



## Rules & Policies Agenda for Board Meeting November 9, 2022

- A. Rule Review Update
  - B. Light-Based Medical Device Rules
  - C. Mental or Physical Impairment Rules
  - D. Controlled Substance Prescribing Rules
  - E. Rule 4731-11-14, Chronic Pain
  - F. Legislative Update
  - G. Approval of 2024 Board Meeting Dates
-



**MEMORANDUM**

TO: Betty Montgomery, President  
Members, State Medical Board of Ohio

FROM: Kimberly C. Anderson, Chief Legal Counsel

RE: Rule Review Update

DATE: October 31, 2022

---

Attached please find the Rule Schedule and Spreadsheet for November 2022.

No comments were received on the following rule packages currently pending at CSI:

- Chapter 4731-1, Limited Branch rules;
- Chapter 4731-5, Examinations;
- Rule 4731-6-04, Demonstration of Proficiency in Spoken English;
- Chapter 4731-12, Podiatric Licensure

**Requested Action:** No action requested.

---

# Legal Dept. Rules Schedule

As of October 28, 2022

## **RULES TO NOVEMBER BOARD MEETING**

### **Rules Filed with CSI (comments due 10/14/22)**

#### Massage Therapy Rules

4731-1-01      4731-1-02      4731-1-03  
4731-1-04      4731-1-05      4731-1-07  
4731-1-08      4731-1-09      4731-1-10  
4731-1-11      4731-1-12      4731-1-15  
4731-1-16      4731-1-17      4731-1-18  
4731-1-19

#### Light Based Medical Device Rules

4731-18-01    4731-18-02  
4731-18-03

#### Controlled Substance & Weight Loss Rules

4731-11-03    4731-11-04    4731-11-04.1

#### Podiatric Licensure Rules

4731-12-01  
4731-12-02  
4731-12-03  
4731-12-04  
4731-12-05  
4731-12-06  
4731-12-07

#### Examinations

4731-5-01  
4731-5-02  
4731-5-03  
4731-5-04

#### Demonstration of Proficiency in Spoken English

4731-6-04

## **Rules Filed with JCARR**

### Public Notice of Rules Procedures

4731-2-01-No change rule filed 9.28.22  
JCARR jurisdiction ends 12.27.22

## **Rules Ready to File with JCARR**

### Telehealth Rules

4731-11-09    4731-37-01





4731-1-04	Scope of Practice: Mechanotherapy	06/17/21		09/22/22						12/31/18	12/31/23
4731-1-05	Scope of Practice: Massage Therapy	06/17/21		09/22/22						11/05/19	11/05/24
4731-1-06	Scope of Practice: Naprathy									08/31/18	08/31/23
4731-1-07	<i>Eligibility of Electrologists Licensed by the Ohio State Board of Cosmetology to Obtain Licensure as Cosmetic Therapists Pursuant to Chapter 4731 ORC and Subsequent Limitations</i>	06/17/21		09/22/22						12/31/18	12/31/23
4731-1-08	<i>Continuing Cosmetic Therapy Education Requirements for Registration or Reinstatement of a License to Practice Cosmetic Therapy</i>	06/17/21		09/22/22						09/30/19	09/30/24
4731-1-09	<i>Cosmetic Therapy Curriculum Requirements</i>	06/17/21		09/22/22							08/31/23
4731-1-10	<i>Distance Education</i>	06/17/21		09/22/22						01/31/19	01/31/24
4731-1-11	<i>Application and Certification for certificate to practice cosmetic therapy</i>	06/17/21		09/22/22						03/30/20	03/30/25
4731-1-12	<i>Examination</i>			09/22/22						11/30/16	11/30/21
4731-1-15	<i>Determination of Standing of School, College or Institution</i>	06/17/21		09/22/22						12/31/18	12/31/23
4731-1-16	<i>Massage Therapy curriculum rule (Five year review)</i>	06/17/21		09/22/22						01/31/19	11/30/21
4731-1-17	<i>Instructional Staff</i>	06/17/21		09/22/22						05/31/19	05/31/24
4731-1-18	<i>Grounds for Suspension, Revocation or Denial of Certificate of Good Standing, Hearing Rights</i>	06/17/21		09/22/22						03/30/20	03/30/25
4731-1-19	<i>Probationary Status of a limited branch school</i>	06/17/21		09/22/22						03/30/20	03/30/25
4731-1-24	<i>Massage Therapy Continuing Education</i>	03/09/16		10/26/16	04/24/19	04/29/19	06/05/19				
4731-2-01	<i>Public Notice of Rules Procedure</i>	05/15/22				09/28/22				09/28/22	09/28/27
4731-4-01	<i>Criminal Records Checks - Definitions</i>									09/30/19	09/30/24
4731-4-02	<i>Criminal Records Checks</i>									09/30/19	09/30/24
4731-5-01	<i>Admission to Examinations</i>	05/15/22		09/22/22						06/09/17	06/09/22
4731-5-02	<i>Examination Failure; Inspection and Regrading</i>	05/15/22		09/22/22						06/09/17	06/09/22
4731-5-03	<i>Conduct During Examinations</i>	05/15/22		09/22/22						06/09/17	06/09/22
4731-5-04	<i>Termination of Examinations</i>	05/15/22		09/22/22						06/09/17	06/09/22
4731-6-01	<i>Medical or Osteopathic Licensure: Definitions</i>									07/31/19	07/31/24
4731-6-02	<i>Preliminary Education for Medical and Osteopathic Licensure</i>									07/31/19	07/31/24

4731-6-04	Demonstration of proficiency in spoken English	05/15/22		09/22/22						06/09/17	06/09/22
4731-6-05	Format of Medical and Osteopathic Examination		09/08/21	09/24/21	10/27/21	10/29/21	12/03/21		01/12/22	01/31/22	01/31/27
4731-6-14	Examination for physician licensure	09/03/20								07/31/19	07/31/24
4731-6-15	Eligibility for Licensure of National Board Diplomats and Medical Council of Canada Licentiates									07/31/19	07/31/24
4731-6-21	Application Procedures for Certificate Issuance; Investigation; Notice of Hearing Rights									07/31/19	07/31/24
4731-6-22	Abandonment and Withdrawal of Medical and Osteopathic Licensure Applications									07/31/19	07/31/24
4731-6-30	Training Certificates									07/31/19	07/31/24
4731-6-31	Limited Preexamination Registration and Limited Certification									07/31/19	07/31/24
4731-6-33	Special Activity Certificates									07/31/19	07/31/24
4731-6-34	Volunteer's Certificates									07/31/19	07/31/24
4731-7-01	Method of Notice of Meetings									07/31/19	07/31/24
4731-8-01	Personal Information Systems	04/29/20		10/05/20	11/18/20	02/11/21			no change	02/11/21	02/11/26
4731-8-02	Definitions	04/29/20		10/05/20	11/18/20	02/11/21			no change	02/11/21	02/11/26
4731-8-03	Procedures for accessing confidential personal information	04/29/20		10/05/20	11/18/20	02/11/21			no change	02/11/21	02/11/26
4731-8-04	Valid reasons for accessing confidential personal information	04/29/20		10/05/20	11/18/20	02/11/21	03/15/21	03/29/21	05/12/21	05/31/21	05/31/26
4731-8-05	Confidentiality Statutes	04/29/20		10/05/20	11/18/20	02/11/21	03/15/21	03/29/21	05/12/21	05/31/21	05/31/26
4731-8-06	Restricting & Logging access to confidential personal information	04/29/20		10/05/20	11/18/20	02/11/21			no change	02/11/21	02/11/26
4731-9-01	Record of Board Meetings; Recording, Filming, and Photographing of Meetings									09/15/19	06/17/24
4731-10-01	Definitions	10/25/19		05/26/20		Revised filing 11/3/20 10/30/20	12/04/20	12/07/20	05/12/21	05/31/21	05/31/26
4731-10-02	Requisite Hours of Continuing Medical Education for License Renewal or Reinstatement	10/25/19		05/26/20		Revised filing 11/3/20 10/30/20	03/15/21	03/29/21	05/12/21	05/31/21	05/31/26
4731-10-03	CME Waiver	10/25/19		05/26/20		Revised filings 11/24 & 11/3 - orig 10/30/20	12/04/20	12/07/20	05/12/21	05/31/21	05/31/26
4731-10-04	Continuing Medical Education Requirements for Restoration of a License	10/25/19		05/26/20		Revised filings 11/24 & 11/3 - orig 10/30/20	12/04/20	12/07/20	05/12/21	05/31/21	05/31/26

4371-10-08	Evidence of Continuing Medical Education	10/25/19		05/26/20		Revised filings 11/24 & 11/3 - orig 10/30/20	03/15/21	03/29/21	05/12/21	05/31/21	05/31/26
4731-11-01	Controlled substances; General Provisions Definitions	02/12/22								10/31/20	10/31/25
4731-11-02	Controlled Substances - General Provisions	07/26/19	11/13/19	10/05/20		05/27/21			no change		05/27/26
4731-11-03	Schedule II Controlled Substance Stimulants			09/22/22						12/31/15	12/31/20
4731-11-04	Controlled Substances: Utilization for Weight Reduction			09/22/22						02/29/16	02/28/21
4731-11-04.1	Controlled substances: Utilization for chronic weight management			09/22/22						12/31/15	12/31/20
4731-11-07	Research Utilizing Controlled Substances	07/26/19	11/13/19	10/05/20		05/27/21			no change		05/27/26
4731-11-08	Utilizing Controlled Substances for Self and Family Members	01/25/21	03/10/21	03/18/21	04/23/21	05/27/21			no change		05/27/26
4731-11-09	Prescribing to persons the physician has never personally examined.	02/12/22	05/11/22	05/16/22						03/23/17	09/19/22
4731-11-11	Standards and procedures for review of "Ohio Automated Rx Reporting System" (OARRS).	07/26/19	11/13/19	10/05/20		05/27/21	06/28/21		09/08/21	09/30/21	09/30/26
4731-11-13	Prescribing of Opioid Analgesics for Acute Pain									08/31/17	08/31/22
4731-11-14	Prescribing for subacute and chronic pain			3/21/19	11/14/19	corrected-7/16/20 6/18/2020	07/23/20	08/17/20	10/14/20	10/31/20	12/23/23
4731-12-01	Preliminary Education for Licensure in Podiatric Medicine and Surgery	04/18/22		09/22/22						06/30/17	06/30/22
4731-12-02	Standing of Colleges of Podiatric Surgery and Medicine	04/18/22		09/22/22						06/30/17	06/30/22
4731-12-03	Eligibility for the Examination in Podiatric Surgery and Medicine (see note below)	04/18/22		09/22/22						04/19/17	10/16/22
4731-12-04	Eligibility of Licensure in Podiatric Medicine and Surgery by Endorsement from Another State	04/18/22		09/22/22						06/30/17	06/30/22
4731-12-05	Application Procedures for Licensure in Podiatric Medicine and Surgery, Investigation, Notice of Hearing Rights.	04/18/22		09/22/22						06/30/17	06/30/22
4731-12-06	Visiting Podiatric Faculty Certificates	04/18/22		09/22/22						06/30/17	06/30/22
4731-12-07	Podiatric Training Certificates	04/18/22		09/22/22						06/30/17	06/30/22
4731-13-01	Conduct of Hearings - Representative; Appearances	08/26/20	10/14/20	10/23/20	04/02/21	04/12/21	05/17/21	06/07/21	07/14/21	07/31/21	07/31/26
4731-13-02	Filing Request for Hearing	08/26/20	10/14/20	10/23/20	04/02/21	04/12/21	No change				04/12/26

4731-13-03	Authority and Duties of Hearing Examiners	08/26/20	10/14/20	amended filing 1/6/21 10/23/20	04/02/21	04/12/21	05/17/21	06/07/21	07/14/21	07/31/21	07/31/26
4731-13-04	Consolidation	08/26/20	10/14/20	10/23/20	04/02/21	04/12/21	no change				04/12/26
4731-13-05	Intervention	08/26/20	10/14/20	10/23/20	04/02/21	04/12/21	no change				04/12/26
4731-13-06	Continuance of Hearing	08/26/20	10/14/20	10/23/20	04/02/21	04/12/21	05/17/21	06/07/21	07/14/21	07/31/21	07/31/26
4731-13-07	Motions	08/26/20	10/14/20	10/23/20	04/02/21	04/12/21	05/17/21	06/07/21	07/14/21	07/31/21	07/31/26
4731-13-07.1	Form and page limitations for briefs and memoranda	08/26/20	10/14/20	10/23/20	04/02/21	04/12/21	05/17/21	06/07/21	07/14/21	07/31/21	07/31/26
4731-13-08	Filing	08/26/20	10/14/20	10/23/20	04/02/21	04/12/21	05/17/21	06/07/21	07/14/21	07/31/21	07/31/26
4731-13-09	Service	08/26/20	10/14/20	10/23/20	04/02/21	04/12/21	05/17/21	06/07/21	07/14/21	07/31/21	07/31/26
4731-13-10	Computation and Extension of Time	08/26/20	10/14/20	10/23/20	04/02/21	04/12/21	no change				04/12/26
4731-13-11	Notice of Hearings	08/26/20	10/14/20	10/23/20	04/02/21	04/12/21	no change				04/12/26
4731-13-12	Transcripts	08/26/20	10/14/20	10/23/20	04/02/21	04/12/21	no change				04/12/26
4731-13-13	Subpoenas for Purposes of Hearing	08/26/20	10/14/20	10/23/20	04/02/21	04/12/21	05/17/21	06/07/21	07/14/21	07/31/21	07/31/26
4731-13-14	Mileage Reimbursement and Witness Fees	08/26/20	10/14/20	10/23/20	04/02/21	04/12/21	no change				04/12/26
4731-13-15	Reports and Recommendations	08/26/20	10/14/20	10/23/20	04/02/21	04/12/21	05/17/21	06/07/21	07/14/21	07/31/21	07/31/26
4731-13-16	Reinstatement or Restoration of Certificate	08/26/20	10/14/20	10/23/20	04/02/21	04/12/21	05/17/21	06/07/21	07/14/21	07/31/21	07/31/26
4731-13-17	Settlements, Dismissals, and Voluntary Surrenders	08/26/20	10/14/20	10/23/20	04/02/21	04/12/21	05/17/21	06/07/21	07/14/21	07/31/21	07/31/26
4731-13-18	Exchange of Documents and Witness Lists	08/26/20	10/14/20	10/23/20	04/02/21	04/12/21	no change				04/12/26
4731-13-20	Depositions in Lieu of Live Testimony and Transcripts in place of Prior Testimony	08/26/20	10/14/20	10/23/20	04/02/21	04/12/21	no change				04/12/26
4731-13-20.1	Electronic Testimony	08/26/20	10/14/20	10/23/20	04/02/21	04/12/21	no change				04/12/26
4731-13-21	Prior Action by the State Medical Board	08/26/20	10/14/20	10/23/20	04/02/21	04/12/21	no change				04/12/26
4731-13-22	Stipulation of Facts	08/26/20	10/14/20	10/23/20	04/02/21	04/12/21	no change				04/12/26
4731-13-23	Witnesses	08/26/20	10/14/20	10/23/20	04/02/21	04/12/21	no change				04/12/26
4731-13-24	Conviction of a Crime	08/26/20	10/14/20	10/23/20	04/02/21	04/12/21	no change				04/12/26
4731-13-25	Evidence	08/26/20	10/14/20	10/23/20	04/02/21	04/12/21	no change				04/12/26
4731-13-26	Broadcasting and Photographing Administrative Hearings	08/26/20	10/14/20	10/23/20	04/02/21	04/12/21	no change				04/12/26
4731-13-27	Sexual Misconduct Evidence	08/26/20	10/14/20	10/23/20	04/02/21	04/12/21	no change				04/12/26
4731-13-28	Supervision of Hearing Examiners	08/26/20	10/14/20	10/23/20	04/02/21	04/12/21	no change				04/12/26
4731-13-30	Prehearing Conference	08/26/20	10/14/20	10/23/20	04/02/21	04/12/21	no change				04/12/26
4731-13-31	Transcripts of Prior Testimony	08/26/20	10/14/20	10/23/20	04/02/21	04/12/21	no change				04/12/26
4731-13-32	Prior Statements of the Respondent	08/26/20	10/14/20	10/23/20	04/02/21	04/12/21	no change				04/12/26

4731-13-33	Physician's Desk Physician	08/26/20	10/14/20	10/23/20	04/02/21	04/12/21	05/17/21	06/07/21	07/14/21	07/31/21	07/31/26
4731-13-34	Ex Parte Communication	08/26/20	10/14/20	10/23/20	04/02/21	04/12/21	no change				04/12/26
4731-13-35	Severability	08/26/20	10/14/20	10/23/20	04/02/21	04/12/21	no change				04/12/26
4731-13-36	Disciplinary Actions	08/26/20	10/14/20	10/23/20	04/02/21	04/12/21	05/17/21	06/07/21	07/14/21	07/31/21	07/31/26
4731-14-01	Pronouncement of Death	01/25/21	03/10/21	03/18/21		05/27/21	06/28/21		09/08/21	09/30/21	09/30/26
4731-15-01	Licensee Reporting Requirement; Exceptions									11/17/17	05/17/23
4731-15-02	Healthcare Facility Reporting Requirement									11/17/17	05/17/23
4731-15-03	Malpractice Reporting Requirement									11/17/17	05/17/23
4731-15-04	Professional Society Reporting									11/17/17	05/17/23
4731-15-05	Liability; Reporting Forms; Confidentially and Disclosure									11/17/17	05/17/23
4731-16-01	Rules governing impaired physicians and approval of treatments programs - Definitions									11/17/17	05/17/23
4731-16-02	General Procedures in Impairment Cases	06/17/21	09/08/21	09/24/21	10/27/21	10/29/21	12/03/21		01/12/22	01/31/22	05/17/23
4731-16-04	Other Violations									11/17/17	05/17/23
4731-16-05	Examinations	06/17/21	09/08/21	09/24/21	10/27/21	10/29/21	12/03/21		01/12/22	01/31/22	05/17/23
4731-16-06	Consent Agreements and Orders for Reinstatement of Impaired Practitioners								01/12/22	01/31/22	05/17/23
4731-16-07	Treatment Provider Program Obligations									11/17/17	05/17/23
4731-16-08	Criteria for Approval	06/17/21	09/08/21	09/24/21	10/27/21	10/29/21	12/03/21			11/17/17	05/17/23
4731-16-09	Procedures for Approval									11/17/17	05/17/23
4731-16-10	Aftercare Contracts									11/17/17	05/17/23
4731-16-11	Revocation, Suspension, or Denial of Certificate of Good Standing									11/17/17	05/17/23
4731-16-12	Out-of-State Impairment Cases									11/17/17	05/17/23
4731-16-13	Patient Consent; Revocation of Consent									11/17/17	05/17/23
4731-16-14	Caffeine, Nicotine, and Over-The Counter Drugs									11/17/17	05/17/23
4731-16-15	Patient Rights									11/17/17	05/17/23
4731-16-17	Requirements for the one-bite program									01/31/19	01/31/24
4731-16-18	Eligibility for the one-bite program									01/31/19	01/31/24
4731-16-19	Monitoring organization for one-bite program									01/31/19	01/31/24
4731-16-20	Treatment providers in the one-bite program									01/31/19	01/31/24
4731-16-21	Continuing care for the one-bite program									01/31/19	01/31/24

4731-17-01	Exposure-Prone Invasive Procedure Precautions - Definitions	08/26/20	10/14/20	10/23/20	11/24/20	02/11/21	03/15/21	03/29/21	05/12/21	05/31/21	05/31/26
4731-17-02	Universal Precautions	08/26/20	10/14/20	10/23/20	11/24/20	02/11/21			no change		02/11/26
4731-17-03	Hand Washing	08/26/20	10/14/20	10/23/20	11/24/20	02/11/21			no change		02/11/26
4731-17-04	Disinfection and Sterilization	08/26/20	10/14/20	10/23/20	11/24/20	02/11/21	03/15/21	03/29/21	05/12/21	05/31/21	05/31/26
4731-17-05	Handling and Disposal of Sharps and Wastes	08/26/20	10/14/20	10/23/20	11/24/20	02/11/21	03/15/21	03/29/21	05/12/21	05/31/21	05/31/26
4731-17-06	Barrier Techniques	08/26/20	10/14/20	10/23/20	11/24/20	02/11/21			no change		02/11/26
4731-17-07	Violations	08/26/20	10/14/20	10/23/20	11/24/20	02/11/21	03/15/21	03/29/21	05/12/21	05/31/21	05/31/26
4731-18-01	Definitions			09/22/22						07/31/21	07/31/26
4731-18-02	Use of Light Based Medical Devices			09/22/22						07/31/21	07/31/26
4731-18-03	Delegation of the Use of Light Based Medical Devices			09/22/22						07/31/21	07/31/26
4731-18-04	Delegation of phototherapy and photodynamic therapy	01/10/18	01/20/20	05/12/20	04/05/21	04/09/21	refiled 6-9-21 5/17/2021	06/25/21	07/14/21	07/31/21	07/31/26
4731-20-01	Surgery Privileges of Podiatrist - Definition of Foot									05/31/18	05/31/23
4731-20-02	Surgery: Ankle Joint									05/31/18	05/31/23
4731-22-01	Emeritus Registration - Definitions									08/31/17	08/31/22
4731-22-02	Application									08/31/17	08/31/22
4731-22-03	Status of Registrant									05/12/17	05/12/22
4731-22-04	Continuing Education Requirements									05/12/17	05/12/22
4731-22-06	Renewal of Cycle of Fees									05/12/17	05/12/22
4731-22-07	Change to Active Status	06/17/21	09/08/21	09/24/21	10/27/21	10/29/21	12/03/21		01/12/22	01/31/22	08/31/22
4731-22-08	Cancellation of or Refusal to Issue an Emeritus Registration									05/12/17	05/12/22
4731-23-01	Delegation of Medical Tasks - Definitions	01/25/21	03/10/21	03/18/21	04/23/21	05/27/21			no change		05/27/26
4731-23-02	Delegation of Medical Tasks	01/25/21	03/10/21	03/18/21	04/23/21	refiled 7/14/21 5/27/2021	06/28/21		09/08/21	09/30/21	09/30/26
4731-23-03	Delegation of Medical Tasks: Prohibitions	01/25/21	03/10/21	03/18/21	04/23/21	05/27/21			no change		05/27/26
4731-23-04	Violations	01/25/21	03/10/21	03/18/21	04/23/21	05/27/21			no change		05/27/26
4731-24-01	Anesthesiologist Assistants - Definitions									07/31/19	07/31/24
4731-24-02	Anesthesiologist Assistants; Supervision									07/31/19	07/31/24
4731-24-03	Anesthesiologist Assistants; Enhanced Supervision									07/31/19	07/31/24
4731-25-01	Office-Based Surgery - Definition of Terms										03/01/23
4731-25-02	General Provisions									05/31/18	05/31/23
4731-25-03	Standards for Surgery Using Moderate Sedation/Analgesia									05/31/18	08/31/23

4731-25-04	Standards for Surgery Using Anesthesia Services									05/31/18	05/31/23
4731-25-05	Liposuction in the Office Setting									03/01/18	03/01/23
4731-25-07	Accreditation of Office Settings									05/31/18	05/31/23
4731-25-08	Standards for Surgery									09/30/19	09/30/24
4731-26-01	Sexual Misconduct - Definitions	01/25/21	03/10/21	03/18/21	04/23/21	refiled 7/14/21 5/27/2021	06/28/21		09/08/21	09/30/21	09/30/26
4731-26-02	Prohibitions	01/25/21	03/10/21	03/18/21	04/23/21	05/27/21	06/28/21		09/08/21	09/30/21	09/30/26
4731-26-03	Violations; Miscellaneous	01/25/21	03/10/21	03/18/21	04/23/21	05/27/21	06/28/21		09/08/21	09/30/21	09/30/26
4731-27-01	Definitions									02/04/19	02/02/24
4731-27-02	Dismissing a patient from the medical practice									05/31/19	05/31/24
4731-27-03	Notice of termination of physician employment or physician leaving a practice, selling a practice, or retiring from the practice of medicine									05/31/19	05/31/24
4731-28-01	Mental or Physical Impairment									08/31/17	08/31/22
4731-28-02	Eligibility for confidential monitoring program									08/31/18	08/31/23
4731-28-03	Participation in the confidential monitoring program									08/31/18	08/31/23
4731-28-04	Disqualification from continued participation in the confidential monitoring program									08/31/18	08/31/23
4731-28-05	Termination of the participation agreement for the confidential monitoring program									08/31/18	08/31/23
4731-29-01	Standards and procedures for operation of a pain management clinic.									06/30/17	06/30/22
4731-30-01	Internal Management Definitions									09/23/18	09/23/23
4731-30-02	Internal Management Board Metrics	07/26/19								09/23/18	09/23/23
4731-30-03	Approval of Licensure Applications	06/17/21				refiled 11-4-21 5/7/2020			01/12/22	01/31/22	10/17/24
4731-30-04	Maintenance of List of Disqualifying Criminal Offenses	08/13/21				refiled 11-4-21			09/08/21	12/31/21	12/31/26
4731-31-01	Requirements for assessing and granting clearance for return to practice or competition. (concussion rule)					04/10/19	05/13/19			11/30/19	11/30/24
4731-32-01	Definition of Terms									09/08/17	09/08/22
4731-32-02	Certificate to Recommend Medical Marijuana									09/08/17	09/08/22

4731-32-03	Standard of Care									09/08/17	09/08/22
4731-32-04	Suspension and Revocation of Certificate to Recommend									09/08/17	09/08/22
4731-32-05	Petition to Request Additional Qualifying Condition or Disease									09/08/17	09/08/22
4731-33-01	Definitions	05/09/19		11/15/19	05/20/20	06/18/20	07/23/20	08/17/20	10/14/20	10/31/20	04/30/24
4731-33-02	Standards and procedures for withdrawal management for drug or alcohol addiction	05/09/19		11/15/19	05/20/20	06/18/20	07/23/20	08/17/20	10/14/20	10/31/20	10/31/25
4731-33-03	Office-Based Treatment for Opioid Addiction									04/30/19	04/30/24
4731-33-04	Medication Assisted Treatment Using Naltrexone									04/30/19	04/30/24
4731-34-01	Standards and Procedures to be followed by physicians when prescribing a dangerous drug that may be administered by a pharmacist by injection.									07/31/19	07/31/24
4731-35-01	Consult Agreements	01/25/21	04/14/21	04/26/21	06/04/21	09/22/21	10/29/21	11/08/21	12/08/21	12/31/21	10/31/25
4731-35-02	Standards for managing drug therapy	01/25/21	04/14/21	04/26/21	06/04/21	09/22/21	10/29/21	11/08/21	12/08/21	12/31/21	10/31/25
4731-36-01	Military provisions related to education and experience requirements for licensure	06/17/21	09/08/21	09/24/21	10/27/21	10/29/21	12/03/21		01/12/22	01/31/22	10/29/21
4731-36-02	Military provisions related to renewal of license and continuing education	03/22/19	06/12/19	12/05/19	09/11/20	09/25/20	10/27/20	11/16/20	12/09/20	12/31/20	12/31/25
4731-36-03	Processing applications from service members, veterans, or spouses of service members or veterans.	03/22/19	06/12/19	12/05/19	09/11/20	09/25/20	10/27/20	11/16/20	12/09/20	12/31/20	12/31/25
4731-36-04	Temporary license for military spouse	02/11/20	02/12/20	02/14/20		02/11/21	03/15/21	03/29/21	05/12/21	05/31/21	05/31/26
4731-37-01	Telemedicine	02/12/22	05/11/22	05/16/22							
4731-38-01	Licenses Issued or Renewed Under the Interstate Medical Licensure Compact	11/12/21	01/12/22	01/14/22	02/14/22	02/18/22	03/25/22		05/11/22	05/31/22	05/31/27
4759-2-01	Definitions									11/30/19	11/30/24
4759-4-01	Applications									11/30/19	11/30/24
4759-4-02	Preprofessional experience										08/28/24
4759-4-03	Examination									11/30/19	11/30/24
4759-4-04	Continuing Education	08/27/19		11/10/20	04/02/21	04/09/21	05/17/21	06/07/21	07/14/21	07/31/21	07/31/26
4759-4-08	Limited permit	8/27/19 4/19/18	07/11/18	11/10/20	04/02/21	04/09/21	05/17/21	06/07/21	07/14/21	07/31/21	07/31/26
4759-4-09	License certificates and permits	04/19/18	07/11/18	09/25/18						11/30/19	11/30/24
4759-5-01	Supervision of persons claiming exemption									08/28/19	08/28/24



4759-5-02	Student practice exemption										11/30/19	11/30/24
4759-5-03	Plan of treatment exemption										11/30/19	11/30/24
4759-5-04	Additional nutritional activities exemption											07/01/24
4759-5-05	Distribution of literature exemption											07/01/24
4759-5-06	Weight control program exemption											07/01/24
4759-6-01	Standards of practice innutrition care										11/30/19	11/30/24
4759-6-02	Standards of professional performance	04/19/18	07/11/18	11/10/20	04/02/21	refiled 6/9/21 4/9/2021	05/17/21	06/25/21	07/14/21	07/31/21	07/31/26	
4759-6-03	Interpretation of standards										11/30/19	11/30/24
4759-9-01	Severability										11/30/19	11/30/24
4759-11-01	Miscellaneous Provisions	02/12/22	05/11/22	05/16/22							11/30/19	11/30/24
4761-2-03	Board Records										02/28/19	02/28/24
4761-3-01	Definition of terms										02/28/19	02/28/24
4761-4-01	Approval of educational programs										02/28/19	02/28/24
4761-4-02	Monitoring of Ohio respiratory care educational programs										02/28/19	02/28/24
4761-5-01	Waiver of licensing requirements pursuant to division (B) of section 4761.04 or the Revised Code	04/23/19	06/12/19	11/06/19	01/10/20	06/18/20	07/23/20	08/17/20	09/09/20	09/30/20	09/30/25	
4761-5-02	Admission to the Ohio credentialing examination	04/23/19	06/12/19	11/06/19	01/10/20	06/19/20	No change rule				09/19/20	06/19/25
4761-5-04	License application procedure	04/23/19	06/12/19	11/06/19	01/10/20	06/18/20	07/23/20	08/17/20	09/09/20	09/30/20	09/30/25	
4761-5-06	Respiratory care practice by polysomnographic technologists	04/23/19	06/12/19	11/06/19	01/10/20	06/18/20	No change rule				09/18/20	06/18/25
4761-6-01	Limited permit application procedure	04/23/19	06/12/19	11/06/19	01/10/20	06/18/20	07/23/20	08/17/20	09/09/20	09/30/20	02/28/24	
4761-7-01	Original license or permit, identification card or electronic license verification										02/28/19	02/28/24
4761-7-03	Scope of respiratory care defined											11/15/23
4761-7-04	Supervision			11/06/19	01/10/20	06/18/20	07/23/20	08/17/20	09/09/20	09/30/20	09/30/25	
4761-7-05	Administration of medicines											11/15/23
4761-8-01	Renewal of license or permits	03/22/19	06/12/19	12/05/19	09/11/20	09/25/20	10/27/20	11/16/20	12/09/20	12/31/20	12/31/25	
4761-9-01	Definition of respiratory care continuing education			11/06/19	01/10/20	06/18/20	07/23/20	08/17/20	09/09/20	09/30/20	02/28/24	
4761-9-02	General RCCE requirements and reporting mechanism	03/22/19	06/12/19	12/05/19	09/11/20	09/25/20	10/27/20	11/16/20	12/09/20	12/31/20	12/31/25	
4761-9-03	Activities which do not meet the Ohio RCCE requirements										02/28/19	02/28/24
4761-9-04	Ohio respiratory care law and professional ethics course criteria			11/06/19	01/10/20	Refiled 8/24/20 6/18/2020	9/24/20 7/23/2020	08/17/20	11/10/20		02/28/24	
4761-9-05	Approved sources of RCCE			11/06/19	01/10/20	06/18/20	07/23/20	08/17/20	09/09/20	09/30/20	02/28/24	

4761-9-07	Auditing for compliance with RCCE requirements			11/06/19	01/10/20	06/18/20	07/23/20	08/17/20	09/09/20	09/30/20	09/30/25
4761-10-01	Ethical and professional conduct									02/28/19	02/28/24
4761-10-02	Proper use of credentials										11/15/23
4761-10-03	Providing information to the Board	04/23/19	06/12/19	11/06/19	01/10/20	06/18/20	07/23/20	08/17/20	09/09/20	09/30/20	09/30/25
4761-15-01	Miscellaneous Provisions	02/12/22	05/11/22	05/16/22						02/28/19	02/28/24
4774-1-01	Definitions	04/29/20	10/14/20	10/23/20	11/24/20	02/11/21			no change	02/11/21	02/11/26
4774-1-02	Application for Certificate to Practice	04/29/20	10/14/20	10/23/20	11/24/20	02/11/21	03/15/21	03/29/21	05/12/21	05/31/21	05/31/26
4774-1-03	Renewal of Certificate to Practice	04/29/20	10/14/20	10/23/20	11/24/20	02/11/21	03/15/21	03/29/21	05/12/21	05/31/21	05/31/26
4774-1-04	Miscellaneous Provisions	04/29/20	10/14/20	10/23/20	11/24/20	02/11/21			no change	02/11/21	02/11/26
4778-1-01	Definition									01/29/19	01/24/24
4778-1-02	Application									04/30/19	04/30/24
4778-1-03	Special Activity License									01/24/19	01/24/24
4778-1-05	Collaboration Agreement									04/30/19	04/30/24
4778-1-06	Miscellaneous Provisions	02/12/22	05/11/22	05/16/22						04/30/19	04/30/24



**MEMORANDUM**

TO: Betty Montgomery, President  
Members, State Medical Board of Ohio

FROM: Kimberly C. Anderson, Chief Legal Counsel

RE: Light Based Medical Device Rules (4731-18-01, 4731-18-02, 4731-18-03, OAC)

DATE: October 31, 2022

---

Rules 4731-18-01, 4731-18-02, and 4731-18-03 were filed with the Common Sense Initiative with comments due October 14, 2022. The rules were recently updated in 2021, but statutory changes related to laser hair removal required some clean-up of the rules. A copy of the Business Impact Analysis and proposed rules are attached for your review.

The Board received comments from the Cosmetic Therapy Association of Ohio, which are attached for your review. In addition, on October 17, 2022, the Board received an inquiry from Erin Hennessey asking whether late comments would be received. Ms. Hennessey was advised that late comments would be reviewed so long as they were received within a few days of October 17, 2022. To date, no additional comments have been received.

Amanda Nelson of the Cosmetic Therapy Association requests that cosmetic therapists are added to the professionals to whom the use of a vascular laser for non-ablative dermatologic procedures may be delegated. Currently, a physician may delegate the use of a non-ablative dermatologic procedure may be delegated to a physician assistant, registered nurse or licensed practical nurse. The Board reviewed a similar comment from the Cosmetic Therapy Association in April 2022 and declined to make that change because cosmetic therapist training is focused on hair removal.

**Requested Action:** Determine whether to make the requested change to the rule and authorize the communication of the decision to the Cosmetic Therapy Association and the Common Sense Initiative.

---



# Common Sense Initiative

**Mike DeWine**, Governor  
**Jon Husted**, Lt. Governor

**Sean McCullough**, Director

## Business Impact Analysis

Agency, Board, or Commission Name: State Medical Board of Ohio

Rule Contact Name and Contact Information:

Kimberly Anderson, [Kimberly.Anderson@med.ohio.gov](mailto:Kimberly.Anderson@med.ohio.gov), (614) 466-7207

Regulation/Package Title (a general description of the rules' substantive content):

Light Based Medical Device Rules

Rule Number(s): 4731-18-01, 4731-18-02, 4731-18-03

Date of Submission for CSI Review: 9/22/22

Public Comment Period End Date: 10/14/22

**Rule Type/Number of Rules:**

New/ 1 rules

No Change/      rules (FYR?     )

Amended/ 2 rules (FYR?     )

Rescinded/ 1 rules (FYR?     )

The Common Sense Initiative is established in R.C. 107.61 to eliminate excessive and duplicative rules and regulations that stand in the way of job creation. Under the Common Sense Initiative, agencies must balance the critical objectives of regulations that have an adverse impact on business with the costs of compliance by the regulated parties. Agencies should promote transparency, responsiveness, predictability, and flexibility while developing

77 SOUTH HIGH STREET | 30TH FLOOR | COLUMBUS, OHIO 43215-6117

[CSIPublicComments@governor.ohio.gov](mailto:CSIPublicComments@governor.ohio.gov)

regulations that are fair and easy to follow. Agencies should prioritize compliance over punishment, and to that end, should utilize plain language in the development of regulations.

### **Reason for Submission**

1. R.C. 106.03 and 106.031 require agencies, when reviewing a rule, to determine whether the rule has an adverse impact on businesses as defined by R.C. 107.52. If the agency determines that it does, it must complete a business impact analysis and submit the rule for CSI review.

Which adverse impact(s) to businesses has the agency determined the rule(s) create?

The rule(s):

- a.  Requires a license, permit, or any other prior authorization to engage in or operate a line of business.
- b.  Imposes a criminal penalty, a civil penalty, or another sanction, or creates a cause of action for failure to comply with its terms.
- c.  Requires specific expenditures or the report of information as a condition of compliance.
- d.  Is likely to directly reduce the revenue or increase the expenses of the lines of business to which it will apply or applies.

### **Regulatory Intent**

2. Please briefly describe the draft regulation in plain language.

*Please include the key provisions of the regulation as well as any proposed amendments.*

Rule 4731-18-01: Establishes the definitions for this rule chapter.

Rule 4731-18-02: Establishes the use of light based medical devices is the practice of medicine and provides general information regarding the delegation of certain types of light based medical devices.

Rule 4731-18-03: Provides detail regarding the delegation of light based medical devices for specified non-ablative procedures.

3. Please list the Ohio statute(s) that authorize the agency, board or commission to adopt the rule(s) and the statute(s) that amplify that authority.

Authorized by: 4730.07, 4731.05, 4731.33

77 SOUTH HIGH STREET | 30TH FLOOR | COLUMBUS, OHIO 43215-6117

[CSIPublicComments@governor.ohio.gov](mailto:CSIPublicComments@governor.ohio.gov)

Amplifies: 4730.07, 4731.05, 4731.33, 4731.22, 4730.21, 4730.25, 4731.22, 4731.41

- 4. Does the regulation implement a federal requirement? Is the proposed regulation being adopted or amended to enable the state to obtain or maintain approval to administer and enforce a federal law or to participate in a federal program?**

*If yes, please briefly explain the source and substance of the federal requirement.*

No.

- 5. If the regulation includes provisions not specifically required by the federal government, please explain the rationale for exceeding the federal requirement.**

Not applicable.

- 6. What is the public purpose for this regulation (i.e., why does the Agency feel that there needs to be any regulation in this area at all)?**

The public purpose of the proposed rules is to ensure public safety in the practice of medicine and surgery and the competent application of certain light based medical devices. The purpose of this particular filing is to align the rules with R.C. 4731.33 related to the delegation of light based medical devices for hair removal.

- 7. How will the Agency measure the success of this regulation in terms of outputs and/or outcomes?**

The success of these regulations will be measured by the safe application of certain light based medical devices with minimal adverse events; the rules being written in plain, understandable language, licensee compliance with the rules; and minimal questions from the licensees about the proposed rules.

- 8. Are any of the proposed rules contained in this rule package being submitted pursuant to R.C. 101.352, 101.353, 106.032, 121.93, or 121.931?**

*If yes, please specify the rule number(s), the specific R.C. section requiring this submission, and a detailed explanation.*

No.

### **Development of the Regulation**

- 9. Please list the stakeholders included by the Agency in the development or initial review of the draft regulation.**

*If applicable, please include the date and medium by which the stakeholders were initially contacted.*

In November 2021, the Medical Board circulated the proposed rules to interested parties who have requested to receive rule updates, including the Ohio State Medical Association, the Academy of Medicine of Cleveland and Northern Ohio, the Ohio Hospital Association, the

77 SOUTH HIGH STREET | 30TH FLOOR | COLUMBUS, OHIO 43215-6117

[CSIPublicComments@governor.ohio.gov](mailto:CSIPublicComments@governor.ohio.gov)

Ohio Physician Assistant Association, attorneys interested in matters before the Medical Board, and the Ohio Board of Nursing. The proposed rules were also posted on the Medical Board's website and were provided to the members of the Physician Assistant Policy Committee in February of 2022.

**10. What input was provided by the stakeholders, and how did that input affect the draft regulation being proposed by the Agency?**

Four comments were received. Beth Adamson of the Ohio Association of Physician Assistants requested that the definition of "Ablative dermatologic procedure" in 4731-18-01(D) be updated because physician assistants are already performing procedures in office beneath the dermo-epidermal junction to the subcutaneous fact (such as excisions with intermediate and complex closures) without direct supervision. Ms. Adamson requested a change to Rule 4731-18-02(D) to state that a physician may delegate the application of light based medical devices for hair removal, resurfacing and dermatologic purposes because the current language is restrictive to specialty physician practices such as dermatology, ENT, facial plastic surgery and plastic and reconstructive surgery. Ms. Adamson requests the removal of paragraphs (A)(3), (4), and (5) of Rule 4731-18-03 because the requirement for the physician to evaluate the patient creates more work for the provider. Matthew Ernst and Jo Kelton of Removery, LLC recommended changes to the rules to allow delegation of laser tattoo removal to cosmetic therapists, physician assistants, registered nurses and licensed practical nurses. Amanda Nelson of the Cosmetic Therapy Association of Ohio recommended changes to Rules 4731-18-01 through 4731-18-03 which would allow cosmetic therapists to be delegated the use of light based medical devices for non-ablative vascular treatments.

The rules and comments were discussed at the February meeting of the Physician Assistant Policy Council. The members did not recommend any specific rule changes.

The Medical Board reviewed the comments at its meeting on April 13, 2022 and after a full discussion, determined not to make the proposed changes. The purpose of this rule review is to correct any discrepancies between the statute and the rules, which were finalized less than one year ago, after a very lengthy rule-making process. The rules were changed to allow physician assistants and nurses to be delegated the use of non-ablative vascular lasers because these are the safest for patients. Tattoo removal does not use a non-ablative vascular laser and is more complicated due to the different pigments used in tattoos. The Board wanted to keep the physician evaluation in paragraphs (A)(3) and (4) to ensure patient safety and that the use of the non-ablative vascular laser was appropriate for the patient's condition.

**11. What scientific data was used to develop the rule or the measurable outcomes of the rule? How does this data support the regulation being proposed?**

The Board used its medical expertise to develop the rules with a focus on ensuring patient safety.

**12. What alternative regulations (or specific provisions within the regulation) did the Agency consider, and why did it determine that these alternatives were not appropriate? If none, why didn't the Agency consider regulatory alternatives?**

77 SOUTH HIGH STREET | 30TH FLOOR | COLUMBUS, OHIO 43215-6117

[CSIPublicComments@governor.ohio.gov](mailto:CSIPublicComments@governor.ohio.gov)

The Board carefully considered the comments but determined not to make substantive changes regarding the procedures around delegation of non-ablative vascular lasers nor to add tattoo removal as a laser procedure that could be delegated to physician assistants or nurses. The purpose of the amendments is to align the rules with the newly passed statute regarding laser hair removal.

- 13. Did the Agency specifically consider a performance-based regulation? Please explain. *Performance-based regulations define the required outcome, but don't dictate the process the regulated stakeholders must use to achieve compliance.***

The Medical Board did not consider a performance-based regulation because these proposed rules do not define the required outcome and instead seek to prevent adverse events.

- 14. What measures did the Agency take to ensure that this regulation does not duplicate an existing Ohio regulation?**

The rule amendments are proposed to ensure that the rule does not duplicate or conflict with R.C. 4731.33.

- 15. Please describe the Agency's plan for implementation of the regulation, including any measures to ensure that the regulation is applied consistently and predictably for the regulated community.**

The rules will be posted on the Medical Board's website and notice of the rules will be circulated to the interested parties. Medical Board staff members will be available to answer questions regarding the rules. Board staff will be made aware of the rules' provisions so that the rules can be fairly, consistently, and predictably applied to the regulated community.

### **Adverse Impact to Business**

- 16. Provide a summary of the estimated cost of compliance with the rule. Specifically, please do the following:**

- a. Identify the scope of the impacted business community; and**
- b. Identify the nature of all adverse impact (e.g., fees, fines, employer time for compliance); and**
- c. Quantify the expected adverse impact from the regulation. *The adverse impact can be quantified in terms of dollars, hours to comply, or other factors; and may be estimated for the entire regulated population or for a "representative business." Please include the source for your information/estimated impact.***

The impacted business community includes physicians utilizing light-based medical devices in their practice, licensees to whom tasks are delegated, such as physician assistants, registered nurses and licensed practical nurses. The nature of the adverse impact is the

77 SOUTH HIGH STREET | 30TH FLOOR | COLUMBUS, OHIO 43215-6117

[CSIPublicComments@governor.ohio.gov](mailto:CSIPublicComments@governor.ohio.gov)



eight hours of basic education that must be completed for the delegation of non-ablative procedures. In addition, the physicians will need to have the delegated licensees observe procedures and then provide direct physical oversight before the licensees can perform on their own. In addition, physicians who violate these rules are subject to disciplinary action and fines up to \$20,000 from the Medical Board.

**17. Why did the Agency determine that the regulatory intent justifies the adverse impact to the regulated business community?**

The Medical Board determined that the regulatory intent justifies the adverse impact to the regulated business community because the Board endeavors to protect patients and ensure the competent application of the specified light based medical devices.

**Regulatory Flexibility**

**18. Does the regulation provide any exemptions or alternative means of compliance for small businesses? Please explain.**

No, the regulation does not provide exemptions or alternative means of compliance for small business. All practitioners utilizing light-based medical devices need to follow the same regulations for patient safety.

**19. How will the agency apply Ohio Revised Code section 119.14 (waiver of fines and penalties for paperwork violations and first-time offenders) into implementation of the regulation?**

Due process requires the Medical Board to consistently apply its rules such that all licensees using light-based medical devices are equally treated.

**20. What resources are available to assist small businesses with compliance of the regulation?**

Medical Board staff members are available by telephone and e-mail to answer questions.

4731-18-01

**Definitions.**

As used in this chapter of the Administrative Code:

- (A) “Light based medical device ” means any device that can be made to produce or amplify electromagnetic radiation at wavelengths equal to or greater than one hundred eighty nm but less than or equal to  $1.0 \times 10^6$  nm [ten to the sixth power] and that is manufactured, designed, intended or promoted for irradiation of any part of the human body for the purpose of affecting the structure or function of the body.
- (B) “Phototherapy” means the following:
- (1) For paragraph (A) of rule 4731-18-04 of the Administrative Code, phototherapy means the application of light for the treatment of hyperbilirubinemia in neonates.
  - (2) For paragraphs (B) and (C) of rule 4731-18-04 of the Administrative Code, phototherapy means the application of ultraviolet light for the treatment of psoriasis and similar skin diseases. This application can occur with any device cleared or approved by the United States food and drug administration for the indicated use that can be made to produce irradiation with broadband ultraviolet B (290-320nm), narrowband ultraviolet B (311-313 nm), excimer light based (308nm), ultraviolet A1 (340-400nm), or UVA (320-400nm) plus oral psoralen called PUVA.
- (C) “Photodynamic therapy” means light therapy involving the activation of a photosensitizer by visible light in the presence of oxygen, resulting in the creation of reactive oxygen species, which selectively destroy the target tissue.
- (D) “Ablative dermatologic procedure” means a dermatologic procedure that is expected to excise, burn, or vaporize the skin below the dermo-epidermal junction.
- (E) “Non-ablative dermatologic procedure” means a dermatologic procedure that is not expected or intended to excise, burn, or vaporize the epidermal surface of the skin.
- (F) “Physician means a person authorized to practice medicine and surgery, osteopathic medicine and surgery, or podiatric medicine and surgery under Chapter 4731. of the Revised Code and acting within the scope of their practice.
- (G) “Delegation” means the assignment of the performance of a service to a person who is not a physician.

(H) "On-site supervision" means the physical presence of the supervising physician is required in the same location (i.e., the physician's office suite) as the delegate of the light based medical device but does not require the physician's presence in the same room.

~~(I) "Off-site supervision" means that the supervising physician shall be continuously available for direct communication with the cosmetic therapist.~~

~~(I)~~(I) "Direct physical oversight" means the physical presence of the supervising physician is required in the same room to directly observe the delegate of the light based medical device.

~~(K)~~(J) "Vascular laser" means light-based medical devices including lasers and intense pulsed light apparatuses whose primary cutaneous target structures are telangiectasia, venulectasia, and superficial cutaneous vascular structures. In general, these lasers have wavelengths that correspond to the hemoglobin absorption spectrum.

4731-18-02

**Use of light based medical devices.**

- (A) The application of light based medical devices to the human body is the practice of medicine and surgery, osteopathic medicine and surgery, or podiatric medicine and surgery.
- (B) A physician shall not delegate the application of light based medical devices for ablative procedures.
- (C) A physician may delegate the application of a vascular laser for non-ablative dermatologic procedures according to the requirements in paragraph (A) of rule 4731-18-03 of the Administrative Code.
- (D) A physician may delegate the application of light based medical devices for the purpose of hair removal according to the ~~respective~~ requirements [of section 4731.33 of the Revised Code](#).~~in paragraphs (B) and (C) of rule 4731-18-03 of the Administrative Code.~~
- (E) A physician may delegate the application of phototherapy for the treatment of hyperbilirubinemia in neonates according to the requirements in paragraph (A) of rule 4731-18-04 of the Administrative Code.
- (F) A physician may delegate the application of phototherapy and photodynamic therapy only for dermatologic purposes according to the requirements of paragraphs (B) and (C) of rule 4731-18-04 of the Administrative Code.
- (G) A violation of paragraph (B) of this rule shall constitute "a departure from, or the failure to conform to, minimal standards of care of similar practitioners under the same or similar circumstances, whether or not actual injury to a patient is established," as that clause is used in division (B)(6) of section 4731.22 of the Revised Code and "violating or attempting to violate, directly or indirectly, or assisting in or abetting the violation of, or conspiring to violate, any provisions of this chapter or any rule promulgated by the board," as that clause is used in division (B)(20) of section 4731.22 of the Revised Code, to wit: section 4731.41 of the Revised Code.

4731-18-03

Delegation of the use of light based medical devices for specified non-ablative procedures.

(A) A physician may delegate the application of a vascular laser for non-ablative dermatologic procedures only if all the following conditions are met:

(1) The vascular laser has been specifically cleared or approved by the United States food and drug administration for the specific intended non-ablative dermatologic procedure;

(2) The use of the vascular laser for the specific non-ablative dermatologic use is within the physician's normal course of practice and expertise;

(3) The physician has seen and evaluated the patient to determine whether the proposed application of the specific vascular laser is appropriate;

(4) The physician has seen and evaluated the patient following the initial application of the specific vascular laser, but prior to any continuation of treatment in order to determine that the patient responded well to the initial application of the specific vascular laser;

(5) The person to whom the delegation is made is one of the following:

(a) A physician assistant licensed under Chapter 4730. of the Revised Code with whom the physician has an effective supervision agreement; or,

(b) A registered nurse or licensed practical nurse licensed under Chapter 4723. of the Revised Code;

(6) For a physician assistant, the authorization must meet the requirements of section 4730.21 of the Revised Code.

(7) For a registered nurse or licensed practical nurse, the physician must ensure that the person to whom the delegation is made has received adequate education and training to provide the level of skill and care required including:

(a) Eight hours of basic education that must include the following topics: light based procedure physics, tissue interaction in light based procedures, light based procedure safety including use of proper safety equipment, clinical application of light based procedures, pre and post-operative care of light based procedure patients, and reporting of adverse events;

(b) Observation of fifteen procedures for each specific type of vascular laser non-ablative procedure delegated. The procedures observed must be performed by a physician for whom the use of this specific vascular laser procedure is within the physicians normal course of practice and expertise; and

(c) Performance of twenty procedures under the direct physical oversight of the physician on each specific type of vascular laser non-ablative procedure delegated. The physician overseeing the performance of these procedures must use this specific vascular laser procedure within the physicians normal course of practice and expertise;

(d) Satisfactory completion of training shall be documented and retained by each physician delegating and the delegate. The education requirement in paragraph (A)(7)(a) of this rule must only be completed once by the delegate regardless of the number of types of specific vascular laser procedures delegated and the number of delegating physicians. The training requirements in paragraphs (A)(7)(b) and (A)(7)(c) of this rule must be completed by the delegate once for each specific type of vascular laser procedure delegated regardless of the number of delegating physician;

(8) For delegation to a registered nurse or licensed practical nurse, the physician provides on-site supervision at all times that the person to whom the delegation is made is applying the vascular laser; and,

(9) For delegation to a registered nurse or licensed practical nurse, the physician supervises no more than two persons pursuant to this rule at the same time.

(B) A physician may delegate the application of light based medical devices for the purpose of hair removal in accordance with the requirements of section 4731.33 of the Revised Code.

(C) The physician assistant, registered nurse or licensed practical nurse shall immediately report to the supervising physician any clinically significant side effect following the application of the light based medical device or any failure of the treatment to progress as was expected at the time the delegation was made. The physician shall see and personally evaluate the patient who has experienced the clinically significant side effect or whose treatment is not progressing as expected as soon as practicable.

(D) A violation of paragraph (A), (B), or (C) of this rule by a physician shall constitute "a departure from, or the failure to conform to, minimal standards of care of similar practitioners under the same or similar circumstances, whether or not actual injury to a patient is established," as that clause is used in division (B)(6) of section 4731.22 of the Revised Code.

(E) A violation of division (A)(5) of this rule shall constitute "violating or attempting to violate, directly or indirectly, or assisting in or abetting the violation of, or conspiring to violate, any provisions of this chapter or any rule promulgated by the board," as that clause is used in division (B)(20) of section 4731.22 of the Revised Code, to wit: section 4731.41 of the Revised Code.

(F) A violation of paragraph (C) of this rule by a physician assistant shall constitute "a departure from, or failure to conform to, minimal standards of care of similar physician assistants under the same or similar circumstances, regardless of whether actual injury to patient is established," as that clause is used in division (B)(19) of section 4730.25 of the Revised Code.

\*\*\* DRAFT - NOT YET FILED \*\*\*

4731-18-03

**Delegation of the use of light based medical devices for specified non-ablative procedures.**

- (A) A physician may delegate the application of a vascular laser for non-ablative dermatologic procedures only if all the following conditions are met:
- (1) The vascular laser has been specifically cleared or approved by the United States food and drug administration for the specific intended non-ablative dermatologic procedure;
  - (2) The use of the vascular laser for the specific non-ablative dermatologic use is within the physician's normal course of practice and expertise;
  - (3) The physician has seen and evaluated the patient to determine whether the proposed application of the specific vascular laser is appropriate;
  - (4) The physician has seen and evaluated the patient following the initial application of the specific vascular laser, but prior to any continuation of treatment in order to determine that the patient responded well to the initial application of the specific vascular laser;
  - (5) The person to whom the delegation is made is one of the following:
    - (a) A physician assistant licensed under Chapter 4730. of the Revised Code with whom the physician has an effective supervision agreement; or,
    - (b) A registered nurse or licensed practical nurse licensed under Chapter 4723. of the Revised Code;
  - (6) For a physician assistant, the authorization must meet the requirements of section 4730.21 of the Revised Code.
  - (7) For a registered nurse or licensed practical nurse, the physician must ensure that the person to whom the delegation is made has received adequate education and training to provide the level of skill and care required including:
    - (a) Eight hours of basic education that must include the following topics: light based procedure physics, tissue interaction in light based procedures, light based procedure safety including use of proper safety equipment, clinical application of light based procedures, pre and post-operative care of light based procedure patients, and reporting of adverse events;



- (b) Observation of fifteen procedures for each specific type of vascular laser non-ablative procedure delegated. The procedures observed must be performed by a physician for whom the use of this specific vascular laser procedure is within the physician's normal course of practice and expertise; and
  - (c) Performance of twenty procedures under the direct physical oversight of the physician on each specific type of vascular laser non-ablative procedure delegated. The physician overseeing the performance of these procedures must use this specific vascular laser procedure within the physician's normal course of practice and expertise;
  - (d) Satisfactory completion of training shall be documented and retained by each physician delegating and the delegate. The education requirement in paragraph (A)(7)(a) of this rule must only be completed once by the delegate regardless of the number of types of specific vascular laser procedures delegated and the number of delegating physicians. The training requirements in paragraphs (A)(7)(b) and (A)(7)(c) of this rule must be completed by the delegate once for each specific type of vascular laser procedure delegated regardless of the number of delegating physician;
- (8) For delegation to a registered nurse or licensed practical nurse, the physician provides on-site supervision at all times that the person to whom the delegation is made is applying the vascular laser; and,
- (9) For delegation to a registered nurse or licensed practical nurse, the physician supervises no more than two persons pursuant to this rule at the same time.
- (B) A physician may delegate the application of light based medical devices for the purpose of hair removal only if all the following conditions are met:
- (1) The light based medical device has been specifically cleared or approved by the United States food and drug administration for the removal of hair from the human body;
  - (2) The use of the light based medical device for the purpose of hair removal is within the physician's normal course of practice and expertise;
  - (3) The physician has seen and evaluated the patient to determine whether the proposed application of the specific light based medical device is appropriate;

- (4) The physician has seen and evaluated the patient following the initial application of the specific light based medical device, but prior to any continuation of treatment in order to determine that the patient responded well to that initial application of the specific light based medical device;
- (5) The person to whom the delegation is made is one of the following:
  - (a) A physician assistant licensed under Chapter 4730. of the Revised Code with whom the physician has an effective supervision agreement;
  - (b) A cosmetic therapist who was licensed under Chapter 4731. of the Revised Code on April 11, 2021 or who has completed a cosmetic therapy course of instruction for a minimum of seven hundred fifty clock hours and received a passing score on the “Certified Laser Hair Removal Professional ® Examination” administered by “The Society for Clinical and Medical Hair Removal”; or,
  - (c) A registered nurse or licensed practical nurse licensed under Chapter 4723. of the Revised Code.
- (6) For a physician assistant, the authorization must meet the requirements of section 4730.21 of the Revised Code.
- (7) For cosmetic therapists, registered nurses and licensed practical nurses, the physician shall ensure the person to whom the delegation is made has received adequate education and training to provide the level of skill and care required including:
  - (a) Eight hours of basic education that must include the following topics: light based procedure physics, tissue interaction in light based procedures, light based procedure safety including use of proper safety equipment, clinical application of light based procedures, pre and post-operative care of light based procedure patients, and reporting of adverse events;
  - (b) Observation of fifteen procedures for each specific type of light based medical device procedure for hair removal delegated. The procedures observed must be performed by a physician for whom the use of this specific light based medical device procedure for hair removal is within the physician’s normal course of practice and expertise; and

- (c) Performance of twenty procedures under the direct physical oversight of the physician on each specific type of light based medical device procedure for hair removal delegated. The physician overseeing the performance of these procedures must use this specific light based medical device procedure for hair removal within the physician's normal course of practice and expertise;
  - (d) Satisfactory completion of training shall be documented and retained by each physician delegating and the delegate. The education requirement in paragraph (A)(7)(a) of this rule must only be completed once by the delegate regardless of the number of types of specific light based medical device procedures for hair removal delegated and the number of delegating physicians. The training requirements of paragraphs (A)(7)(b) and (A)(7)(c) of this rule must be completed by the delegate once for each specific type of light based medical device procedure for hair removal delegated regardless of the number of delegating physicians;
  - (e) Delegates who, prior to the effective date of this rule, have been applying a specific type of light based medical device procedure for hair removal for at least two years through a lawful delegation by a physician, shall be exempted from the education and training requirements of paragraphs (A)(7)(a), (A)(7)(b), and (A)(7)(c) of this rule for that type of procedure provided that they obtain a written certification from one of their current delegating physicians stating that the delegate has received sufficient education and training to competently apply that type of light based medical device procedure. This written certification must be completed no later than sixty days after the effective date of this rule, and a copy of the certification shall be retained by each delegating physician and each delegate.
  - (f) For cosmetic therapists, the education and training requirements of paragraph (A)(7)(a), (A)(7)(b), or (A)(7)(c) of this rule may be satisfied through the cosmetic therapy course of instruction in paragraph (B)(5)(b) of this rule if the program provides written verification to the physician that the cosmetic therapist completed the requirements of paragraph (A)(7)(a), (A)(7)(b), or (A)(7)(c) of this rule as part of the cosmetic therapy course of instruction.
- (8) For cosmetic therapists, registered nurses and licensed practical nurses, the physician provides on-site supervision at all times that the person to whom the delegation is made is applying the light based medical device; and,

- (9) For cosmetic therapists, registered nurses and licensed practical nurses, the physician supervises no more than two persons pursuant to this rule at the same time.
- (C) Notwithstanding paragraph (B)(8) of this rule, the physician may provide off-site supervision when the light based medical device is applied for the purpose of hair removal to an established patient if the person to whom the delegation is made pursuant to paragraph (B) of this rule is a cosmetic therapist who meets all of the following criteria:
- (1) The cosmetic therapist has successfully completed a course in the use of light based medical devices for the purpose of hair removal that has been approved by the delegating physician;
  - (2) The course consisted of at least fifty hours of training, at least thirty hours of which was clinical experience; and
  - (3) The cosmetic therapist has worked under the on-site supervision of the physician making the delegation a sufficient period of time that the physician is satisfied that the cosmetic therapist is capable of competently performing the service with off-site supervision.

The cosmetic therapist shall maintain documentation of the successful completion of the required training.

- (D) The cosmetic therapist, physician assistant, registered nurse or licensed practical nurse shall immediately report to the supervising physician any clinically significant side effect following the application of the light based medical device or any failure of the treatment to progress as was expected at the time the delegation was made. The physician shall see and personally evaluate the patient who has experienced the clinically significant side effect or whose treatment is not progressing as expected as soon as practicable.
- (E) A violation of paragraph (A), (B), (C), or (D) of this rule by a physician shall constitute "a departure from, or the failure to conform to, minimal standards of care of similar practitioners under the same or similar circumstances, whether or not actual injury to a patient is established," as that clause is used in division (B)(6) of section 4731.22 of the Revised Code.
- (F) A violation of division (A)(5) or (B)(5) of this rule shall constitute "violating or attempting to violate, directly or indirectly, or assisting in or abetting the violation of, or conspiring to violate, any provisions of this chapter or any rule promulgated

by the board," as that clause is used in division (B)(20) of section 4731.22 of the Revised Code, to wit: section 4731.41 of the Revised Code.

(G) A violation of paragraph (C) or (D) of this rule by a cosmetic therapist shall constitute the unauthorized practice of medicine pursuant to section 4731.41 of the Revised Code.

(H) A violation of paragraph (D) of this rule by a physician assistant shall constitute "a departure from, or failure to conform to, minimal standards of care of similar physician assistants under the same or similar circumstances, regardless of whether actual injury to patient is established," as that clause is used in division (B)(19) of section 4730.25 of the Revised Code.

October 14, 2022

To:  
Kimberly Anderson, Chief Legal Counsel  
State Medical Board of Ohio

[CSIPublicComments@governor.ohio.gov](mailto:CSIPublicComments@governor.ohio.gov)

We appreciate the opportunity to provide public comment from those who own and operate light-based medical devices regarding the upcoming changes to rules 4731-18-01 through 4731-18-03. The State Medical Board of Ohio (SMBO) has implied in the Business Impact Analysis (BIA) that the purpose of the rule change is to align it with law change that occurred in September of 2021. The cosmetic therapy profession would like the state that we were unfairly pushed out of the verbally proposed changes due to the unexpected unlicensure of our profession from SMBO earlier that year. The portion of concern relates to the statement under question 10 of the BIA that says the “change to allow physicians assistants and nurses to be delegated non-ablative vascular lasers because these are the safest for patients”. The cosmetic therapy profession has a documented history of asking for delegation of vascular lasers going back to at least February of 2018 and has a written record of being considered a competent profession to be delegated to. Please allow us to summarize our experience with the rule change that occurred.

In the BIA, SMBO does admit that the light-based rule has been going through amendment changes for a very long time. In January 2021’s SMBO meeting minutes referenced at the bottom of this letter, show a Rule Spreadsheet that provides the “current review date” for the light-based medical device rule recorded as 06/2005 but that it was not sent for initial public comment until 01/2018 (page 16, pictured below), almost 13 years passed the expected rule review timeline. In these same meeting minutes, SMBO’s then President Dr. Bechtel said “that vascular lasers are probably the safest of all the lasers and have a lower risk of scarring, and that is why the vascular laser was chosen for expansion into the scope of practice of nurses and cosmetic therapists” (page 3).

Rule Number	Rule Description	Sent for Initial Comment	Board Approval to File with CSI	CSI filing	CSI recommendation	JCARR filing	Rules Hearing	JCARR Hearing	Board Adoption	New Effective Date	Current Review Date
4731-16-14	Caffeine, Nicotine, and Over-The Counter Drugs									11/17/17	11/17/22
4731-16-15	Patient Rights									11/17/17	11/17/22
4731-16-17	Requirements for the one-bite program									01/31/19	01/31/24
4731-16-18	Eligibility for the one-bite program									01/31/19	01/31/24
4731-16-19	Monitoring organization for one-bite program									01/31/19	01/31/24
4731-16-20	Treatment providers in the one-bite program									01/31/19	01/31/24
4731-16-21	Continuing care for the one-bite program									01/31/19	01/31/24
4731-17-01	Exposure-Prone Invasive Procedure Precautions - Definitions	08/26/20	10/14/20	10/23/20	11/24/20					12/31/16	12/31/21
4731-17-02	Universal Precautions	08/26/20	10/14/20	10/23/20	11/24/20					11/30/16	11/30/21
4731-17-03	Hand Washing	08/26/20	10/14/20	10/23/20	11/24/20						08/17/21
4731-17-04	Disinfection and Sterilization	08/26/20	10/14/20	10/23/20	11/24/20					12/31/16	12/31/21
4731-17-05	Handling and Disposal of Sharps and Wastes	08/26/20	10/14/20	10/23/20	11/24/20						08/17/21
4731-17-06	Barrier Techniques	08/26/20	10/14/20	10/23/20	11/24/20						08/17/21
4731-17-07	Violations	08/26/20	10/14/20	10/23/20	11/24/20					11/09/16	11/30/21
4731-18-01	Definitions	01/10/18	01/20/20	05/12/20							
4731-18-02	Use of Light Based Medical Devices	01/10/18	01/20/20	05/12/20						05/31/02	06/30/05
4731-18-03	Delegation of the Use of Light Based Medical Devices	01/10/18	01/20/20	05/12/20						06/30/00	06/30/05

Reference: Board Meetings & Minutes *Rule and Policy's January 13, 2021*, State Medical Board of Ohio, Feb. 2021, [https://med.ohio.gov/Portals/0/For%20The%20Public/Board%20Meetings%20and%20Minutes/2021/Board%20Meetings/Jan\\_%202021%20Rules%20and%20Policies%20Packet\\_1.pdf?ver=OnjgTpZntpaT-QefKLy8g%3d%3d](https://med.ohio.gov/Portals/0/For%20The%20Public/Board%20Meetings%20and%20Minutes/2021/Board%20Meetings/Jan_%202021%20Rules%20and%20Policies%20Packet_1.pdf?ver=OnjgTpZntpaT-QefKLy8g%3d%3d).

Unfortunately, legislation occurred shortly after that unlicensed our profession which put us at risk of falling out of compliance with the light based delegation rule for hair removal, which accounts for the majority of what a cosmetic therapist does in today's industry. It was decided that an Emergency Rule had to be enacted in April, 2021 to bridge a gap to allow the majority of women-owned small businesses within the cosmetic therapy industry to continue client care uninterrupted. SMBO was able to detail training requirements for all delegates during this first official update to the rule in over twenty years but it clearly was not inclusive of everything that they wanted to achieve. As Emergency Rules are only active for a short period of time, the rule finally passed through the standard process in July 2021. Although our community had asked for vascular delegation again in May's open comments and public hearing, it was not included. We feel this was in retaliation to our field's unlicensure and does not consider cosmetic therapy's hour-based training requirements that far exceeds the newly adopted vascular training requirements in the application of a device that has similar light wavelengths, mechanism of action, and depth into the skin layers as laser hair removal.

Worrying that SMBO had the power to write us out of the laser delegation rule as a newly unlicensed profession at any point in future rule reviews, it was decided by legislators in Ohio's 133<sup>rd</sup> General Assembly to pull the laser hair removal portion of the rule into its own law, ORC 4731.33. We wish to argue we are as just as competent to perform vascular treatment, if not more so than the other professions as the newly adopted vascular training was built out using cosmetic therapy's laser hair removal delegation as a starting guide. Cosmetic therapy laser training had always required 50 hours of education and clinical experience since its effective date in 2000. Although it did not specify the number of observed/supervised treatments the new rule states, our hour-based requirement more than covers the number of training treatments that the new rule for vascular delegation entails. Vascular treatments can be performed quickly and a trainee can observe up to 4 treatments per hour. Combining the required observed/supervised and 8 hours of education can easily be completed in as little as 16 hours. By law, cosmetic therapists study the same educational content for over three times as many hours.

During those first twenty years the rule only listed the other delegated professions as requiring a subjective "adequate training" in the eyes of the delegating doctor that wasn't further defined until the Emergency Rule was enacted last year. It is our understanding that the legislators of the had leaned hard on SMBO's recommendation on how this law should be worded, as told to us by the lobbying group, The Buckeye Institute, who was the initial entity that recommended our unlicensure. Ironically, the law retracted the robust laser hair removal training requirements for physician assistants (PA) and nurses (approximately 16 hours) that the medical board had spent two years building out and it once again only applies to cosmetic therapists. Currently, PA's and nurses have no training requirements for laser hair removal and SMBO no longer has regulation over enforcing hair removal training, only training requirements for vascular laser delegation going forward.

We would also like to note that cosmetic therapists have no history of public harm or safety complaints from our application of laser treatments for hair removal in our over twenty-year history of delegation. We deserve to be considered for vascular delegation especially now that we were unlicensed which created a business impact to our ability to be hired in our industry. The BIA says there are no exemptions for small businesses however by adding cosmetic therapists to the approved delegated list for vascular treatments several mostly woman owned small businesses would greatly benefit from being able to expand these types of treatments into their service options. Cosmetic therapists have typically been the most cost-effective profession for a med-spa or doctor's office to hire to perform laser hair removal and could lead to more job creation for our field if we were allowed this ability to be delegated vascular light-based medical devices.



If history repeats itself, we cannot wait another twenty years for this rule to complete the next scheduled review process and this is our last chance to ask for the delegation that would make our profession's employability more desirable. Additionally, allowing our cosmetic therapist owned small businesses the ability to add these services would increase our profitability which would lend to us being able to hire within our own field to cover the increased service demand and create jobs for our upcoming students within the cosmetic therapy profession.

Sincerely,

A handwritten signature in cursive script that reads "Amanda Nelson".

Amanda Nelson, CT, Trustee  
The Cosmetic Therapy Association of Ohio Board





Rules and Policies  
January 13, 2021

1. Adoption of December policy meeting minutes
  2. Rule Review Update
    - a. Rules for initial review
    - b. Rules at CSI
    - c. Comments received on weight-loss rules
    - d. Adoption of CME rules
  3. Legislative Update
    - a. Summary of lame duck (see attached memos on SB 310, HB 263 and HB 442)
    - b. Legislative outreach initiatives
-



State Medical Board of Ohio

**POLICY COMMITTEE MEETING**

**December 9, 2020**

via live-streamed video conference

<p><b>Members:</b> Amol Soin, M.D., Chair Robert Giacalone, R.Ph., J.D. Mark Bechtel, M.D. Betty Montgomery Sherry Johnson, D.O.</p> <p><b>Other Board Members present:</b> Michael Schottenstein, M.D. Kim Rothermel, M.D. Bruce Saferin, D.P.M. Jonathan Feibel, M.D. Harish Kakarala, M.D.</p>	<p><b>Staff:</b> Stephanie Loucka, Executive Director Kimberly Anderson, Chief Legal Counsel Nathan Smith, Senior Legal and Policy Counsel Chelsea Wonski, Legislative Director Julie Williams, Public Information Officer Benton Taylor, Board Parliamentarian</p>
---	---

Dr. Soin called the meeting to order at 9:01 a.m.

### Minutes Review

**Dr. Bechtel moved to approve the draft minutes of the November 10, 2020 meeting of the Policy Committee. Mr. Giacalone seconded the motion. The motion carried.**

### Rule Review Update

Ms. Anderson stated that there will be fewer rules to be reviewed in 2021, but the group will include rules that are used by the Board often. Among the rules scheduled for review in 2021 are the sexual misconduct rules, the delegation rules, and the rules on prescribing controlled substances for self and family. The 2021 rule review schedule is included in the meeting materials.

Ms. Anderson stated that the Board is scheduled to adopt new rules at today's Board meeting. The continuing medical education (CME) rules, including the mandatory one hour of education on the duty-to-report, has been through the required hearings and will be ready for adoption by the Board at its January 2021 meeting.

### Rules with the Common Sense Initiative

#### Temporary Military Licensure

Ms. Anderson stated that the Board is scheduled to adopt rules this afternoon regarding military licensure. The Common Sense Initiative (CSI) required changes to proposed Rule 4731-36-04 to

reference the Board's processes as described in proposed Rule 4731-36-03. CSI also requested that language be added to explain that licensure fees would be waived. Ms. Anderson noted that statute requires the fee to be waived, and this is why the explanation was not initially included in the proposed Rule. The explanation of the waived licensure fees has been added to the proposed Rule as Paragraph H.

In response to a question from Dr. Bechtel, Ms. Anderson stated that although licensure fees will be waived, the applicant will still be responsible for paying for the background check as required by statute. Ms. Montgomery asked that measures be taken to ensure that the Board does not end up absorbing the costs of the background checks. Ms. Anderson stated that she will work with Mr. Turek to make sure the instructions for the applicants is clear on that point.

**Dr. Bechtel moved to recommend approval of the proposed amendments to Rule 4731-36-04, to be filed with the Joint Committee on Agency Rule Review. Dr. Johnson seconded the motion.** The motion carried.

### **Light-Based Medical Devices**

Ms. Anderson stated that many comments were received on the proposed light-based medical devices rule and have been included in the Committee materials packet. The rules have been discussed with the Physician Assistant Policy Committee as well. Ms. Anderson stated that the physician assistant statutes, especially 4730.21, Ohio Revised Code, already specify how a supervising physician and a physician assistant should work together with respect to the competence of the physician assistant to utilize light-based medical devices, the type of supervision to be given by the supervising physician, and the number of physician assistants that may be supervised at one time. These statutory provisions are slightly different from what has been proposed in this rule.

Ms. Anderson has drafted changes to the rule to address these concerns and to treat physician assistants differently in accordance with statute. For registered nurses, licensed practical nurses, and in some cases cosmetic therapists, the rule would establish a number of procedures to be viewed, require on-site supervision, and limit the physician to supervising up to two individuals.

Because these changes are significant, Ms. Anderson wished to consult with the Physician Assistant Policy Committee and ensure their concerns are being addressed, as well as the Board of Nursing since the rule would affect some of their licensees. Ms. Anderson also asked for the Committee's input on the definitional concerns that were raised in the public comments.

Ms. Montgomery asked for clarification of whether the rule applies to vascular lasers, which was one of the questions in the public comments. Dr. Bechtel stated that the rule specifically discusses what types of skin lesions are considered vascular in nature and therefore amenable to treatment. Dr. Bechtel stated that the energy of vascular lasers is absorbed by the hemoglobin in the blood, which dissipates energy and causes blood vessels to branch down. Dr. Bechtel was satisfied with the rule's description of what skin lesions are considered vascular. Dr. Bechtel was also comfortable with defining vascular lasers as light-based medical devices. Ms. Anderson thanked Dr. Bechtel for clarifying that issue.

Dr. Bechtel continued that the rule is focused on patient safety. Dr. Bechtel stated that vascular lasers are probably the safest of all the lasers and have a lower risk of scarring, and that is why the vascular laser was chosen for expansion into the scope of practice of nurses and cosmetic therapists. The rule also includes rigorous educational requirements, including eight hours of classroom education. The

practitioners are required to observe 15 cases and then perform 20 cases under direct supervision of a physician. Also, physicians cannot supervise more than two individuals at one time. In response to two articles on laser safety sent by the Cleveland Clinic, Dr. Bechtel stated that one article was on ablative lasers, which are not expanded by this rule because of the greater risk of scarring. The other article was published outside the United States. Dr. Bechtel reiterated that he is comfortable that the guardrails and educational requirements in the rule will promote patient safety.

Dr. Schottenstein asked if the Board of Nursing has statutes that governs their licensees' authorization for supervision that could potentially allow them more leeway than this proposed rule would. Ms. Anderson replied that she did not believe that was the case, but she would like to get input from the Board of Nursing.

Regarding the scope of cosmetic therapists, Mr. Giacalone asked Dr. Bechtel to comment on what makes hair removal and tattoo removal different from vascular treatment. Dr. Bechtel responded that cosmetic therapists can perform laser hair removal and those who already do so can continue under this rule. However, the rule would require cosmetic therapists who are beginning to practice laser hair removal to undergo extensive educational instruction. Dr. Bechtel stated that removal of tattoos is very complicated and requires a laser to be specifically chosen based on the tattoo pigment. Tattoo removal also has a much higher incidence of scarring. While allowing cosmetic therapists to use laser for tattoo removal may be something the Board could consider in the future, it is not included in the current proposed rule due to the challenging process and potential risks.

**Dr. Bechtel moved to circulate the proposed changes to the proposed rule to the Physician Assistant Policy Committee and the Board of Nursing for input. Dr. Johnson seconded the motion.** The motion carried.

### **Weight-Loss Prescribing Rules**

Dr. Soin stated that last month the Committee decided to gather additional information on this topic. Since that time, Dr. Soin reached out to key opinion leaders in this field, as well as pharmacists, physicians who treat obesity, and representatives from national obesity associations. Dr. Soin remarked that he received a great deal of valuable information and feedback from these interactions. At the Board's request, these experts also provided written comments that Dr. Soin found to be excellent and well-written. Dr. Soin stated that it would be helpful to have additional time to review the written comments and provide a more robust update next month.

Dr. Soin observed that there were two general themes in the comments. One theme was the potential opportunity to enhance telemedicine visits for some of the wellness checks that are required by rule. Secondly, the vast majority of comments were on the issue phentermine being labeled as an acute treatment and whether there are any opportunities for chronic use. Dr. Soin stated the more information will be gathered for review next month.

### **Hearing Rules**

Ms. Anderson stated that though minor changes to the hearing rules have already been approved by the Board, the Hearing Examiners have requested that the rule be amended so they would have the ability to hold virtual hearings via video conference upon motion from a party or from the Hearing Examiner, even when the current emergency is over. Ms. Montgomery was in favor of this change because of the added flexibility it could provide to licensees and the potential to increase the number of hearings held.

**Ms. Montgomery moved to refile the hearing rule with the proposed change. Dr. Bechtel seconded the motion.** The motion carried.

### **Consult Agreement Rules**

Ms. Anderson stated that the Board of Pharmacy is required by statute to submit any proposed changes to its consult agreement rules to the Medical Board for input. The Board has had an opportunity to review the Board of Pharmacy's proposed changes and Ms. Anderson has been notified of some minor typographical errors. Likewise, the Medical Board is required by statute to submit any potential changes to its consult agreement rules to the Board of Pharmacy for their input.

**Dr. Johnson moved to communicate to the Board of Pharmacy the Board's comments on the Board of Pharmacy's proposed consult agreement rules. Dr. Johnson further moved to approve submission of the Medical Board's proposed consult agreement rules to the Board of Pharmacy for consultation as required in Section 4729.39(E)(2), ORC. Dr. Bechtel seconded the motion.** The motion carried.

### **Legislative Update**

**Senate Bill 246, Occupational Licensing Reciprocity:** Ms. Wonski stated that the legislative staff has worked with the bill's sponsor and the committee chair to address concerns for retaining the Board's ability to make determinations on whether an applicant has adequately met Ohio's qualifications for licensure. Last week, the Senate committee adopted the Board's requested changes. These amendments allow greater flexibility for all licensing boards in making determinations on applicants' fitness to practice. Ms. Wonski thanked Mr. Smith, who was instrumental in both drafting and negotiating the amendments.

Ms. Montgomery asked if there has been discussion on allowing the Board to consider applicants' offenses beyond the five-year limit for cases of violence or sexually-related offenses. Ms. Wonski replied that the fitness-to-practice language allows the Board more flexibility to consider older offenses if they resulted in action on the applicant's license in another state. Mr. Smith commented that Ms. Wonski is working diligently on House Bill 263 to request a longer look-back period on convictions.

**House Bill 263, Occupational Licensing:** Ms. Wonski stated that this legislation would require the Board to provide a comprehensive list of criminal offenses that would prevent a person from becoming licensed in Ohio. The legislative staff has worked with several other health care boards, as well as the bill sponsor and committee chair, to develop solutions to the boards' issues. The Senate Transportation, Commerce, and Workforce Committee had a third hearing on this bill last week. The Board submitted testimony expressing its concerns with the language and offered suggested changes. The bill is scheduled for its fifth hearing today.

**Senate Bill 364, Interstate Medical Licensure Compact:** Ms. Wonski stated that this bill would require Ohio to join the Interstate Medical Licensure Compact. This legislation has not moved recently, but the staff continues to monitor it closely. Ms. Wonski did not expect the bill to move during this General Assembly, but this language may be seen again early next year.

**House Bill 492, Physician Assistants:** Ms. Wonski stated that this bill would expand the ability of physician assistants to perform procedural sedation for the purpose of rapid intubation. Ms. Wonski

stated that several stakeholders have expressed opposition to the bill. The bill has not moved much through the legislative process, but the staff is monitoring it closely.

**Senate Bill 236, Radiation Control and Radiation Technology Professionals:** Ms. Wonski stated that this legislation would authorize the State Director of Health, when adopting rules for Ohio's radiation control program, to deviate from the suggested state regulations for control of radiation if doing so is warranted and does not pose a health, environmental, or safety risk. The staff is watching this legislation because an amendment was added that would grant anesthesiologist assistants the ability to order or direct others to administer drugs under a supervision agreement. The Ohio State Medical Association and the Ohio Society of Anesthesiologists have expressed a neutral position on the amendment.

**Senate Bill 305, Telemedicine:** Ms. Wonski stated that this bill would require insurers to provide coverage for telehealth services during a state of emergency. If the bill begins to move, the Committee will be updated at the next meeting.

**House Bill 388, Out-of-Network Care (Surprise Billing):** Ms. Montgomery asked Ms. Wonski for her evaluation of this bill's progress and flexibility. Ms. Wonski stated that under this legislation, hospitals would be required to notify patients if a test or other service is out of the patient's insurance network, inform the patient if there is way to obtain that service in-network, and provide the cost of any such services if they are not emergency in nature. The bill has had its third hearing in the Senate, so it is possible that it may pass in this legislative session. This bill has the support of the Ohio Department of Insurance.

**Federal Legislation:** Dr. Schottenstein asked if the Board has the ability to provide input on federal legislation. Ms. Wonski stated that the four pieces of federal legislation that is listed in the legislative tracker are not expected to move this year. If there is federal legislation that could potentially move and the Board feels strongly about, the legislative staff can weigh in with Ohio's congressional representatives and senators to make the Board's position known.

### **Pharmacy Board Updates**

There were no Pharmacy Board updates at this time.

### **Adjourn**

**Dr. Bechtel moved to adjourn the meeting. Dr. Johnson seconded the motion.** All Committee members voted aye. The motion carried.

The meeting adjourned at 9:43 a.m.

bt



**MEMORANDUM**

TO: Mark Bechtel, M.D., President  
Members, State Medical Board of Ohio

FROM: Kimberly C. Anderson, Chief Legal Counsel

RE: Rule Review Update

DATE: December 29, 2021

---

Attached are the updated rule schedule and rule spreadsheet. Please let me know if you have any questions.

**Action Requested: No action requested**

---

# Legal Dept. Rules Schedule

As of December 29, 2020

## To January Board Meeting for Adoption

4731-10 CME rules  
JCARR jurisdiction ends 1/3/2021

### **RULES AT CSI**

#### **Comment Deadline 5/27/20**

4731-18 – Light Based Medical Device Rules

#### **Comment Deadline 10/19/20**

4731-11-02    4731-11-03    4731-11-04  
4731-11-04.1    4731-11-07    4731-11-11

#### **Comment Deadline 11/6/20**

4731 Chapter 13 – 36 rules

#### **Comment Deadline 11/23/20**

4759-4-04    4759-4-08    4759-6-02

### **RULES SENT FOR INITIAL CIRCULATION**

#### **Comment Deadline – September 25, 2020**

4731-6-14

## **RULES AT JCARR**

### **Ready to be filed with JCARR**

4731-8-01	4731-8-02	4731-8-03
4731-8-04	4731-8-05	4731-8-06
4774-1-01	4774-1-02	4774-1-03
4774-1-04	4731-17-01	4731-17-02
4731-17-03	4731-17-04	4731-17-05
4731-17-06	4731-17-07	4731-36-04

### **Rules for review in 2021**

4731-1-12-Examination-Due 11.30.21  
4731-1-16-Massage Therapy Curriculum-Due  
11.30.21  
4731-11-08-Utilizing controlled substances for self  
and family members-Due 8.17.21  
4731-14-01-Pronouncement of Death-Due 6.30.21  
4731-23-01-Delegation of Medical Tasks-Definitions-  
Due 11.30.21  
4731-23-02-Delegation of Medical Tasks-Due  
11.30.21  
4731-23-03-Delegation of Medical Tasks-  
Prohibitions-Due 8.17.21  
4731-23-04-Violations-Due 8.17.21  
4731-26-01-Sexual Misconduct Definitions-Due-  
6.30.21  
4731-26-02-Prohibitions-Due 6.14.21  
4731-26-03-Violations; Miscellaneous-Due 6.30.21



Rule Number	Rule Description	Sent for Initial Comment	Board Approval to File with CSI	CSI filing	CSI recommendation	JCARR filing	Rules Hearing	JCARR Hearing	Board Adoption	New Effective Date	Current Review Date
4730-1-01	Regulation of Physician Assistants - Definitions		06/12/19	07/16/19	11/07/19	06/18/20	No change rule			09/16/20	06/18/25
4730-1-05	Quality Assurance System		06/12/19	07/16/19	11/07/19	06/19/20	No change rule			09/17/20	06/19/25
4730-1-06	Licensure as a physician assistant	03/22/19	06/12/19	12/04/19		06/18/20	07/23/20	08/17/20	09/09/20	12/31/20	09/30/23
4730-1-07	Miscellaneous Provisions		06/12/19	07/16/19	11/07/19	06/18/20	07/23/20	08/17/20	09/09/20	09/30/20	09/30/23
4730-2-01	Physician Delegated Prescriptive Authority - Definitions		06/12/19	07/16/19	11/07/19	06/18/20	No change rule			09/18/20	06/18/25
4730-2-04	Period of on-site supervision of physician-delegated prescriptive authority		06/12/19	07/16/19	11/07/19	06/18/20	07/23/20	08/17/20	09/09/20	09/30/20	11/15/23
4730-2-05	Addition of valid prescriber number after initial licensure		06/12/19	07/16/19	11/07/19	06/18/20	07/23/20	08/17/20	09/09/20	09/30/20	09/30/23
4730-2-07	Standards for Prescribing		06/12/19	07/16/19	11/07/19	06/18/20	07/23/20	08/17/20	09/09/20	09/30/20	09/30/25
4730-2-10	Standards and Procedures for use of OARRS		06/12/19	07/16/19	11/07/19	06/18/20	07/23/20	08/17/20	09/09/20	09/30/20	09/30/23
4730-4-01	Definitions	05/09/19		11/15/19	05/20/20	06/18/20	07/23/20	08/17/20	10/14/20	10/31/20	04/30/24
4730-4-02	Standards and procedures for withdrawal management for drug or alcohol addiction	05/09/19		11/15/19	05/20/20	06/18/20	07/23/20	08/17/20	10/14/20	10/31/20	10/31/25
4730-4-03	Office Based Treatment for Opioid addiction									04/30/19	04/30/24
4730-4-04	Medication assisted treatment using naltrexone									04/30/19	04/30/24
4730-5-01											
4730-5-02											
4731-1-01	Limited Practitioners - Definition of Terms									03/30/20	03/30/25
4731-1-02	Application of Rules Governing Limited Branches of Medicine or Surgery									07/31/19	07/31/24
4731-1-03	General Prohibitions										08/31/23
4731-1-04	Scope of Practice: Mechanotherapy									12/31/18	12/31/23
4731-1-05	Scope of Practice: Massage Therapy				04/24/19	Refiled 8/20/19 4/29/19	06/05/19		10/16/19	11/05/19	11/05/24
4731-1-06	Scope of Practice: Naprapathy									08/31/18	08/31/23

Rule Number	Rule Description	Sent for Initial Comment	Board Approval to File with CSI	CSI filing	CSI recommendation	JCARR filing	Rules Hearing	JCARR Hearing	Board Adoption	New Effective Date	Current Review Date
4731-1-07	Eligibility of Electrologists Licensed by the Ohio State Board of Cosmetology to Obtain Licensure as Cosmetic Therapists Pursuant to Chapter 4731 ORC and Subsequent Limitations									12/31/18	12/31/23
4731-1-08	Continuing Cosmetic Therapy Education Requirements for Registration or Reinstatement of a License to Practice Cosmetic Therapy									09/30/19	09/30/24
4731-1-09	Cosmetic Therapy Curriculum Requirements										08/31/23
4731-1-10	Distance Education									01/31/19	01/31/24
4731-1-11	Application and Certification for certificate to practice cosmetic therapy									03/30/20	03/30/25
4731-1-12	Examination									11/30/16	11/30/21
4731-1-15	Determination of Standing of School, College or Institution									12/31/18	12/31/23
4731-1-16	Massage Therapy curriculum rule (Five year review)									01/31/19	11/30/21
4731-1-17	Instructional Staff									05/31/19	05/31/24
4731-1-18	Grounds for Suspension, Revocation or Denial of Certificate of Good Standing, Hearing Rights									03/30/20	03/30/25
4731-1-19	Probationary Status of a limited branch school									03/30/20	03/30/25
4731-1-24	Massage Therapy Continuing Education	03/09/16		10/26/16	04/24/19	04/29/19	06/05/19				
4731-2-01	Public Notice of Rules Procedure									12/07/17	12/07/22
4731-4-01	Criminal Records Checks - Definitions									09/30/19	09/30/24
4731-4-02	Criminal Records Checks									09/30/19	09/30/24
4731-5-01	Admission to Examinations									06/09/17	06/09/22
4731-5-02	Examination Failure; Inspection and Regrading									06/09/17	06/09/22
4731-5-03	Conduct During Examinations									06/09/17	06/09/22
4731-5-04	Termination of Examinations									06/09/17	06/09/22
4731-6-01	Medical or Osteopathic Licensure: Definitions									07/31/19	07/31/24
4731-6-02	Preliminary Education for Medical and Osteopathic Licensure									07/31/19	07/31/24

Rule Number	Rule Description	Sent for Initial Comment	Board Approval to File with CSI	CSI filing	CSI recommendation	JCARR filing	Rules Hearing	JCARR Hearing	Board Adoption	New Effective Date	Current Review Date
4731-6-04	Demonstration of proficiency in spoken English									06/09/17	06/09/22
4731-6-05	Format of Medical and Osteopathic Examination									07/31/19	07/31/24
4731-6-14	Examination for physician licensure	09/03/20								07/31/19	07/31/24
4731-6-15	Eligibility for Licensure of National Board Diplomats and Medical Council of Canada Licentiates									07/31/19	07/31/24
4731-6-21	Application Procedures for Certificate Issuance; Investigation; Notice of Hearing Rights									07/31/19	07/31/24
4731-6-22	Abandonment and Withdrawal of Medical and Osteopathic Licensure Applications									07/31/19	07/31/24
4731-6-30	Training Certificates									07/31/19	07/31/24
4731-6-31	Limited Preexamination Registration and Limited Certification									07/31/19	07/31/24
4731-6-33	Special Activity Certificates									07/31/19	07/31/24
4731-6-34	Volunteer's Certificates									07/31/19	07/31/24
4731-7-01	Method of Notice of Meetings									07/31/19	07/31/24
4731-8-01	Personal Information Systems	04/29/20		10/05/20	11/18/20					04/21/16	04/21/21
4731-8-02	Definitions	04/29/20		10/05/20	11/18/20					04/21/16	04/21/21
4731-8-03	Procedures for accessing confidential personal information	04/29/20		10/05/20	11/18/20					04/21/16	04/21/21
4731-8-04	Valid reasons for accessing confidential personal information	04/29/20		10/05/20	11/18/20					04/21/16	04/21/21
4731-8-05	Confidentiality Statutes	04/29/20		10/05/20	11/18/20					07/31/16	07/31/21
4731-8-06	Restricting & Logging access to confidential personal information	04/29/20		10/05/20	11/18/20					04/21/16	04/21/21
4731-9-01	Record of Board Meetings; Recording, Filming, and Photographing of Meetings									09/15/19	06/17/24
4731-10-01	Definitions	10/25/19		05/26/20		Revised filing 11/3/20 10/30/20	12/04/20	12/07/20		02/02/18	02/02/23
4731-10-02	Requisite Hours of Continuing Medical Education for License Renewal or Reinstatement	10/25/19		05/26/20		Revised filing 11/3/20 10/30/20	12/04/20	12/07/20		05/31/18	05/31/23

Rule Number	Rule Description	Sent for Initial Comment	Board Approval to File with CSI	CSI filing	CSI recommendation	JCARR filing	Rules Hearing	JCARR Hearing	Board Adoption	New Effective Date	Current Review Date
4731-10-03	CME Waiver	10/25/19		05/26/20		Revised filings 11/24 & 11/3 - orig 10/30/20	12/04/20	12/07/20		05/31/18	05/31/23
4731-10-04	Continuing Medical Education Requirements for Restoration of a License	10/25/19		05/26/20		Revised filings 11/24 & 11/3 - orig 10/30/20	12/04/20	12/07/20		05/31/18	05/31/23
4731-10-05	<i>Out-of-State Licensees</i>	10/25/19		05/26/20		<i>Revised filings 11/24 &amp; 11/3 - orig 10/30/20</i>	12/04/20	12/07/20		05/31/18	05/31/23
4731-10-06	<i>Licensure After Cutoff for Preparation of Registration Notices</i>	10/25/19		05/26/20		<i>Revised filings 11/24 &amp; 11/3 - orig 10/30/20</i>	12/04/20	12/07/20		05/31/18	05/31/23
4371-10-07	<i>Internships, Residencies and Fellowships</i>	10/25/19		05/26/20		<i>Revised filings 11/24 &amp; 11/3 - orig 10/30/20</i>	12/04/20	12/07/20		05/31/18	05/31/23
4371-10-08	Evidence of Continuing Medical Education	10/25/19		05/26/20		Revised filings 11/24 & 11/3 - orig 10/30/20	12/04/20	12/07/20		05/31/18	05/31/23
4731-10-09	<i>Continuing Medical Education Requirement for Mid-term Licensees</i>	10/25/19		05/26/20		<i>Revised filings 11/24 &amp; 11/3 - orig 10/30/20</i>	12/04/20	12/07/20		05/31/18	05/31/23

Rule Number	Rule Description	Sent for Initial Comment	Board Approval to File with CSI	CSI filing	CSI recommendation	JCARR filing	Rules Hearing	JCARR Hearing	Board Adoption	New Effective Date	Current Review Date
4731-10-10	Continuing Medical Education Requirements Following License Restoration	10/25/19		05/26/20		Revised filings 11/24 & 11/3 - orig 10/30/20	12/04/20	12/07/20		05/31/18	05/31/23
4731-10-11	Telemedicine Certificates	10/25/19		05/26/20		Revised filings 11/24 & 11/3 - orig 10/30/20	12/04/20	12/07/20		05/31/18	05/31/23
4731-11-01	Controlled substances; General Provisions Definitions				11/14/19	corrected-7/16/20 6/18/2020	07/23/20	08/17/20	10/14/20	10/31/20	10/31/25
4731-11-02	Controlled Substances - General Provisions	07/26/19	11/13/19	10/05/20						04/30/19	12/31/20
4731-11-03	Schedule II Controlled Substance Stimulants	07/26/19	11/13/19	10/05/20						12/31/15	12/31/20
4731-11-04	Controlled Substances: Utilization for Weight Reduction	07/26/19	11/13/19	10/05/20						02/29/16	02/28/21
4731-11-04.1	Controlled substances: Utilization for chronic weight management	07/26/19	11/13/19	10/05/20						12/31/15	12/31/20
4731-11-07	Research Utilizing Controlled Substances	07/26/19	11/13/19	10/05/20						09/30/15	09/30/20
4731-11-08	Utilizing Controlled Substances for Self and Family Members									08/17/16	08/17/21
4731-11-09	Prescribing to persons the physician has never personally examined.									03/23/17	03/23/22
4731-11-11	Standards and procedures for review of "Ohio Automated Rx Reporting System" (OARRS).	07/26/19	11/13/19	10/05/20						12/31/15	12/31/20
4731-11-13	Prescribing of Opioid Analgesics for Acute Pain									08/31/17	08/31/22
4731-11-14	Prescribing for subacute and chronic pain			3/21/19	11/14/19	corrected-7/16/20 6/18/2020	07/23/20	08/17/20	10/14/20	10/31/20	12/23/23
4731-12-01	Preliminary Education for Licensure in Podiatric Medicine and Surgery									06/30/17	06/30/22
4731-12-02	Standing of Colleges of Podiatric Surgery and Medicine									06/30/17	06/30/22

Rule Number	Rule Description	Sent for Initial Comment	Board Approval to File with CSI	CSI filing	CSI recommendation	JCARR filing	Rules Hearing	JCARR Hearing	Board Adoption	New Effective Date	Current Review Date
4731-12-03	Eligibility for the Examination in Podiatric Surgery and Medicine <b>(see note below)</b>									04/19/17	04/19/22
4731-12-04	Eligibility of Licensure in Podiatric Medicine and Surgery by Endorsement from Another State									06/30/17	06/30/22
4731-12-05	Application Procedures for Licensure in Podiatric Medicine and Surgery, Investigation, Notice of Hearing Rights.									06/30/17	06/30/22
4731-12-06	Visiting Podiatric Faculty Certificates									06/30/17	06/30/22
4731-12-07	Podiatric Training Certificates									06/30/17	06/30/22
4731-13-01	Conduct of Hearings - Representative; Appearances	08/26/20	10/14/20	10/23/20						07/31/16	07/31/21
4731-13-02	Filing Request for Hearing	08/26/20	10/14/20	10/23/20						07/31/16	07/31/21
4731-13-03	Authority and Duties of Hearing Examiners	08/26/20	10/14/20	10/23/20						09/30/18	07/31/21
4731-13-04	Consolidation	08/26/20	10/14/20	10/23/20							04/21/21
4731-13-05	Intervention	08/26/20	10/14/20	10/23/20							04/21/21
4731-13-06	Continuance of Hearing	08/26/20	10/14/20	10/23/20						09/30/16	09/30/21
4731-13-07	Motions	08/26/20	10/14/20	10/23/20						09/30/18	04/21/21
4731-13-07.1	Form and page limitations for briefs and memoranda	08/26/20	10/14/20	10/23/20						09/30/18	09/30/23
4731-13-08	Filing	08/26/20	10/14/20	10/23/20						07/31/16	07/31/21
4731-13-09	Service	08/26/20	10/14/20	10/23/20						07/31/16	07/31/21
4731-13-10	Computation and Extension of Time	08/26/20	10/14/20	10/23/20						07/31/16	07/31/21
4731-13-11	Notice of Hearings	08/26/20	10/14/20	10/23/20						07/31/16	07/31/21
4731-13-12	Transcripts	08/26/20	10/14/20	10/23/20						07/31/16	07/31/21
4731-13-13	Subpoenas for Purposes of Hearing	08/26/20	10/14/20	10/23/20						07/31/16	07/31/21
4731-13-14	Mileage Reimbursement and Witness Fees	08/26/20	10/14/20	10/23/20							04/21/21
4731-13-15	Reports and Recommendations	08/26/20	10/14/20	10/23/20						07/31/16	07/31/21
4731-13-16	Reinstatement or Restoration of Certificate	08/26/20	10/14/20	10/23/20						07/31/16	07/31/21
4731-13-17	Settlements, Dismissals, and Voluntary Surrenders	08/26/20	10/14/20	10/23/20						04/21/16	04/21/21
4731-13-18	Exchange of Documents and Witness Lists	08/26/20	10/14/20	10/23/20						07/31/16	07/31/21
4731-13-20	Depositions in Lieu of Live Testimony and Transcripts in place of Prior Testimony	08/26/20	10/14/20	10/23/20						07/31/16	07/31/21
4731-13-20.1	Electronic Testimony	08/26/20	10/14/20	10/23/20						07/31/16	07/31/21
4731-13-21	Prior Action by the State Medical Board	08/26/20	10/14/20	10/23/20						04/21/16	04/21/21
4731-13-22	Stipulation of Facts	08/26/20	10/14/20	10/23/20						04/21/16	04/21/21
4731-13-23	Witnesses	08/26/20	10/14/20	10/23/20						09/14/16	09/30/21

Rule Number	Rule Description	Sent for Initial Comment	Board Approval to File with CSI	CSI filing	CSI recommendation	JCARR filing	Rules Hearing	JCARR Hearing	Board Adoption	New Effective Date	Current Review Date
4731-13-24	Conviction of a Crime	08/26/20	10/14/20	10/23/20						04/21/16	04/21/21
4731-13-25	Evidence	08/26/20	10/14/20	10/23/20						07/31/16	07/31/21
4731-13-26	Broadcasting and Photographing Administrative Hearings	08/26/20	10/14/20	10/23/20						04/21/16	04/21/21
4731-13-27	Sexual Misconduct Evidence	08/26/20	10/14/20	10/23/20						04/21/16	04/21/21
4731-13-28	Supervision of Hearing Examiners	08/26/20	10/14/20	10/23/20						04/21/16	04/21/21
4731-13-30	Prehearing Conference	08/26/20	10/14/20	10/23/20						04/21/16	04/21/21
4731-13-31	Transcripts of Prior Testimony	08/26/20	10/14/20	10/23/20						04/21/16	04/21/21
4731-13-32	Prior Statements of the Respondent	08/26/20	10/14/20	10/23/20						04/21/16	04/21/21
4731-13-33	Physician's Desk Physician	08/26/20	10/14/20	10/23/20						04/21/16	04/21/21
4731-13-34	Ex Parte Communication	08/26/20	10/14/20	10/23/20						07/31/16	07/31/21
4731-13-35	Severability	08/26/20	10/14/20	10/23/20						04/21/16	04/21/21
4731-13-36	Disciplinary Actions	08/26/20	10/14/20	10/23/20						07/31/16	07/31/21
4731-14-01	Pronouncement of Death									06/30/16	06/30/21
4731-15-01	Licensee Reporting Requirement; Exceptions									11/17/17	11/17/22
4731-15-02	Healthcare Facility Reporting Requirement									11/17/17	11/17/22
4731-15-03	Malpractice Reporting Requirement									11/17/17	11/17/22
4731-15-04	Professional Society Reporting									11/17/17	11/17/22
4731-15-05	Liability; Reporting Forms; Confidentially and Disclosure									11/17/17	11/17/22
4731-16-01	Rules governing impaired physicians and approval of treatments programs - Definitions									11/17/17	11/17/22
4731-16-02	General Procedures in Impairment Cases									11/17/17	11/17/22
4731-16-04	Other Violations									11/17/17	11/17/22
4731-16-05	Examinations									11/17/17	11/17/22
4731-16-06	Consent Agreements and Orders for Reinstatement of Impaired Practitioners									11/17/17	11/17/22
4731-16-07	Treatment Provider Program Obligations									11/17/17	11/17/22
4731-16-08	Criteria for Approval									11/17/17	11/17/22
4731-16-09	Procedures for Approval									11/17/17	11/17/22
4731-16-10	Aftercare Contracts									11/17/17	11/17/22
4731-16-11	Revocation, Suspension, or Denial of Certificate of Good Standing									11/17/17	11/17/22
4731-16-12	Out-of-State Impairment Cases									11/17/17	11/17/22
4731-16-13	Patient Consent; Revocation of Consent									11/17/17	11/17/22

Rule Number	Rule Description	Sent for Initial Comment	Board Approval to File with CSI	CSI filing	CSI recommendation	JCARR filing	Rules Hearing	JCARR Hearing	Board Adoption	New Effective Date	Current Review Date
4731-16-14	Caffeine, Nicotine, and Over-The Counter Drugs									11/17/17	11/17/22
4731-16-15	Patient Rights									11/17/17	11/17/22
4731-16-17	Requirements for the one-bite program									01/31/19	01/31/24
4731-16-18	Eligibility for the one-bite program									01/31/19	01/31/24
4731-16-19	Monitoring organization for one-bite program									01/31/19	01/31/24
4731-16-20	Treatment providers in the one-bite program									01/31/19	01/31/24
4731-16-21	Continuing care for the one-bite program									01/31/19	01/31/24
4731-17-01	Exposure-Prone Invasive Procedure Precautions - Definitions	08/26/20	10/14/20	10/23/20	11/24/20					12/31/16	12/31/21
4731-17-02	Universal Precautions	08/26/20	10/14/20	10/23/20	11/24/20					11/30/16	11/30/21
4731-17-03	Hand Washing	08/26/20	10/14/20	10/23/20	11/24/20						08/17/21
4731-17-04	Disinfection and Sterilization	08/26/20	10/14/20	10/23/20	11/24/20					12/31/16	12/31/21
4731-17-05	Handling and Disposal of Sharps and Wastes	08/26/20	10/14/20	10/23/20	11/24/20						08/17/21
4731-17-06	Barrier Techniques	08/26/20	10/14/20	10/23/20	11/24/20						08/17/21
4731-17-07	Violations	08/26/20	10/14/20	10/23/20	11/24/20					11/09/16	11/30/21
4731-18-01	Definitions	01/10/18	01/20/20	05/12/20							
4731-18-02	Use of Light Based Medical Devices	01/10/18	01/20/20	05/12/20						05/31/02	06/30/05
4731-18-03	Delegation of the Use of Light Based Medical Devices	01/10/18	01/20/20	05/12/20						06/30/00	06/30/05
4731-18-04	Delegation of phototherapy and photodynamic therapy	01/10/18	01/20/20	05/12/20						05/31/02	05/31/07
4731-20-01	Surgery Privileges of Podiatrist - Definition of Foot									05/31/18	05/31/23
4731-20-02	Surgery: Ankle Joint									05/31/18	05/31/23
4731-22-01	Emeritus Registration - Definitions									08/31/17	08/31/22
4731-22-02	Application									08/31/17	08/31/22
4731-22-03	Status of Registrant									05/12/17	05/12/22
4731-22-04	Continuing Education Requirements									05/12/17	05/12/22
4731-22-06	Renewal of Cycle of Fees									05/12/17	05/12/22
4731-22-07	Change to Active Status									08/31/17	08/31/22
4731-22-08	Cancellation of or Refusal to Issue an Emeritus Registration									05/12/17	05/12/22
4731-23-01	Delegation of Medical Tasks - Definitions									11/30/16	11/30/21
4731-23-02	Delegation of Medical Tasks									11/30/16	11/30/21



Rule Number	Rule Description	Sent for Initial Comment	Board Approval to File with CSI	CSI filing	CSI recommendation	JCARR filing	Rules Hearing	JCARR Hearing	Board Adoption	New Effective Date	Current Review Date
4731-23-03	Delegation of Medical Tasks: Prohibitions									08/17/16	08/17/21
4731-23-04	Violations									08/17/16	08/17/21
4731-24-01	Anesthesiologist Assistants - Definitions									07/31/19	07/31/24
4731-24-02	Anesthesiologist Assistants; Supervision									07/31/19	07/31/24
4731-24-03	Anesthesiologist Assistants; Enhanced Supervision									07/31/19	07/31/24
4731-25-01	Office-Based Surgery - Definition of Terms										03/01/23
4731-25-02	General Provisions									05/31/18	05/31/23
4731-25-03	Standards for Surgery Using Moderate Sedation/Analgesia									05/31/18	08/31/23
4731-25-04	Standards for Surgery Using Anesthesia Services									05/31/18	05/31/23
4731-25-05	Liposuction in the Office Setting									03/01/18	03/01/23
4731-25-07	Accreditation of Office Settings									05/31/18	05/31/23
4731-25-08	Standards for Surgery									09/30/19	09/30/24
4731-26-01	Sexual Misconduct - Definitions									06/30/16	06/30/21
4731-26-02	Prohibitions									06/14/16	06/14/21
4731-26-03	Violations; Miscellaneous									06/30/16	06/30/21
4731-27-01	Definitions									02/04/19	02/02/24
4731-27-02	Dismissing a patient from the medical practice									05/31/19	05/31/24
4731-27-03	Notice of termination of physician employment or physician leaving a practice, selling a practice, or retiring from the practice of medicine									05/31/19	05/31/24
4731-28-01	Mental or Physical Impairment									08/31/17	08/31/22
4731-28-02	Eligibility for confidential monitoring program									08/31/18	08/31/23
4731-28-03	Participation in the confidential monitoring program									08/31/18	08/31/23
4731-28-04	Disqualification from continued participation in the confidential monitoring program									08/31/18	08/31/23
4731-28-05	Termination of the participation agreement for the confidential monitoring program									08/31/18	08/31/23
4731-29-01	Standards and procedures for operation of a pain management clinic.									06/30/17	06/30/22
4731-30-01	Internal Management Definitions									09/23/18	09/23/23

Rule Number	Rule Description	Sent for Initial Comment	Board Approval to File with CSI	CSI filing	CSI recommendation	JCARR filing	Rules Hearing	JCARR Hearing	Board Adoption	New Effective Date	Current Review Date
4731-30-02	Internal Management Board Metrics	07/26/19								09/23/18	09/23/23
4731-30-03	Approval of Licensure Applications					05/07/20				10/17/19	10/17/24
4731-31-01	Requirements for assessing and granting clearance for return to practice or competition. (concussion rule)					04/10/19	05/13/19			11/30/19	11/30/24
4731-32-01	Definition of Terms									09/08/17	09/08/22
4731-32-02	Certificate to Recommend Medical Marijuana									09/08/17	09/08/22
4731-32-03	Standard of Care									09/08/17	09/08/22
4731-32-04	Suspension and Revocation of Certificate to Recommend									09/08/17	09/08/22
4731-32-05	Petition to Request Additional Qualifying Condition or Disease									09/08/17	09/08/22
4731-33-01	Definitions	05/09/19		11/15/19	05/20/20	06/18/20	07/23/20	08/17/20	10/14/20	10/31/20	04/30/24
4731-33-02	Standards and procedures for withdrawal management for drug or alcohol addiction	05/09/19		11/15/19	05/20/20	06/18/20	07/23/20	08/17/20	10/14/20	10/31/20	10/31/25
4731-33-03	Office-Based Treatment for Opioid Addiction									04/30/19	04/30/24
4731-33-04	Medication Assisted Treatment Using Naltrexone									04/30/19	04/30/24
4731-34-01	Standards and Procedures to be followed by physicians when prescribing a dangerous drug that may be administered by a pharmacist by injection.									07/31/19	07/31/24
4731-35-01	Consult Agreements	01/18/19		03/21/19	11/14/19	06/18/20	07/23/20	08/17/20	10/14/20	10/31/20	10/31/25
4731-35-02	Standards for managing drug therapy	01/18/19		03/21/19	11/14/19	06/18/20	07/23/20	08/17/20	10/14/20	10/31/20	10/31/25
4731-36-01	Military provisions related to education and experience requirements for licensure	03/22/19	06/12/19	12/05/19	09/11/20	09/25/20	10/27/20	11/16/20	12/09/20	12/31/20	12/31/25
4731-36-02	Military provisions related to renewal of license and continuing education	03/22/19	06/12/19	12/05/19	09/11/20	09/25/20	10/27/20	11/16/20	12/09/20	12/31/20	12/31/25
4731-36-03	Processing applications from service members, veterans, or spouses of service members or veterans.	03/22/19	06/12/19	12/05/19	09/11/20	09/25/20	10/27/20	11/16/20	12/09/20	12/31/20	12/31/25
4731-36-04	Temporary license for military spouse	02/11/20	02/12/20	02/14/20							
4759-2-01	Definitions									11/30/19	11/30/24
4759-4-01	Applications									11/30/19	11/30/24
4759-4-02	Preprofessional experience										08/28/24
4759-4-03	Examination									11/30/19	11/30/24

Rule Number	Rule Description	Sent for Initial Comment	Board Approval to File with CSI	CSI filing	CSI recommendation	JCARR filing	Rules Hearing	JCARR Hearing	Board Adoption	New Effective Date	Current Review Date
4759-4-04	Continuing Education	08/27/19		11/10/20						11/30/19	11/30/24
4759-4-08	Limited permit	8/27/19 4/19/18	07/11/18	11/10/20						11/30/19	11/30/24
4759-4-09	License certificates and permits	04/19/18	07/11/18	09/25/18						11/30/19	11/30/24
4759-5-01	Supervision of persons claiming exemption									08/28/19	08/28/24
4759-5-02	Student practice exemption									11/30/19	11/30/24
4759-5-03	Plan of treatment exemption									11/30/19	11/30/24
4759-5-04	Additional nutritional activities exemption										07/01/24
4759-5-05	Distribution of literature exemption										07/01/24
4759-5-06	Weight control program exemption										07/01/24
4759-6-01	Standards of practice innutrition care									11/30/19	11/30/24
4759-6-02	Standards of professional performance	04/19/18	07/11/18	11/10/20							12/18/17
4759-6-03	Interpretation of standards									11/30/19	11/30/24
4759-9-01	Severability									11/30/19	11/30/24
4759-11-01	Miscellaneous Provisions									11/30/19	11/30/24
4761-2-03	Board Records									02/28/19	02/28/24
4761-3-01	Definition of terms									02/28/19	02/28/24
4761-4-01	Approval of educational programs									02/28/19	02/28/24
4761-4-02	Monitoring of Ohio respiratory care educational programs									02/28/19	02/28/24
4761-5-01	Waiver of licensing requirements pursuant to division (B) of section 4761.04 or the Revised Code	04/23/19	06/12/19	11/06/19	01/10/20	06/18/20	07/23/20	08/17/20	09/09/20	09/30/20	09/30/25
4761-5-02	Admission to the Ohio credentialing examination	04/23/19	06/12/19	11/06/19	01/10/20	06/19/20	No change rule			09/19/20	06/19/25
4761-5-04	License application procedure	04/23/19	06/12/19	11/06/19	01/10/20	06/18/20	07/23/20	08/17/20	09/09/20	09/30/20	09/30/25
4761-5-06	Respiratory care practice by polysomnographic technologists	04/23/19	06/12/19	11/06/19	01/10/20	06/18/20	No change rule			09/18/20	06/18/25
4761-6-01	Limited permit application procedure	04/23/19	06/12/19	11/06/19	01/10/20	06/18/20	07/23/20	08/17/20	09/09/20	09/30/20	02/28/24
4761-7-01	Original license or permit, identification card or electronic license verification									02/28/19	02/28/24
4761-7-03	Scope of respiratory care defined										11/15/23
4761-7-04	Supervision			11/06/19	01/10/20	06/18/20	07/23/20	08/17/20	09/09/20	09/30/20	09/30/25
4761-7-05	Administration of medicines										11/15/23
4761-8-01	Renewal of license or permits	03/22/19	06/12/19	12/05/19	09/11/20	09/25/20	10/27/20	11/16/20	12/09/20	12/31/20	12/31/25
4761-9-01	Definition of respiratory care continuing education			11/06/19	01/10/20	06/18/20	07/23/20	08/17/20	09/09/20	09/30/20	02/28/24

Rule Number	Rule Description	Sent for Initial Comment	Board Approval to File with CSI	CSI filing	CSI recommendation	JCARR filing	Rules Hearing	JCARR Hearing	Board Adoption	New Effective Date	Current Review Date
4761-9-02	General RCCE requirements and reporting mechanism	03/22/19	06/12/19	12/05/19	09/11/20	09/25/20	10/27/20	11/16/20	12/09/20	12/31/20	12/31/25
4761-9-03	Activities which do not meet the Ohio RCCE requirements									02/28/19	02/28/24
4761-9-04	Ohio respiratory care law and professional ethics course criteria			11/06/19	01/10/20	Refiled 8/24/20 6/18/2020	9/24/20 7/23/2020	08/17/20	11/10/20		02/28/24
4761-9-05	Approved sources of RCCE			11/06/19	01/10/20	06/18/20	07/23/20	08/17/20	09/09/20	09/30/20	02/28/24
4761-9-07	Auditing for compliance with RCCE requirements			11/06/19	01/10/20	06/18/20	07/23/20	08/17/20	09/09/20	09/30/20	09/30/25
4761-10-01	Ethical and professional conduct									02/28/19	02/28/24
4761-10-02	Proper use of credentials										11/15/23
4761-10-03	Providing information to the Board	04/23/19	06/12/19	11/06/19	01/10/20	06/18/20	07/23/20	08/17/20	09/09/20	09/30/20	09/30/25
4761-15-01	Miscellaneous Provisions									02/28/19	02/28/24
4774-1-01	Definitions	04/29/20	10/14/20	10/23/20	11/24/20					12/31/16	12/31/21
4774-1-02	Application for Certificate to Practice	04/29/20	10/14/20	10/23/20	11/24/20					11/30/16	11/30/21
4774-1-03	Renewal of Certificate to Practice	04/29/20	10/14/20	10/23/20	11/24/20					11/30/16	11/30/21
4774-1-04	Miscellaneous Provisions	04/29/20	10/14/20	10/23/20	11/24/20					08/17/16	08/17/21
4778-1-01	Definition									01/29/19	01/24/24
4778-1-02	Application									04/30/19	04/30/24
4778-1-03	Special Activity License									01/24/19	01/24/24
4778-1-05	Collaboration Agreement									04/30/19	04/30/24
4778-1-06	Miscellaneous Provisions									04/30/19	04/30/24



**MEMORANDUM**

TO: Mark Bechtel, M.D., President  
Members, State Medical Board of Ohio

FROM: Kimberly C. Anderson, Chief Legal Counsel

RE: Comments Received regarding Weight Loss Rules, 4731-11-04 and 4731-11-04.1,  
OAC

DATE: December 30, 2020

---

Rules 4731-11-04 and 4731-11-04.1 are currently pending at CSI. One comment was received, from Jennifer Hayhurst at OSMA, requesting that the Board consult with experts in obesity medicine to obtain comments regarding the proposed rules. The Policy Committee agreed to consult with experts and Dr. Soin convened a meeting on November 23, 2020. All interested parties were invited to make a presentation and to provide written comments regarding the rules.

Attached you will find written materials provided by the following individuals:

1. Ethan Lazarus, M.D., Clinical Nutrition Center, Greenwood Village, CO;
2. Barto Burguera, M.D., Ph.D., Marcio Griebeler, M.D., Diana Isaacs, PharmD, W. Scott Butsch, M.D., Cleveland Clinic
3. Bruce Barker, M.D., Ohio Health, Delaware, OH
4. Elizabeth W. Adamson, Executive Director, Ohio Association of Physician Assistants
5. Chris Gallagher, Obesity Action Coalition
6. Ted Kyle, RPh, MBA, ConscienHealth, Pittsburgh, PA
7. Angela Kay Fitch, M.D., MGH Weight Center, Boston, MA

I have also attached the proposed rules, 4731-11-04 and 4731-11-04.1, OAC.

**Recommended Action: Review the comments and advise as to next steps.**

---



# Clinical Nutrition Center

MEDICAL WEIGHT LOSS  
INTEGRATION

November 20<sup>th</sup>, 2020

Dear Honorable Members of the State Medical Board of Ohio:

Thank you so much for the opportunity to testify on your upcoming proposed rule OAC 4731-11-04 (weight loss) that is currently pending with the State of Ohio's Common Sense Initiative (CSI). I am sorry that I am not able to testify in-person or by phone, but I would like to provide some additional commentary as you consider this rule.

As written, I am concerned that this rule will HURT more people than it will help. Let me try to explain.

People with obesity are already highly stigmatized for their disease. Yet, this disease is serious. This is now being exacerbated by COVID-19. People with obesity are 3-6x more likely to die or require a ventilator.

The explanation that this rule has served Ohioans well for many years and therefore should be reaffirmed is short-sighted, and doesn't take into account changes with regards to our understanding of obesity as a disease (recognized by the American Medical Association in 2013). It is not consistent with the way in which obesity care is delivered in the rest of America. This policy would be like telling people with depression to simply "Think happy thoughts." Treating depression this way is unlikely to help people, and very likely to cause harm vs. offering patients the current standards of care with regards to depression pharmacotherapy. Obesity treatment is no different.

This rule is in direct conflict with an evidence-based guideline published by the Endocrine Society in 2014 stating that long-term phentermine prescribing is appropriate (Endocrine society pharmacotherapy 2014 guideline, pp 357-358, attached).

This rule is in direct conflict with the position statement of the Obesity Medicine Association, a group of over 3,000 physicians, Nurse Practitioners and Physician Assistants (attached).

This rule is not consistent with American Medical Association policy calling on the AMA to "Work with state and specialty societies to identify states in which physicians are restricted from providing the current standard of care with regards to obesity treatment" and to "work with interested state medical societies and other interested stakeholders to remove out-of-date restrictions at the state and federal levels prohibiting healthcare providers from



# Clinical Nutrition Center

MEDICAL WEIGHT LOSS  
INTEGRATION

providing the current standard of care to patients affected by obesity.” I have spoken with the AMA Council on Legislation and they would be happy to assist you with this policy.

I understand your concerns that Phentermine is a controlled substance; however, decades of experience have shown it to be well tolerated and have very low potential for addiction (Hendricks article attached).

Another study of 13,972 adults treated with phentermine was published in 2019 showed “Greater weight loss without increased risk of incident CVD or death in patients using phentermine monotherapy for longer than 3 months... This study supports the effectiveness and safety of longer-term phentermine use for low-risk individuals.” (Lewis et al, attached).

Long-term phentermine and topiramate have been shown to safely improve weight loss and reduce the failure rate after gastric bypass surgery (attached).

Continuing on your current path of not allowing physicians to practice medicine which is the standard of care in the rest of the country leaves millions of vulnerable Ohioans living with obesity at risk for serious complications of obesity ranging from medical (diabetes, hypertension, heart disease, COVID-19 complications, cancer) to functional impairments (inability to walk comfortably, back, pain, joint pain) to mental health (decreased quality of life, increased depression) and even financial loss (wage bias and job bias against those living with obesity, being forced to pay for expensive brand-name anti-obesity medications when inexpensive generics are readily available, as in study above).

Your policy would allow the on-label prescribing of Phentermine at 15 mg/d if it is part of the brand-name drug Qsymia, but not allow its generic counterparts to be used *at exactly the same dosage of phentermine*. Because Qsymia is expensive and not on most formularies, this is in effect telling your population that they must use a brand name drug but will not allow the same components to be used, at much lower cost, with no reasonable explanation given.

Now is the time to trust your physicians to practice good medicine. Allow your physicians to treat their patients. Stop singling out obesity as this is simply an extension of decades old weight bias. You are not instructing your physicians how to treat diabetes, depression or hypertension. Don't tell your physicians how to treat obesity. Finally, today, you have a chance to adopt the same policies as the rest of the country. It is time for Ohio to emerge from the 1980's and accept the current standards of care for obesity.

I urge you to retire the entire statement around weight management, or if you find yourselves unable to commit to that, to at least remove the language singling out phentermine.



# Clinical Nutrition Center

MEDICAL WEIGHT LOSS  
INTEGRATION

Thank you for your consideration.

Sincerely,



*Ethan Lazarus MD.*

Ethan Lazarus, MD

Obesity Medicine Physician since 2004  
Board Certified: American Board of Family Medicine  
Diplomate: American Board of Obesity Medicine  
Obesity Medicine Association President-Elect  
The Obesity Society - Member  
American Medical Association - Delegate



## Pharmacological Management of Obesity: An Endocrine Society Clinical Practice Guideline

Caroline M. Apovian, Louis J. Aronne, Daniel H. Bessesen, Marie E. McDonnell, M. Hassan Murad, Uberto Pagotto, Donna H. Ryan, and Christopher D. Still

Boston University School of Medicine and Boston Medical Center (C.M.A.), Boston, Massachusetts 02118; Weill-Cornell Medical College (L.J.A.), New York, New York 10065; Denver Health Medical Center (D.H.B.), Denver, Colorado 80204; Brigham and Women's Hospital (M.E.M.), Boston, Massachusetts 02115; Mayo Clinic, Division of Preventative Medicine (M.H.M.), Rochester, Minnesota 55905; Alma Mater University of Bologna (U.P.), S. Orsola-Malpighi Hospital Endocrinology Unit, 40138 Bologna, Italy; Pennington Biomedical Research Center (D.H.R.), Baton Rouge, Louisiana 70808; and Geisinger Health Care System (C.D.S.), Danville, Pennsylvania 17822

**Objective:** To formulate clinical practice guidelines for the pharmacological management of obesity.

**Participants:** An Endocrine Society-appointed Task Force of experts, a methodologist, and a medical writer. This guideline was co-sponsored by the European Society of Endocrinology and The Obesity Society.

**Evidence:** This evidence-based guideline was developed using the Grading of Recommendations, Assessment, Development, and Evaluation (GRADE) system to describe the strength of recommendations and the quality of evidence.

**Consensus Process:** One group meeting, several conference calls, and e-mail communications enabled consensus. Committees and members of the Endocrine Society, the European Society of Endocrinology, and The Obesity Society reviewed and commented on preliminary drafts of these guidelines. Two systematic reviews were conducted to summarize some of the supporting evidence.

**Conclusions:** Weight loss is a pathway to health improvement for patients with obesity-associated risk factors and comorbidities. Medications approved for chronic weight management can be useful adjuncts to lifestyle change for patients who have been unsuccessful with diet and exercise alone. Many medications commonly prescribed for diabetes, depression, and other chronic diseases have weight effects, either to promote weight gain or produce weight loss. Knowledgeable prescribing of medications, choosing whenever possible those with favorable weight profiles, can aid in the prevention and management of obesity and thus improve health. (*J Clin Endocrinol Metab* 100: 342–362, 2015)

### Summary of Recommendations

#### 1.0 Care of the patient who is overweight or obese

1.1 We recommend that diet, exercise, and behavioral modification be included in all obesity management ap-

proaches for body mass index (BMI)  $\geq 25$  kg/m<sup>2</sup> and that other tools such as pharmacotherapy (BMI  $\geq 27$  kg/m<sup>2</sup> with comorbidity or BMI over 30 kg/m<sup>2</sup>) and bariatric surgery (BMI  $\geq 35$  kg/m<sup>2</sup> with comorbidity or BMI over 40 kg/m<sup>2</sup>) be used as adjuncts to behavioral modification

ISSN Print 0021-972X ISSN Online 1945-7197

Printed in U.S.A.

Copyright © 2015 by the Endocrine Society

Received September 3, 2014. Accepted December 8, 2014.

First Published Online January 15, 2015

For article see page 363

Abbreviations: ACE, angiotensin-converting enzyme; AED, antiepileptic drug; ARB, angiotensin receptor blocker; BID, twice a day; BMI, body mass index; BP, blood pressure; CCK, cholecystokinin; CI, confidence interval; DPP-4, dipeptidyl peptidase IV; ER, extended release; GLP-1, glucagon-like peptide-1; H1, histamine; HbA1c, glycated hemoglobin; POMC, pro-opiomelanocortin; PYY, peptide YY; QD, every day; RCT, randomized controlled trial; SC, subcutaneous; SGLT, sodium-glucose-linked transporter; SNRI, serotonin-norepinephrine reuptake inhibitor; SSRI, selective serotonin reuptake inhibitor; T2DM, type 2 diabetes; TID, three times a day.

to reduce food intake and increase physical activity when this is possible. Drugs may amplify adherence to behavior change and may improve physical functioning such that increased physical activity is easier in those who cannot exercise initially. Patients who have a history of being unable to successfully lose and maintain weight and who meet label indications are candidates for weight loss medications. (1|⊕⊕⊕⊕)

1.2 In order to promote long-term weight maintenance, we suggest the use of approved<sup>1</sup> weight loss medication (over no pharmacological therapy) to ameliorate comorbidities and amplify adherence to behavior changes, which may improve physical functioning and allow for greater physical activity in individuals with a BMI  $\geq 30$  kg/m<sup>2</sup> or in individuals with a BMI of  $\geq 27$  kg/m<sup>2</sup> and at least one associated comorbid medical condition such as hypertension, dyslipidemia, type 2 diabetes (T2DM), and obstructive sleep apnea. (2|⊕⊕⊕⊕)

1.3 In patients with uncontrolled hypertension or a history of heart disease, we recommend against using the sympathomimetic agents phentermine and diethylpropion. (1|⊕⊕⊕⊕)

1.4 We suggest assessment of efficacy and safety at least monthly for the first 3 months, then at least every 3 months in all patients prescribed weight loss medications. (2|⊕⊕⊕⊕)

1.5 If a patient's response to a weight loss medication is deemed effective (weight loss  $\geq 5\%$  of body weight at 3 mo) and safe, we recommend that the medication be continued. If deemed ineffective (weight loss  $< 5\%$  at 3 mo) or if there are safety or tolerability issues at any time, we recommend that the medication be discontinued and alternative medications or referral for alternative treatment approaches be considered. (1|⊕⊕⊕⊕)

1.6 If medication for chronic obesity management is prescribed as adjunctive therapy to comprehensive lifestyle intervention, we suggest initiating therapy with dose escalation based on efficacy and tolerability to the recommended dose and not exceeding the upper approved dose boundaries. (2|⊕⊕⊕⊕)

1.7 In patients with T2DM who are overweight or obese, we suggest the use of antidiabetic medications that have additional actions to promote weight loss (such as glucagon-like peptide-1 [GLP-1] analogs or sodium-glucose-linked transporter-2 [SGLT-2] inhibitors), in addition to the first-line agent for T2DM and obesity, metformin. (2|⊕⊕⊕⊕)

1.8 In patients with cardiovascular disease who seek pharmacological treatment for weight loss, we suggest us-

ing medications that are not sympathomimetics such as lorcaserin and/or orlistat. (2|⊕⊕⊕⊕)

## 2.0 Drugs that cause weight gain and some alternatives

2.1 We recommend weight-losing and weight-neutral medications as first- and second-line agents in the management of a patient with T2DM who is overweight or obese. Clinicians should discuss possible weight effects of glucose-lowering medications with patients and consider the use of antihyperglycemic medications that are weight neutral or promote weight loss. (1|⊕⊕⊕⊕)

2.2 In obese patients with T2DM requiring insulin therapy, we suggest adding at least one of the following: metformin, pramlintide, or GLP-1 agonists to mitigate associated weight gain due to insulin. The first-line insulin for this type of patient should be basal insulin. This is preferable to using either insulin alone or insulin with sulfonylurea. We also suggest that the insulin therapy strategy be considered a preferential trial of basal insulin prior to premixed insulins or combination insulin therapy. (2|⊕⊕⊕⊕)

2.3 We recommend angiotensin-converting enzyme (ACE) inhibitors, angiotensin receptor blockers (ARBs), and calcium channel blockers rather than  $\beta$ -adrenergic blockers as first-line therapy for hypertension in patients with T2DM who are obese. (1|⊕⊕⊕⊕)

2.4 When antidepressant therapy is indicated, we recommend a shared decision-making process that provides patients with quantitative estimates of the expected weight effect of the antidepressant to make an informed decision about drug choice. Other factors that need to be taken into consideration include the expected length of treatment. (1|⊕⊕⊕⊕)

2.5 We recommend using weight-neutral antipsychotic alternatives when clinically indicated, rather than those that cause weight gain, and the use of a shared decision-making process that provides patients with quantitative estimates of the expected weight effect of the alternative treatments to make an informed decision about drug choice. (1|⊕⊕⊕⊕)

2.6 We recommend considering weight gain potential in choosing an antiepileptic drug (AED) for any given patient, and the use of a shared decision-making process that provides patients with quantitative estimates of the expected weight effect of the drugs to make an informed decision about drug choice. (1|⊕⊕⊕⊕)

2.7 In women with a BMI  $> 27$  kg/m<sup>2</sup> with comorbidities or BMI  $> 30$  kg/m<sup>2</sup> seeking contraception, we suggest oral contraceptives over injectable medications due to

<sup>1</sup> Approval in the United States is based on FDA determination. Approval in Europe is based on EMA determination.

weight gain with injectables, provided that women are well-informed about the risks and benefits (ie, oral contraceptives are not contraindicated). (2|⊕○○○)

2.8 We suggest monitoring the weight and waist circumference of patients on antiretroviral therapy due to unavoidable weight gain, weight redistribution, and associated cardiovascular risk. (2|⊕⊕⊕○)

2.9 We suggest the use of nonsteroidal anti-inflammatory drugs and disease-modifying antirheumatic drugs when possible in patients with chronic inflammatory disease like rheumatoid arthritis because corticosteroids commonly produce weight gain. (2|⊕⊕⊕○)

2.10 We suggest the use of antihistamines with less central nervous system activity (less sedation) to limit weight gain. (2|⊕⊕○○)

### 3.0 Off-label use of drugs approved for other indications for chronic obesity management

3.1 We suggest against the off-label use of medications approved for other disease states for the sole purpose of producing weight loss. A trial of such therapy can be attempted in the context of research and by healthcare providers with expertise in weight management dealing with a well-informed patient. (Ungraded Best Practice Recommendation)

## Method of Development of Evidence-Based Clinical Practice Guidelines

The Clinical Guidelines Subcommittee (CGS) of the Endocrine Society deemed the pharmacological management of obesity a priority area in need of practice guidelines and appointed a Task Force to formulate evidence-based recommendations. The Task Force followed the approach recommended by the Grading of Recommendations, Assessment, Development, and Evaluation (GRADE) group, an international group with expertise in the development and implementation of evidence-based guidelines (1). A detailed description of the grading scheme has been published elsewhere (2). The Task Force used the best available research evidence to develop the recommendations. The Task Force also used consistent language and graphical descriptions of both the strength of a recommendation and the quality of evidence. In terms of the strength of the recommendation, strong recommendations use the phrase “we recommend” and the number 1, and weak recommendations use the phrase “we suggest” and the number 2. Cross-filled circles indicate the quality of the evidence, such that ⊕○○○ denotes very low quality evidence; ⊕⊕○○, low quality; ⊕⊕⊕○, moderate quality; and ⊕⊕⊕⊕, high quality. The Task Force

has confidence that persons who receive care according to the strong recommendations will derive, on average, more good than harm. Weak recommendations require more careful consideration of the person’s circumstances, values, and preferences to determine the best course of action. Linked to each *recommendation* is a description of the *evidence* and the *values* that panelists considered in making the recommendation; in some instances, there are *remarks*, a section in which panelists offer technical suggestions for testing conditions, dosing, and monitoring. These technical comments reflect the best available evidence applied to a typical person being treated. Often this evidence comes from the unsystematic observations of the panelists and their values and preferences; therefore, these remarks should be considered suggestions.

The Endocrine Society maintains a rigorous conflict-of-interest review process for the development of clinical practice guidelines. All Task Force members must declare any potential conflicts of interest, which are reviewed before they are approved to serve on the Task Force and periodically during the development of the guideline. The conflict-of-interest forms are vetted by the CGS before the members are approved by the Society’s Council to participate on the guideline Task Force. Participants in the guideline development must include a majority of individuals without conflicts of interest in the matter under study. Participants with conflicts of interest may participate in the development of the guideline, but they must have disclosed all conflicts. The CGS and the Task Force have reviewed all disclosures for this guideline and resolved or managed all identified conflicts of interest.

Conflicts of interest are defined as remuneration in any amount from the commercial interest(s) in the form of grants; research support; consulting fees; salary; ownership interest (eg, stocks, stock options, or ownership interest excluding diversified mutual funds); honoraria or other payments for participation in speakers’ bureaus, advisory boards, or boards of directors; or other financial benefits. Completed forms are available through the Endocrine Society office.

Funding for this guideline was derived solely from the Endocrine Society, and thus the Task Force received no funding or remuneration from commercial or other entities.

A systematic review was commissioned by the Endocrine Society to quantify weight gain and weight loss associated with a discrete list of drugs chosen a priori by this guideline Task Force (3). The systematic review compared a list of 54 commonly used drugs chosen a priori by the Task Force (drugs suspected of having weight implications) that were compared to placebo in randomized controlled trials. For trials to be included, the length of treatment had to be  $\geq 30$  days. The outcome of interest for the review was weight change (expressed in absolute and rel-

ative terms). The Task Force also used evidence derived from existing systematic reviews, randomized trials, and observational studies on the management of medications for other conditions that may result in weight gain. Economic analyses and cost effectiveness studies were not reviewed or considered as a basis for the recommendations. Drugs associated with weight gain and suggested alternatives are presented in [Supplemental Table 1](#).

In several of the recommendations, we used evidence derived from randomized clinical trials about the benefits of shared decision making in terms of improving patients' knowledge, reducing decisional conflict and regret, and enhancing the likelihood of patients making decisions consistent with their own values (4). Although there is abundant evidence for the value of shared decision making across several clinical scenarios, specific evidence for obesity management is scant. This highlights a limitation of the existing literature and poses a challenge for implementing a specific strategy for shared decision making in managing obesity.

### Medical management of the disease of obesity

The Task Force agrees with the opinion of prominent medical societies that current scientific evidence supports the view that obesity is a disease (5).

Weight loss produces many benefits including risk factor improvement, prevention of disease, and improvements in feeling and function. Greater weight loss produces greater benefits, but modest (5 to 10%) weight loss, such as that produced by lifestyle modifications and medications, has been shown to produce significant improvements in many conditions (5, 6).

Medications used for the management of conditions other than obesity can contribute to or exacerbate weight gain in susceptible individuals. Many of these conditions are also associated with obesity. Healthcare providers can help patients prevent or attenuate weight gain by appropriately prescribing medications that would promote weight loss or minimize weight gain when treating these conditions. Healthcare providers can help selected patients successfully lose weight by appropriately prescribing weight loss medications or in some cases surgical intervention as an adjunct to lifestyle change.

This guideline will target how providers can use medications as an adjunct to lifestyle change therapy to promote weight loss and maintenance. It will also address how prescribers can prevent or attenuate weight gain when prescribing for diabetes, depression, and chronic diseases often associated with obesity. The evidence review addresses medications with a weight loss indication, as well as those medications that affect weight when prescribed for a nonobesity indication, ie, that have been as-

sociated with significant weight gain and increase in risk of comorbidities or with weight loss.

### Clinical encounter with the patient who is overweight or obese

There are a number of steps a clinician should take in the clinical encounter.

- Annual and symptom-based screening for major chronic conditions associated with obesity in all adult patients with a BMI of 30 kg/m<sup>2</sup> or above. These include T2DM, cardiovascular disease, hypertension, hyperlipidemia, obstructive sleep apnea, nonalcoholic fatty liver disease, osteoarthritis, and major depression.
- Timely adherence to national cancer screening guidelines with the understanding that individuals who are obese are at increased risk for many malignancies (7).
- Identification of contributing factors, including family history, sleep disorders, disordered eating, genetics, and environmental or socioeconomic causes.
- Identification of and appropriate screening for secondary causes of obesity (Table 1). These need not be automatically screened for unless the history and/or physical examination suggests the diagnosis or suspicion of the diagnosis.
- Adherence to the AHA/ACC/TOS Guideline for the Management of Overweight and Obesity in Adults (8), which was updated in 2013 and includes recommendations for assessment and treatment with diet and exercise, as well as bariatric surgery for appropriate candidates.
- Identification of medications that contribute to weight gain. Prescribe drugs that are weight neutral or that promote weight loss when possible.
- Formulation of a treatment plan based on diet, exercise, and behavior modifications as above.

### Rationale for pharmacological treatment of obesity

#### *The challenge of weight reduction*

If permanent weight loss could be achieved exclusively with behavioral reductions in food intake and increases in energy expenditure, medications for obesity would not be needed. Weight loss is difficult for most patients, and the patient's desire to restrict food and energy intake is counteracted by adaptive biological responses to weight loss (9–12). The fall in energy expenditure (out of proportion to reduction in body mass) and increase in appetite that are observed after weight loss are associated with changes in a range of hormones (12–14). Some of these changes represent adaptive responses to weight loss and result in al-



**Table 1.** Causes of Obesity

Primary Causes
Genetic causes
Monogenic disorders
Melanocortin-4 receptor mutation
Leptin deficiency
POMC deficiency
Syndromes
Prader-Willi
Bardet-Biedl
Cohen
Alström
Froehlich
Secondary Causes
Neurological
Brain injury
Brain tumor
Consequences of cranial irradiation
Hypothalamic obesity
Endocrine
Hypothyroidism <sup>a</sup>
Cushing syndrome
GH deficiency
Pseudohypoparathyroidism
Psychological
Depression <sup>b</sup>
Eating disorders
Drug-Induced
Tricyclic antidepressants
Oral contraceptives
Antipsychotics
Anticonvulsants
Glucocorticoids
Sulfonylureas
Glitazones
$\beta$ blockers

<sup>a</sup> Controversial whether hypothyroidism causes obesity or exacerbates obesity.

<sup>b</sup> Depression associated with overeating or bingeing.

tered physiology that promotes weight regain. Other changes reflect improvements in dysfunctional hormonal systems that occur as a patient moves from being obese to being closer to a healthy weight. These latter changes underlie many of the health benefits of weight loss.

No approved weight loss medication appears to promote long-term thermogenesis. These medications promote weight loss through effects on appetite, increasing satiety, and decreasing hunger, perhaps by aiding in resisting food cues or by reducing caloric absorption (14).

As discussed above, weight loss is usually associated with a reduction in total energy expenditure that is out of proportion to changes in lean body mass; the primary determinant of resting energy expenditure appears to persist indefinitely as long as the reduced weight is maintained. Clinically, this means that the individual must reduce energy intake or increase energy expenditure indefinitely to sustain weight loss.

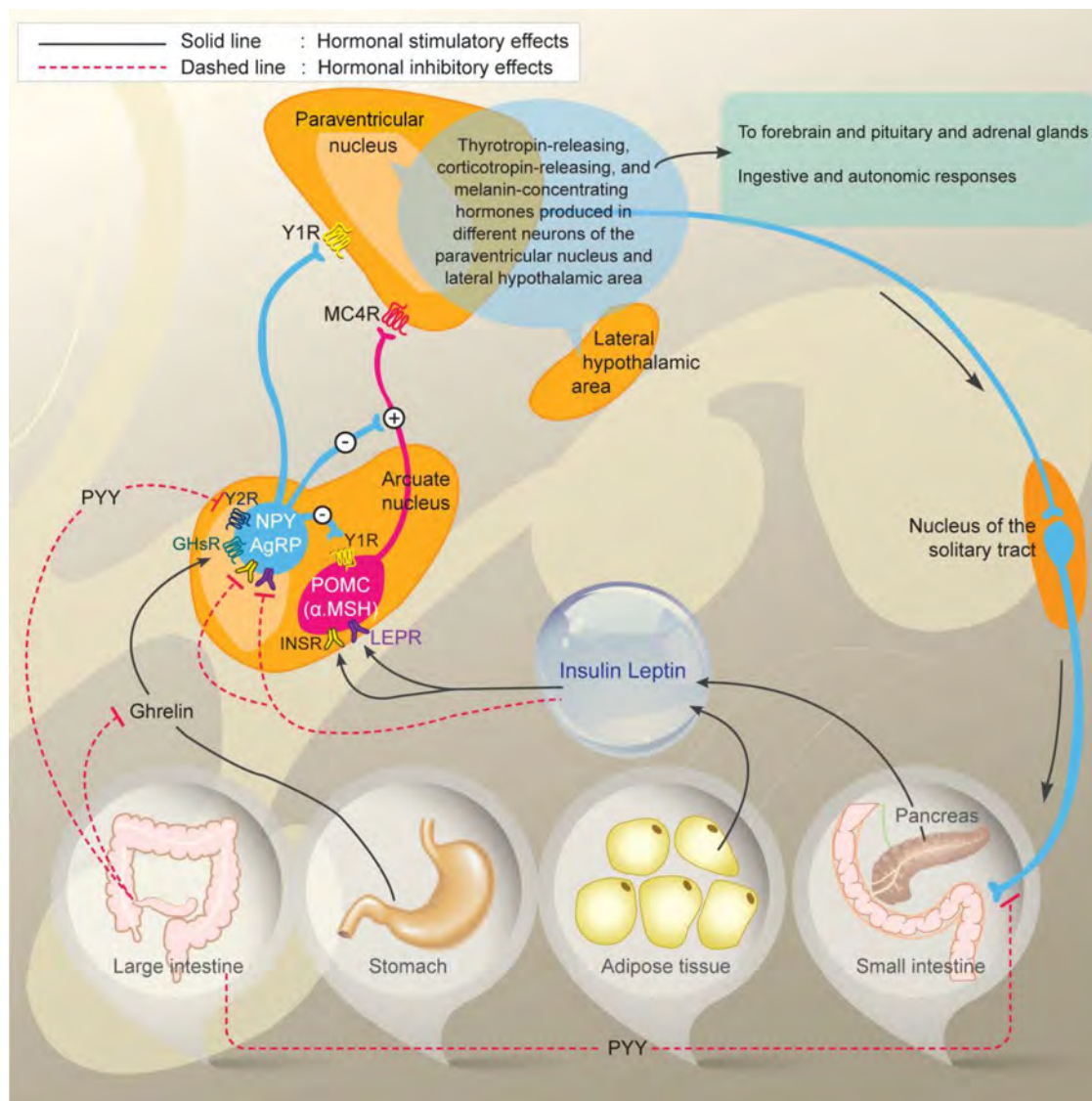
## Neuroendocrine dysregulation of energy intake and energy expenditure in obesity

Signals to appetite and controlling centers within the central nervous system and in particular the hypothalamus and the brainstem come from the gut, adipose tissue, liver, and pancreas (Figure 1). Distention of the gastrointestinal tract is communicated to the brain. In the process of food intake, gut hormones are secreted that signal satiety in the hindgut primarily; these include most notably peptide YY (PYY; secreted in ileum and colon) and cholecystokinin (CCK; in duodenum), but also gastric inhibitory polypeptide (K cells in duodenum and jejunum) and GLP-1 (L cells in ileum), which are primarily secreted in response to glucose and promote insulin release from the pancreas as well as satiety. Ghrelin is produced in the stomach, and it is unique among gut hormones in that it is orexigenic and levels increase with time since the last meal. These hormones signal areas in the hindbrain and arcuate nucleus, as do insulin and leptin. Leptin is secreted from adipose tissue, and circulating levels are proportional to fat mass. It is an anorectic hormone, which exerts its effects by inhibiting neuropeptide Y/Agouti-related peptide neurons and activating pro-opiomelanocortin (POMC)/cocaine amphetamine-related transcript neurons in the arcuate nucleus, resulting in decreased food intake and increased energy expenditure, although the increase in energy expenditure has been disputed in leptin-deficient humans treated with leptin (15).

Obesity in humans is almost universally associated with high leptin levels and failure to respond to exogenous leptin; thus, leptin analogs have not been found to be useful so far in the treatment of obesity. In humans, many other cues such as reward and emotional factors play a role in food intake aside from hunger, and another pathway is responsible for reward-associated feeding behavior. Increased hunger and decreased satiety after weight loss are associated with an increase in the 24-hour profile of circulating levels of the orexigenic hormone ghrelin and reductions in the levels of the anorexigenic hormones PYY, CCK, leptin, and insulin. These changes in appetite-related hormones appear to persist for at least 1 year after weight reduction and may remain altered indefinitely in a manner that promotes increased energy intake and ultimately weight regain (14, 16–23)

## Mechanisms of action of pharmacological agents

With the exception of orlistat, medications indicated for obesity target appetite mechanisms. The medications available for obesity treatment work primarily in the arcuate nucleus to stimulate the POMC neurons, which promote satiety. Some of the medications discussed in Section 1.0 are serotonergic, dopaminergic, or norepinephrine-



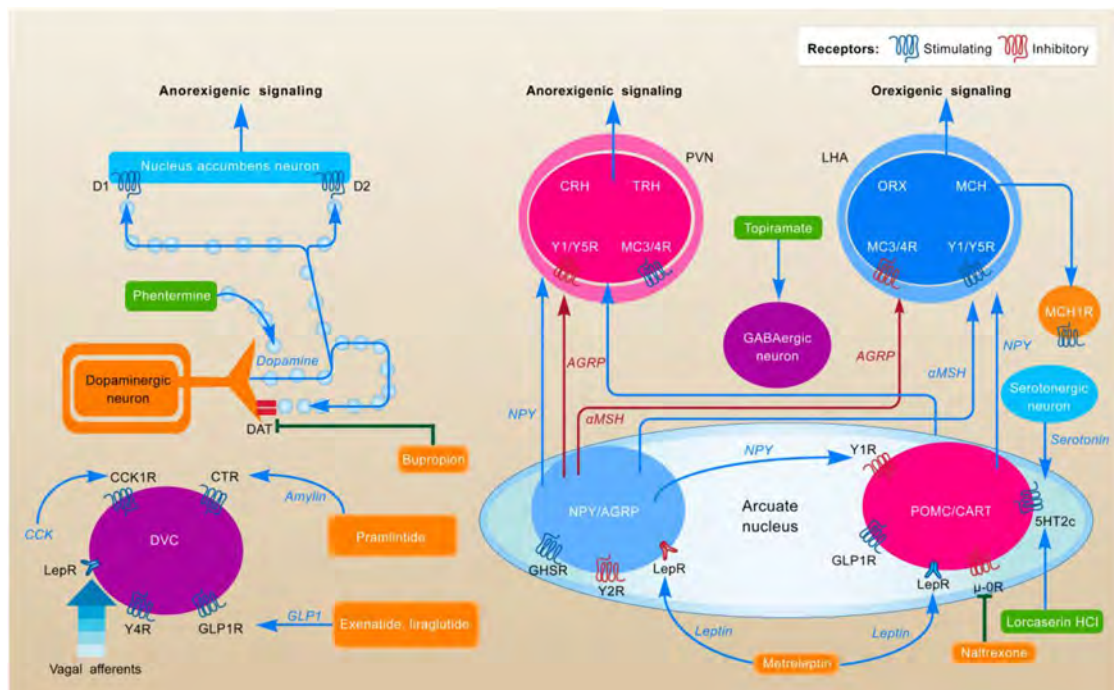
**Figure 1.** Interactions among hormonal and neural pathways that regulate food intake and body-fat mass.  $\alpha$ -MSH,  $\alpha$ -melanocyte-stimulating hormone; GhRsR, GH secretagogue receptor; INSR, insulin receptor; LEPR, leptin receptor; MC4R, melanocortin receptor type 4; Y1R, Y1 receptor; Y2R, Y2 receptor. [Adapted from J. Korner and R. L. Leibel: To eat or not to eat - how the gut talks to the brain. *N Engl J Med.* 2003;349:926–928 (24), with permission. © Massachusetts Medical Society.]

releasing agents/reuptake inhibitors (Figure 2) (24). Phentermine is primarily a noradrenergic and possibly dopaminergic sympathomimetic amine. Lorcaserin is a serotonin agent specifically stimulating the serotonin type 2c receptor (25). The combination of phentermine and topiramate, which is a neurostabilizer and antiseizure medication, seems to be additive (26); however, it is unclear how topiramate enhances appetite suppression. Bupropion is a dopamine and norepinephrine reuptake inhibitor (27), which stimulates POMC neurons. In combination with naltrexone, bupropion enhances efficacy due to the release of feedback inhibition of POMC neurons that naltrexone potentiates. GLP-1 agonists also affect the POMC neurons and cause satiety (18). Orlistat blocks absorption of 25 to 30% of fat calories and is not

appreciably absorbed systemically (28, 29). Another class of medications is associated with weight loss without an effect on appetite. This class is the SGLT-2 inhibitors for T2DM, which promote weight loss by preventing the reabsorption of glucose as well as water in the renal tubules (30).

## 1.0 Care of the patient who is overweight or obese

1.1 We recommend that diet, exercise, and behavioral modification be included in all overweight and obesity management approaches for BMI  $\geq 25$  kg/m<sup>2</sup> and that other tools such as pharmacotherapy (BMI  $\geq 27$  kg/m<sup>2</sup> with comorbidity or BMI over 30 kg/m<sup>2</sup>) and bariatric surgery (BMI  $\geq 35$  kg/m<sup>2</sup> with comorbidity or BMI over



**Figure 2.** Antiobesity agents and their mechanism of action. AGRP, Agouti-related peptide; CART, cocaine amphetamine-related transcript; CCK1R, CCK1 receptor; GLP1R, GLP-1 receptor; CTR, calcitonin receptor; D1, dopamine 1 receptor; D2, dopamine 2 receptor; DAT, dopamine active transporter; DVC, dorsal vagal complex; GHSR, GH secretagogue receptor; LepR, leptin receptor; MC3/4R, melanocortin receptor type 3/4; MCH1R, melanin-concentrating hormone 1 receptor; NPY, neuropeptide Y; PVN, paraventricular nucleus; Y1/Y5R, Y1/Y5 receptor; Y2R, Y2 receptor; Y4R, Y4 receptor; αMSH, α melanocyte-stimulating hormone; μ-OR, μ-opioid receptor. [Adapted from G. W. Kim et al: Antiobesity pharmacotherapy: new drugs and emerging targets. *Clin Pharmacol Ther.* 2014;95:53–66 (25), with permission. © American Society for Clinical Pharmacology and Therapeutics.

40 kg/m<sup>2</sup>) be used as adjuncts to behavioral modification to reduce food intake and increase physical activity when this is possible. Drugs may amplify adherence to behavior change and may improve physical functioning such that increased physical activity is easier in those who cannot exercise initially. Patients who have a history of being unable to successfully lose and maintain weight and who

meet label indications are candidates for weight loss medications. (1|⊕⊕⊕⊕) (Table 2 and Supplemental Table 1)

**Evidence and relevant values**

Weight loss medications reinforce behavioral strategies to create negative energy balance. Most weight loss medications affect appetite and, as a result, promote adherence

**Table 2.** Advantages and Disadvantages Associated with Weight Loss Medications

Drug	Advantages	Disadvantages
Phentermine	Inexpensive (\$)	Side effect profile
Topiramate/phentermine	Greater weight loss <sup>a</sup>	No long-term data <sup>b</sup>
Lorcaserin	Robust weight loss <sup>a</sup>	Expensive (\$\$\$)
Orlistat, prescription	Long-term data <sup>b</sup>	Teratogen
Orlistat, over-the-counter	Side effect profile	Expensive (\$\$\$)
Naltrexone/bupropion	Long-term data <sup>b</sup>	Less weight loss <sup>a</sup>
Liraglutide	Nonsystemic	Side effect profile
	Long term data <sup>b</sup>	Less weight loss <sup>a</sup>
	Inexpensive (\$)	Side effect profile
	Greater weight loss <sup>a</sup>	Mid-level price range (\$\$)
	Food addiction	
	Long-term data <sup>b</sup>	
	Side effect profile	
	Long-term data <sup>b</sup>	Expensive (\$\$\$)
		Injectable

<sup>a</sup> Less weight loss = 2–3%; greater weight loss = >3–5%; robust weight loss = >5%.

<sup>b</sup> Long term is 1–2 years.



**Table 3.** Comorbid Conditions in Obesity and Evidence for Amelioration With Weight Reduction

Comorbidity	Improvement After Weight Loss	First Author, Year (Ref)
T2DM	Yes	Cohen, 2012 (132); Mingrone, 2012 (133) <sup>a</sup> ; Schauer, 2012 (134); Buchwald, 2009 (135)
Hypertension	Yes	llane-Parikka, 2008 (136); Phelan, 2007 (137); Zanella, 2006 (138)
Dyslipidemia and metabolic syndrome	Yes	llane-Parikka, 2008 (136); Phelan, 2007 (137); Zanella, 2006 (138)
Cardiovascular disease	Yes	Wannamethee, 2005 (139)
NAFLD	Variable outcomes	Andersen, 1991 (140); Huang, 2005 (141); Palmer, 1990 (142); Ueno, 1997 (143)
Osteoarthritis	Yes	Christensen, 2007 (144); Fransen, 2004 (145); Huang, 2000 (146); Messier, 2004 (147); van Gool, 2005 (148)
Cancer	Yes	Adams, 2009 (149); Sjöström, 2009 (150)
Major depression	Insufficient evidence	
Sleep apnea	Yes	Kuna, 2013 (151)

Abbreviation: NAFLD, nonalcoholic fatty liver disease.

<sup>a</sup> This study showed that weight gain within the normal-weight BMI category (ie, increase from 23 to 25 kg/m<sup>2</sup>) increased risk of T2DM 4-fold.

to the diet. The medication that blocks fat absorption reinforces avoidance of high-fat (energy-dense) foods, in addition to promoting malabsorption of fat calories. Medications act to amplify the effect of the behavioral changes to consume fewer calories. They do not “work on their own.” To get maximal efficacy, obesity drugs should be used as adjuncts to lifestyle change therapy, and in some cases weight loss is limited without lifestyle change. Whatever baseline behavioral treatment is given, the effect of the drug will be static (33, 34). Just as increasing the dose of medication increases weight loss, increasing the intensity of behavioral modification increases weight loss (33). Patients should be made aware that lifestyle changes are needed when using a weight loss medication and that the addition of a weight loss medication to a lifestyle program will likely result in greater weight loss (6, 35–38).

In making this recommendation, the Task Force acknowledges the variation in the strength of evidence for the different lifestyle interventions and pharmacological interventions for obesity. However, the strong recommendation for reserving pharmacological interventions as an adjunct therapy also depends on values and preferences, with an emphasis on avoiding the side effects, burden, and cost of medications while promoting a healthier lifestyle that has benefit beyond weight loss.

1.2 In order to promote long-term weight maintenance, we suggest the use of approved (see Footnote 1) weight loss medications (over no pharmacological therapy) to ameliorate comorbidities and amplify adherence to behavior changes, which may improve physical functioning and allow for greater physical activity in individuals with a BMI  $\geq 30$  kg/m<sup>2</sup> or in individuals with a BMI of  $\geq 27$  kg/m<sup>2</sup> and at least one associated comorbid medical con-

dition such as hypertension, dyslipidemia, T2DM, and obstructive sleep apnea. (2|⊕⊕○○)

### Evidence

Caloric restriction through diet and behavior modification has been shown to produce modest but effective weight loss for controlling comorbid medical problems such as diabetes, hypertension, and obstructive sleep apnea (39, 40) (Table 3). Moreover, the adjunctive use of weight loss medication can produce even greater weight loss and cardiometabolic improvements (36, 37, 41–45). Although all of these medications and others have been shown to be effective as adjunctive treatment, none have been shown to be effective on their own. The systematic reviews conducted to support the 2013 AHA/ACC/TOS Guideline for the Management of Overweight and Obesity in Adults (8) evaluated the observational literature about the association of various BMI cutoffs and the incidence of death and cardiovascular disease. That guideline adopted the arbitrary BMI cutpoints of  $\geq 30$  kg/m<sup>2</sup> ( $\geq 27$  kg/m<sup>2</sup> with medical related comorbidity) that had been determined by the U.S. Food and Drug Administration (FDA) and listed on the package inserts of FDA-approved obesity medications. Our Task Force adopted these cutpoints, realizing that they are arbitrary and only low-quality evidence supports associations determined by these cutpoints. Nevertheless, we had to use cutpoints to provide patients and clinicians with specific implementable and practical recommendations.

The only medication available in the European Union for chronic obesity management is orlistat. We encourage additional scrutiny of medications available in the United States by the European Medicines Agency (EMA) and the



funding of additional long-term clinical trials in the European Union and elsewhere to study the safety and efficacy of these medications, with the goal of providing access to medications for chronic obesity management to patients in need across the world.

1.3 In patients with uncontrolled hypertension or a history of heart disease, we recommend against using sympathomimetic agents phentermine and diethylpropion. (1|⊕⊕⊕⊕) (Table 4)

### Evidence

The product labels for medications approved for chronic weight management (46–49) include contraindications and cautions based on clinical data submission on > 1500 individuals treated with each medication before approval. These contraindications are detailed in Table 4. Prescribers should be familiar with these product labels in order to avoid contraindications and to judiciously choose patients based on product cautions.

For the sympathomimetic agents phentermine and diethylpropion, regulatory approval was given based on a smaller clinical profile and without a cardiovascular outcomes study. There is thus a lack of evidence on safety for these products across broad populations. In making a strong recommendation, the panel placed a high value on avoiding harm and a lower value on potential short-term weight loss.

### Implementation remarks

Because phentermine and diethylpropion are associated with elevations in mean blood pressure (BP) and pulse rate in treated populations, we do not advocate their prescription in patients with a history of cardiovascular disease, and we suggest caution and careful monitoring in patients with hypertension history. Thus, caution is advised in prescribing these agents in patients with hypertension, history of cardiac arrhythmia, or seizures. A serotonin receptor agonist such as lorcaserin would be a better choice in a patient with these conditions.

Another example is the patient with obesity and depression on a selective serotonin reuptake inhibitor (SSRI) or serotonin-norepinephrine reuptake inhibitor (SNRI). In these patients, lorcaserin would not be the best choice due to the potential for serotonin syndrome. A better choice would be phentermine/topiramate or phentermine alone. Orlistat is likely to be safe in all instances due to its mechanism of action. Other cautionary instances are outlined in Table 4.

1.4 We suggest assessment of efficacy and safety at least monthly for the first 3 months, then at least every

3 months in all patients prescribed weight loss medications. (2|⊕⊕⊕⊕)

### Evidence

Diet, behavior modification, and, if appropriate, pharmacotherapy have been shown to be safe and effective in producing modest but effective weight loss and amelioration of comorbid medical problems. To promote maximum effectiveness, frequent assessments are indicated to assess effectiveness of the treatment, ensure accountability, and monitor safety and efficacy of the weight loss medications. The more accountable patients are to weight loss programs, the better the outcomes that are expected. Moreover, any adverse side effects of the weight loss medications can be detected early and rectified (8). The AHA/ACC/TOS Guideline for the Management of Overweight and Obesity in Adults reviewed randomized clinical trials on weight loss interventions and determined that the best weight loss outcomes occur with frequent face-to-face visits (16 visits per year on average) (8, 38).

1.5 If a patient's response to a weight loss medication is deemed effective (weight loss  $\geq 5\%$  of body weight at 3 mo) and safe, we recommend that the medication be continued. If deemed ineffective (weight loss  $< 5\%$  at 3 mo) or if there are safety or tolerability issues at any time, we recommend that the medication be discontinued and alternative medications or referral for alternative treatment approaches be considered. (1|⊕⊕⊕⊕)

### Evidence

Weight loss medications do not change the underlying physiology of weight regulation in any permanent way. Trials of weight loss medication that have used a crossover design have demonstrated that the weight loss effects of these medications are only sustained as long as they are taken and these same benefits occur on introducing the medication in patients previously treated with lifestyle alone. Historically, patients and providers thought that weight loss medications could be used to produce an initial weight loss that could subsequently be sustained by behavioral means. The available evidence does not support this view. Much as antihypertensive medications lower BP to a new steady state with BP rising to baseline levels upon discontinuing medication, weight loss medications promote weight loss to a new steady state with gradual weight gain typically occurring when medications are stopped (50, 51).

1.6 If medication for obesity management is prescribed as adjunctive therapy to comprehensive lifestyle intervention, we suggest initiating therapy with dose escalation based on efficacy and tolerability to the recommended

**Table 4.** Pharmacotherapy for Obesity in the United States (December 2014)

Drug (Generic)	Dosage	Mechanism of Action	Weight Loss Above Diet and Lifestyle Alone, Mean Weight Loss, % or kg <sup>a</sup> ; Duration of Clinical Studies	Status	Common Side Effects	Contraindications
Phentermine resin	AdipexP (37.5 mg), 37.5 mg/d Ionamin (30 mg), 30–37.5 mg/d	Norepinephrine-releasing agent	3.6 kg (7.9 lb); 2–24 wk	Approved in 1960s for short-term use (3 mo)	Headache, elevated BP, elevated HR, insomnia, dry mouth, constipation, anxiety Cardiovascular: palpitation, tachycardia, elevated BP, ischemic events Central nervous system: overstimulation, restlessness, dizziness, insomnia, euphoria, dysphoria, tremor, headache, psychosis Gastrointestinal: dryness of the mouth, unpleasant taste, diarrhea, constipation, other gastrointestinal disturbances Allergic: urticaria Endocrine: impotence, changes in libido	Anxiety disorders (agitated states), history of heart disease, uncontrolled hypertension, seizure, MAO inhibitors, pregnancy and breastfeeding, hyperthyroidism, glaucoma, history of drug abuse, sympathomimetic amines
Diethylpropion	Tenuate (75 mg), 75 mg/d	Norepinephrine-releasing agents	3.0 kg (6.6 lb); 6–52 wk	FDA approved in 1960s for short-term use (3 mo)	See phentermine resin	See phentermine resin
Orlistat, prescription (120 mg)	120 mg TID	Pancreatic and gastric lipase inhibitor	2.9–3.4 kg (6.5–7.5 lb), 2.9–3.4%; 1 y	FDA approved in 1999 for chronic weight management	Decreased absorption of fat-soluble vitamins, steatorrhea, oily spotting, flatulence with discharge, fecal urgency, oily evacuation, increased defecation, fecal incontinence	Cyclosporine (taken 2 h before or after orlistat dose), chronic malabsorption syndrome, pregnancy and breastfeeding, cholestasis, levothyroxine, warfarin, antiepileptic drugs
Orlistat, over-the-counter (60 mg)	60–120 mg TID	Pancreatic and gastric lipase inhibitor	2.9–3.4 kg (6.5–7.5 lb), 2.9–3.4%; 1 y	FDA approved in 1999 for chronic weight management	See Orlistat, prescription	See Orlistat, prescription
Lorcaserin (10 mg)	10 mg BID	5HT <sub>2c</sub> receptor agonist	3.6 kg (7.9 lb), 3.6%; 1 y	FDA approved in 2012 for chronic weight management	Headache, nausea, dry mouth, dizziness, fatigue, constipation	Pregnancy and breastfeeding <b>Use with caution:</b> SSRI, SNRI/MAOI, St John's wort, triptans, bupropion, dextromethorphan
Phentermine (P)/topiramate (T)	3.75 mg P/23 mg T ER QD (starting dose) 7.5 mg P/46 mg T ER daily (recommended dose) 15 mg P/92 mg P/T ER daily (high dose)	GABA receptor modulation (T) plus norepinephrine-releasing agent (P)	6.6 kg (14.5 lb) (recommended dose), 6.6% 8.6 kg (18.9 lb) (high dose), 8.6%; 1 y	FDA approved in 2012 for chronic weight management	Insomnia, dry mouth, constipation, paraesthesia, dizziness, dysgeusia	Pregnancy and breastfeeding, hyperthyroidism, glaucoma, MAO inhibitor, sympathomimetic amines
Naltrexone/bupropion	32 mg/360 mg 2 tablets QID (high dose)	Reuptake inhibitor of dopamine and norepinephrine (bupropion) and opioid antagonist (naltrexone)	4.8%; 1 y (Ref. 79)	FDA approved in 2014 for chronic weight management	Nausea, constipation, headache, vomiting, dizziness	Uncontrolled hypertension, seizure disorders, anorexia nervosa or bulimia, drug or alcohol withdrawal, MAO inhibitors
Liraglutide	3.0 mg injectable	GLP-1 agonist	5.8 kg; 1 y (Ref. 30, 31)	FDA approved in 2014 for chronic weight management	Nausea, vomiting, pancreatitis	Medullary thyroid cancer history, multiple endocrine neoplasia type 2 history

Abbreviations: GABA,  $\gamma$ -aminobutyric acid; HR, heart rate; MAO, monoamine oxidase (Ref. 46–49).<sup>a</sup> Mean weight loss in excess of placebo as percentage of initial body weight or mean kilogram weight loss over placebo.

dose and not exceeding the upper approved dose boundaries. (2|⊕⊕○○)

### Evidence

For the medications approved for long-term treatment for obesity, the recommended doses are as follows: orlistat, 120 mg three times a day (TID); phentermine/topiramate, 7.5 mg/46 mg every day (QD); lorcaserin, 10 mg twice a day (BID); naltrexone/bupropion, 8 mg/90 mg, 2 tablets BID; and for liraglutide, 3.0 mg SC QD (46–49).

For orlistat, the drug is available over the counter at a dosage of 60 mg TID. This dosage has been shown to produce greater weight loss than placebo (52). The recommended prescription dosage is 120 mg TID. Given the favorable safety profile and weight loss efficacy of orlistat at 120 mg TID, it is the preferred dose for prescription (47). There is no evidence from clinical trials using dosages higher than 120 mg TID that efficacy is greater at higher dosages, and prescribers should not exceed 120 mg TID. Orlistat, 120 mg TID, has been studied and approved for treatment of adolescents with obesity (58–60).

For phentermine/topiramate extended release (ER), it is necessary to escalate the dose when starting the medication. The clinical trial data support starting at a dosage of 3.75 mg/23 mg QD and maintaining this for at least 2 weeks. If the patient tolerates the medication, an increase to 7.5 mg/46 mg is in order. Because of the more favorable tolerability profile in clinical studies of the 7.5 mg/46 mg dose, further escalation is only recommended for patients who have not lost 3% of their body weight at 12 weeks. In that case, the dose can be increased to 11.25 mg/69 mg, and then to 15 mg/92 mg. The product label recommends a gradual reduction of dose over 3–5 days because of the observation of seizures occurring when topiramate was stopped abruptly in patients with epilepsy (41, 43, 61).

For lorcaserin, the recommended dosage is 10 mg BID. In clinical trials, lorcaserin 10 mg QD produced nearly as much weight loss as 10 mg BID (42, 44, 45).

Naltrexone/bupropion is available in 8mg/90mg combination tablets. One tablet should be started in the morning and in 1 week 1 tablet added before dinner. As tolerated, the dose should be increased to 2 tablets in the morning the 3rd week, and 2 tablets before the evening meal the 4th week to the maximum of 2 tablets twice daily. If side effects such as nausea develop during dose escalation, the dose should not be increased further until tolerated. If a patient has not lost more than 5% of body weight at 12 weeks, naltrexone/bupropion should be discontinued (79, 93).

Liraglutide should be initiated at a dose of 0.6 mg daily by SC injection. The dose can be increased by 0.6 mg per week up to a maximum of 3.0 mg. If side effects such as

nausea develop during dose escalation, the dose should not be increased further until tolerated (31).

There are no comparative data of different doses of phentermine and other sympathomimetics used as a single agent. Therefore, the once-daily doses of 30 mg phentermine (37.5 mg as resin) or 75 mg tenate should not be exceeded.

1.7 In patients with T2DM who are overweight or obese, we suggest the use of antidiabetic medications that have additional actions to promote weight loss (such as GLP-1 analogs or SGLT-2 inhibitors) in addition to the first-line agent for T2DM and obesity, metformin (63). (2|⊕⊕○○)

### Evidence

Individuals with obesity and T2DM may have the dual benefit of weight loss and glycemic control while prescribed a regimen including one or more of three currently available drug classes: metformin, the GLP-1 agonists (exenatide, liraglutide), and the new class of SGLT-2 inhibitors. For the goal of clinically significant weight loss, trials comparing GLP-1 agonists and other antihyperglycemic agents have shown weight loss in some subjects in higher ranges between 5.5 and 8 kg (62). Although other agents including metformin and SGLT-2 inhibitors produce more modest weight loss, ie, in the 1- to 3-kg range in most studies, these agents have not been studied in the setting of concomitant behavioral therapy, and the full weight loss potential is therefore not yet known. In summary, because a subset of diabetes patients may have substantial weight loss on certain diabetes agents that also lower blood glucose, most patients with diabetes should try one or more of these before being considered for additional medications designed for the specific goal of weight loss. The most substantial evidence supports a trial of GLP-1 agonists (see recommendation 2.1).

1.8 In patients with cardiovascular disease who seek pharmacological treatment for weight loss, we suggest using medications that are not sympathomimetics, such as lorcaserin and/or orlistat. (2|⊕○○○)

### Evidence

Because patients with a prior history of cardiovascular disease may be susceptible to sympathetic stimulation, agents without cardiovascular signals (increased BP and pulse) should be used preferentially. For patients with established cardiovascular disease who require medication for weight loss, orlistat and lorcaserin should be used. These drugs have a lower risk of increased BP than phentermine and topiramate ER. Lorcaserin showed a reduc-

tion in pulse and BP greater than placebo in randomized placebo-controlled trials (44).

## 2.0 Drugs that cause weight gain and some alternatives

A variety of prescription medications have been associated with weight gain. Drug-induced weight gain is a preventable cause of obesity. For all patients, and particularly for patients who have a BMI > 27 kg/m<sup>2</sup> with comorbidities or BMI > 30 kg/m<sup>2</sup>, the desired level of clinical efficacy for a chosen therapy should be balanced against side effects, including the likelihood of weight gain. In cases where there are no acceptable therapeutic alternatives, the minimal dose required to produce clinical efficacy may prevent drug-induced weight gain. Patients' initial weight status, the presence of risk factors for cardiovascular disease, diabetes, and other obesity-related health complications, as well as the benefits of pharmacological therapies warrant careful consideration when prescribing a first-line therapy or change in medication.

2.1 We recommend weight-losing and weight-neutral medications as first- and second-line agents in the management of a patient with T2DM who is overweight or obese. (1|⊕⊕⊕⊕)

### Evidence

The effect of metformin for promoting mild weight loss is likely due to multiple mechanisms (63). However, in animal models, metformin mediates a phenotypic shift away from lipid accretion through AMP-activated Protein Kinase-Nicotinamide phosphoribosyltransferase-Sirtuin 1-mediated changes in metabolism supporting treatment for obesity (64). GLP-1 agonists such as exenatide and liraglutide have also been shown to promote mild weight loss. Pramlintide is an amylin analog that promotes weight loss by increasing satiety and decreasing food intake (65, 66). Dipeptidyl peptidase IV (DPP-4) inhibitors appear to be weight neutral or may lead to minimal weight change.  $\alpha$ -Glucosidase inhibitors such as acarbose and miglitol may be weight neutral or lead to a small change in weight (152, 153).

Clinicians should discuss possible weight effects of glucose-lowering medications with patients and consider the use of antihyperglycemic medications that are weight neutral or promote weight loss.

Weight gain is often associated with many diabetes therapies. Patients can gain as much as 10 kg in a relatively short period (3 to 6 mo) after initiating treatment with insulin, sulfonylureas, and other insulin secretagogues like glitinides and thiazolidinediones. Participants in the Diabetes Prevention Program with impaired glucose tolerance who took metformin (850 mg BID) lost 2.1 kg compared

with a weight loss of 0.1 kg in the placebo group (69). A recent study comparing sitagliptin plus metformin with pioglitazone in drug-naive patients with T2DM showed that the sitagliptin-metformin combination resulted in weight loss (−1.4 kg) whereas pioglitazone led to weight gain (3.0 kg) (70). A retrospective analysis of exenatide (n = 6280), sitagliptin (n = 5861), and insulin (n = 32 398) indicated that exenatide-treated subjects lost an average of 3.0 kg, sitagliptin-treated subjects lost 1.1 kg, and insulin-treated subjects gained 0.6 kg (71).

In a 1-year trial comparing two doses of liraglutide (1.2 and 1.8 mg) with glimepiride 8 mg, subjects lost 2.05 and 2.45 kg in the 1.2- and 1.8-mg groups, respectively, compared with a 1.12-kg weight gain in the glimepiride group. Glycated hemoglobin (HbA1c) significantly ( $P = .0014$ ) decreased by 0.84% with liraglutide 1.2 mg and by 1.14% with liraglutide 1.8 mg ( $P < .0001$ ) compared to 0.51% with glimepiride (72). An analysis of 17 randomized placebo-controlled trials showed that all GLP-1 agonists reduced HbA1c levels by about 1% (62). The DPP-4 inhibitors sitagliptin and vildagliptin have also been shown in a meta-analysis of 25 studies to lower HbA1c by approximately 0.7 and 0.6%, respectively, in comparison with placebo (73).

A recent review of direct comparisons with active glucose-lowering agents in drug-naive patients demonstrated that DPP-4 inhibitors reduce HbA1c slightly less than metformin (by approximately 0.28) and provide similar glucose-lowering effects as a thiazolidinedione. DPP-4 inhibitors have better gastrointestinal tolerability than metformin yet are weight neutral (74, 75). Another meta-analysis found that an increase in body weight (1.8 to 3.0 kg) was observed with most second-line therapies, the exceptions being DPP-4 inhibitors,  $\alpha$ -glucosidase inhibitors, and GLP-1 analogs (+0.6 to −1.8 kg) (76). Pramlintide, indicated as an adjunct to insulin, may also aid with weight loss. A meta-analysis demonstrated a weight loss of −2.57 kg for those taking pramlintide vs the control groups (77).

The SGLT-2 inhibitors dapagliflozin and canagliflozin are a new class of antidiabetic drugs that reduce renal glucose reabsorption in the proximal convoluted tubule, leading to increased urinary glucose excretion (78). A recent systematic review and meta-analysis (79) looks at not only the effect of these medications on glycemic indices but also their effects on body weight. Compared with placebo, the mean percentage change in body weight from baseline in eight studies of > 12 weeks comparing the SGLT-2 inhibitor to placebo was −2.37% (95% confidence interval [CI], −2.73 to −2.02). Canagliflozin appears to produce slightly more weight loss on average because three studies with dapagliflozin vs placebo showed mean loss of −2.06% of initial body weight (95% CI, −2.38 to



–1.74), and five studies of canagliflozin vs placebo showed –2.61% loss (95% CI, –3.09 to –2.13); however, this was not statistically significant. This analysis may underestimate the weight loss effects of these drugs because studies of 12 weeks were included. In 52-week observations, there is no weight regain after maximal loss at 24 weeks.

In addition, because weight-sparing medications are unique in that they do not independently cause hypoglycemia, they have a lower potential for hindering an exercise program. Exercise adjustment is generally necessary only with insulin and with medications that can promote endogenous insulin secretion despite decreasing glucose levels, such as the sulfonylurea and glinide classes of agents (80). Hence, prioritizing metformin, incretin-based medications, and SGLT-2s as therapeutic strategies can reduce exercise-related hypoglycemia and potentially increase the safety and efficacy of exercise in patients with diabetes, thus supporting this important weight-reduction strategy (67, 68).

2.2 In obese patients with T2DM requiring insulin therapy, we suggest adding at least one of the following: metformin, pramlintide, or GLP-1 agonists to mitigate associated weight gain due to insulin. The first-line insulin for this type of patient should be basal insulin. This is preferable to using either insulin alone or insulin with a sulfonylurea. We also suggest that the insulin therapy strategy be considered a preferential trial of basal insulin prior to premixed insulins or combination insulin therapy. (2|⊕⊕⊕⊕)

### Evidence

Insulin remains the most effective agent to control serum glucose (81). However, multiple large studies typically show weight gain associated with insulin use, either as monotherapy or in combination with oral antidiabetic agents (82–85). Treatment with both metformin and insulin, or when metformin is prescribed in addition to an insulin program, yields similar glycemic benefit to insulin alone without excessive additional weight gain, as shown by meta-analyses and randomized trials (86–88).

Amylin analogs are FDA approved for use in combination with existing insulin treatment. A dose-finding study with pramlintide added to a variety of insulin regimens showed weight loss (–1.4 kg) in treatment groups (89), with HbA1c reductions of 0.62 to 0.68% in the 120- $\mu$ g dose group. Additionally, weight gain was prevented when pramlintide was added to the basal insulins glargine or detemir. Other studies have found more substantial weight loss of over 3 kg with the use of pramlintide (90).

Other weight-sparing regimens have been studied, including the combination of basal insulin with the weight-

neutral DPP-4 inhibitor sitagliptin (91) and weight-reducing combination therapy with liraglutide and metformin. Buse et al (92) investigated the addition of exenatide or placebo to regimens of insulin glargine alone, or in combination with metformin or pioglitazone or both, in adult T2DM patients with HbA1c of 7.1 to 10.5%. Despite superior HbA1c reduction, weight also decreased by 1.8 kg in the exenatide group compared with an increase of 1.0 kg in the placebo group (between-group difference, –2.7 kg; 95% CI, –3.7 to –1.7).

Finally, some weight benefits have been seen with the basal insulin analogs relative to biphasic and prandial insulin analog regimens. The Treating To Target in Type 2 Diabetes trial in patients receiving metformin/ sulfonylurea compared the initiation of basal insulin detemir (twice daily, if required) to that of biphasic insulin aspart BID or prandial insulin aspart TID. Basal insulin use was associated with the least weight gain at 1 year (+1.9 vs +4.7 vs +5.7 kg, detemir vs biphasic vs prandial, respectively) (93), and the weight advantage persisted during the 3-year trial (94).

2.3 We recommend ACE inhibitors, ARBs, and calcium channel blockers rather than  $\beta$ -adrenergic blockers as first-line therapy for hypertension in patients with T2DM who are obese. (1|⊕⊕⊕⊕)

### Evidence

Angiotensin is overexpressed in obesity, directly contributing to obesity-related hypertension, providing support for the use of an ACE inhibitor as a first-line agent. Calcium channel blockers are also effective in the treatment of obesity-related hypertension and have not been associated with weight gain or adverse changes in lipids. ACE inhibitors and ARBs have not been associated with weight gain or insulin resistance and provide renal protection in diabetes (95).

If required, selective or nonselective  $\beta$ -blockers with a vasodilating component such as carvedilol and nebivolol are recommended because these agents appear to have less weight gain potential and less of an impact on glucose and lipid metabolism than other nonselective  $\beta$ -blockers (96, 97).

A study in patients taking metoprolol tartrate compared with those taking carvedilol for hypertension showed a mean weight gain of 1.19 kg, suggesting that weight gain is not a class effect of the  $\beta$ -adrenergic blockers (98). A meta-analysis of body weight changes in a series of randomized controlled hypertension trials of at least 6-month duration showed that body weight was higher in the  $\beta$ -blocker group, with a median difference of 1.2 kg between the  $\beta$ -blocker group and the control group (97). The Second Australian National Blood Pressure Trial re-

ported slightly better cardiovascular outcomes in hypertensive men treated with a regimen that began with an ACE inhibitor compared with a regimen starting with a diuretic (95).

2.4 When antidepressant therapy is indicated, we recommend a shared decision-making process that provides patients with quantitative estimates of the expected weight effect of the antidepressant to make an informed decision about drug choice. Other factors that need to be taken into consideration include the expected length of treatment. (1|⊕⊕⊕○)

### Evidence

The antidepressants vary considerably with respect to their long-term weight gain potential. Serretti and Mandelli (99) evaluated the relative risk of weight gain associated with drugs within the major classes of antidepressant medications in a recent meta-analysis. Paroxetine is considered to be the SSRI associated with the greatest long-term increase in body weight (100), amitriptyline is the most potent inducer of weight gain among the tricyclic antidepressants (99), and mirtazapine (a noradrenergic and specific serotonergic antidepressant) is also associated with weight gain in the long term (101). Other specific tricyclics that have been associated with weight gain include nortriptyline (102), whereas the effect of imipramine seems to be neutral (99). SSRIs such as fluoxetine and sertraline have been associated with weight loss during acute treatment (4–12 wk) and with weight neutrality in the maintenance (>4 mo) phase (99). No significant effect could be observed for citalopram or escitalopram on body weight (99). Among the serotonin and norepinephrine reuptake inhibitors, venlafaxine and duloxetine have been reported to slightly increase body weight over long-term treatment, although long-term data for venlafaxine are scarce (99). Bupropion selectively inhibits reuptake of dopamine and, to a lesser extent, norepinephrine. It is the only antidepressant that consistently causes weight loss (103). It was originally approved both for treating depression and for inducing smoking cessation. During clinical trials, it suppressed appetite and food cravings and significantly decreased body weight (103). The commissioned systematic review accompanying this guideline (3) was only able to demonstrate weight gain with amitriptyline (1.8 kg) and mirtazapine (1.5 kg) and weight loss with bupropion (−1.3 kg) and fluoxetine (−1.3 kg). The evidence for weight changes with other antidepressants was of lower quality.

2.5 We recommend using weight-neutral antipsychotic alternatives when clinically indicated, rather than those that cause weight gain, and the use of a shared decision-

making process that provides patients with quantitative estimates of the expected weight effect of the alternative treatments to make an informed decision about drug choice. (1|⊕⊕⊕○)

### Evidence

Although better tolerated than the older antipsychotics, many of the new atypical antipsychotic agents have weight gain as a side effect (104). This weight gain is of clinical concern because it impedes patient compliance and has deleterious health consequences (104, 105) in patients who are often overweight or obese to begin with. The differential effect of atypical antipsychotics on histamine (H1) receptors, anticholinergic effects, and serotonin type 2C antagonistic effects may explain differences in weight gain among the drugs. Henderson et al (106) demonstrated that weight gain associated with clozapine treatment continued for as long as 46 months and was accompanied by a significant increase in triglyceride levels and a 37% increase in the incidence of T2DM over the 5-year period of observation. A randomized trial investigating the effectiveness of five antipsychotic medications found that a weight gain of > 7% from baseline occurred in 30% of those taking olanzapine, 16% for quetiapine, 14% for risperidone, 12% for perphenazine, and 7% of those taking ziprasidone (107). Allison and Casey (104) noted that patients lost weight when switched from olanzapine to ziprasidone, and this weight loss was associated with improvements in their serum lipid profile and glucose tolerance. In a 6-week, double-blind trial, patients were randomly assigned to receive ziprasidone (n = 136) or olanzapine (n = 133). Body weight increased significantly in those taking olanzapine (3.6 kg) compared with those taking ziprasidone (1.0 kg) (108). A review of nine randomized controlled trials comparing ziprasidone with amisulpride, clozapine, olanzapine, quetiapine, and risperidone showed that ziprasidone produced less weight gain than olanzapine (five RCTs; n = 1659; mean difference, −3.82; 95% CI, −4.69 to −2.96), quetiapine (two randomized controlled trials [RCTs]; n = 754; relative risk, 0.45; 95% CI, 0.28 to 0.74), or risperidone (three RCTs; n = 1063; relative risk, 0.49; 95% CI, 0.33 to 0.74). Ziprasidone was also associated with less cholesterol increase than olanzapine, quetiapine, and risperidone (109). Finally, a review of 34 trials of antipsychotics in youth with psychotic and bipolar disorders found that weight gain ranged from 3.8 to 16.2 kg with olanzapine, 0.9 to 9.5 kg with clozapine, 1.9 to 7.2 kg with risperidone, 2.3 to 6.1 kg with quetiapine, and 0 to 4.4 kg with aripiprazole (110). Despite the variable effects on weight gain among the antipsychotic agents, the prediabetes ef-

fect may be similar via weight-independent mechanisms (111).

2.6 We recommend considering weight gain potential in choosing an AED for any given patient, and the use of a shared decision-making process that provides patients with quantitative estimates of the expected weight effect of the drugs to make an informed decision about drug choice. (1|⊕⊕⊕⊕)

### Evidence

AEDs associated with weight loss are felbamate, topiramate, and zonisamide. AEDs associated with weight gain are gabapentin, pregabalin, valproic acid, vigabatrin, and carbamazepine. Weight-neutral AEDs are lamotrigine, levetiracetam, and phenytoin. In clinical practice, it is critical to weigh patients regularly, and AED selection should be based on each patient's profile without sacrificing therapeutic efficacy (112).

Valproic acid has been shown to cause weight gain in both adults and children (113). A retrospective study of long-term weight gain in adult epileptic patients on valproic acid mono- or polytherapy showed that mild-to-moderate weight gain (5 to 10% of baseline weight) was shown in 24% of patients, whereas marked weight gain (>10% gain of baseline weight) was shown in 47% of patients (114). A study of patients taking gabapentin for 12 months or more showed that of 44 patients, 57% gained more than 5% of their baseline body weight; of these, 10 patients (23%) gained more than 10% of their baseline weight (115). Our commissioned systematic review (3) suggested weight gain with gabapentin (2.2 kg after 1.5 mo of use) and divalproex (relative risk for weight gain, 2.8; 95% CI, 1.30, 6.02). Carbamazepine is an older AED and has also been associated with weight gain, although not as significant as valproic acid or gabapentin (116). A study of 66 patients taking AEDs showed that 66.7% of those on carbamazepine had gained an average of 1.5 kg at a 6- to 8-month follow-up visit (117).

2.7 In women with a BMI > 27 kg/m<sup>2</sup> with comorbidities or BMI > 30 kg/m<sup>2</sup> seeking contraception, we suggest oral contraceptives over injectable medications due to weight gain with injectables, provided that women are well-informed about the risks and benefits (ie, oral contraceptives are not contraindicated). (2|⊕○○○)

### Evidence

Contraceptive drugs are available in different dosages and formulations and are composed of progestins alone or in combination with estrogens. Some progestins have androgenic/antiandrogenic properties. The research on contraceptives and weight gain is conflicting, and the studies

conducted so far are difficult to compare because of the different formulations of contraceptives containing variable doses of estrogens, and with the progestins having different androgenic/antiandrogenic profiles. Moreover, randomized controlled trials comparing hormonal contraceptive methods with a placebo usually raise ethical issues. As recently documented by Gallo et al (118), only four trials included a placebo group or no intervention group, and no evidence has been found to support the association between combination (estrogen plus a progestin) hormonal contraception and weight change. In addition, the same authors, by examining 79 trials of combination contraceptives, concluded that no substantial difference in weight could be found. Moreover, discontinuation of combination contraceptives because of weight change did not differ between groups where this was studied (118).

There is limited evidence of weight gain when using progestin-only contraceptives. Mean gain was less than 2 kg for most studies up to 12 months (119). However, it should be noted that most of the trials were conducted in normal-weight women and excluded obese subjects.

### Remarks

Selected studies have reported an increase in contraceptive failure in women with a BMI > 27 kg/m<sup>2</sup>. Data on this issue are conflicting but should be discussed with the appropriate patients on an individual basis.

2.8 We suggest monitoring the weight and waist circumference of patients on antiretroviral therapy due to unavoidable weight gain, weight redistribution, and associated cardiovascular risk. (2|⊕⊕⊕⊕)

### Evidence

Treatments for human immunodeficiency disease include administration of antiretroviral therapy and protease inhibitors. Although effective for suppressing HIV viral activity, which should be associated with appropriate weight gain, such treatments are associated with increased deposition of visceral adipose tissue (120) and lipodystrophy (121). One study of 10 HIV patients treated with protease inhibitor-containing regimens found that patients gained an average of 8.6 kg ( $P = .006$ ) after 6 months (120).

2.9 We suggest the use of nonsteroidal anti-inflammatory drugs and disease-modifying antirheumatic drugs when possible in patients with chronic inflammatory disease like rheumatoid arthritis because corticosteroids commonly produce weight gain. (2|⊕⊕⊕⊕)

## Evidence

When possible, chronic steroid therapy should be avoided in the treatment of chronic inflammatory disease to avoid weight gain in individuals who are overweight or obese. Weight gain and its effects on comorbidities should be considered among the commonly known side effects of glucocorticoid therapy. This is particularly important in rheumatic diseases because, for example, obesity in the setting of osteoarthritis leads to more severe disability and reduced exercise capacity, ambulatory capacity, and quality of life (122). A systematic review reported that, based on data from four RCTs in rheumatoid arthritis, glucocorticoids cause a weight increase of 4 to 8% (123, 124). An additional study showed that, when compared with sulfasalazine, glucocorticoid therapy was associated with a 1.7-kg weight gain after 1 year of treatment (125, 126), and another showed a 2.0-kg weight gain after 24 weeks in patients taking prednisone (127).

2.10 We suggest the use of antihistamines with less central nervous system activity (less sedation) to limit weight gain. (2|⊕⊕○○)

## Evidence

Research is inconclusive regarding differences in the weight gain potential of sedating vs nonsedating antihistamines because weight has rarely been an outcome in studies of antihistamines, but it appears that the more potent the antihistamine, the greater the potential for weight gain (128). A recent study demonstrated that the odds ratio for being overweight was increased in prescription H1 antihistamine users (129). Furthermore, a study using data from the 2005–2006 National Health and Nutrition Examination Survey found that prescription H1 antihistamine users had a significantly higher weight, waist circumference, and insulin concentration than matched controls (129).

### 3.0 Off-label use of drugs approved for other indications for chronic obesity management

3.1 We suggest against the off-label use of medications approved for other disease states for the sole purpose of producing weight loss. A trial of such therapy can be attempted in the context of research and by healthcare providers with expertise in weight management dealing with a well-informed patient. (Ungraded Best Practice Recommendation)

## Evidence

A variety of drug classes approved for other uses have been utilized off-label by some prescribers to promote weight loss in patients who are obese. Categories of drugs used may include the antiseizure medication topiramate as

well as zonisamide, metformin, GLP-1 agonists such as exenatide and liraglutide, the antidepressant bupropion, as well as drugs for attention deficit hyperactivity disorder such as methylphenidate, and thyroid hormones. Combination treatments of these drugs also represent off-label use, although they have been utilized by some practitioners. Physicians without expertise in weight management or endocrinology are advised against prescribing off-label medications.

If a provider chooses to prescribe a medication for weight loss that is not FDA approved for this indication or is not approved for chronic administration, at minimum they should advise patients that this approach has not been evaluated for safety and efficacy and is not approved by the FDA. This discussion as well as details of the risks and benefits of the treatment approach that were presented to the patient should be documented in the medical record. The provider should discuss medications that are FDA approved for weight loss with the patient and document why an off-label medication was chosen over one of these. Practices such as selling weight loss medications out of the office should be avoided because they could be interpreted as representing a conflict of interest for the provider.

### Long-term prescribing of phentermine

Although phentermine is FDA approved for weight loss, it is not approved for long-term use. This presents a conundrum for clinicians because it is clear that weight regain will likely occur once the medication is stopped. One approach that has been tried to avoid this situation is intermittent therapy (130). Although this approach appears to work and might be appropriate when a patient is intermittently exposed to environmental factors that promote weight gain, it is not a logical way to prescribe given what is understood about the effects of weight loss medications on weight regulation. The question then is whether or not it is reasonable to prescribe phentermine off-label long term. In making this decision with a patient, direction and guidance provided by State Medical Boards and local laws always take precedence. However, in the many locations where these sources have not provided clear advice, clinicians are left to make their own best professional judgments.

Phentermine is currently the most widely prescribed weight loss medication, and it is likely that much of this prescribing is off label. This is likely a reflection of the low cost of phentermine as compared to other weight loss medications. There currently are no long-term data on safety or efficacy, although recent data on 269 patients treated long term with phentermine suggest that the addiction potential is low (131). In addition, recent data on single and combination agents for weight loss document phen-



termine 15 mg alone as able to induce over 7% weight loss at 6 months (26). There currently is minimal evidence of any serious long-term side effects when phentermine is used alone for weight loss. Given the wide clinical prescribing of phentermine for more than 20 years and the lack of evidence of serious side effects, even in the absence of long-term controlled safety and efficacy data, it seems reasonable for clinicians to prescribe phentermine long term as long as the patient: 1) has no evidence of serious cardiovascular disease; 2) does not have serious psychiatric disease or a history of substance abuse; 3) has been informed about weight loss medications that are FDA approved for long-term use and told that these have been documented to be safe and effective whereas phentermine has not; 4) does not demonstrate a clinically significant increase in pulse or BP when taking phentermine; and 5) demonstrates a significant weight loss while using the medication. These aspects of care should be documented in the patient's medical record, and the off-label nature of the prescribing should be documented at each visit. Medication should be started at 7.5 or 15 mg/d initially and only increased if the patient is not achieving clinically significant weight loss. Patients should be followed at least monthly during dose escalation and then at least every 3 months when on a stable dose.

## Acknowledgments

Address all correspondence and requests for reprints to: The Endocrine Society, 2055 L Street NW, Suite 600, Washington, DC 20036. E-mail: govt-prof@endocrine.org. Telephone: 202-971-3636. Address all commercial reprint requests for orders 101 and more to: <https://www.endocrine.org/corporate-relations/commercial-reprints>. Address all reprint requests for orders for 100 or fewer to Society Services, Telephone: 202-971-3636. E-mail: [societyservices@endocrine.org](mailto:societyservices@endocrine.org), or Fax: 202-736-9705.

Co-sponsoring Associations: European Society of Endocrinology and The Obesity Society.

Disclosure Summary: The authors have nothing to declare.

## Financial Disclosures of the Task Force

**Caroline M. Apovian, MD (chair)**—Financial or Business/Organizational Interests: none declared; Significant Financial Interest or Leadership Position: Zafgen, Inc, MYOS Corporation, Eisai, Vivus, Orexigen Therapeutics, Takeda, NIH grantee or reviewer. **Louis J. Aronne, MD, FACP**—Financial or Business/Organizational Interests: American Board of Obesity Medicine; Significant Financial Interest or Leadership Position: Jamieson Laboratories, Pfizer Inc, Healthcare Research Consulting Group,

Marwood Group, Novo Nordisk A/S, Eisai Inc, Rhythm, Johnson & Johnson, Ethicon Endo-Surgery Inc, GI Dynamics, Zafgen Inc, GLG, VIVUS Inc, MYOS Corporation, and BMIQ. **Daniel H. Bessesen, MD**—Financial or Business/Organizational Interests: The Obesity Society, NIH Grantee and Reviewer, PCORI contract recipient, Enteromedics Inc; Significant Financial Interest or Leadership Position: none declared. **Marie E. McDonnell, MD**—Financial or Business/Organizational Interests: none declared; Significant Financial Interest or Leadership Position: none declared. **M. Hassan Murad, MD, MPH\***—Financial or Business/Organizational Interests: Mayo Clinic, Division of Preventive Medicine; Significant Financial Interest or Leadership Position: none declared. **Uberto Pagotto, MD, PhD**—Financial or Business/Organizational Interests: none declared; Significant Financial Interest or Leadership Position: none declared. **Donna Ryan, MD**—Financial or Business/Organizational Interests: The Obesity Society; Significant Financial Interest or Leadership Position: Vivus, Eisai, Inc, Janssen, Novo Nordisk, Takeda, Scientific Intake. **Christopher D. Still, DO, FACP, FACP**—Financial or Business/Organizational Interests: Obesity Action Coalition, American Board of Physician Nutrition Specialists (ABPNS Board Member); Significant Financial Interest or Leadership Position: none declared.

\*Evidence-based reviews for this guideline were prepared under contract with the Endocrine Society.

## References

1. Atkins D, Best D, Briss PA, et al. Grading quality of evidence and strength of recommendations. *BMJ*. 2004;328:1490.
2. Swiglo BA, Murad MH, Schünemann HJ, et al. A case for clarity, consistency, and helpfulness: state-of-the-art clinical practice guidelines in endocrinology using the grading of recommendations, assessment, development, and evaluation system. *J Clin Endocrinol Metab*. 2008;93:666–673.
3. Domecq JP, Prutsky G, Leppin A, et al. Drugs commonly associated with weight change: a systematic review and meta-analysis. *J Clin Endocrinol Metab*. 2015;100:363–370.
4. Stacey D, Légaré F, Col NF, et al. Decision aids for people facing health treatment or screening decisions. *Cochrane Database Syst Rev*. 2014;1:CD001431.
5. American Medical Association. Policy H-440.842. Recognition of Obesity as a Disease; 2013.
6. Allison DB, Downey M, Atkinson RL, et al. Obesity as a disease: a white paper on evidence and arguments commissioned by the Council of the Obesity Society. *Obesity (Silver Spring)*. 2008;16:1161–1177.
7. Calle EE, Rodriguez C, Walker-Thurmond K, Thun MJ. Overweight, obesity, and mortality from cancer in a prospectively studied cohort of U.S. adults. *N Engl J Med*. 2003;348(17):1625–1638.
8. Jensen MD, Ryan DH, Apovian CM, et al. 2013 AHA/ACC/TOS guideline for the management of overweight and obesity in adults: a report of the American College of Cardiology/American Heart

- Association Task Force on Practice Guidelines and The Obesity Society. *Circulation*. 2014;129(25 suppl 2):S102–S138.
9. Rosenbaum M, Goldsmith R, Bloomfield D, et al. Low-dose leptin reverses skeletal muscle, autonomic, and neuroendocrine adaptations to maintenance of reduced weight. *J Clin Invest*. 2005;115:3579–3586.
  10. Hinkle W, Cordell M, Leibel R, Rosenbaum M, Hirsch J. Effects of reduced weight maintenance and leptin repletion on functional connectivity of the hypothalamus in obese humans. *PLoS One*. 2013;8:e59114.
  11. Goldsmith R, Joannisse DR, Gallagher D, et al. Effects of experimental weight perturbation on skeletal muscle work efficiency, fuel utilization, and biochemistry in human subjects. *Am J Physiol Regul Integr Comp Physiol*. 2010;298:R79–R88.
  12. Rosenbaum M, Hirsch J, Gallagher DA, Leibel RL. Long-term persistence of adaptive thermogenesis in subjects who have maintained a reduced body weight. *Am J Clin Nutr*. 2008;88:906–912.
  13. Pasman WJ, Saris WH, Muls E, Vansant G, Westerterp-Plantenga MS. Effect of exercise training on long-term weight maintenance in weight-reduced men. *Metabolism*. 1999;48(1):15–21.
  14. Sumithran P, Prendergast LA, Delbridge E, et al. Long-term persistence of hormonal adaptations to weight loss. *N Engl J Med*. 2011;365:1597–1604.
  15. Farooqi IS, Wangensteen T, Collins S, et al. Clinical and molecular genetic spectrum of congenital deficiency of the leptin receptor. *N Engl J Med*. 2007;356(3):237–247.
  16. Leibel RL. Molecular physiology of weight regulation in mice and humans. *Int J Obes (Lond)*. 2008;32(suppl 7):S98–S108.
  17. Yu JH, Kim MS. Molecular mechanisms of appetite regulation. *Diabetes Metab J*. 2012;36:391–398.
  18. Morton GJ, Cummings DE, Baskin DG, Barsh GS, Schwartz MW. Central nervous system control of food intake and body weight. *Nature*. 2006;443:289–295.
  19. Stahl SM. Impulsivity, compulsivity, and addiction. In: *Stahl's Essential Psychopharmacology*. 4th ed. New York, NY: Cambridge University Press; 2013:537–575.
  20. Lutter M, Nestler EJ. Homeostatic and hedonic signals interact in the regulation of food intake. *J Nutr*. 2009;139:629–632.
  21. Volkow ND, Wang GJ, Tomasi D, Baler RD. Obesity and addiction: neurobiological overlaps. *Obes Rev*. 2013;14:2–18.
  22. Mendieta-Zerón H, López M, Diéguez C. Gastrointestinal peptides controlling body weight homeostasis. *Gen Comp Endocrinol*. 2008;155:481–495.
  23. Cone RD. Anatomy and regulation of the central melanocortin system. *Nat Neurosci*. 2005;8:571–578.
  24. Korner J, Leibel RL. To eat or not to eat - how the gut talks to the brain. *N Engl J Med*. 2003;349:926–928.
  25. Kim GW, Lin JE, Bloman ES, Waldman SA. Antiobesity pharmacotherapy: new drugs and emerging targets. *Clin Pharmacol Ther*. 2014;95:53–66.
  26. Aronne LJ, Wadden TA, Peterson C, Winslow D, Odeh S, Gadde KM. Evaluation of phentermine and topiramate versus phentermine/topiramate extended-release in obese adults. *Obesity (Silver Spring)*. 2013;21:2163–2171.
  27. Carroll FI, Blough BE, Mascarella SW, Navarro HA, Lukas RJ, Damaj MI. Bupropion and bupropion analogs as treatments for CNS disorders. *Adv Pharmacol*. 2014;69:177–216.
  28. Davidson MH, Hauptman J, DiGirolamo M, et al. Weight control and risk factor reduction in obese subjects treated for 2 years with orlistat: a randomized, controlled trial. *JAMA*. 1999;281:235–242.
  29. Torgerson JS, Hauptman J, Boldrin MN, Sjöström L. XENical in the prevention of diabetes in obese subjects (XENDOS) study: a randomized study of orlistat as an adjunct to lifestyle changes for the prevention of type 2 diabetes in obese patients. *Diabetes Care*. 2004;27(1):155–161.
  30. Wadden TA, Hollander P, Klein S, et al. Weight maintenance and additional weight loss with liraglutide after low-calorie-diet-induced weight loss: the SCALE Maintenance randomized study. *Int J Obes (Lond)*. 2013;37:1443–1451.
  31. Astrup A, Carraro R, Finer N, et al. Safety, tolerability and sustained weight loss over 2 years with the once-daily human GLP-1 analog, liraglutide. *Int J Obes (Lond)* [Errata (2012) 36:890 and (2013) 37:322]. 2012;36:843–854.
  32. Vasilakou D, Karagiannis T, Athanasiadou E, et al. Sodium-glucose cotransporter 2 inhibitors for type 2 diabetes: a systematic review and meta-analysis. *Ann Intern Med*. 2013;159:262–274.
  33. Wadden TA, Berkowitz RI, Sarwer DB, Prus-Wisniewski R, Steinberg C. Benefits of lifestyle modification in the pharmacologic treatment of obesity: a randomized trial. *Arch Intern Med*. 2001;161:218–227.
  34. Yanovski SZ, Yanovski JA. Long-term drug treatment for obesity: a systematic and clinical review. *JAMA*. 2014;311:74–86.
  35. Avenell A, Brown TJ, McGee MA, et al. What interventions should we add to weight reducing diets in adults with obesity? A systematic review of randomized controlled trials of adding drug therapy, exercise, behaviour therapy or combinations of these interventions. *J Hum Nutr Diet*. 2004;17:293–316.
  36. Wadden TA, Berkowitz RI, Womble LG, et al. Randomized trial of lifestyle modification and pharmacotherapy for obesity. *N Engl J Med*. 2005;353:2111–2120.
  37. Wadden TA, Foreyt JP, Foster GD, et al. Weight loss with naltrexone SR/bupropion SR combination therapy as an adjunct to behavior modification: the COR-BMOD trial. *Obesity (Silver Spring)*. 2011;19:110–120.
  38. Tuomilehto J, Lindström J, Eriksson JG, et al. Prevention of type 2 diabetes mellitus by changes in lifestyle among subjects with impaired glucose tolerance. *N Engl J Med*. 2001;344:1343–1350.
  39. Hamman RF, Wing RR, Edelstein SL, et al. Effect of weight loss with lifestyle intervention on risk of diabetes. *Diabetes Care*. 2006;29:2102–2107.
  40. Unick JL, Beavers D, Jakicic JM, et al. Effectiveness of lifestyle interventions for individuals with severe obesity and type 2 diabetes: results from the Look AHEAD trial. *Diabetes Care*. 2011;34:2152–2157.
  41. Garvey WT, Ryan DH, Look M, et al. Two-year sustained weight loss and metabolic benefits with controlled-release phentermine/topiramate in obese and overweight adults (SEQUEL): a randomized, placebo-controlled, phase 3 extension study. *Am J Clin Nutr*. 2012;95:297–308.
  42. Fidler MC, Sanchez M, Raether B, et al. A one-year randomized trial of lorcaserin for weight loss in obese and overweight adults: the BLOSSOM trial. *J Clin Endocrinol Metab*. 2011;96:3067–3077.
  43. Gadde KM, Allison DB, Ryan DH, et al. Effects of low-dose, controlled-release, phentermine plus topiramate combination on weight and associated comorbidities in overweight and obese adults (CONQUER): a randomised, placebo-controlled, phase 3 trial. *Lancet*. 2011;377:1341–1352.
  44. Smith SR, Weissman NJ, Anderson CM, et al. Multicenter, placebo-controlled trial of lorcaserin for weight management. *N Engl J Med*. 2010;363:245–256.
  45. O'Neil PM, Smith SR, Weissman NJ, et al. Randomized placebo-controlled clinical trial of lorcaserin for weight loss in type 2 diabetes mellitus: the BLOOM-DM study. *Obesity (Silver Spring)*. 2012;20:1426–1436.
  46. Qsymia (phentermine and topiramate extended-release) [prescribing information]. Mountain View, CA: Vivus Inc. <http://www.qsymia.com/pdf/prescribing-information.pdf>. Accessed July 2, 2014.
  47. Xenical (orlistat) [prescribing information]. South San Francisco, CA: Genentech USA Inc. [http://www.gene.com/download/pdf/xenical\\_prescribing.pdf](http://www.gene.com/download/pdf/xenical_prescribing.pdf). Accessed July 2, 2014.
  48. Alli (orlistat) [label]. Moon Township, PA: GlaxoSmithKline. [http://www.accessdata.fda.gov/drugsatfda\\_docs/label/2007/021887lbl.pdf](http://www.accessdata.fda.gov/drugsatfda_docs/label/2007/021887lbl.pdf). Approved February 7, 2007. Accessed July 2, 2014.
  49. Belviq (lorcaserin) [prescribing information]. Zofingen, Switzer-

- land: Arena Pharmaceuticals GmbH. [https://www.belviqhcp.com/media/1001/belviq\\_prescribing\\_information.pdf](https://www.belviqhcp.com/media/1001/belviq_prescribing_information.pdf). Accessed July 2, 2014.
50. Fanghänel G, Cortinas L, Sánchez-Reyes L, Berber A. Second phase of a double-blind study clinical trial on Sibutramine for the treatment of patients suffering essential obesity: 6 months after treatment cross-over. *Int J Obes Relat Metab Disord*. 2001;25:741–747.
  51. Sjöström L, Rissanen A, Andersen T, et al. Randomised placebo-controlled trial of orlistat for weight loss and prevention of weight regain in obese patients. European Multicentre Orlistat Study Group. *Lancet*. 1998;352:167–172.
  52. Anderson JW, Schwartz SM, Hauptman J, et al. Low-dose orlistat effects on body weight of mildly to moderately overweight individuals: a 16 week, double-blind, placebo-controlled trial. *Ann Pharmacother*. 2006;40:1717–1723.
  53. Haddock CK, Poston WS, Dill PL, Foreyt JP, Ericsson M. Pharmacotherapy for obesity: a quantitative analysis of four decades of published randomized clinical trials. *Int J Obes Relat Metab Disord*. 2002;26:262–273.
  54. Li D, Morris JS, Liu J, et al. Body mass index and risk, age of onset, and survival in patients with pancreatic cancer. *JAMA*. 2009;301:2553–2562.
  55. Avenell A, Broom J, Brown TJ, et al. Systematic review of the long-term effects and economic consequences of treatments for obesity and implications for health improvement. *Health Technol Assess*. 2004;8:iii-iv,1–182.
  56. Rucker D, Padwal R, Li SK, Curioni C, Lau DC. Long term pharmacotherapy for obesity and overweight: updated meta-analysis. *BMJ*. 2007;335(7631):1194–1199.
  57. Leblanc ES, O'Connor E, Whitlock EP, Patnode CD, Kapka T. Effectiveness of primary care-relevant treatments for obesity in adults: a systematic evidence review for the U.S. Preventive Services Task Force. *Ann Intern Med*. 2011;155:434–447.
  58. Maahs D, de Serna DG, Kolotkin RL, et al. Randomized, double-blind, placebo-controlled trial of orlistat for weight loss in adolescents. *Endocr Pract*. 2006;12:18–28.
  59. McDuffie JR, Calis KA, Booth SL, Uwaiwo GI, Yanovski JA. Effects of orlistat on fat-soluble vitamins in obese adolescents. *Pharmacotherapy*. 2002;22:814–822.
  60. McGovern L, Johnson JN, Rullo R, et al. Clinical review: treatment of pediatric obesity: a systematic review and meta-analysis of randomized trials. *J Clin Endocrinol Metab*. 2008;93:4600–4605.
  61. Allison DB, Gadde KM, Garvey WT, et al. Controlled-release phentermine/topiramate in severely obese adults: a randomized controlled trial (EQUIP). *Obesity (Silver Spring)*. 2012;20:330–342.
  62. Shyangdan DS, Royle P, Clar C, Sharma P, Waugh N, Snaith A. Glucagon-like peptide analogues for type 2 diabetes mellitus. *Cochrane Database Syst Rev*. 2011;10:CD006423.
  63. Malin SK, Kashyap SR. Effects of metformin on weight loss: potential mechanisms. *Curr Opin Endocrinol Diabetes Obes*. 2014;21(5):323–329.
  64. Caton PW, Kieswich J, Yaqoob MM, Holness MJ, Sugden MC. Metformin opposes impaired AMPK and SIRT1 function and deleterious changes in core clock protein expression in white adipose tissue of genetically-obese db/db mice. *Diabetes Obes Metab*. 2011;13(12):1097–1104.
  65. Chapman I, Parker B, Doran S, et al. Effect of pramlintide on satiety and food intake in obese subjects and subjects with type 2 diabetes. *Diabetologia*. 2005;48(5):838–848.
  66. Smith SR, Blundell JE, Burns C, et al. Pramlintide treatment reduces 24-h caloric intake and meal sizes and improves control of eating in obese subjects: a 6-wk translational research study. *Am J Physiol Endocrinol Metab*. 2007;293(2):E620–E627.
  67. Bolinder J, Ljunggren Ö, Kullberg J, et al. Effects of dapagliflozin on body weight, total fat mass, and regional adipose tissue distribution in patients with type 2 diabetes mellitus with inadequate glycemic control on metformin. *J Clin Endocrinol Metab*. 2012;97:1020–1031.
  68. Grandy S, Hashemi M, Langkilde AM, Parikh S, Sjöström CD. Changes in weight loss-related quality of life among type 2 diabetes mellitus patients treated with dapagliflozin. *Diabetes Obes Metab*. 2014;16:645–650.
  69. Knowler WC, Barrett-Connor E, Fowler SE, et al. Reduction in the incidence of type 2 diabetes with lifestyle intervention or metformin. *N Engl J Med*. 2002;346:393–403.
  70. Wainstein J, Katz L, Engel SS, et al. Initial therapy with the fixed-dose combination of sitagliptin and metformin results in greater improvement in glycaemic control compared with pioglitazone monotherapy in patients with type 2 diabetes. *Diabetes Obes Metab*. 2012;14(5):409–418.
  71. Horton ES, Silberman C, Davis KL, Berria R. Weight loss, glycemic control, and changes in cardiovascular biomarkers in patients with type 2 diabetes receiving incretin therapies or insulin in a large cohort database. *Diabetes Care*. 2010;33:1759–1765.
  72. Garber A, Henry R, Ratner R, et al. Liraglutide versus glimepiride monotherapy for type 2 diabetes (LEAD-3 Mono): a randomised, 52-week, phase III, double-blind, parallel-treatment trial. *Lancet*. 2009;373(9662):473–481.
  73. Richter B, Bandeira-Echtler E, Bergerhoff K, Lerch CL. Dipeptidyl peptidase-4 (DPP-4) inhibitors for type 2 diabetes mellitus. *Cochrane Database Syst Rev*. 2008;2:CD006739.
  74. Wu D, Li L, Liu C. Efficacy and safety of dipeptidyl peptidase-4 inhibitors and metformin as initial combination therapy and as monotherapy in patients with type 2 diabetes mellitus: a meta-analysis. *Diabetes Obes Metab*. 2014;16(1):30–37.
  75. Scheen AJ. DPP-4 inhibitors in the management of type 2 diabetes: a critical review of head-to-head trials. *Diabetes Metab*. 2012;38:89–101.
  76. McIntosh B, Cameron C, Singh SR, et al. Second-line therapy in patients with type 2 diabetes inadequately controlled with metformin monotherapy: a systematic review and mixed-treatment comparison meta-analysis. *Open Med*. 2011;5:e35–e48.
  77. Singh-Franco D, Perez A, Harrington C. The effect of pramlintide acetate on glycemic control and weight in patients with type 2 diabetes mellitus and in obese patients without diabetes: a systematic review and meta-analysis. *Diabetes Obes Metab*. 2011;13:169–180.
  78. Ferrannini E, Solini A. SGLT2 inhibition in diabetes mellitus: rationale and clinical prospects. *Nat Rev Endocrinol*. 2012;8:495–502.
  79. Greenway FL, Fujioka K, Plodkanski RA, et al. COR I Study Group. *Lancet*. 2010;376:595–605.
  80. McDonnell ME. Combination therapy with new targets in type 2 diabetes: a review of available agents with a focus on pre-exercise adjustment. *J Cardiopulm Rehabil Prev*. 2007;27:193–201.
  81. Nathan DM, Buse JB, Davidson MB, et al. Medical management of hyperglycemia in type 2 diabetes: a consensus algorithm for the initiation and adjustment of therapy: a consensus statement of the American Diabetes Association and the European Association for the Study of Diabetes. *Diabetes Care*. 2009;32:193–203.
  82. Jacob AN, Salinas K, Adams-Huet B, Raskin P. Weight gain in type 2 diabetes mellitus. *Diabetes Obes Metab*. 2007;9:386–393.
  83. Raslová K, Tamer SC, Clauson P, Karl D. Insulin detemir results in less weight gain than NPH insulin when used in basal-bolus therapy for type 2 diabetes mellitus, and this advantage increases with baseline body mass index. *Clin Drug Investig*. 2007;27:279–285.
  84. Hermansen K, Davies M. Does insulin detemir have a role in reducing risk of insulin-associated weight gain? *Diabetes Obes Metab*. 2007;9:209–217.
  85. Holman RR, Thorne KI, Farmer AJ, et al. Addition of biphasic, prandial, or basal insulin to oral therapy in type 2 diabetes. *N Engl J Med*. 2007;357:1716–1730.
  86. Goudswaard AN, Furlong NJ, Rutten GE, Stolk RP, Valk GD. Insulin monotherapy versus combinations of insulin with oral hy-



- poglycaemic agents in patients with type 2 diabetes mellitus. *Cochrane Database Syst Rev.* 2004;4:CD003418.
87. Chow CC, Tsang LW, Sorensen JP, Cockram CS. Comparison of insulin with or without continuation of oral hypoglycemic agents in the treatment of secondary failure in NIDDM patients. *Diabetes Care.* 1995;18:307–314.
  88. Mäkimmattila S, Nikkilä K, Yki-Järvinen H. Causes of weight gain during insulin therapy with and without metformin in patients with type II diabetes mellitus. *Diabetologia.* 1999;42:406–412.
  89. Hollander PA, Levy P, Fineman MS, et al. Pramlintide as an adjunct to insulin therapy improves long-term glycemic and weight control in patients with type 2 diabetes: a 1-year randomized controlled trial. *Diabetes Care.* 2003;26:784–790.
  90. Aronne L, Fujioka K, Aroda V, et al. Progressive reduction in body weight after treatment with the amylin analog pramlintide in obese subjects: a phase 2, randomized, placebo-controlled, dose-escalation study. *J Clin Endocrinol Metab.* 2007;92:2977–2983.
  91. Hollander P, Raslova K, Skjøth TV, Råstam J, Liutkus JF. Efficacy and safety of insulin detemir once daily in combination with sitagliptin and metformin: the TRANSITION randomized controlled trial. *Diabetes Obes Metab.* 2011;13:268–275.
  92. Buse JB, Bergenstal RM, Glass LC, et al. Use of twice-daily exenatide in basal insulin-treated patients with type 2 diabetes: a randomized, controlled trial. *Ann Intern Med.* 2011;154:103–112.
  93. Contrave [package insert]. Deerfield, IL: Takeda Pharmaceuticals USA Inc. <http://general.takedapharm.com/content/file.aspx?filetypecode=CONTRAVEPI&CountryCode=US&LanguageCode=EN&cacheRandomizer=bc8d4bba-8158-44f2-92b3-1e1ba338af0a>. Accessed January 5, 2015.
  94. Holman RR, Farmer AJ, Davies MJ, et al. Three-year efficacy of complex insulin regimens in type 2 diabetes. *N Engl J Med.* 2009;361:1736–1747.
  95. Wing LM, Reid CM, Ryan P, et al. A comparison of outcomes with angiotensin-converting–enzyme inhibitors and diuretics for hypertension in the elderly. *N Engl J Med.* 2003;348:583–592.
  96. Manrique C, Whaley-Connell A, Sowers JR. Nebivolol in obese and non-obese hypertensive patients. *J Clin Hypertens (Greenwich).* 2009;11:309–315.
  97. Sharma AM, Pischon T, Hardt S, Kunz I, Luft FC. Hypothesis:  $\beta$ -adrenergic receptor blockers and weight gain: a systematic analysis. *Hypertension.* 2001;37:250–254.
  98. Messerli FH, Bell DS, Fonseca V, et al. Body weight changes with  $\beta$ -blocker use: results from GEMINI. *Am J Med.* 2007;120:610–615.
  99. Serretti A, Mandelli L. Antidepressants and body weight: a comprehensive review and meta-analysis. *J Clin Psychiatry.* 2010;71:1259–1272.
  100. Rosenzweig-Lipson S, Beyer CE, Hughes ZA, et al. Differentiating antidepressants of the future: efficacy and safety. *Pharmacol Ther.* 2007;113:134–153.
  101. Nutt DJ. Tolerability and safety aspects of mirtazapine. *Hum Psychopharmacol.* 2002;17(suppl 1):S37–S41.
  102. Weber E, Stack J, Pollock BG, et al. Weight change in older depressed patients during acute pharmacotherapy with paroxetine and nortriptyline: a double-blind randomized trial. *Am J Geriatr Psychiatry.* 2000;8:245–250.
  103. Gadde KM, Xiong GL. Bupropion for weight reduction. *Expert Rev Neurother.* 2007;7:17–24.
  104. Allison DB, Casey DE. Antipsychotic-induced weight gain: a review of the literature. *J Clin Psychiatry.* 2001;62(suppl 7):22–31.
  105. Kurzthaler I, Fleischhacker WW. The clinical implications of weight gain in schizophrenia. *J Clin Psychiatry.* 2001;62(Suppl 7):32–37.
  106. Henderson DC, Cagliero E, Gray C, et al. Clozapine, diabetes mellitus, weight gain, and lipid abnormalities: a five-year naturalistic study. *Am J Psychiatry.* 2000;157:975–981.
  107. Lieberman JA, Stroup TS, McEvoy JP, et al. Effectiveness of anti-psychotic drugs in patients with chronic schizophrenia. *N Engl J Med.* 2005;353:1209–1223.
  108. Simpson GM, Glick ID, Weiden PJ, Romano SJ, Siu CO. Randomized, controlled, double-blind multicenter comparison of the efficacy and tolerability of ziprasidone and olanzapine in acutely ill inpatients with schizophrenia or schizoaffective disorder. *Am J Psychiatry.* 2004;161:1837–1847.
  109. Komossa K, Rummel-Kluge C, Hunger H, et al. Ziprasidone versus other atypical antipsychotics for schizophrenia. *Cochrane Database Syst Rev.* 2009;4:CD006627.
  110. Maayan L, Correll CU. Weight gain and metabolic risks associated with antipsychotic medications in children and adolescents. *J Child Adolesc Psychopharmacol.* 2011;21:517–535.
  111. Ballon JS, Pajvani U, Freyberg Z, Leibel RL, Lieberman JA. Molecular pathophysiology of metabolic effects of antipsychotic medications. *Trends Endocrinol Metab.* 2014;25(11):593–600.
  112. Ben-Menachem E. Weight issues for people with epilepsy—a review. *Epilepsia.* 2007;48(suppl 9):42–45.
  113. Verrotti A, D’Egidio C, Mohn A, Coppola G, Chiarelli F. Weight gain following treatment with valproic acid: pathogenetic mechanisms and clinical implications. *Obes Rev.* 2011;12:e32–e43.
  114. Corman CL, Leung NM, Guberman AH. Weight gain in epileptic patients during treatment with valproic acid: a retrospective study. *Can J Neurol Sci.* 1997;24:240–244.
  115. DeToledo JC, Toledo C, DeCerce J, Ramsay RE. Changes in body weight with chronic, high-dose gabapentin therapy. *Ther Drug Monit.* 1997;19:394–396.
  116. Jallon P, Picard F. Bodyweight gain and anticonvulsants: a comparative review. *Drug Saf.* 2001;24:969–978.
  117. Gaspari CN, Guerreiro CA. Modification in body weight associated with antiepileptic drugs. *Arq Neuropsiquiatr.* 2010;68:277–281.
  118. Gallo MF, Lopez LM, Grimes DA, Carayon F, Schulz KF, Helmerhorst FM. Combination contraceptives: effects on weight. *Cochrane Database Syst Rev.* 2014;1:CD003987.
  119. Lopez LM, Edelman A, Chen M, Otterness C, Trussell J, Helmerhorst FM. Progestin-only contraceptives: effects on weight. *Cochrane Database Syst Rev.* 2013;7:CD008815.
  120. Stricker RB, Goldberg B. Weight gain associated with protease inhibitor therapy in HIV-infected patients. *Res Virol.* 1998;149:123–126.
  121. Reust CE. Common adverse effects of antiretroviral therapy for HIV disease. *Am Fam Physician.* 2011;83:1443–1451.
  122. Sutbeyaz ST, Sezer N, Koseoglu BF, Ibrahimoglu F, Tekin D. Influence of knee osteoarthritis on exercise capacity and quality of life in obese adults. *Obesity.* 2007;15:2071–2076.
  123. Da Silva JA, Jacobs JW, Bijlsma JW. Revisiting the toxicity of low-dose glucocorticoids: risks and fears. *Ann NY Acad Sci.* 2006;1069:275–288.
  124. Jacobs JW, Boers M, Kirwan JR, Bijlsma JW. The benefit of low-dose glucocorticoid treatment in early rheumatoid arthritis may outweigh the risk: comment on the editorial by Harris. *Arthritis Rheum.* 2006;54(6):2031–2032; author reply 2032.
  125. Landewé RB, Boers M, Verhoeven AC, et al. COBRA combination therapy in patients with early rheumatoid arthritis: long-term structural benefits of a brief intervention. *Arthritis Rheum.* 2002;46:347–356.
  126. Boers M, van der Heijde DM. Prevention or retardation of joint damage in rheumatoid arthritis: issues of definition, evaluation and interpretation of plain radiographs. *Drugs.* 2002;62(12):1717–1724.
  127. Prummel MF, Mourits MP, Blank L, Berghout A, Koornneef L, Wiersinga WM. Randomized double-blind trial of prednisone versus radiotherapy in Graves’ ophthalmopathy. *Lancet.* 1993;342(8877):949–954.
  128. Aronne LJ. Drug-induced weight gain: non-CNS medications. In: Aronne LJ, ed. *A Practical Guide to Drug-Induced Weight Gain.* Minneapolis, MN: McGraw-Hill; 2002:77–91.

129. Ratliff JC, Barber JA, Palmese LB, Reutenauer EL, Tek C. Association of prescription H1 antihistamine use with obesity: results from the National Health and Nutrition Examination Survey. *Obesity (Silver Spring)*. 2010;18:2398–2400.
130. Weintraub M, Sundareshan PR, Schuster B, et al. Long-term weight control study. II (weeks 34 to 104). An open-label study of continuous fenfluramine plus phentermine versus targeted intermittent medication as adjuncts to behavior modification, caloric restriction, and exercise. *Clin Pharmacol Ther*. 1992;51:595–601.
131. Hendricks EJ, Srisurapanont M, Schmidt SL, et al. Addiction potential of phentermine prescribed during long-term treatment of obesity. *Int J Obes (Lond)*. 2014;38:292–298.
132. Cohen, RV, Pinheiro JC, Schiavon CA, Salles JE, Wajchenberg BL, Cummings DE. Effects of gastric bypass surgery in patients with type 2 diabetes and only mild obesity. *Diabetes Care*. 2012;35:1420–1428.
133. Mingrone G, Panunzi S, De Gaetano A, et al. Bariatric surgery versus conventional medical therapy for type 2 diabetes. *N Engl J Med*. 2012;366:1577–1585.
134. Schauer PR, Kashyap SR, Wolski K, et al. Bariatric surgery versus intensive medical therapy in obese patients with diabetes. *N Engl J Med*. 2012;366:1567–1576.
135. Buchwald H, Estok R, Fahrbach K, et al. Weight and type 2 diabetes after bariatric surgery: systematic review and meta-analysis. *Am J Med*. 2009;122:248–256.e5.
136. Ilanne-Parikka P, Eriksson JG, Lindström J, et al. Effect of lifestyle intervention on the occurrence of metabolic syndrome and its components in the Finnish Diabetes Prevention Study. *Diabetes Care*. 2008;31:805–807.
137. Phelan S, Wadden TA, Berkowitz RI, et al. Impact of weight loss on the metabolic syndrome. *Int J Obes (Lond)*. 2007;31:1442–1448.
138. Zanella MT, Uehara MH, Ribeiro AB, Bertolami M, Falsetti AC, Yunes MA. Orlistat and cardiovascular risk profile in hypertensive patients with metabolic syndrome: the ARCOS study. *Arq Bras Endocrinol Metabol*. 2006;50:368–376.
139. Wannamethee SG, Shaper AG, Walker M. Overweight and obesity and weight change in middle aged men: impact on cardiovascular disease and diabetes. *J Epidemiol Community Health*. 2005;59:134–139.
140. Andersen T, Gluud C, Franzmann MB, Christoffersen P. Hepatic effects of dietary weight loss in morbidly obese subjects. *J Hepatol*. 1991;12:224–229.
141. Huang MA, Greenon JK, Chao C, et al. One-year intense nutritional counseling results in histological improvement in patients with non-alcoholic steatohepatitis: a pilot study. *Am J Gastroenterol*. 2005;100:1072–1081.
142. Palmer M, Schaffner F. Effect of weight reduction on hepatic abnormalities in overweight patients. *Gastroenterology*. 1990;99(5):1408–1413.
143. Ueno T, Sugawara H, Sujaku K, et al. Therapeutic effects of restricted diet and exercise in obese patients with fatty liver. *J Hepatol*. 1997;27:103–107.
144. Christensen R, Bartels EM, Astrup A, Bliddal H. Effect of weight reduction in obese patients diagnosed with knee osteoarthritis: a systematic review and meta-analysis. *Ann Rheum Dis*. 2007;66:433–439.
145. Fransen M. Dietary weight loss and exercise for obese adults with knee osteoarthritis: modest weight loss targets, mild exercise, modest effects. *Arthritis Rheum*. 2004;50:1366–1369.
146. Huang MH, Chen CH, Chen TW, Weng MC, Wang WT, Wang YL. The effects of weight reduction on the rehabilitation of patients with knee osteoarthritis and obesity. *Arthritis Care Res*. 2000;13:398–405.
147. Messier SP, Loeser RF, Miller GD, et al. Exercise and dietary weight loss in overweight and obese older adults with knee osteoarthritis: the Arthritis, Diet, and Activity Promotion Trial. *Arthritis Rheum*. 2004;50:1501–1510.
148. van Gool CH, Penninx BW, Kempen GI, et al. Effects of exercise adherence on physical function among overweight older adults with knee osteoarthritis. *Arthritis Rheum*. 2005;53:24–32.
149. Adams TD, Stroup AM, Gress RE, et al. Cancer incidence and mortality after gastric bypass surgery. *Obesity*. 2009;17:796–802.
150. Sjöström L, Gummesson A, Sjöström CD, et al. Effects of bariatric surgery on cancer incidence in obese patients in Sweden (Swedish Obese Subjects Study): a prospective, controlled intervention trial. *Lancet Oncol*. 2009;10:653–662.
151. Kuna ST, Reboussin DM, Borradaile KE, et al. Long-term effect of weight loss on obstructive sleep apnea severity in obese patients with type 2 diabetes. *Sleep*. 2013;36:641–649A.
152. van de Laar FA, Lucassen PL, Akkermans RP, et al. Alpha-glucosidase inhibitors for patients with type 2 diabetes: results from a Cochrane systematic review and meta-analysis. *Diabetes Care*. 2005; 28(1):154–163.
153. Lee A, Patrick P, Wishart J, Horowitz M, Morley JE. The effects of miglitol on glucagon-like peptide-1 secretion and appetite sensations in obese type 2 diabetics. *Diabetes Obes Metab*. 202;4(5):329–335.

Original Article

# Addiction potential of phentermine prescribed during long-term treatment of obesity

E J Hendricks, M Srisurapanont, S L Schmidt, M Haggard, S Souter, C L Mitchell, D G De Marco, M J Hendricks, Y Istratiy & F L Greenway

*International Journal of Obesity* **38**, 292–298 (2014)

doi:10.1038/ijo.2013.74

Download Citation

Addiction Drug therapy Obesity

Received: 11 February 2013

Revised: 07 April 2013

Accepted: 10 April 2013

Published online: 17 May 2013

## Abstract

---

### Objective:

To investigate if phentermine treatment induces phentermine abuse, psychological dependence (addiction) or phentermine drug craving in overweight, obese and weight loss maintenance patients. To investigate whether amphetamine-like withdrawal occurs after abrupt cessation of long-term phentermine treatment.

### Design:

Clinical intervention trial with interruption of phentermine treatment in long-term patients.

### Subjects:

269 obese, overweight or formerly obese subjects (age: 20–88 years, BMI: 21–74 kg m<sup>-2</sup>) treated with phentermine long-term (LTP, N=117), 1.1–21.1 years, or short-term (ATP, N=152), 4–22 days, with phentermine doses of 18.75–112.5 (LTP) and 15–93.75 (ATP) mg per day.

## Measurements:

Module K of the Mini International Neuropsychiatric Interview modified for phentermine (MINI-SUD), Severity of Dependence Scale (SDS), 45-item Cocaine Craving Questionnaire-NOW (CCQ-NOW) modified for phentermine (PCQ-NOW), and Amphetamine Withdrawal Questionnaire (AWQ) modified for phentermine (PWQ).

## Results:

MINI-SUD interviews were negative for phentermine abuse or psychological dependence in all LTP patients. SDS examination scores were low for all LTP and ATP patients, indicating they were not psychologically dependent upon phentermine. PCQ-NOW scores were low for all LTP and ATP patients, indicating neither short-term nor long-term phentermine treatment had induced phentermine craving. Other than an increase in hunger or eating, amphetamine-like withdrawal symptoms did not occur upon abrupt phentermine cessation as measured by sequential PWQ scores.

## Conclusions:

Phentermine abuse or psychological dependence (addiction) does not occur in patients treated with phentermine for obesity. Phentermine treatment does not induce phentermine drug craving, a hallmark sign of addiction. Amphetamine-like withdrawal does not occur upon abrupt treatment cessation even at doses much higher than commonly recommended and after treatment durations of up to 21 years.

Subscribe to *International Journal of Obesity* for full access:

**\$652**

Subscribe

READCUBE ACCESS:

**\$4.99**

rent

**\$20.00**

buy

Buy/Rent now

**Additional access options:**

Already a subscriber? [Log in now](#) or [Register](#) for online access.

[Login via Athens](#) | [Login via Shibboleth](#) | [Use a document delivery service](#) | [Purchase a site license](#)

## References

---

1. Samaranayake NR, Ong KL, Leung RY, Cheung BM. Management of obesity in the National Health and Nutrition Examination Survey (NHANES), 2007-2008. *Ann Epidemiol* 2012; **22**: 349-353.

---

2. Colman E. Anorectics on trial: a half century of federal regulation of prescription appetite suppressants. *Ann Intern Med* 2005; **143**: 380-385.

---

3. Glazer G. Long-term pharmacotherapy of obesity 2000: a review of efficacy and safety. *Arch Intern Med* 2001; **161**: 1814-1824.

---

4. Ioannides-Demos LL, Piccenna L, McNeil JJ. Pharmacotherapies for obesity: past, current, and future therapies. *J Obes* 2011; **2011**: 179674.

---

5. Kang JG, Park CY, Kang JH, Park YW, Park SW. Randomized controlled trial to investigate the effects of a newly developed formulation of phentermine diffuse-controlled release for obesity. *Diabetes Obes Metab* 2010; **12**: 876-882.

---

6. Kim KK, Cho HJ, Kang HC, Youn BB, Lee KR. Effects on weight reduction and safety of short-term phentermine administration in Korean obese people. *Yonsei Med J* 2006; **47**: 614-625.

---

7. Frank A. The long-term management of obesity with continuing pharmacotherapy. *Obes Res* 2004; **12**: 1821-1827.

---

8. Hendricks EJ, Greenway FL, Westman EC, Gupta AK. Blood pressure and heart rate effects, weight loss and maintenance during long-term phentermine pharmacotherapy for obesity. *Obesity (Silver Spring)* 2011; **19**: 2351-2360.

---



9. Rothman RB. Treatment of obesity with 'combination' pharmacotherapy. *Am J Ther* 2010; **17**: 596–603.

---

10. Hendricks EJ, Rothman RB, Greenway FL. How physician obesity specialists use drugs to treat obesity. *Obesity (Silver Spring)* 2009; **17**: 1730–1735.

---

11. Hendricks EJ, Greenway FL. A study of abrupt phentermine cessation in patients in a weight management program. *Am J Ther* 2011; **18**: 292–299.

---

12. Sheehan DV, Lecrubier Y, Sheehan KH, Amorim P, Janavs J, Weiller E *et al.* The Mini-International Neuropsychiatric Interview (M.I.N.I.): the development and validation of a structured diagnostic psychiatric interview for DSM-IV and ICD-10. *J Clin Psychiatry* 1998; **59** (Suppl 20): 22–33 quiz 34–57.

---

13. Gossop M, Darke S, Griffiths P, Hando J, Powis B, Hall W *et al.* The Severity of Dependence Scale (SDS): psychometric properties of the SDS in English and Australian samples of heroin, cocaine and amphetamine users. *Addiction* 1995; **90**: 607–614.

---

14. Tiffany ST, Singleton E, Haertzen CA, Henningfield JE. The development of a cocaine craving questionnaire. *Drug Alcohol Depend* 1993; **34**: 19–28.

---

15. McGregor C Amphetamine withdrawal:nature, time course, and treatment. PhD Thesis. Department of Clinical and Experimental Pharmacology, University of Adelaide, Adelaide, 2005, 224pp.

---

16. Srisurapanont M, Jarusuraisin N, Jittiwutikan J. Amphetamine withdrawal: I. Reliability, validity and factor structure of a measure. *Aust N Z J Psychiatry* 1999; **33**: 89–93.

---

17. Heinz AJ, Epstein DH, Schroeder JR, Singleton EG, Heishman SJ, Preston KL. Heroin and cocaine craving and use during treatment: measurement validation and potential relationships. *J Subst Abuse Treat* 2006; **31**: 355–364.

---

18. Bruno R, Matthews AJ, Topp L, Degenhardt L, Gomez R, Dunn M. Can the severity of dependence scale be usefully applied to 'ecstasy'? *Neuropsychobiology* 2009; **60**: 137–147.

---

19. Topp L, Mattick RP. Choosing a cut-off on the Severity of Dependence Scale (SDS) for amphetamine users. *Addiction* 1997; **92**: 839–845.

---

20. Kaye S, Darke S. Determining a diagnostic cut-off on the Severity of Dependence Scale (SDS) for cocaine dependence. *Addiction* 2002; **97**: 727–731.

---

21. Martin G, Copeland J, Gates P, Gilmour S. The Severity of Dependence Scale (SDS) in an adolescent population of cannabis users: reliability, validity and diagnostic cut-off. *Drug Alcohol Depend* 2006; **83**: 90–93.

---

22. Tiffany ST, Wray JM. The clinical significance of drug craving. *Ann N Y Acad Sci* 2012; **1248**: 1–17.

---

23. Newton TF, De La Garza R 2nd, Kalechstein AD, Tziortzis D, Jacobsen CA. Theories of addiction: methamphetamine users' explanations for continuing drug use and relapse. *Am J Addict* 2009; **18**: 294–300.

---

24. McGregor C, Srisurapanont M, Jittiwutikarn J, Laobhripatr S, Wongtan T, White JM. The nature, time course and severity of methamphetamine withdrawal. *Addiction* 2005; **100**: 1320–1329.

---

25. van Rossum JM, Simons F. Locomotor activity and anorexogenic action. *Psychopharmacologia* 1969; **14**: 248–254.

---

26. Srisurapanont M, Arunpongpaisal S, Wada K, Marsden J, Ali R, Kongsakon R. Comparisons of methamphetamine psychotic and schizophrenic symptoms: a differential item functioning analysis. *Prog Neuropsychopharmacol Biol Psychiatry* 2011; **35**: 959–964.

---

27. Kish SJ. Pharmacologic mechanisms of crystal meth. *CMAJ* 2008; **178**: 1679–1682.

---

28. Zorick T, Nestor L, Miotto K, Sugar C, Hellemann G, Scanlon G *et al.* Withdrawal symptoms in abstinent methamphetamine-dependent subjects. *Addiction* 2010; **105**: 1809–1818.

---

29. Brauer LH, Johanson CE, Schuster CR, Rothman RB, de Wit H. Evaluation of phentermine and fenfluramine, alone and in combination, in normal, healthy volunteers. *Neuropsychopharmacology* 1996; **14**: 233–241.

---

30. Jasinski DR, Faries DE, Moore RJ, Schuh LM, Allen AJ. Abuse liability assessment of atomoxetine in a drug-abusing population. *Drug Alcohol Depend* 2008; **95**: 140–146.

---

31. Schoedel KA, Addy C, Chakraborty B, Rosko K, Dunbar S, Maes A *et al.* Human abuse potential and cognitive effects of taranabant, a cannabinoid 1 receptor inverse agonist: a randomized, double-blind, placebo- and active-controlled, crossover study in recreational polydrug users. *J Clin Psychopharmacol* 2012; **32**: 492–502.

---

32. Couper FJ, Pemberton M, Jarvis A, Hughes M, Logan BK. Prevalence of drug use in commercial tractor-trailer drivers. *J Forensic Sci* 2002; **47**: 562–567.

---

33. Lee S, Kim J, In S, Choi H, Chung H, Chung KH. Detection of phentermine in hair samples from drug suspects. *Forensic Sci Int* 2011; **207**: e5–e7.

---

34. Jain NC, Budd RD, Sneath TC. Frequency of use or abuse of amphetamine-related drugs. *Am J Drug Alcohol Abuse* 1979; **6**: 53–57.

---

35. Greene WM, Sylvester M, Abraham J. Addiction liability of pharmacotherapeutic interventions in obesity. *Curr Pharm Des* 2011; **17**: 1188–1192.

---

36. American Psychiatric Association. *Diagnostic and Statistical Manual of Mental Disorders* 4th edn American Psychiatric Association: Washington, DC, USA, 2000.

---

37. O'Brien CP, Volkow N, Li TK. What's in a word? Addiction versus dependence in DSM-V. *Am J Psychiatry* 2006; **163**: 764–765.

---

38. Kampman KM, Volpicelli JR, McGinnis DE, Alterman AI, Weinrieb RM, D'Angelo L et al. Reliability and validity of the Cocaine Selective Severity Assessment. *Addict Behav* 1998; **23**: 449–461.
- 
39. Shoptaw SJ, Kao U, Heinzerling K, Ling W. Treatment for amphetamine withdrawal. *Cochrane Database Syst Rev* 2009; CD003021 doi: 10.1002/14651858.
- 
40. Ahmadi J, Kampman K, Dackis C. Outcome predictors in cocaine dependence treatment trials. *Am J Addict* 2006; **15**: 434–439.
- 
41. Ahmadi J, Kampman KM, Oslin DM, Pettinati HM, Dackis C, Sparkman T. Predictors of treatment outcome in outpatient cocaine and alcohol dependence treatment. *Am J Addict* 2009; **18**: 81–86.
- 

## Author information

---

### Affiliations

Center for Weight Management, Roseville, CA, USA

E J Hendricks, M Haggard, S Souter, C L Mitchell, D G De Marco, M J Hendricks & Y Istratiy

Department of Psychiatry, Chiang Mai University, Chiang Mai, Thailand

M Srisurapanont

Department of Endocrinology, Metabolism & Diabetes, University of Colorado, Anschutz Medical Campus, Aurora, CO, USA

S L Schmidt

Pennington Biomedical Research Center of the Louisiana State University System, Baton Rouge, LA, USA

F L Greenway

### Competing interests

Dr Hendricks has received honoraria from Akramax Pharmaceuticals, Eurodrug Laboratories, Citius Pharmaceuticals and Vivus pharmaceuticals. Dr Greenway has received honoraria from Baronova, Basic Research, Citius, Diabetic Living, Eisai, GNC, Jenny Craig, Lithera, Merck, Naturalpha, Nume Health, Orexigen, Plensat, Takeda, Thetis, Unigene and Zafgen. The remaining authors declare no conflict of interest.

### **Corresponding author**

Correspondence to E J Hendricks.

*International Journal of Obesity* ISSN 1476-5497 (online)

---

**SPRINGER NATURE**

© 2018 Macmillan Publishers Limited, part of Springer Nature. All rights reserved.

# Safety and Effectiveness of Longer-Term Phentermine Use: Clinical Outcomes from an Electronic Health Record Cohort

Kristina H. Lewis<sup>1,2</sup>, Heidi Fischer<sup>3</sup>, Jany Ard<sup>3</sup>, Lee Barton<sup>3</sup>, Daniel H. Bessessen<sup>4</sup>, Matthew F. Daley<sup>5</sup>, Jay Desai<sup>6</sup>, Stephanie L. Fitzpatrick<sup>7</sup>, Michael Horber<sup>8</sup>, Corinna Koebnick<sup>3</sup>, Caryn Oshiro<sup>9</sup>, Aya Yamamoto<sup>3</sup>, Deborah R. Young<sup>3</sup>, and David E. Arterburn<sup>10</sup>

**Objective:** The aim of this work was to study weight loss and risk of cardiovascular disease (CVD) or death associated with longer-term phentermine use.

**Methods:** Using electronic health record data, 13,972 adults were identified with a first phentermine fill in 2010 to 2015, creating exposure categories according to a patient's duration of use (referent:  $\leq 3$  months). Multivariable linear models were used to compare percent weight loss across categories at 6, 12, and 24 months, and Cox proportional hazards models were used to compare risk of composite CVD or death, up to 3 years after starting phentermine.

**Results:** The cohort was 84% female and 45% white, with a mean (SD) baseline age 43.5 (10.7) years and BMI of 37.8 (7.2) kg/m<sup>2</sup>. In multivariable models, longer-term users of phentermine experienced more weight loss; patients using continuously for  $> 12$  months lost 7.4% more than the referent group at 24 months ( $P < 0.001$ ). The composite CVD or death outcome was rare (0.3%, 41 events), with no significant difference in hazard ratios between groups.

**Conclusions:** Greater weight loss without increased risk of incident CVD or death was observed in patients using phentermine monotherapy for longer than 3 months. Despite the limitations of the observational design, this study supports the effectiveness and safety of longer-term phentermine use for low-risk individuals.

*Obesity* (2019) 27, 591-602. doi:10.1002/oby.22430

## Introduction

Lifestyle interventions remain the cornerstone of treatment for patients with obesity, typically yielding a peak weight loss of 5% to 10% after 6 months (1). However, up to one-third of patients do not respond to such programs (2,3), and weight regain is common following intervention cessation (4,5). Pharmacotherapy can increase the proportion of individuals who respond to lifestyle interventions as well as the duration and magnitude of response (6). Clinically significant durable weight loss has been demonstrated in placebo-controlled trials of antiobesity medications (7-14), but broader use of medications

remains limited because of concerns about cost, efficacy, and adverse events (15). The most commonly used weight-loss medication in the United States is phentermine (16,17), a sympathomimetic amine that acts by inhibiting appetite and that was originally approved for weight loss in 1959 (18,19). Most studies examining phentermine monotherapy have limited treatment duration to less than 12 weeks (20), aligning with a package insert that recommends that the medication be used as "a short-term adjunct (a few weeks)" to lifestyle-based programs (21). Concerns about longer-term phentermine use include increased risk

<sup>1</sup> Department of Epidemiology and Prevention, Division of Public Health Sciences, Wake Forest School of Medicine, Winston-Salem, North Carolina, USA. Correspondence: Kristina H. Lewis (khlewis@wakehealth.edu) <sup>2</sup> Department of Implementation Science, Division of Public Health Sciences, Wake Forest School of Medicine, Winston-Salem, North Carolina, USA. <sup>3</sup> Department of Research and Evaluation, Kaiser Permanente Southern California, Pasadena, California, USA <sup>4</sup> Diabetes & Endocrinology Division, Denver Health Medical Center, Denver, Colorado, USA <sup>5</sup> Institute for Health Research, Kaiser Permanente Colorado, Aurora, Colorado, USA <sup>6</sup> HealthPartners Institute, Bloomington, Minnesota, USA <sup>7</sup> Kaiser Permanente Center for Health Research, Portland, Oregon, USA <sup>8</sup> Mid-Atlantic Permanente Research Institute, Kaiser Permanente Mid-Atlantic States, Rockville, Maryland, USA <sup>9</sup> Center for Health Research, Kaiser Permanente Hawaii, Honolulu, Hawaii, USA <sup>10</sup> Kaiser Permanente Washington Health Research Institute, Seattle, Washington, USA.

**Funding agencies:** This work was supported by Patient-Centered Outcomes Research Institute (PCORI) as part of the Patient Outcomes Research to Advance Learning (PORTAL) project (PCORI CD RN 1306-04681).  
**Disclosure:** The authors declared no conflicts of interest.  
**Author contributions:** Study concept and design: KHL, DEA, and JA; acquisition, analysis, and interpretation of data: all authors; drafting of manuscript: KHL and HF; critical revision of manuscript: all authors; statistical analysis plan: HF, KHL, and DEA; graphical support: CK; supervision: KHL, DEA, and DRY.  
**Received:** 9 November 2018; **Accepted:** 9 January 2019; **Published online 22 March 2019.** doi:10.1002/oby.22430

of cardiovascular disease (CVD) (6,17) and potential for addiction (22).

Weight-loss treatment approaches are evolving to favor long-term therapy, aligning with the new chronic disease model of obesity. Newer antiobesity medications have, accordingly, been approved by the Food and Drug Administration (FDA) for long-term use (i.e., more than 12 months) (20). If phentermine monotherapy, which is widely available and low cost, was found to be safe and effective for long-term use, the impact for obesity treatment could be significant.

Using data from electronic health records (EHRs), we studied whether adults prescribed phentermine for longer than 12 weeks experienced differential weight loss, change in blood pressure (BP) or heart rate (HR), or increased risk of incident CVD or death compared with adults prescribed phentermine in an on-label short-term episode. Our primary hypothesis was that longer-term users would experience greater weight loss without increased risk of CVD or death.

## Methods

### Study design, health care systems, and data sources

The data sources for this retrospective cohort study were EHRs abstracted from the Patient Outcomes Research to Advance Learning (PORTAL) cohort, a collaborative data effort across several integrated health insurance and care-delivery systems in the United States as part of the National Patient-Centered Clinical Research Network (PCORnet) initiative (23,24). Data elements included membership status, demographics, vital signs, health care use, laboratory values, and pharmacy dispensing. This cohort included data from Kaiser Permanente (Southern California, Colorado, Northwest, Washington state, Hawaii, and Mid-Atlantic States [Maryland, Virginia, District of Columbia]) and from Denver Health and HealthPartners (Minnesota). The study was approved by the Kaiser Permanente Southern California Institutional Review Board, with other sites ceding primary review.

### Study population

We identified adult health plan members 18 to 64 years old with a “first” phentermine fill (dose  $\leq 37.5$  mg/d) between January 1, 2010, and September 30, 2015. To find likely incident users, we limited selection to patients with at least 12 months of continuous baseline enrollment, during which there were no prior phentermine prescriptions (25). We chose the study end date to coincide with the *International Classification of Diseases, Ninth Revision to Tenth Revision* transition, after which changes in diagnosis coding could have led to systematic differences in detection of outcomes and covariates.

We required patients to have BMI  $\geq 27$  kg/m<sup>2</sup> within 3 months prior to their first phentermine fill. We excluded those with history of bariatric surgery or cancer diagnosis (other than nonmelanoma skin cancer). We also excluded anyone with baseline year evidence of pregnancy, use of other weight-loss medications, palliative care encounters, or diagnosis and/or procedure codes for any cardiovascular outcomes of interest, including myocardial infarction, stroke, angina, coronary artery bypass grafting, or carotid artery procedures (Figure 1). Weight, BP, and HR analyses were limited to individuals with at least one relevant measurement before and after initiating phentermine.

## Exposure

Our exposure of interest was a patient’s pattern of phentermine use in follow-up, characterized based on duration and persistence of use. For each individual, we first created episodes of phentermine use and mapped them across follow-up time (26-28). See Supporting Information Figure S1 for details on how episodes were created.

Individuals with one phentermine treatment episode lasting  $\leq 112$  days and no subsequent use during follow-up were treated as our referent or “short-term” use group, reflecting FDA-approved use of the medication. This episode duration ( $\leq 112$  days) was based on multiplying the on-label duration of 90 days by a factor of 1.25 to account for days in the episode when a patient was between fills (28). Patients with a single phentermine treatment episode lasting  $> 112$  and up to 365 days, but with no subsequent treatment episodes, were labeled “medium-term continuous” users. Patients with a single continuous episode lasting  $> 365$  days were labeled “long-term continuous” users.

In clinical practice, patients often take phentermine intermittently over time. To separately capture these individuals and allow for follow-up beyond the first treatment episode, we created two additional groups. Persons with two or more separate treatment episodes in which no episode exceeded 112 days were termed “short-term intermittent” users. Those with two or more episodes in which at least one episode exceeded 112 days were termed “medium-term intermittent” users.

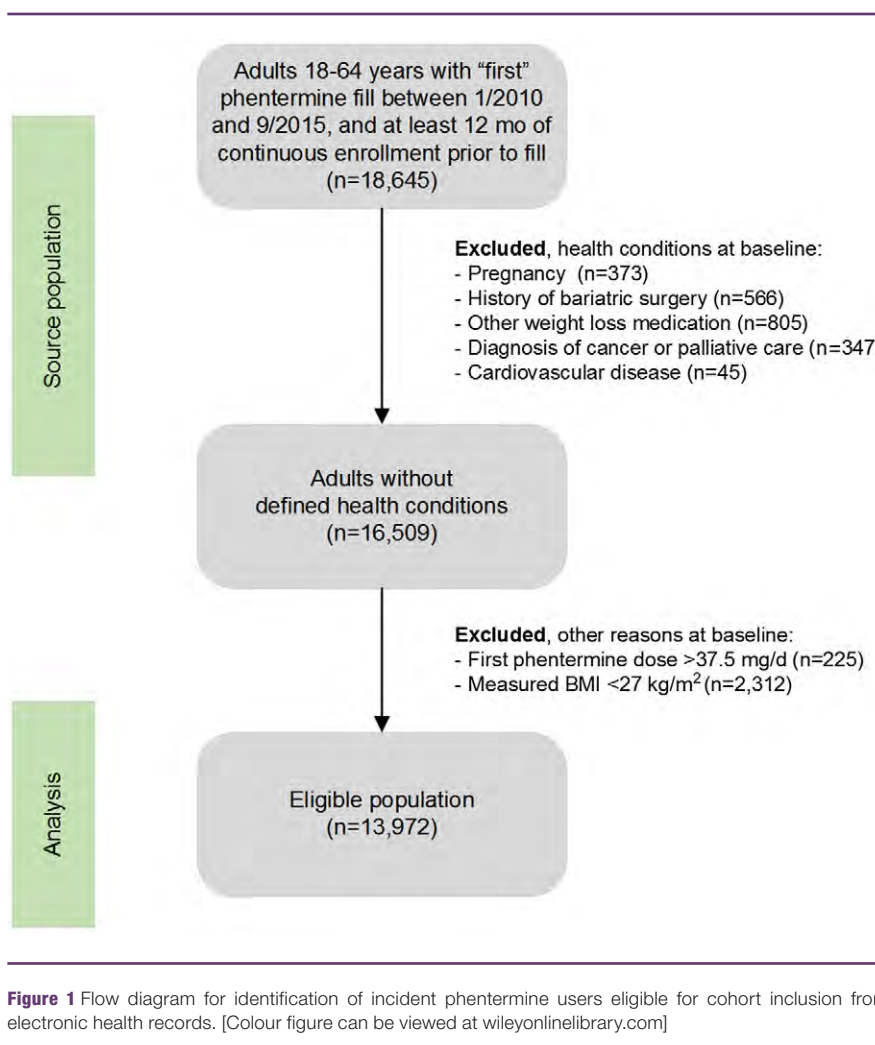
We treated phentermine use as a time-varying exposure. A patient’s inclusion in a particular exposure category was dependent on his or her exposure pattern up to the time point of interest, meaning that patients could change exposure categories over time. For example, at the 6-month mark, we could not yet classify anyone as being in the long-term continuous group because less than a year of phentermine exposure had elapsed. Therefore, these individuals were included in our medium-term continuous group for 6-month analyses, only separating out as a distinct group after 12 months of continuous exposure to phentermine.

## Outcomes

Our outcome for drug effectiveness was percent change in weight from baseline, measured at 6, 12, and 24 months after initial phentermine dispensing. We abstracted all weights recorded in the outpatient setting. We selected baseline weight (kilograms) as the nearest measure on or within 90 days prior to the index date. Because we were working with clinical data, follow-up did not occur precisely at 6, 12, or 24 months for most individuals. We accepted weights for each follow-up point based on a variable window that enlarged as follow-up time progressed. For our 6-month outcome, we accepted the nearest weight measure within  $-30$  to  $+90$  days; at 12 months, we accepted the nearest weight measure within  $-90$  to  $+90$  days; and at 24 months, we accepted the nearest weight measure within  $-180$  to  $+180$  days.

We examined changes in systolic BP (SBP), diastolic BP (DBP) (mmHg), and HR (beats per minute [bpm]) from baseline as intermediate outcomes for cardiovascular risk because of the sympathomimetic effect of phentermine. We derived change in HR, SBP, and DBP from outpatient measures, selecting the nearest measure per window per patient for analysis. Additional rules used for cleaning vital sign data are available in Supporting Information Table S1.

Our distal outcome measure for cardiovascular risk was a composite measure of incident myocardial infarction, stroke, angina, coronary artery



bypass grafting, carotid artery intervention, or death. We abstracted all relevant *International Classification of Diseases, Ninth Revision* diagnosis or procedure and Current Procedural Terminology procedure codes (Supporting Information Table S2) and used a previously published method to assign incident events (29). Information about date of death came from a combination of EHR, administrative, and state mortality databases (30).

### Covariates

All models included EHR-derived covariates for sex, race or ethnicity (non-Hispanic white, non-Hispanic black, Hispanic, Asian, other), age group (18-34, 35-49, 50-64), baseline BMI category (27-29.9, 30-34.9, 35-39.9, 40-49.9, or  $\geq 50$ ), hypertension, diabetes, smoking status, health care system, calendar year of phentermine initiation, and average daily dose category of phentermine (37.5 mg/d or <37.5 mg/d). BP and HR models were adjusted for baseline tertile of each measure.

We used demographic information from geographic information systems to create a covariate for area-level measure of poverty (percent of households in census block below poverty level: <5%, 5% to <10%, 10% to <20% or  $\geq 20\%$ ) (31). We assigned the rare patients missing

phentermine dose ( $n = 39$ ) or poverty ( $n = 538$ ) the modal values for their region.

### Statistical analysis

We built separate multivariable linear models at 6, 12, and 24 months of follow-up to examine the outcomes of percent change in weight and change in SBP, DBP, and HR. In weight analyses, we limited inclusion in the referent group to patients with at least one refill because patients with a single fill were likely intolerant to phentermine. Their inclusion would have biased weight loss results in favor of longer-term users.

We used Cox proportional hazards models with phentermine treated as a time-varying covariate to examine the composite outcome of incident CVD or death in a time-to-event fashion up to 3 years after the index date. Patients achieving any one of the submeasures composing our composite outcome were considered to have the outcome at that time.

Patients were not included in multivariable linear models if any of the following occurred before a time point of interest: health insurance plan disenrollment, > 18 months since any clinical care or encounters



TABLE 1 Characteristics of phentermine users according to final exposure categorization<sup>a</sup>

	On-label users		Off-label users			Total (N = 13,972)
	Short-term referent (n = 6,764)	Short-term intermittent (n = 2,938)	Medium-term continuous (n = 1,703)	Medium-term intermittent (n = 2,423)	Long-term continuous (n = 144)	
<b>Sex<sup>b</sup></b>						
Female	5,611 (83.1%)	2,523 (85.8%)	1,402 (82.3%)	2,047 (84.3%)	116 (80.6%)	11,699 (83.7%)
<b>Race/ethnicity<sup>c</sup></b>						
Non-Hispanic white	3,007 (44.5%)	1,093 (37.2%)	894 (52.5%)	1,181 (48.6%)	80 (55.6%)	6,255 (44.8%)
Non-Hispanic black	1,370 (20.3%)	786 (26.7%)	253 (14.9%)	446 (18.4%)	19 (13.2%)	2,874 (20.6%)
Hispanic	1,749 (25.9%)	764 (26.0%)	367 (21.6%)	564 (23.2%)	27 (18.8%)	3,471 (24.8%)
Asian	305 (4.5%)	137 (4.7%)	101 (5.9%)	107 (4.4%)	12 (8.3%)	662 (4.7%)
Other	324 (4.8%)	162 (5.5%)	88 (5.2%)	130 (5.4%)	6 (4.2%)	710 (5.1%)
<b>Age (y)<sup>c</sup></b>	43.7 (10.9)	42.3 (10.6)	44.3 (10.4)	43.7 (10.5)	46.5 (10.0)	43.5 (10.7)
<b>BMI (kg/m<sup>2</sup>)<sup>c</sup></b>						
Mean (SD)	38.0 (7.5)	37.0 (6.9)	38.4 (7.0)	37.6 (6.8)	37.5 (7.1)	37.8 (7.2)
27-29.9	687 (10.2%)	381 (13%)	118 (6.9%)	234 (9.6%)	14 (9.7%)	1,434 (10.3%)
30-34.9	1,977 (29.3%)	979 (33.3%)	477 (28%)	738 (30.4%)	45 (31.3%)	4,216 (30.2%)
35-39.9	1,890 (28.0%)	773 (26.3%)	519 (30.5%)	735 (30.3%)	46 (31.9%)	3,963 (28.4%)
40-49.9	1,733 (25.7%)	673 (22.9%)	472 (27.7%)	593 (24.4%)	30 (20.8%)	3,501 (25.1%)
≥ 50.0	468 (6.9%)	136 (4.6%)	117 (6.9%)	128 (5.3%)	9 (6.3%)	858 (6.1%)
<b>Hypertension diagnosis<sup>d</sup></b>	1,443 (21.4%)	578 (19.6%)	357 (21%)	476 (19.6%)	35 (24.3%)	2,889 (20.7%)
<b>Diabetes diagnosis<sup>c,d</sup></b>	824 (12.2%)	299 (10.2%)	224 (13.2%)	253 (10.4%)	24 (16.7%)	1,624 (11.6%)
<b>Smoking status<sup>c,e</sup></b>						
Never users	4,211 (62.3%)	1,870 (63.6%)	1,035 (60.8%)	1,469 (60.5%)	69 (47.9%)	8,654 (61.9%)
Ever users	2,298 (34%)	944 (32.1%)	612 (35.9%)	849 (35%)	65 (45.1%)	4,768 (34.1%)
Missing/unknown	246 (3.6%)	128 (4.4%)	56 (3.3%)	110 (4.5%)	10 (6.9%)	550 (3.9%)
<b>Area families below poverty level<sup>f</sup></b>						
Missing <sup>e,g</sup>	234 (3.5%)	146 (5%)	56 (3.3%)	93 (3.8%)	9 (6.3%)	538 (3.9%)
< 5%	1,568 (23.2%)	686 (23.3%)	445 (26%)	612 (25.2%)	38 (26.4%)	3,349 (24%)
5-< 10%	1,779 (26.3%)	769 (26.1%)	448 (26.2%)	656 (27%)	37 (25.7%)	3,682 (26.4%)
10-< 20%	1,812 (26.8%)	798 (27.1%)	443 (25.9%)	629 (25.9%)	35 (24.3%)	3,717 (26.6%)
≥ 20%	1,362 (20.2%)	543 (18.5%)	318 (18.6%)	438 (18%)	25 (17.4%)	2,686 (19.2%)
<b>Follow-up duration (y)<sup>c</sup></b>	1.6 (1.1)	2.2 (0.9)	1.6 (1.0)	2.4 (0.8)	2.3 (0.8)	1.9 (1.0)
<b>Median percent of follow-up on phentermine</b>	9%	16%	33%	42%	75%	19%
<b>Daily phentermine dose<sup>c</sup></b>						
< 37.5 mg	3,688 (54.6%)	1,528 (51.9%)	1,120 (65.8%)	1,526 (62.9%)	89 (61.8%)	7,951 (56.9%)
37.5 mg	3,053 (45.2%)	1,404 (47.7%)	580 (34.1%)	892 (36.7%)	53 (36.8%)	5,982 (42.8%)
Missing <sup>g</sup>	14 (0.2%)	10 (0.3%)	3 (0.2%)	10 (0.4%)	2 (1.4%)	39 (0.3%)

Data given as n (%) for categorical variables and mean (SD) for continuous variables.

<sup>a</sup>On-label short-term users (referent) had a single phentermine use episode ≤ 112 days. Short-term intermittent users rotated on and off phentermine but never remained on the drug for longer than 112 days. Off-label user groups defined as follows: medium-term continuous users had a single phentermine treatment episode lasting > 112 but ≤ 365 days; medium-term intermittent users had multiple treatment episodes in which at least one exceeded 112 days; and long-term continuous users had a single episode lasting > 365 days. Note that “n” in each column corresponds to final exposure assignment at end of follow-up. Because of the time-varying nature of the exposure, relative size of groups and distribution of characteristics may differ between time points in early follow-up (e.g., at 6 and 12 months).

<sup>b</sup>P = 0.004 for  $\chi^2$  test.

<sup>c</sup>P < 0.001 for difference across groups using  $\chi^2$  test for categorical and Kruskal-Wallis test for continuous variables.

<sup>d</sup>Defined as one relevant inpatient or two outpatient *International Classification of Diseases, Ninth Revision* codes in year prior to index phentermine prescription.

<sup>e</sup>Tobacco “ever users” includes current and historical smokers.

<sup>f</sup>Using geographic information systems measures mapping to 2010 census block group socioeconomic status data, categories go from highest to lowest SES vertically.

<sup>g</sup>For analyses, patients missing either the area-level poverty measure or daily phentermine dose had these values set to modal value for patients in their region. A sensitivity analysis was conducted excluding these patients entirely from analyses and results did not change.

**TABLE 2** Difference in percent weight loss over follow-up: results from multivariable linear models using time-varying exposure<sup>a</sup>

	6 months		12 months		24 months	
	Parameter estimate (95% CI)	n (% of enrolled with weight data available) <sup>b</sup>	Parameter estimate (95% CI)	n (% of enrolled with weight data available) <sup>b</sup>	Parameter estimate (95% CI)	n (% of enrolled with weight data available) <sup>b</sup>
Intercept <sup>c</sup>	-2.68 (-3.28 to -2.08) <sup>d,e</sup>		-1.38 (-2.08 to -0.67) <sup>f</sup>		-0.16 (-1.07 to 0.75)	
Short-term <sup>c</sup>	Referent	2,555 (66%)	Referent	2,074 (78%)	Referent	1,323 (90%)
Short-term intermittent <sup>c</sup>	-1.75 (-2.13 to -1.37) <sup>d,g</sup>	1,450 (73%)	-1.36 (-1.80 to -0.93) <sup>g</sup>	1,743 (82%)	-0.26 (-0.83 to 0.32) <sup>g</sup>	1,545 (92%)
Medium-term continuous <sup>c</sup>	-5.07 (-5.40 to -4.73) <sup>d,g</sup>	2,352 (74%)	-4.66 (-5.13 to -4.19) <sup>g</sup>	1,371 (78%)	-1.71 (-2.46 to -0.96) <sup>g</sup>	613 (89%)
Medium-term intermittent <sup>c</sup>	-4.22 (-5.11 to -3.33) <sup>d,g</sup>	179 (78%)	-5.63 (-6.13 to -5.13) <sup>g</sup>	1,178 (86%)	-3.48 (-4.07 to -2.88) <sup>g</sup>	1,368 (93%)
Long-term continuous <sup>c</sup>	n/a		n/a		-7.36 (-8.96 to -5.76) <sup>g</sup>	98 (89%)

<sup>a</sup>Separate models built for each time point, all adjusted for gender, race and ethnicity, smoking, diabetes, hypertension, baseline BMI, average medication strength, year of original prescription, and site.  
<sup>b</sup>n (%) by exposure category within each time point references those with a weight measure versus total number assigned to that exposure category at that time point.  
<sup>c</sup>Short-term users (referent) had a single phentermine use episode ≤ 112 days; short-term intermittent users rotated on and off phentermine but never remained on the drug for longer than 112 days. Off-label user groups were defined as follows: medium-term continuous users had a single phentermine treatment episode lasting > 112 but ≤ 365 days; medium-term intermittent users had multiple treatment episodes in which at least one exceeded 112 days; and long-term continuous users had a single episode lasting > 365 days.  
<sup>d</sup>Parameter estimates for intercept approximate percent weight loss of referent group when all covariates are set to their referent value, and parameter estimates for comparison groups should be interpreted as difference in percent weight loss compared with referent group.  
<sup>e</sup>p < 0.0001 for comparing intercept to zero.  
<sup>f</sup>p < 0.001 for comparing intercept to zero.  
<sup>g</sup>p < 0.0001 for comparing percent weight loss in comparison groups to referent group.  
n/a, not applicable.

in their health system, incident pregnancies, bariatric procedures, prescription of any weight-loss medication besides phentermine, prescription for phentermine >37.5 mg/d, CVD outcome (e.g., myocardial infarction), or death. Patients were censored at these times in the Cox model.

### Sensitivity analyses

Unmeasured patient characteristics or differential response to phentermine could predict greater medication persistence and more weight loss. Therefore, we conducted two sensitivity analyses to assess whether patients who used phentermine for longer did so because the medication was working better for them. In the first sensitivity analysis, we treated phentermine use over follow-up as a fixed exposure, allowing patients to populate their final exposure categories artificially early. We then conducted weight-loss analysis using these fixed exposure categories, beginning at 3 months, when phentermine duration should have been relatively equal between categories.

Second, we conducted a separate “responders-only” sensitivity analysis. In this analysis, we limited inclusion in the cohort to patients who achieved  $\geq 3\%$  weight loss by 3 months. Our goal with this analysis was to reduce the potential impact of phentermine nonresponders on lower weight loss in the referent group. The responder analysis was also conducted in two ways, treating phentermine as both time varying and fixed.

To test the sensitivity of our weight findings to varying acceptable time windows for follow-up measures, we reran models using acceptable windows of  $-/+90$  days,  $+90$  days,  $-/+60$  days,  $+60$  days,  $-30/+90$  days, and  $-30/+60$  days at each time point (6, 12, and 24 months).

To examine whether a higher-risk subgroup of patients might be more likely to experience adverse effects, we repeated HR and BP analyses on the subset of individuals with baseline hypertension diagnoses.

## Results

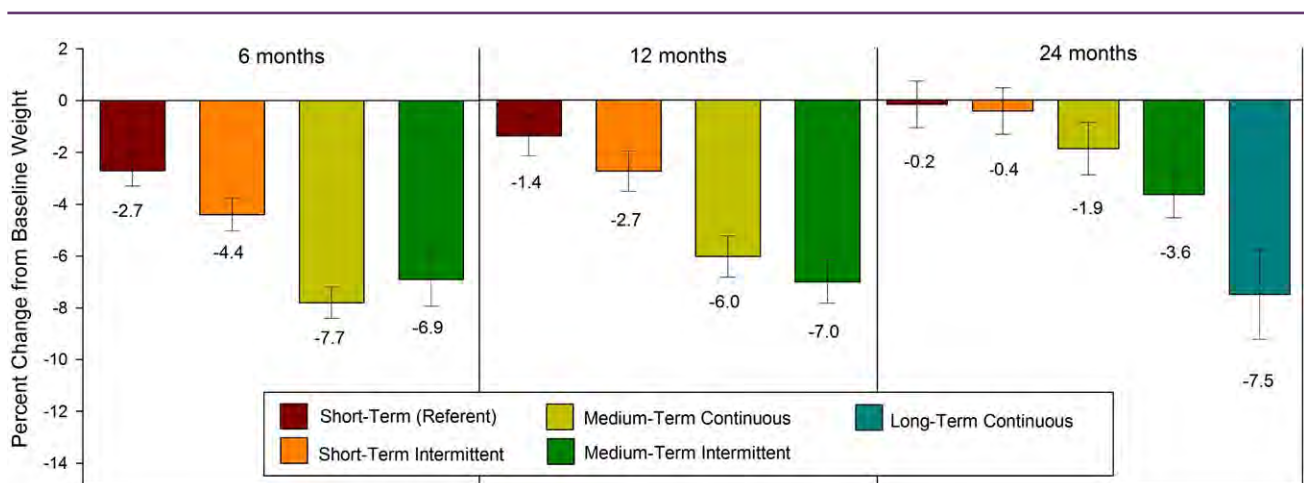
### Study population

We identified 13,972 incident phentermine users (Figure 1). Most were women (84%), and the mean (SD) baseline age was 43.5 (10.7) years; just under half (45%) were non-Hispanic white (Table 1). Baseline BMI was 37.8 (7.2) kg/m<sup>2</sup>, 21% carried a diagnosis of hypertension at baseline, and 12% had a diagnosis of diabetes. Phentermine use groups differed by baseline characteristics, with on-label users slightly more likely to be minorities, younger, not diabetic, and never smokers compared with off-label groups. Off-label groups included a higher proportion of patients taking a lower daily dose of phentermine.

### Weight loss

At 6, 12, and 24 months after phentermine initiation, weight loss was greater among off-label and intermittent short-term users than our referent short-term single episode users (Table 2). The mean weight change for short-term single episode (referent) phentermine use can be approximated by examining the intercept values for models at each time point (Table 2, Figure 2). By 6 months after drug initiation (or  $\sim 3$  months after discontinuing phentermine), short-term users averaged 2.7% (95% CI: 2.1%-3.3%) total weight loss. By 12 months, their weight loss was 1.4% (95% CI: 0.7%-2.1%), and by 24 months, the weight change in this group was not different from zero.

The magnitude of difference in weight loss between comparison groups and the referent group varied with duration of follow-up (Table 2, Figure 2). At 6 months, short-term intermittent users lost 1.8% (95% CI: 1.4%-2.1%) additional body weight relative to short-term single episode (referent) users, while medium-term continuous users lost 5.1% (95% CI: 4.7%-5.4%) more. At 12 months, the medium-term intermittent group lost 5.6% (95% CI: 5.1%-6.1%) more weight than short-term single episode users. At 24 months after phentermine initiation,



**Figure 2** Estimated percent weight loss at 6 months and 1 and 2 years after phentermine initiation; results from multivariable linear models. Estimates at each time point are from separate multivariable linear models, and  $n$  (%) by group over follow-up is presented in Table 2. Note that because real clinical follow-up does not occur at exact 6-month intervals, weights were drawn from an acceptable time window of outpatient visits around each time point of interest, as outlined in *Methods*. Estimates for the referent group (on-label continuous) were based on the y-intercept of multivariable models in the case in which all covariates are set to referent. Estimates for comparison groups were generated by summing the intercept weight loss and the additional change in weight by group at each time point. Error bars represent 95% CI for each estimate.

**TABLE 3** Difference in percent weight loss over follow-up: results from multivariable linear models using time-varying exposure among early phentermine responders<sup>a</sup>

	6 months		12 months		24 months	
	Parameter estimate (95% CI)	n (% of enrolled with weight data available) <sup>b</sup>	Parameter estimate (95% CI)	n (% of enrolled with weight data available) <sup>b</sup>	Parameter estimate (95% CI)	n (% of enrolled with weight data available) <sup>b</sup>
Intercept <sup>c</sup>	-6.26 (-7.09 to -5.43) <sup>d,e</sup>		-4.07 (-5.20 to -2.94) <sup>e</sup>		-3.01 (-4.53 to -1.48) <sup>f</sup>	
Short-term <sup>c</sup>	Referent	767 (70%)	Referent	604 (82%)	Referent	364 (94%)
Short-term intermittent <sup>c</sup>	-1.54 (-2.12 to -0.97) <sup>d,g</sup>	565 (78%)	-1.75 (-2.49 to -1.02) <sup>g</sup>	604 (84%)	-0.07 (-1.16 to 1.02) <sup>g</sup>	495 (93%)
Medium-term continuous <sup>c</sup>	-3.35 (-3.82 to -2.88) <sup>d,g</sup>	1,574 (78%)	-3.64 (-4.33 to -2.95) <sup>g</sup>	848 (80%)	-0.54 (-1.71 to 0.64) <sup>g</sup>	364 (89%)
Medium-term intermittent <sup>c</sup>	-2.25 (-3.34 to -1.15) <sup>d,g</sup>	103 (82%)	-4.21 (-4.93 to -3.48) <sup>g</sup>	744 (90%)	-2.47 (-3.49 to -1.46) <sup>g</sup>	788 (94%)
Long-term continuous <sup>c</sup>	n/a		n/a		-7.68 (-10.02 to -5.34) <sup>g</sup>	52 (91%)

<sup>a</sup>Separate models built for each time point, all adjusted for gender, race and ethnicity, smoking, diabetes, hypertension, baseline BMI, average medication strength, year of original prescription, and site. Models include only patients who had documented weight loss of  $\geq 3\%$  by 3 months after starting phentermine.

<sup>b</sup>n (%) by exposure category within each time point references those with a weight measure versus total number assigned to that exposure category at that time point.

<sup>c</sup>Short-term users (referent) had a single phentermine use episode  $\leq 112$  days; short-term intermittent users rotated on and off phentermine but never remained on drug for longer than 112 days. Off-label user groups were defined as follows: medium-term continuous users had a single phentermine treatment episode lasting  $> 112$  but  $\leq 365$  days; medium-term intermittent users had multiple treatment episodes in which at least one exceeded 112 days; and long-term continuous users had a single episode lasting  $> 365$  days.

<sup>d</sup>Parameter estimates for intercept approximate percent weight loss of referent group when all covariates are set to their referent value, and parameter estimates for comparison groups should be interpreted as difference in percent weight loss compared with referent group.

<sup>e</sup>P < 0.0001 for comparing intercept to zero.

<sup>f</sup>P < 0.0001 for comparing intercept to zero.

<sup>g</sup>P < 0.0001 for comparing percent weight loss in comparison groups with referent group.

n/a, not applicable.

long-term continuous (>12 months) users lost 7.4% (95% CI: 5.8%-9.0%) more weight than short-term single episode users.

When we examined weight change at 3 months using final assigned exposure categories rather than time-varying exposure, individuals in the off-label and intermittent use categories already had greater weight loss than those in the referent group (Supporting Information Table S3). In these models, short-term users had lost 3.5% (95% CI: 3.1%-4.0%) body weight at 3 months, with additional weight loss by group as follows: short-term intermittent, 0.4% (95% CI: 0.1%-0.7%); medium-term continuous, 2.6% (95% CI: 2.3%-2.9%); medium-term intermittent, 3.0% (95% CI: 2.7%-3.3%); and long-term continuous, 3.4% (95% CI: 2.6%-4.3%). Referent and between-group patterns for weight loss at 6, 12, and 24 months in this sensitivity analysis using fixed phentermine use groups were otherwise similar to our main findings.

Our responders-only analysis for weight loss included 4,340 individuals who experienced  $\geq 3\%$  weight loss by 3 months, representing 62% of the 7,043 patients who had weight data available at that time point. In multivariable models treating phentermine as a time-varying exposure among responders, referent group weight loss was greater than in our main analyses, as follows: 6.3% (95% CI: 5.4%-7.1%) at 6 months, 4.1% (95% CI: 2.9%-5.2%) at 12 months, and 3.0% (95% CI: 1.5%-4.5%) at 24 months (Table 3, Figure 3). Despite selecting for individuals with more initial success, weight loss in our comparison groups was still greater than the referent group at all time points in follow-up. Comparison groups displayed a similar magnitude of difference as observed in our main analysis (Table 3) but with greater overall weight loss for all groups (Figure 3). The sensitivity analysis for responders using end-group assignments and examining early (3 month) weight loss between groups showed slightly greater early weight loss among comparison groups compared with the referent group; however, between-group differences at this early time point were attenuated (Supporting Information Table S4).

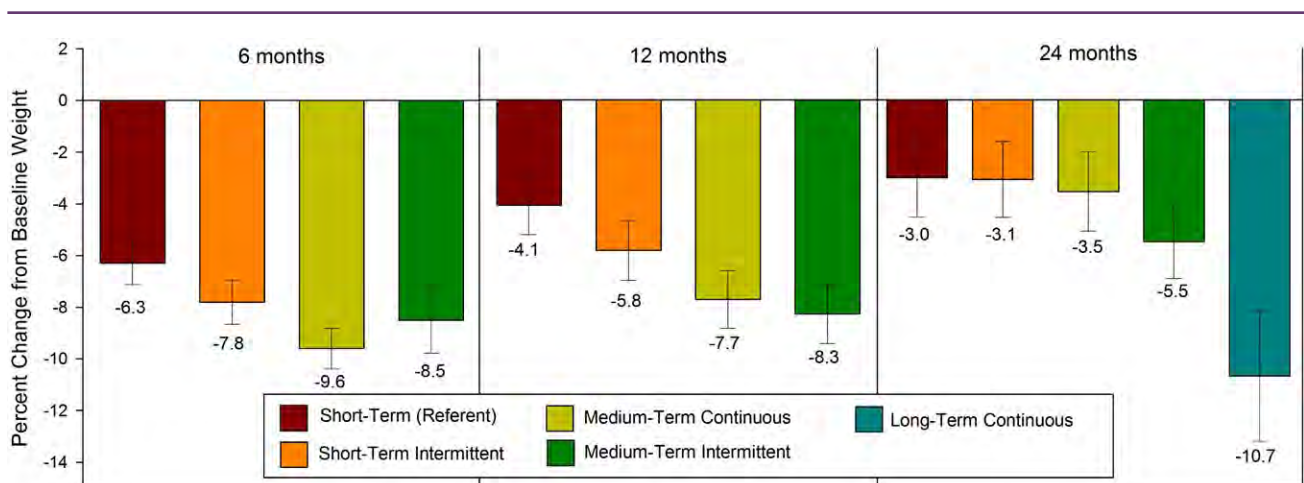
Varying the time window for acceptable EHR weight measures did not appreciably change referent or between-group results compared with our main analysis despite a large amount of variability in missingness that occurred as a result of requiring narrower or wider time windows around each point (Supporting Information Table S5). Related to missingness, the reader will note that the number of patients in each exposure category varies over follow-up. In part, this is due to the time-varying nature of our exposure; however, additional reasons for missingness are summarized in Supporting Information Table S6.

### Changes in BP and HR

At baseline, mean (SD) HR was 79 (12) bpm, and mean (SD) BP was 122 (12)/74 (9). Patients in the short-term single episode (referent) group had no significant change in HR at 6, 12, or 24 months (Table 4). The greatest relative HR increase among medium-term continuous users was at 6 months and was 1.6 (95% CI: 1.0-2.2) bpm higher than the referent group; among medium-term intermittent users, at 12 months, it was 1.1 (95% CI: 0.3-1.9) bpm higher than the referent group. Comparison group changes in HR did not differ from the referent group at 24 months.

SBP in the referent group was stable at 6 and 12 months, but at 24 months, it had increased by 1.8 (0.5-3.2) mmHg, relative to baseline. There was no between-group difference in SBP change at 6 months; however, the comparison groups on the whole had slightly lower BP than the referent group at 12 and 24 months, again with variability in magnitude of difference by group. For example, at 24 months, patients in the long-term continuous user group experienced SBP  $\Delta$ -3.3 (-0.8 to -5.9) mmHg relative to the on-label users.

DBP in the referent (short-term) group was stable relative to baseline at 6, 12, and 24 months, and there were no significant between-group differences in DBP over follow-up.



**Figure 3** Estimated percent weight loss at 6 months and 1 and 2 years after phentermine initiation among responders; results from multivariable linear models. Models include only phentermine responders, patients who had lost  $\geq 3\%$  body weight by 3 months after initiating medication. Estimates at each time point are from separate multivariable linear models, and  $n$  (%) by group over follow-up is presented in Table 2. Note that because real clinical follow-up does not occur at exact 6-month intervals, weights were drawn from an acceptable time window of outpatient visits around each time point of interest, as outlined in *Methods*. Estimates for the referent group (on-label continuous) were based on the y-intercept of multivariable models in the case in which all covariates are set to referent. Estimates for comparison groups were generated by summing the intercept weight loss and the additional change in weight by group at each time point. Error bars represent 95% CI for each estimate.



**TABLE 4 Change in heart rate (HR) and blood pressure (BP) over follow-up: results from multivariable linear models using time-varying exposure<sup>a</sup>**

	Heart rate results					
	6 months		12 months		24 months	
	Parameter estimate ΔHR (bpm) (95% CI)	n (%) enrolled with VS data <sup>b</sup>	Parameter estimate ΔHR (bpm) (95% CI)	n (%) enrolled with VS data <sup>b</sup>	Parameter estimate ΔHR (bpm) (95% CI)	n (%) enrolled with VS data <sup>b</sup>
Intercept <sup>c</sup>	1.01 (-0.13 to 2.16) <sup>d</sup>	n/a	0.64 (-0.51 to 1.80)	n/a	0.55 (-0.77 to 1.86)	n/a
Short-term <sup>c</sup>	Ref	4,268 (68%)	Ref	3,672 (79%)	Ref	2,534 (91%)
Short-term intermittent <sup>c</sup>	0.81 (0.08 to 1.53) <sup>d,e</sup>	1,439 (74%)	0.27 (-0.43 to 0.96) <sup>f</sup>	1,723 (83%)	0.13 (-0.65 to 0.91)	1,533 (93%)
Medium-term continuous <sup>c</sup>	1.61 (0.99 to 2.24) <sup>d,e</sup>	2,353 (75%)	1.16 (0.40 to 1.92) <sup>f</sup>	1,362 (79%)	-0.19 (-1.28 to 0.90)	610 (90%)
Medium-term intermittent <sup>c</sup>	-0.77 (-2.57 to 1.04) <sup>d,e</sup>	181 (80%)	1.09 (0.28 to 1.90) <sup>f</sup>	1,184 (88%)	0.67 (-0.14 to 1.49)	1,360 (95%)
Long-term continuous <sup>c</sup>	n/a		n/a		2.64 (0.15 to 5.14)	96 (90%)

	Blood pressure results					
	6 months		12 months		24 months	
	Parameter estimate (95% CI)	n (%) enrolled with VS data <sup>b</sup>	Parameter estimate (95% CI)	n (%) enrolled with VS data <sup>b</sup>	Parameter estimate (95% CI)	n (%) enrolled with VS data <sup>b</sup>
Intercept <sup>c</sup>	-0.99 (-2.13 to 0.14) <sup>d</sup>	n/a	-0.19 (-1.37 to 0.99)	n/a	1.83 (0.48 to 3.19) <sup>g</sup>	n/a
Short-term <sup>c</sup>	Ref	4,377 (68%)	Ref	3,742 (79%)	Referent	2,592 (92%)
Short-term intermittent <sup>c</sup>	-0.78 (-1.49 to -0.06) <sup>d</sup>	1,468 (75%)	-0.41 (-1.11 to 0.30) <sup>h</sup>	1,759 (83%)	0.2 (-0.60 to 1.00) <sup>i</sup>	1,560 (94%)
Medium-term continuous <sup>c</sup>	0.08 (-0.46 to 0.61) <sup>d</sup>	2,402 (76%)	0.21 (-0.31 to 0.73)	1,395 (80%)	0.4 (-0.18 to 0.98)	622 (90%)
Medium-term intermittent <sup>c</sup>	-0.5 (-1.12 to 0.12) <sup>d</sup>	183 (80%)	-1.11 (-1.88 to -0.33) <sup>h</sup>	1,200 (88%)	-0.94 (-2.05 to 0.17) <sup>j</sup>	1,383 (95%)
Long-term continuous <sup>c</sup>	0.36 (-0.11 to 0.82) <sup>d</sup>		-0.39 (-0.95 to 0.18)		-0.12 (-0.93 to 0.69)	
	-1.18 (-2.98 to 0.61) <sup>d</sup>		-0.92 (-1.74 to -0.09) <sup>h</sup>		-0.41 (-1.25 to 0.43) <sup>j</sup>	
	-0.81 (-2.16 to 0.53) <sup>d</sup>		-0.19 (-0.79 to 0.41)		0.12 (-0.49 to 0.73)	
	n/a		n/a		-3.31 (-5.85 to -0.76) <sup>j</sup>	99 (91%)
					-0.69 (-2.54 to 1.16)	

<sup>a</sup>Separate models built for each time point, all adjusted for gender, race and ethnicity, smoking, diabetes, hypertension, baseline HR or BP tertile, average medication strength, year of original prescription, and site.  
<sup>b</sup>n (%) by exposure category within each time point references those with a HR measure versus total number assigned to that exposure category at that time point.  
<sup>c</sup>Short-term users (referent) had a single phentermine use episode ≤ 112 days; short-term intermittent users rotated on and off phentermine but never remained on the drug for longer than 112 days. Off-label user groups were defined as follows: medium-term continuous users had a single phentermine treatment episode lasting > 112 but ≤ 365 days; medium-term intermittent users had multiple treatment episodes in which at least one exceeded 112 days; and long-term continuous users had a single episode lasting > 365 days.  
<sup>d</sup>Parameter estimates for intercept approximate change from baseline in BP or HR of referent group when all covariates are set to their referent value, and parameter estimates for comparison groups should be interpreted as difference in BP or HR compared with referent group.  
<sup>e</sup>p < 0.0001 for comparing HR and BP change in comparison groups with referent group.  
<sup>f</sup>p = 0.005 for comparing HR change in comparison groups with referent group.  
<sup>g</sup>p = 0.008 for comparing SBP change in comparison groups with referent group.  
<sup>h</sup>p = 0.02 for comparing SBP change in comparison groups with referent group.  
<sup>i</sup>p = 0.03 for comparing SBP change in comparison groups with referent group.  
 VS, vital signs; n/a, not applicable.

**TABLE 5** Results from multivariable Cox models<sup>a</sup>: hazard ratio for composite outcome of incident myocardial infarction, stroke, CVD intervention, or death up to 3 years after phentermine initiation

	Hazard ratio	CI <sup>b</sup>
Short-term (referent)	Reference	
Short-term intermittent	0.74	0.29-1.91
Medium-term intermittent	0.50	0.14-1.74
Medium & long-term continuous combined <sup>c</sup>	1.58	0.69-3.63

<sup>a</sup>Models include phentermine exposure as time-varying covariate as well as gender, race and ethnicity, smoking, diabetes, hypertension, baseline BMI, average medication strength, year of original prescription, and site.

<sup>b</sup> $P = 0.30$  for examining differences between groups.

<sup>c</sup>There were no events in long-term continuous subgroup; therefore, to allow this group to contribute person-time to the models, it was grouped with the medium-term continuous exposure category.

Among patients with baseline hypertension, BP increased more over time than in our main cohort (Supporting Information Table S7), but there were no 6- or 12-month differences by phentermine exposure category. By 24 months, SBP in longer-term phentermine use groups for hypertensive patients was lower than among short-term hypertensive users. Between-group comparisons for  $\Delta$ HRR among patients with hypertension were similar to our main analysis.

### Incident CVD or death

Up to 3 years after the index date, incidence of composite adverse outcomes was low. Forty-one people out of 13,972 (0.3%) experienced an event (for group-specific event rates, see Supporting Information Table S8). Because there were no qualifying CVD or death events in the long-term continuous user group, these individuals were grouped with the medium-term continuous users for analysis. Multivariable Cox regression models treating phentermine use as a time-varying covariate found no significant difference in risk of incident CVD or death between groups (Table 5).

## Discussion

In this large cohort study, a longer duration of phentermine use was associated with clinically significant greater weight loss up to 2 years after initiating medication, with no observed increase in risk for incident cardiovascular events or death over 3 years of follow-up. Discontinuation of phentermine consistently resulted in weight regain.

There are few prior studies examining long-term use of phentermine, particularly as monotherapy for obesity (6,20,22,32). However, in 2012, a new brand-named drug, Phentermine/Topiramate-CR, earned FDA approval for long-term ( $\geq 12$  months) use as a weight-loss medication. Randomized trial data from patients taking this medication for 24 months showed sustained 9% to 11% weight loss without increased cardiovascular risk (33,34). While these findings suggested possible safety and effectiveness of using phentermine monotherapy for longer than 12 weeks, Phentermine/Topiramate-CR has a lower daily phentermine dose than is typical of monotherapy, necessitating additional studies on this topic to inform clinical care.

Experts now recognize obesity as a chronic disease, best treated with comprehensive intensive lifestyle intervention and long-term follow-up, using tools such as pharmacotherapy and bariatric surgery to supplement lifestyle change as needed (35). There is a need for longer-term effective, safe, and affordable pharmacotherapy that can be used as an adjunct to lifestyle change advice. Longer-term use of phentermine in the United States indeed appears to be a pervasive practice (36); 30% of our cohort was made up of individuals with at least one phentermine episode lasting  $> 12$  weeks.

Our findings show that patients prescribed phentermine for  $\leq 3$  months, as is currently directed by labeling, did not experience durable clinically significant weight loss. In contrast, patients using phentermine off-label for longer periods generally experienced greater weight loss that was sustained so long as they remained on medication. For example, medium-term users (those on phentermine for up to 12 months) averaged significantly greater weight loss than the referent group at 12 months but had regained nearly 70% by 24 months.

Findings from our analysis of phentermine responders, patients with at least 3% weight loss by 3 months after medication initiation, underscore the importance of not continuing to prescribe a medication to patients who do not appear to experience clinical benefit (Figure 2, Figure 3). Patients who responded early across all groups reached clinically significant levels of weight loss ( $\geq 5\%$  on average) by 6 months and generally had more durable weight loss. This finding aligns with similar observations from the literature on diet-induced weight loss, in which early response tends to predict greater overall weight-loss success (2,37).

We observed a slight increase in average HR among phentermine users that normalized after discontinuation. This finding is consistent with the drug's mechanism of action, and the magnitude of increase is similar to prior studies of phentermine-containing medications (33). The relative decrease in SBP associated with longer-term phentermine use, despite the sympathomimetic effect of the drug, may be attributable to greater weight loss, resulting in a net-lowering effect. We observed this relative BP lowering even among patients with baseline hypertension. We cannot exclude the occurrence of rare hypertensive events resulting in emergency department visits because our analyses relied on outpatient information.

Importantly, we did not observe an increase in risk of CVD or death related to the duration of phentermine use up to 3 years after initiating medication. Additional study of these rare outcomes is needed, including research with a larger higher-risk population of long-term users and greater duration of follow-up. Our overall low rate of the composite outcome (0.3% of all patients experienced an event) may be related to the patient population in this study; 85% were women, and we excluded individuals with prevalent CVD. However, our findings are consistent with those from placebo-controlled trials of Phentermine/Topiramate-CR, in which 7 of 2,581 (0.3%) of active drug patients experienced a similar composite outcome (34) and provide some reassurance about the relative safety of phentermine prescribing in low-risk individuals.

Our study has several important limitations. First, we cannot interpret the relationship between duration of phentermine use and percent weight loss as causal. Our referent group likely includes patients who discontinued phentermine because of ineffectiveness, and, conversely,

our comparison groups contained people who remained on medication precisely because it was effective for them. Our sensitivity analyses support this suspicion; differences in weight loss favored longer-term users even at the 3-month mark when phentermine duration was approximately equal between groups. We tried to mitigate this bias by limiting our weight analyses to patients with at least one refill and by conducting a responders-only analysis; however, the possibility for residual confounding and/or reverse causality remains.

Duration of follow-up differed between exposure categories and was systematically greater for longer-term phentermine users. This could have led to an ascertainment bias between categories, but it is not clear in which direction our results would be biased.

We did not address provider- or health-system-level variables, and it is possible that these factors differed systematically between groups in a way that favored longer-term phentermine users. For example, if physicians willing to prescribe phentermine for longer durations are more likely to be obesity specialists (36), or if this pattern of prescribing is more likely to be associated with participation in a comprehensive weight-management program, such differences could confound the relationship between phentermine use duration and weight loss.


Our data should be interpreted with regard to dispensing of phentermine and may not fully indicate whether patients reliably took the medication. Similarly, it is possible that some patients had phentermine or other weight-loss medications filled outside of our systems, going undetected in our data. Although we adjusted for daily dose of phentermine and censored for doses exceeding 37.5 mg/d, we did not specifically study appropriate dosing for longer-term use of this medication. Similarly, we did not examine coadministered medications that could have led to weight loss or gain or changing BP or HR as a side effect (e.g., topiramate, metoprolol). We did censor for incident use of any FDA-approved weight-loss medications in follow-up.

As with any EHR-based study, there was loss to follow-up in our cohort over time, with missingness possibly not at random. We did find that a large portion of the missingness (e.g., 32% at 24 months) was due to patients prescribed phentermine in later years reaching the end of the study period (September 30, 2015), which is unlikely to be a source of bias. On a related note, the number of patients in our “long-term continuous” use group was quite small relative to the other groups; therefore, additional study with a larger group of patients using phentermine for  $\geq 12$  months would help to bolster our findings.

Finally, we did not attempt to characterize other possible adverse outcomes of phentermine use such as anxiety, sleep disturbance, or addiction. A clinical trial with regular standardized outcome assessments at predetermined intervals would be important to accurately describe the risk of such events.

## Conclusion

Recommendations to limit phentermine use to less than 3 months do not align with current concepts of pharmacological treatment for patients with obesity. Our results show that longer-term phentermine users experienced greater weight loss without apparent increases in cardiovascular risk. Given the chronicity of obesity and the paucity of

good long-term treatment options for this condition, these data provide reassurance that longer-term phentermine monotherapy is a reasonable treatment option in low-risk individuals. Still, there is a need for randomized controlled trials to definitively establish the safety and effectiveness of protracted phentermine monotherapy. 

## Acknowledgments

We thank Dr. Sengwee Toh of the Department of Population Medicine at Harvard Pilgrim Healthcare Institute/Harvard Medical School for providing his input and expertise on pharmacoepidemiologic methods for this paper. Additionally, we thank the analysts in each PORTAL region for their time and effort in extracting the EHR data used in this study.

© 2019 The Obesity Society

## References

- Jensen MD, Ryan DH, Donato KA, et al. Guidelines (2013) for managing overweight and obesity in adults. *Obesity* 2014;22:S1-S410.
- Miller CK, Nagaraja HN, Weinhold KR. Early weight-loss success identifies nonresponders after a lifestyle intervention in a worksite diabetes prevention trial. *J Acad Nutr Diet* 2015;115:1464-1471.
- Wadden TA, West DS, Neiberg RH, et al. One-year weight losses in the Look AHEAD study: factors associated with success. *Obesity (Silver Spring)* 2009;17:713-722.
- Barte JC, ter Bogt NC, Bogers RP, et al. Maintenance of weight loss after lifestyle interventions for overweight and obesity, a systematic review. *Obes Rev* 2010;11:899-906.
- Soleymani T, Daniel S, Garvey WT. Weight maintenance: challenges, tools and strategies for primary care physicians. *Obes Rev* 2016;17:81-93.
- Apovian CM, Aronne LJ, Bessesen DH, et al. Pharmacological management of obesity: an Endocrine Society clinical practice guideline. *J Clin Endocrinol Metab* 2015;100:342-362.
- Apovian CM, Aronne L, Rubino D, et al. A randomized, phase 3 trial of naltrexone SR/bupropion SR on weight and obesity-related risk factors (COR-II). *Obesity (Silver Spring)* 2013;21:935-943.
- Gadde KM, Allison DB, Ryan DH, et al. Effects of low-dose, controlled-release, phentermine plus topiramate combination on weight and associated comorbidities in overweight and obese adults (CONQUER): a randomised, placebo-controlled, phase 3 trial. *Lancet* 2011;377:1341-1352.
- Pi-Sunyer X, Astrup A, Fujioka K, et al. Controlled trial of 3.0 mg of liraglutide in weight management. *N Engl J Med* 2015;373:11-22.
- Smith SR, Weissman NJ, Anderson CM, et al. Multicenter, placebo-controlled trial of lorcaserin for weight management. *N Engl J Med* 2010;363:245-256.
- Astrup A, Carraro R, Finer N, et al. Safety, tolerability and sustained weight loss over 2 years with the once-daily human GLP-1 analog, liraglutide. *Int J Obes (Lond)* 2012;36:843-854.
- Fidler MC, Sanchez M, Raether B, et al. A one-year randomized trial of lorcaserin for weight loss in obese and overweight adults: the BLOSSOM trial. *J Clin Endocrinol Metab* 2011;96:3067-3077.
- Greenway FL, Fujioka K, Plodkowski RA, et al. Effect of naltrexone plus bupropion on weight loss in overweight and obese adults (COR-I): a multicentre, randomised, double-blind, placebo-controlled, phase 3 trial. *Lancet* 2010;376:595-605.
- Torgerson JS, Hauptman J, Boldrin MN, Sjostrom L. XENical in the prevention of diabetes in obese subjects (XENDOS) study: a randomized study of orlistat as an adjunct to lifestyle changes for the prevention of type 2 diabetes in obese patients. *Diabetes Care* 2004;27:155-161.
- LeBlanc ESPC, Webber EM, Redmond N, Rushkin M, O'Connor EA. Behavioral and pharmacotherapy weight loss interventions to prevent obesity-related morbidity and mortality in adults: updated evidence report and systematic review for the US Preventive Services Task Force. *JAMA* 2018;320:1172-1191.
- Xia Y, Kelton CM, Guo JJ, Bian B, Heaton PC. Treatment of obesity: pharmacotherapy trends in the United States from 1999 to 2010. *Obesity (Silver Spring)* 2015;23:1721-1728.
- Bray GA, Heisel WE, Afshin A, et al. The science of obesity management: an Endocrine Society scientific statement. *Endocr Rev* 2018;39:79-132.
- Patel D. Pharmacotherapy for the management of obesity. *Metabolism* 2015;64:1376-1385.
- Colman E. Anorectics on trial: a half century of federal regulation of prescription appetite suppressants. *Ann Intern Med* 2005;143:380-385.
- Velazquez A, Apovian CM. Updates on obesity pharmacotherapy. *Ann N Y Acad Sci* 2018;1411:106-119.
- Adipex-P (phentermine hydrochloride) [package insert]. Sellersville, PA: Teva Pharmaceuticals USA; 2012. [https://www.accessdata.fda.gov/drugsatfda\\_docs/label/2012/085128s0651bl.pdf](https://www.accessdata.fda.gov/drugsatfda_docs/label/2012/085128s0651bl.pdf).



22. Hendricks EJ, Srisurapanont M, Schmidt SL, et al. Addiction potential of phentermine prescribed during long-term treatment of obesity. *Int J Obes (Lond)* 2014;38:292-298.
23. Young DR, Waitzfelder BA, Arterburn D, et al. The Patient Outcomes Research to Advance Learning (PORTAL) network adult overweight and obesity cohort: development and description. *JMIR Res Protoc* 2016;5:e87. doi:10.2196/resprot.5589
24. McGlynn EA, Lieu TA, Durham ML, et al. Developing a data infrastructure for a learning health system: the PORTAL network. *J Am Med Inform Assoc* 2014;21:596-601.
25. Johnson ES, Bartman BA, Briesacher BA, et al. The incident user design in comparative effectiveness research. *Pharmacoepidemiol Drug Saf* 2013;22:1-6.
26. Food and Drug Administration. Guidance for Industry and FDA Staff: Best Practices for Conducting and Reporting Pharmacoepidemiologic Safety Studies Using Electronic Healthcare Data. Silver Spring, MD: Food and Drug Administration; 2013.
27. Parker MM, Moffet HH, Adams A, Karter AJ. An algorithm to identify medication nonpersistence using electronic pharmacy databases. *J Am Med Inform Assoc* 2015;22:957-961.
28. Andrade SE, Kahler KH, Frech F, Chan KA. Methods for evaluation of medication adherence and persistence using automated databases. *Pharmacoepidemiol Drug Saf* 2006;15:565-574; discussion 575-577.
29. Fisher DPJE, Haneuse S, Arterburn D, et al. Association between bariatric surgery and macrovascular disease outcomes in patients with type 2 diabetes and severe obesity. *JAMA* 2018;320:1570-1582.
30. Arterburn D, Johnson ES, Butler MG, Fisher D, Bayliss EA. Predicting 90-day mortality after bariatric surgery: an independent, external validation of the OS-MRS prognostic risk score. *Surg Obes Relat Dis* 2014;10:774-779.
31. Krieger N, Chen JT, Waterman PD, Rehkopf DH, Subramanian SV. Race/ethnicity, gender, and monitoring socioeconomic gradients in health: a comparison of area-based socioeconomic measures—the public health disparities geocoding project. *Am J Public Health* 2003;93:1655-1671.
32. Allison DB, Gadde KM, Garvey WT, et al. Controlled-release phentermine/topiramate in severely obese adults: a randomized controlled trial (EQUIP). *Obesity (Silver Spring)* 2012;20:330-342.
33. Garvey WT, Ryan DH, Look M, et al. Two-year sustained weight loss and metabolic benefits with controlled-release phentermine/topiramate in obese and overweight adults (SEQUENCE): a randomized, placebo-controlled, phase 3 extension study. *Am J Clin Nutr* 2012;95:297-308.
34. Jordan J, Astrup A, Engeli S, Narkiewicz K, Day WW, Finer N. Cardiovascular effects of phentermine and topiramate: a new drug combination for the treatment of obesity. *J Hypertens* 2014;32:1178-1188.
35. Bray GA, Kim KK, Wilding JPH; World Obesity Federation. Obesity: a chronic relapsing progressive disease process. A position statement of the World Obesity Federation. *Obes Rev* 2017;18:715-723.
36. Hendricks EJ, Rothman RB, Greenway FL. How physician obesity specialists use drugs to treat obesity. *Obesity (Silver Spring)* 2009;17:1730-1735.
37. Fabricatore AN, Wadden TA, Moore RH, Butryn ML, Heymsfield SB, Nguyen AM. Predictors of attrition and weight loss success: results from a randomized controlled trial. *Behav Res Ther* 2009;47:685-691.

ORIGINAL ARTICLE

# Long-Term Persistence of Hormonal Adaptations to Weight Loss

Priya Sumithran, M.B., B.S., Luke A. Prendergast, Ph.D.,  
Elizabeth Delbridge, Ph.D., Katrina Purcell, B.Sc., Arthur Shulkes, Sc.D.,  
Adamandia Kriketos, Ph.D., and Joseph Proietto, M.B., B.S., Ph.D.

## ABSTRACT

### BACKGROUND

After weight loss, changes in the circulating levels of several peripheral hormones involved in the homeostatic regulation of body weight occur. Whether these changes are transient or persist over time may be important for an understanding of the reasons behind the high rate of weight regain after diet-induced weight loss.

### METHODS

We enrolled 50 overweight or obese patients without diabetes in a 10-week weight-loss program for which a very-low-energy diet was prescribed. At baseline (before weight loss), at 10 weeks (after program completion), and at 62 weeks, we examined circulating levels of leptin, ghrelin, peptide YY, gastric inhibitory polypeptide, glucagon-like peptide 1, amylin, pancreatic polypeptide, cholecystokinin, and insulin and subjective ratings of appetite.

### RESULTS

Weight loss (mean  $\pm$ SE), 13.5 $\pm$ 0.5 kg) led to significant reductions in levels of leptin, peptide YY, cholecystokinin, insulin ( $P < 0.001$  for all comparisons), and amylin ( $P = 0.002$ ) and to increases in levels of ghrelin ( $P < 0.001$ ), gastric inhibitory polypeptide ( $P = 0.004$ ), and pancreatic polypeptide ( $P = 0.008$ ). There was also a significant increase in subjective appetite ( $P < 0.001$ ). One year after the initial weight loss, there were still significant differences from baseline in the mean levels of leptin ( $P < 0.001$ ), peptide YY ( $P < 0.001$ ), cholecystokinin ( $P = 0.04$ ), insulin ( $P = 0.01$ ), ghrelin ( $P < 0.001$ ), gastric inhibitory polypeptide ( $P < 0.001$ ), and pancreatic polypeptide ( $P = 0.002$ ), as well as hunger ( $P < 0.001$ ).

### CONCLUSIONS

One year after initial weight reduction, levels of the circulating mediators of appetite that encourage weight regain after diet-induced weight loss do not revert to the levels recorded before weight loss. Long-term strategies to counteract this change may be needed to prevent obesity relapse. (Funded by the National Health and Medical Research Council and others; ClinicalTrials.gov number, NCT00870259.)

From the Departments of Medicine (P.S., E.D., K.P., A.K., J.P.), and Surgery (A.S.) (Austin and Northern Health), University of Melbourne; and the Department of Mathematics and Statistics, La Trobe University (L.A.P.) — all in Melbourne, VIC, Australia. Address reprint requests to Dr. Proietto at the University of Melbourne, Department of Medicine, Heidelberg Repatriation Hospital, 300 Waterdale Rd., Heidelberg, VIC 3081, Australia, or at [j.proietto@unimelb.edu.au](mailto:j.proietto@unimelb.edu.au).

N Engl J Med 2011;365:1597-604.  
Copyright © 2011 Massachusetts Medical Society.

**W**ORLDWIDE, THERE ARE MORE THAN 1.5 billion overweight adults, including 400 million who are obese.<sup>1</sup> Although dietary restriction often results in initial weight loss, the majority of obese dieters fail to maintain their reduced weight.<sup>2</sup> Understanding the barriers to maintenance of weight loss is crucial for the prevention of relapse.

Body weight is centrally regulated, with peripheral hormonal signals released from the gastrointestinal tract, pancreas, and adipose tissue integrated, primarily in the hypothalamus, to regulate food intake and energy expenditure.<sup>3</sup> The number of identified peripheral modulators of appetite is expanding rapidly and includes leptin, ghrelin, cholecystokinin, peptide YY, insulin, pancreatic polypeptide, and glucagon-like peptide 1 (GLP-1).<sup>4-10</sup>

Caloric restriction results in acute compensatory changes, including profound reductions in energy expenditure<sup>11</sup> and levels of leptin<sup>12</sup> and cholecystokinin<sup>13</sup> and increases in ghrelin<sup>14</sup> and appetite,<sup>15</sup> all of which promote weight regain. It was recently shown that a disproportionate reduction in 24-hour energy expenditure persists in persons who have maintained a reduced body weight for more than 1 year<sup>16</sup>; however, it is not known whether the changes in levels of appetite-regulating hormones that occur during weight reduction are sustained with prolonged maintenance of reduced weight. The present study was designed to address this question, which may be important for understanding the physiological basis of weight regain after weight loss.

## METHODS

### PARTICIPANTS AND STUDY OVERSIGHT

We recruited men and postmenopausal women with a body-mass index (BMI, the weight in kilograms divided by the square of the height in meters) between 27 and 40 by means of newspaper advertisement. Smokers, persons with clinically significant illness, including diabetes, and those taking medications known to affect body weight were excluded. The study was approved by the Austin Health Human Research Ethics Committee, and all participants provided written informed consent.

### STUDY DESIGN

#### *Weight-Loss Phase*

For 8 weeks, participants were instructed to replace all three of their daily meals with a very-low-

energy dietary formulation (Optifast VLCD, Nestlé) and 2 cups of low-starch vegetables, according to the manufacturer's guidelines, which provided 2.1 to 2.3 MJ (500 to 550 kcal) per day. During weeks 9 and 10, participants who had lost 10% or more of their initial body weight were gradually reintroduced to ordinary foods, and weight was stabilized to avoid the potential confounding effect of active weight loss on hormone profiles. Meal replacements were stopped at the end of week 10.

#### *Weight-Maintenance Phase*

At the end of week 10, participants received individual counseling and written advice from a dietitian on a dietary intake that would be consistent with their calculated energy expenditure, with the aim of weight maintenance. No specific macronutrient ratios were prescribed, but carbohydrates with a low glycemic index and a reduced intake of fat were recommended. Participants were also encouraged to engage in 30 minutes of moderately intense physical activity on most days of the week. They visited the clinical research unit at Heidelberg Repatriation Hospital every 2 months, and were contacted by telephone between visits for continued dietary counseling.

#### *Data Collection*

Testing was performed after an overnight fast at baseline (week 0), week 10, and week 62. Participants wore light clothing and were barefoot when anthropometric measurements were made. Bioelectrical impedance was used to measure body weight and composition, with the use of a body-composition analyzer (TBF-300, Tanita). At each of these visits, the first measurement was made while the patient was fasting (baseline). A standardized breakfast was then provided, which consisted of a boiled egg, toast, margarine, orange juice, cereal biscuits (Weet-Bix, Sanitarium), and whole milk. This meal contained 2.3 MJ (550 kcal), with approximately 51% of the energy from carbohydrate, 33% from fat, and 16% from protein. Blood samples were collected 30, 60, 120, 180, and 240 minutes after the meal. Self-reported ratings of appetite were also recorded at these times with the use of a validated 100-mm visual-analogue scale.<sup>17</sup>

### BIOCHEMICAL ASSAYS

Fasting and postprandial plasma levels of acylated ghrelin, active GLP-1, total gastric inhibitory polypeptide, pancreatic polypeptide, amylin, and peptide YY were measured in the same assay with the

use of the human gut hormone panel (LINCOplex Kit, Millipore). Plasma levels of insulin, leptin, and cholecystokinin were measured with the use of a radioimmunoassay. (Additional details on the assays are available in the Supplementary Appendix, available with the full text of this article at NEJM.org.)

#### STATISTICAL ANALYSIS

Two analyses were conducted. In the intention-to-treat analysis, measures that were missing for participants who discontinued the study were replaced with baseline measures. In the second analysis, the only data included were from participants who completed the study (through the 12-month follow-up period). Since our aim was to examine the nature and duration of the physiological changes that occur as a result of diet-induced weight loss, only the data from participants who completed the study are provided for measures of biochemical values and appetite.

Continuous measures were compared with the use of nonparametric tests (the Wilcoxon signed-rank test for pairwise comparison of changes in measurements between study visits, and the Wilcoxon rank-sum test for comparisons between two independent groups). However for the sake of simplicity, descriptive statistics are reported as means  $\pm$ SE unless stated otherwise. Exact P values for Wilcoxon tests were computed with the shift algorithm, which also corrected for ties. Comparisons of independent proportions were calculated with Fisher's exact test. Spearman's rank correlations and associated P values were computed with algorithm AS 89.<sup>18</sup>

Analyses of fasting and 4-hour postprandial hormone profiles and ratings on the visual-analogue scale were carried out by fitting linear mixed-effect models to the data. The linear mixed-effect model, a repeated-measures analysis, included fasting and postprandial measurements and both fixed effects (postprandial time, week, and interaction) and random effects (participant characteristics). Linear mixed-effect estimation was carried out with the use of restricted maximum-likelihood methods, and the overall significance of each fixed effect was assessed by means of Wald tests. When no significant interaction could be detected between postprandial time and week (indicating similar postprandial changes relative to fasting values at different weeks), the model was refitted without interaction, and Tukey's test was used for multiple comparisons of means.

When interaction was present (suggesting an alteration in the postprandial hormone profile after weight loss), significant differences in linear mixed-effect coefficients at weeks 10 and 62, as compared with those at week 0, were reported for individual postprandial time points, and the linear mixed-effect model was restricted to weeks 10 and 62, for a more direct comparison between these weeks. The analysis of gastrointestinal hormones excluded one participant whose biochemical values were more than 5 SD beyond the mean. At baseline, measures of fasting biochemical data were missing for one participant. Less than 2% of the remaining data were missing. Linear mixed-effect analyses were applied to the raw data with no imputation of missing values. To ensure insensitivity of the results to missing data, analyses were repeated after imputation (see the Supplementary Appendix).

## RESULTS

#### STUDY PARTICIPANTS

Among the 50 participants who began the study, 4 withdrew during the first 8 weeks, while they were on the very-low-energy diet. An additional 7 participants did not lose the required 10% of body weight. During the 12-month follow-up period, 5 participants withdrew. Baseline characteristics of all participants who commenced the study and of those who completed it are shown in Table 1. There were no significant differences in any baseline measurements between those who did and those who did not complete the study, but there was a trend toward a younger age among participants who did not complete the study.

#### BODY MEASUREMENTS

Changes in body weight (Fig. 1) were significant in both the intention-to-treat analysis and the analysis that included only those participants who completed the study. Although male participants were significantly heavier than female participants throughout the study period (mean [ $\pm$ SD] baseline weight, 105.9 $\pm$ 12.6 kg vs. 90.5 $\pm$ 11.0 kg;  $P < 0.001$ ), the pattern of weight change was similar for men and women; consequently, the data were combined for the purposes of analysis.

Changes in anthropometric measurements for the participants who completed the study are shown in Table 2. The mean weight loss at the end of week 10 was 13.5 $\pm$ 0.5 kg (14.0% of initial weight). All anthropometric measurements de-

**Table 1. Baseline Characteristics of the Patients.\***

Characteristic	Total (N=50)	Completed Study (N=34)	Did Not Complete Study (N=16)	P Value
Age (yr)	54.4±10.9	56.0±10.6	51.0±11.2	0.05
Female sex (%)	68	68	69	1.00
Weight (kg)	95.4±13.5	96.3±13.7	93.6±13.5	0.47
BMI	34.7±3.2	34.7±3.7	34.5±2.0	0.86
Waist circumference (cm)	103.1±10.0	103.6±10.9	102.1±8.1	0.75
Hip circumference (cm)	120.8±8.0	120.6±8.2	121.2±7.8	0.84
Blood pressure (mm Hg)				
Systolic	135.5±20.2	137.9±20.2	130.3±19.7	0.17
Diastolic	83.1±10.8	82.8±11.8	83.8±8.7	0.71
Heart rate (beats/min)	74.6±8.5	74.9±7.3	74.0±10.8	0.86
Fat (%)	52.1±9.3	51.6±8.5	53.3±11.0	0.68

\* Plus–minus values are means ±SD. BMI denotes body-mass index, calculated as the weight in kilograms divided by the square of the height in meters.

creased significantly between weeks 0 and 10 and remained significantly below baseline values at week 62. Only data from the 34 patients who completed the study are included in the analyses that follow.

#### HORMONAL REGULATORS OF APPETITE

##### *Leptin*

During the weight-loss period, mean fasting plasma levels of leptin decreased by 64.5±3.4% ( $P<0.001$ ). Levels rose between weeks 10 and 62, but at week 62, they remained 35.5±4.7% below baseline levels ( $P<0.001$ ). Reductions in leptin levels from baseline at weeks 10 and 62 remained significant when adjusted for fat mass, and the ratio of leptin to fat mass was significantly lower at week 10 than at week 62 (Table 1 in the Supplementary Appendix). Percentage reductions in leptin and weight correlated strongly at week 10 ( $r=0.78$ ,  $P<0.001$ ) and week 62 ( $r=0.78$ ,  $P<0.001$ ). There was a strong linear relationship between the log-transformed percentage of leptin regained and weight regained, indicating that leptin levels and body weight rose concurrently.

##### *Gastrointestinal Hormones*

Mean fasting and postprandial levels of ghrelin, peptide YY, amylin, and cholecystokinin are shown in Figure 2. (Fig. 1 in the Supplementary Appendix provides these data for the remaining hormones studied, and Table 1 in the Supplementary

Appendix provides information on the area under the curve and the median percentage changes in biochemical values from baseline.)

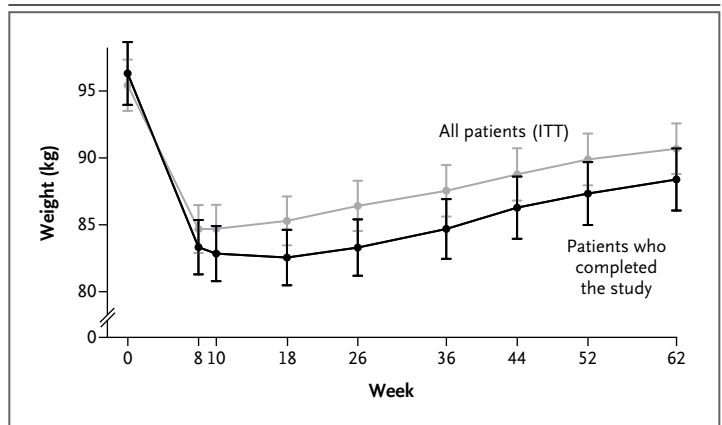
The linear mixed-effect analysis of hormone levels according to postprandial period and study week revealed that postprandial changes were highly significant for each hormone studied ( $P<0.001$  for all comparisons). The interaction between the postprandial period and study week was not significant for ghrelin, peptide YY, GLP-1, cholecystokinin, or pancreatic polypeptide, suggesting that there were similar patterns of postprandial hormone suppression or secretion at baseline and at weeks 10 and 62. For each of these hormones, however, each week was highly significant ( $P\leq 0.001$  for ghrelin, peptide YY, pancreatic polypeptide, and cholecystokinin;  $P=0.008$  for GLP-1), indicating differences in absolute hormone levels at each study week.

Mean levels of ghrelin rose significantly with weight loss ( $P<0.001$  for the change from baseline to week 10). Although ghrelin levels fell between week 10 and week 62 ( $P<0.001$ ), the mean level remained significantly higher at 62 weeks than at baseline ( $P<0.001$ ). For peptide YY, mean levels were significantly lower at weeks 10 and 62 than at baseline ( $P<0.001$  for both comparisons), with levels that were significantly lower at week 62 than those at week 10 ( $P=0.004$ ). For amylin, the interaction between postprandial period and study week was close to being significant ( $P=0.05$ ). Fast-

ing levels of amylin declined significantly with weight loss ( $P=0.008$  for the change from baseline to week 10;  $P=0.05$  for the change from baseline to week 62). The reduction from baseline in amylin secretion within the first 30 minutes after eating was significant at week 10 ( $P=0.002$ ) and approached significance at week 62 ( $P=0.08$ ). The mean level of cholecystikinin was significantly lower at weeks 10 and 62 than at baseline ( $P<0.001$  and  $P=0.04$ , respectively), with no significant difference in levels between weeks 10 and 62.

For gastric inhibitory polypeptide, the interaction between postprandial period and study week was significant ( $P=0.02$ ), owing to the greater secretion of this hormone in the first 60 minutes after meals at weeks 10 and 62 than at baseline ( $P=0.004$  and  $P<0.001$ , respectively). Mean levels of gastric inhibitory polypeptide did not differ significantly between weeks 10 and 62. Mean levels of GLP-1 did not change significantly between baseline and week 10; the levels at week 62 were slightly but significantly lower than baseline levels ( $P=0.005$ ).

Decreases in insulin levels after weight loss were evident, and the interaction between postprandial period and study week was significant ( $P<0.001$ ), with significant reductions in meal-stimulated insulin release 30 and 60 minutes after eating, both from baseline to week 10 ( $P<0.001$  for the two postprandial comparisons) and from baseline to week 62 ( $P<0.001$  for the comparison at 30 minutes;  $P=0.01$  for the comparison at 60 minutes). Mean levels of pancreatic polypeptide were



**Figure 1. Mean ( $\pm$ SE) Changes in Weight from Baseline to Week 62.**

The weight-loss program was started at week 0 and completed at week 10. ITT denotes intention to treat.

significantly higher at week 10 and week 62 than at baseline ( $P=0.008$  and  $P=0.002$ , respectively), with no significant difference between levels at weeks 10 and 62.

#### APPETITE

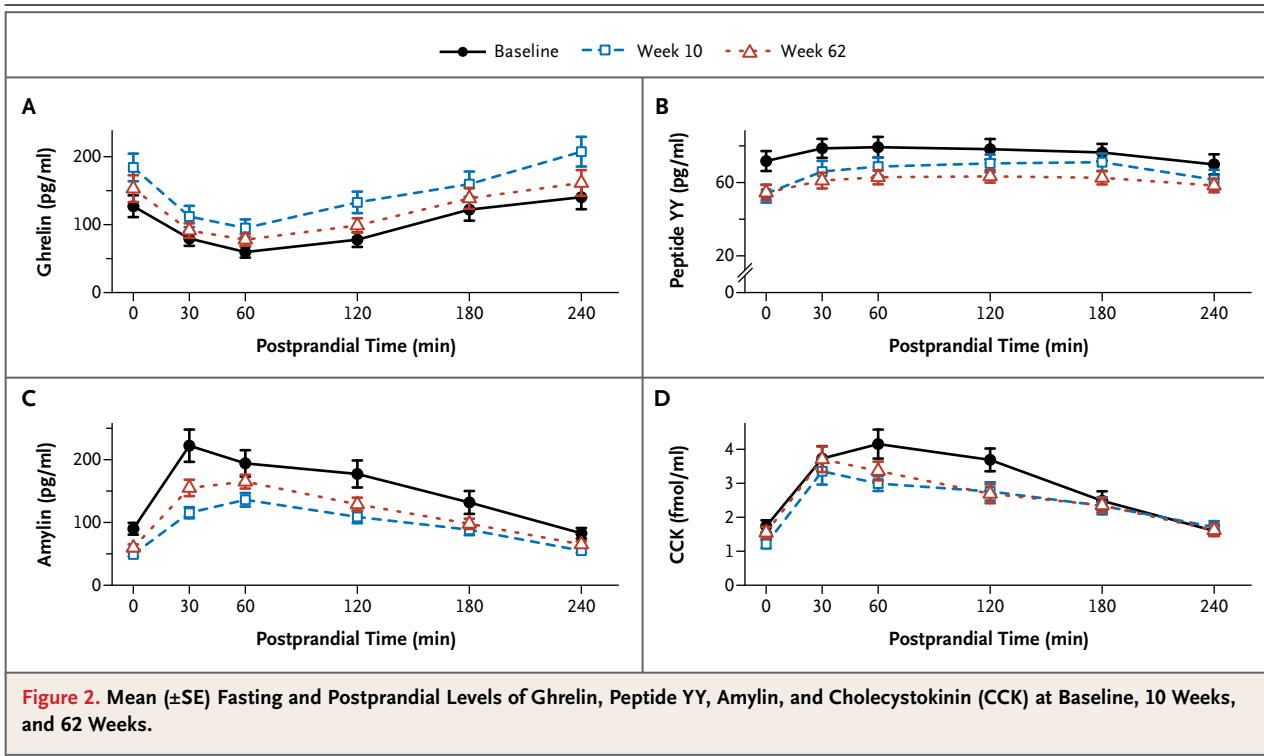
Figure 3 shows mean ratings, on a visual-analogue scale, of fasting and postprandial hunger and desire to eat at baseline and at weeks 10 and 62. (Additional ratings are available in Fig. 2 and Table 2 in the Supplementary Appendix.) The linear mixed-effect analysis revealed that mean ratings of hunger, desire and urge to eat, and prospective consumption were significantly higher at weeks 10 and

**Table 2. Changes in Body Measurements.\***

Variable	Baseline to Wk 10	P Value	Wk 10 to Wk 62	P Value	Baseline to Wk 62	P Value
Weight (kg)	-13.5 $\pm$ 0.5	<0.001	5.5 $\pm$ 1.0	<0.001	-7.9 $\pm$ 1.1	<0.001
Percent change in weight	-14.0 $\pm$ 0.4	<0.001	4.4 $\pm$ 0.7	<0.001	-8.2 $\pm$ 1.1	<0.001
BMI	-4.8 $\pm$ 0.1	<0.001	2.0 $\pm$ 0.3	<0.001	-2.8 $\pm$ 0.4	<0.001
Waist circumference (cm)	-11.1 $\pm$ 0.5	<0.001	4.1 $\pm$ 0.9	<0.001	-7.0 $\pm$ 1.1	<0.001
Hip circumference (cm)	-9.0 $\pm$ 0.4	<0.001	2.5 $\pm$ 0.8	0.002	-6.5 $\pm$ 0.8	<0.001
Blood pressure (mm Hg)						
Systolic	-13.5 $\pm$ 2.7	<0.001	5.9 $\pm$ 3.1	0.05	-7.7 $\pm$ 3.2	0.03
Diastolic	-8.8 $\pm$ 1.7	<0.001	4.9 $\pm$ 1.7	0.009	-4.0 $\pm$ 1.4	0.01
Heart rate (beats/min)	-4.7 $\pm$ 1.6	0.005	1.9 $\pm$ 1.8	0.30	-2.8 $\pm$ 1.8	0.04
Fat (%)	-9.8 $\pm$ 0.7	<0.001	4.5 $\pm$ 0.8	<0.001	-5.3 $\pm$ 0.9	<0.001

\* Plus-minus values are means  $\pm$ SE. P values are for the changes in body measurements within each time period.





62 than at baseline ( $P < 0.001$  for all comparisons), with no significant differences between mean ratings at weeks 10 and 62 and no significant interactions between postprandial period and study week. Ratings for preoccupation with thoughts of food, as compared with baseline ratings, tended to increase at week 10 ( $P = 0.09$ ) and were significantly increased at week 62 ( $P = 0.008$ ). Mean ratings for fullness did not change significantly from baseline to week 10 or week 62 but were significantly lower at week 62 than at week 10 ( $P = 0.03$ ).

## DISCUSSION

Although short-term weight loss is readily achieved through dietary restriction, only a small minority of obese people maintain diet-induced weight loss in the long term.<sup>19</sup> A multitude of hormones, peptides, and nutrients are involved in the homeostatic regulation of body weight, many of which are perturbed after weight loss. Whether these changes represent a transient compensatory response to an energy deficit is unknown, but an important finding of this study is that many of these alterations persist for 12 months after weight loss, even after the onset of weight regain, suggesting that the high rate of relapse among obese people who have lost

weight has a strong physiological basis and is not simply the result of the voluntary resumption of old habits.

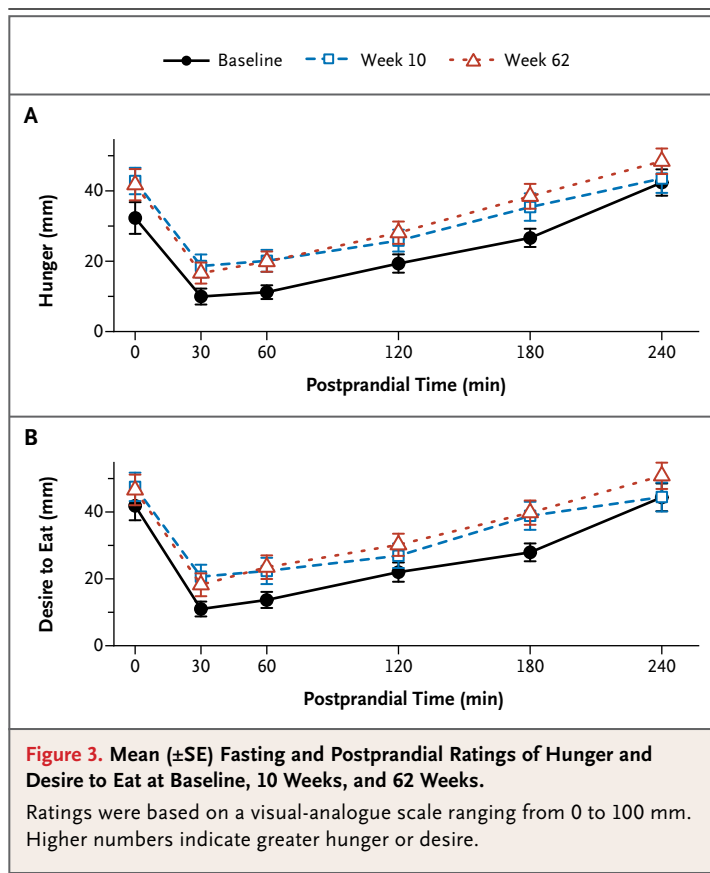
Leptin, an adipocyte hormone, is an indicator of energy stores<sup>20</sup> and acts in the hypothalamus to reduce food intake and increase energy expenditure.<sup>21,22</sup> Ghrelin, peptide YY, gastric inhibitory polypeptide, GLP-1, cholecystokinin, pancreatic polypeptide, and amylin are released from the gastrointestinal tract and pancreas in response to nutrient intake; all but two inhibit intake.<sup>8,10,23-25</sup> The exceptions are ghrelin, which stimulates hunger,<sup>7</sup> and gastric inhibitory polypeptide, which may promote energy storage.<sup>26,27</sup>

Caloric restriction results in a rapid, profound reduction in circulating levels of leptin<sup>28,29</sup> and energy expenditure<sup>30</sup> and an increase in appetite.<sup>15</sup> Other effects of diet-induced weight loss include increased levels of ghrelin<sup>14</sup> and reduced levels of peptide YY<sup>31</sup> and cholecystokinin.<sup>13</sup> Our study shows that after diet-induced weight loss, there are alterations in the postprandial release of amylin and pancreatic polypeptide and, more important, that changes in levels of leptin, ghrelin, peptide YY, gastric inhibitory polypeptide, pancreatic polypeptide, amylin, and cholecystokinin, as well as changes in appetite, persist for 12 months. In ad-

dition, these changes would be expected to facilitate regain of lost weight, with the exception of the change in the level of pancreatic polypeptide, which reduces food intake.<sup>10</sup> However, our findings are consistent with a study of obese children in which levels of pancreatic polypeptide increased after diet-induced weight loss.<sup>32</sup>

A greater-than-predicted decline in 24-hour energy expenditure after weight loss also persists for 1 year or more after the loss in weight has been maintained.<sup>16</sup> In obese rats with diet-induced weight loss, normalization of enhanced metabolic efficiency lags behind weight regain.<sup>33</sup>

Taken together, these findings indicate that in obese persons who have lost weight, multiple compensatory mechanisms encouraging weight gain, which persist for at least 1 year, must be overcome in order to maintain weight loss. These mechanisms would be advantageous for a lean person in an environment where food was scarce, but in an environment in which energy-dense food is abundant and physical activity is largely unnecessary, the high rate of relapse after weight loss is not surprising. Furthermore, the activation of this coordinated response in people who remain obese after weight loss supports the view that there is an elevated body-weight set point in obese persons and that efforts to reduce weight below this point are vigorously resisted. In keeping with this theory, studies have shown that after adjustment for body composition, people whose weight is normal and those who are obese have similar energy requirements for weight maintenance<sup>11</sup> and equivalent reductions in energy expenditure<sup>30</sup> after weight loss. If this is the case, successful management of obesity will require the development of safe, effective, long-term treatments to counteract these compensatory mechanisms and reduce appetite. Given the number of alterations in appetite-regulating mechanisms that have been described so far, a combination of medications will probably be required. Several such combinations are undergoing evaluation,<sup>34,35</sup> but none have been approved by the Food and Drug Administration. Bariatric surgery has well-documented favorable effects on appetite-mediating hormones, hunger, body weight, hypertension, dyslipidemia, type 2 diabetes, and mortality.<sup>36-38</sup> However, because of the attendant costs and long waiting periods, bariatric surgery is not readily accessible to most people.



There are several limitations of this study. First, the attrition rate was high, as it typically is in studies of long-term weight loss.<sup>19</sup> The analyses included only those participants who completed the study, since our intention was to assess the duration of physiological responses to substantial weight loss. However, the possibility that changes in hormone levels and appetite differed in patients who discontinued the study cannot be ruled out. Second, the use of a multiplex assay inevitably results in measurements of individual hormones that are less accurate and precise than those obtained with an optimized assay. However, these factors are likely to minimize the detection of changes occurring after weight loss. Finally, the possibility that weight loss may alter central sensitivity to circulating hormones was not examined.

In conclusion, we found that the compensatory changes in circulating mediators of appetite that encourage weight regain after diet-induced weight loss do not revert to baseline values within 12 months after the initial weight reduction.



Supported by a project grant from the National Health and Medical Research Council (508920), a scholarship from the Endocrine Society of Australia, a Shields Research Scholarship from the Royal Australasian College of Physicians (to Dr. Sumithran), and funding from the Sir Edward Dunlop Medical Research Foundation (to Dr. Proietto).

Disclosure forms provided by the authors are available at NEJM.org.

We thank Celestine Bouniou, John Cardinal, Sherrell Cardinal, Christian Rantzaou, Rebecca Sgambellone, Sherley Visinoni, and Mildred Yim for providing technical assistance.

## REFERENCES

1. Obesity and overweight. Geneva: World Health Organization, 2010. (<http://www.who.int/mediacentre/factsheets/fs311/en/index.html>.)
2. Wing RR, Hill JO. Successful weight loss maintenance. *Annu Rev Nutr* 2001; 21:323-41.
3. Schwartz MW, Woods SC, Porte D Jr, Seeley RJ, Baskin DG. Central nervous system control of food intake. *Nature* 2000;404:661-71.
4. Rezek M. The role of insulin in the glucostatic control of food intake. *Can J Physiol Pharmacol* 1976;54:650-65.
5. Zhang Y, Proenca R, Maffei M, Barone M, Leopold L, Friedman JM. Positional cloning of the mouse obese gene and its human homologue. *Nature* 1994;372:425-32. [Erratum, *Nature* 1995;374:479.]
6. Raben A, Tabliabue A, Christensen NJ, Madsen J, Holst JJ, Astrup A. Resistant starch: the effect on postprandial glycemia, hormonal response, and satiety. *Am J Clin Nutr* 1994;60:544-51.
7. Wren AM, Seal LJ, Cohen MA, et al. Ghrelin enhances appetite and increases food intake in humans. *J Clin Endocrinol Metab* 2001;86:5992-5.
8. Batterham RL, Cowley MA, Small CJ, et al. Gut hormone PYY3-36 physiologically inhibits food intake. *Nature* 2002; 418:650-4.
9. Gutzwiller JP, Göke B, Drewe J, et al. Glucagon-like peptide-1: a potent regulator of food intake in humans. *Gut* 1999; 44:81-6.
10. Batterham RL, Le Roux CW, Cohen MA, et al. Pancreatic polypeptide reduces appetite and food intake in humans. *J Clin Endocrinol Metab* 2003;88:3989-92.
11. Leibel RL, Hirsch J. Diminished energy requirements in reduced-obese patients. *Metabolism* 1984;33:164-70.
12. Geldszus R, Mayr B, Horn R, Geis-thovel F, von zur Mühlen A, Brabant G. Serum leptin and weight reduction in female obesity. *Eur J Endocrinol* 1996;135: 659-62.
13. Chearskul S, Delbridge E, Shulkes A, Proietto J, Kriketos A. Effect of weight loss and ketosis on postprandial cholecystokinin and free fatty acid concentrations. *Am J Clin Nutr* 2008;87:1238-46.
14. Cummings DE, Weigle DS, Frayo S, et al. Plasma ghrelin levels after diet-induced weight loss or gastric bypass surgery. *N Engl J Med* 2002;346:1623-30.
15. Keim NL, Stern JS, Havel PJ. Relation between circulating leptin concentrations and appetite during a prolonged, moderate energy deficit in women. *Am J Clin Nutr* 1998;68:794-801.
16. Rosenbaum M, Hirsch J, Gallagher DA, Leibel RL. Long-term persistence of adaptive thermogenesis in subjects who have maintained a reduced body weight. *Am J Clin Nutr* 2008;88:906-12.
17. Stubbs RJ, Hughes DA, Johnstone AM, et al. The use of visual analogue scales to assess motivation to eat in human subjects: a review of their reliability and validity with an evaluation of new hand-held computerized systems for temporal tracking of appetite ratings. *Br J Nutr* 2000;84:405-15.
18. Best DJ, Roberts DE. Algorithm AS 89: the upper tail probabilities of Spearman's rho. *Appl Stat* 1975;24:377-9.
19. Anderson JW, Konz EC, Frederich RC, Wood CL. Long-term weight-loss maintenance: a meta-analysis of US studies. *Am J Clin Nutr* 2001;74:579-84.
20. Rosenbaum M, Nicolson M, Hirsch J, Murphy E, Chu F, Leibel RL. Effects of weight change on plasma leptin concentrations and energy expenditure. *J Clin Endocrinol Metab* 1997;82:3647-54.
21. Stephens TW, Basinski M, Bristow PK, et al. The role of neuro-peptide Y in the antiobesity action of the obese gene product. *Nature* 1995;377:530-2.
22. Pellemounter MA, Cullen MJ, Baker MB, et al. Effects of the obese gene product on body weight regulation in ob/ob mice. *Science* 1995;269:540-3.
23. Flint A, Raben A, Astrup A, Holst JJ. Glucagon-like peptide 1 promotes satiety and suppresses energy intake in humans. *J Clin Invest* 1998;101:515-20.
24. Morley JE, Flood JF. Amylin decreases food intake in mice. *Peptides* 1991;12:865-9.
25. Gibbs J, Young RC, Smith GP. Cholecystokinin decreases food intake in rats. *J Comp Physiol Psychol* 1973;84:488-95.
26. Hauner H, Glatting G, Kaminska D, Pfeiffer EF. Effects of gastric inhibitory polypeptide on glucose and lipid metabolism of isolated rat adipocytes. *Ann Nutr Metab* 1988;32:282-8.
27. Knapper JM, Puddicombe SM, Morgan LM, Fletcher JM. Investigations into the actions of glucose-dependent insulinotropic polypeptide and glucagon-like peptide-1(7-36)amide on lipoprotein lipase activity in explants of rat adipose tissue. *J Nutr* 1995;125:183-8.
28. Considine RV, Sinha MK, Heiman ML, et al. Serum immunoreactive-leptin concentrations in normal-weight and obese humans. *N Engl J Med* 1996;334:292-5.
29. Havel PJ, Kasim-Karakas S, Mueller W, Johnson PR, Gingerich RL, Stern JS. Relationship of plasma leptin to plasma insulin and adiposity in normal weight and overweight women: effects of dietary fat content and sustained weight loss. *J Clin Endocrinol Metab* 1996;81:4406-13.
30. Leibel RL, Rosenbaum M, Hirsch J. Changes in energy expenditure resulting from altered body weight. *N Engl J Med* 1995;332:621-8. [Erratum, *N Engl J Med* 1995;333:399.]
31. Essah PA, Levy JR, Sistrun SN, Kelly SM, Nestler JE. Effect of weight loss by a low-fat diet and a low-carbohydrate diet on peptide YY levels. *Int J Obes (Lond)* 2010;34:1239-42.
32. Reinehr T, Enriori DJ, Harz K, Cowley MA, Roth CL. Pancreatic polypeptide in obese children before and after weight loss. *Int J Obes (Lond)* 2006;30:1476-81.
33. MacLean PS, Higgins JA, Johnson GC, et al. Enhanced metabolic efficiency contributes to weight regain after weight loss in obesity-prone rats. *Am J Physiol Regul Integr Comp Physiol* 2004;287:R1306-R1315.
34. Greenway FL, Dunayevich E, Tollefson G, et al. Comparison of combined bupropion and naltrexone therapy for obesity with monotherapy and placebo. *J Clin Endocrinol Metab* 2009;94:4898-906.
35. Bays H. Phentermine, topiramate and their combination for the treatment of adiposopathy ("sick fat") and metabolic disease. *Expert Rev Cardiovasc Ther* 2010; 8:1777-801.
36. Sjöström L, Lindroos AK, Peltonen M, et al. Lifestyle, diabetes, and cardiovascular risk factors 10 years after bariatric surgery. *N Engl J Med* 2004;351:2683-93.
37. Le Roux CW, Aylwin SJ, Batterham RL, et al. Gut hormone profiles following bariatric surgery favor an anorectic state, facilitate weight loss, and improve metabolic parameters. *Ann Surg* 2006;243:108-14.
38. Adams TD, Gress RE, Smith SC. Long-term mortality after gastric bypass surgery. *N Engl J Med* 2007;357:753-61.

Copyright © 2011 Massachusetts Medical Society.

It is the position of the Obesity Medicine Association (OMA) that long-term pharmacotherapy represents one important evidence-based treatment strategy for obesity.

Obesity has been recognized as a disease by the American Medical Association. [i] Obesity is a chronic disease that worsens over time. Weight loss does not cure obesity – instead, it triggers adaptations that restore the lost weight. [ii] It is estimated that 85% of self-directed weight loss efforts are met by weight regain.

Pharmacotherapy has been approved by the FDA for chronic weight management. This is different than the prevailing opinion about medications for obesity treatment. Prior to 2012, most medications were indicated only for short-term use to induce weight loss. This is incongruent with current knowledge about the chronic disease of obesity.

Pharmacotherapy has been shown to be both safe and effective. It doubles to triples the odds of losing 5-10% body weight (or more), and also the odds of keeping that weight off. Unfortunately, if treatment is stopped, weight is regained. [iii]

Recent studies have shown the older agents including Phentermine to be safe and effective for long-term use. A study published in 2019 of nearly 14,000 patients on long-term phentermine demonstrated it to be safe and effective for low-risk individuals with responders losing 10.5% body weight. [iv] And, the FDA approved a new version of Phentermine, marketed as Qsymia, for chronic use in 2012.

As a progressive, chronic disease, obesity gets worse over time. Therefore, we also believe that prevention of obesity is just as important as treatment. Drug labels recommend use at a Body Mass Index (BMI) of 27 or more with a compelling comorbidity, or 30 or more without. However, as with other chronic diseases, we know that medications can also be useful in prevention. For example, in an individual with pre-diabetes, metformin can be used off-label to prevent diabetes. Similarly, for a patient at high risk of obesity, medications may be helpful in prevention. Many studies have demonstrated the safety and efficacy of pharmacotherapy. Studies have also shown the older agents to be non-habit-forming. [v]

We would welcome further studies into the safety and efficacy of both old and new agents. In particular, we hope to see well-done, long-term studies on generic phentermine. Nevertheless, we also oppose the current practice of not treating obesity. For example, it is estimated that only 2% of patients with an on-label indication for obesity pharmacotherapy receive treatment. [vi] A more recent study shows only 1.6% of 2.2 million eligible patients are prescribed pharmacotherapy for obesity. [vii] This is in contrast to 85% of those with type 2 diabetes.

Obesity threatens the health of our nation. It is estimated that due to this rise in obesity, by 2030, type 2 diabetes rates will rise from 8.6% to 25% of the population. [viii] Obesity is costing our nation 1.72 trillion dollars annually (47.1% of healthcare spending on chronic disease) and is responsible for 320,000 deaths per year. [ix] Normalizing the BMI can save \$14,059 in healthcare costs and \$28,020 in societal costs per patient over their lifetime. [x]

Only by reducing the burden of the obesity epidemic can we prevent improve these numbers. While we understand that this will take significant work in the public health sector, we cannot continue to deny treatment to those who need it.

Our view is not alone – recent studies published in *Obesity Journal*, and also in *Endocrine Journal* [xi] recommend chronic treatment, even with older agents including phentermine. In spite of this, many providers continue to stop treatment after 3 months, 12 months, or after weight loss stops. Some do this out of fear of repercussion from their state medical, pharmacy and nursing boards. In fact, some states have laws making it illegal to use anti-obesity medications in an off-label way, and specifically single-out phentermine, threatening to take physician licenses if prescribing phentermine for over 3 months. Nurse practitioners and Physician Assistants also sometimes have limitations depending on their local and national certifying organizations that block their ability to provide the current standard of care with regards to anti-obesity pharmacotherapy.

The OMA applauds the AMA for adopting as policy that it is inappropriate for state or federal rules to interfere with evidence-based treatments for obesity that would prohibit a physician from providing the current standard of care with regards to obesity treatment. It is the position of the OMA that long-term prescribing of medications constitutes the current standard of care for obesity treatment, and the OMA opposes these restrictive rules.

Therefore, it is the position of the OMA that:

- 1) The current standard of care with respect to obesity pharmacotherapy is that medications should be prescribed long-term.
- 2) It is medically inappropriate for licensing boards to interfere with a provider's ability to offer standard of care treatment to patients affected by obesity.
- 3) Short-term use of obesity pharmacotherapy is not recommended as it has not been proven to provide a benefit.

---

[i] AMA Policy H440.842, 2013 Annual Meeting of the HOD

[ii] Chaput JP et al. *Obes Rev.* 2012;13:681-691, NHLBI. 2012. [www.nhlbi.gov/health/health-topics/topics/obe/causes#](http://www.nhlbi.gov/health/health-topics/topics/obe/causes#). Accessed May 23rd, 2017.

Schwartz MW et al. *Diabetes.* 2003;52:232-238.

[iii] *Lancet* 2017; Feb 22, 2017, *N Engl J Med* 2010;363:245-56.

[iv] Lewis, K. *Obesity.* 2019; 27(4):591-602

[v] Hendricks EJ et al. Addiction potential of phentermine prescribed during long-term treatment of obesity. *International Journal of Obesity* 38, 292-298 (2014). Doi: 10.1038/ijo.2013.74.

[vi] Thomas CE, Mauer EA, Shukla AP, Rathi S, Aronne LJ. Low adoption of weight loss medications: a comparison of prescribing patterns of antiobesity pharmacotherapies and SGLT2s. *Obesity (Silver Spring).* 2016; 24(9):1955–61.

[vii] Saxon et al. Antiobesity Medication Use in 2.2 Million Adults. 2019;27(12)1975. doi:10.1002/oby.22581

[viii] Rowley WR, Bezold C, Arikan Y, Byrne E, Krohe S. *Diabetes 2030: Insights from Yesterday, Today, and Future Trends.* *Popul Health Manag.* 2017;20(1):6–12. doi:10.1089/pop.2015.0181

[ix] Milken Institute Report. <http://milkeninstitute.org/reports/americas-obesity-crisis-health-and-economic-costs-excess-weight>. Accessed 11/18/2019

[x] *Obesity* (2017) 25, 1809-1815. doi:10.1002/oby.21965

[xi] Apovian, CM et al. *J Clin Endocrinol Metab.* 2015 Feb;100(2):342-62. doi: 10.1210/jc.2014-3415. Epub 2015 Jan 15.

# The Mitigating Effect of Phentermine and Topiramate on Weight Regain After Roux-en-Y Gastric Bypass Surgery

Nawfal W. Istfan <sup>1</sup>, Wendy A. Anderson <sup>2</sup>, Donald T. Hess <sup>2</sup>, Liqun Yu <sup>1</sup>, Brian Carmine <sup>2</sup>, and Caroline M. Apovian <sup>1</sup>

**Objective:** Weight regain (WR) after Roux-en-Y gastric bypass surgery (RYGB) starts to occur 2 years after surgery, ultimately affecting at least 25% of patients. A limited number of studies have evaluated the impact of antiobesity medications (AOMs) on this phenomenon.

**Methods:** This study reviewed the electronic medical records of 1,196 patients who underwent RYGB between 2004 and 2015. WR was evaluated by comparing each patient's weight during subsequent postoperative office visits to nadir weight (lowest weight after RYGB,  $n = 760$ ), taking into consideration the interval during which WR occurred. Patients who were prescribed AOMs and came to follow-up visits were classified as adherent users, whereas those who missed their follow-up visits were considered nonadherent. This study used a linear mixed model, Cox regression, and generalized equation estimator to determine the impact of AOMs on WR trajectory, hazard ratio for time to event, and odds ratio for repeated event occurrence, respectively.

**Results:** Despite the lack of a unified protocol for using AOMs, the three statistical models converged to show that phentermine and topiramate, used individually or in combination, can significantly reduce WR after RYGB.

**Conclusions:** Phentermine and topiramate are effective in mitigating WR after RYGB. Further studies are needed to help ascertain optimal use of AOMs after bariatric surgery.

*Obesity* (2020) **28**, 1023-1030.

## Introduction

Bariatric surgery has evolved as a main treatment strategy for patients with severe obesity, especially in the presence of chronic comorbid conditions such as type 2 diabetes (T2D) and obstructive sleep apnea. One attribute that has increased the popularity of surgical management of obesity is the expectation of durable weight loss (WL), especially for patients with a history of weight cycling. However, several studies have identified an increasing prevalence of weight regain (WR) and subsequent reemergence of obesity-related comorbidities after bariatric surgery (1,2). The lack of a standard measure of WR after bariatric surgery has led to different methods of literature reporting, such as percentage of presurgery weight, nadir weight, or maximum weight lost. It is estimated that in the 5 years following Roux-en-Y gastric bypass surgery

(RYGB), approximately one-half of patients would have regained 15% of the nadir weight, and two-thirds would have regained >20% of the weight lost (2). Given the increasing number of bariatric surgery procedures being performed, the unfavorable impact of WR and the potential for recurrence of metabolic sequelae are likely to be substantial.

We recently showed that, in an 11-year cross-sectional analysis of our ethnically diverse patient population undergoing RYGB, mean WR relative to nadir was approximately 10%, with the highest quartile showing WR in excess of 14.3% of nadir weight. These estimates, which were based on the most recent office visit for each patient, represent a regain of >24% in one-half of the patients and >45% of the weight lost in the highest quartile. Significant factors affecting WR following RYGB were race, age, and presurgical BMI (3).

## Study Importance

### What is already known?

- ▶ The problem of weight regain (WR) after bariatric surgery is increasingly being recognized.
- ▶ Tools to reduce the impact of WR after bariatric surgery are needed.
- ▶ Antiobesity medications (AOMs) have not been extensively used in patients with a history of bariatric surgery.

### What does this study add?

- ▶ Phentermine and topiramate alter the trajectory of WR after Roux-en-Y gastric bypass (RYGB) surgery.
- ▶ Phentermine and topiramate reduce the occurrence of rapid WR after RYGB.

### How might these results change the direction of research?

- ▶ Prospective clinical trials are needed to establish guidelines for use of AOMs in patients with history of bariatric surgery.

<sup>1</sup> Section of Endocrinology, Diabetes, Nutrition, and Weight Management, Department of Medicine, School of Medicine, Boston University/Boston Medical Center, Boston, Massachusetts, USA. Correspondence: Nawfal W. Istfan (nawfal.istfan@bmc.org) <sup>2</sup> Section of Minimally Invasive Surgery, Department of Surgery, School of Medicine, Boston University /Boston Medical Center, Boston, Massachusetts, USA.

See Commentary, pg. 1004.

© 2020 The Obesity Society. Received: 27 November 2019; Accepted: 10 February 2020; Published online 22 May 2020. doi:10.1002/oby.22786



This retrospective study examined the utility of antiobesity medications (AOMs) in treating WR in the same multiethnic patient population after RYGB. We used linear mixed models to evaluate trajectories of weight change relative to the patients' nadir weight. As in our previous study, we classified the rates of WR by quartiles and evaluated the impact of AOMs using three different statistical modeling methodologies. The results of these analyses converge to show that AOMs could play an important role in mitigating WR after RYGB. Although WR has been shown to occur after both sleeve gastrectomy and RYGB, our center is similar to others in that the RYGB population spans a longer follow-up period because sleeve gastrectomy became popular more recently. Therefore, we restricted our analysis to those patients who underwent RYGB during this time period.

## Methods

### Patients

This retrospective study used the electronic medical record data of adult patients who had undergone bariatric surgery, specifically RYGB, at Boston Medical Center (BMC) between 2004 and 2015. This study was approved by the BMC and Boston University Medical Campus Institutional Review Board under protocol H-26417.

### Clinical data

Race and ethnicity were self-identified as Caucasian (CA), black/African American (AA), Hispanic (HA), Asian, American Indian/Native American, Native Hawaiian/Pacific Islander, or not available/declined information. Data were extracted by the Boston University Clinical Data Warehouse and included age at the time of surgery, date of enrollment in the bariatric program, date of the surgery, weight, height, and BMI.

We reviewed data from all patients who underwent bariatric surgery at BMC during this period ( $n=1,516$ ). We limited our study to patients who underwent RYGB from the three most common racial and ethnic groups in our population ( $n=1,196$ ): AA, HA, and CA. Patients who became pregnant after surgery or underwent surgical revisions were excluded. Presurgical medical *International Classification of Diseases, Ninth Revision* codes were used to identify comorbid conditions, including T2D (250 and 790.29), osteoarthritis (715.9 and 716.9), hypertension (401.1, 401.9 and 796.2), dyslipidemia (272), and obstructive sleep apnea (780.57, 780.53 and 327.23).

The zip code for each patient was used to estimate the socioeconomic status (SES) based on the zip code median income. Data on the median income by zip code in 2014 were obtained from the United States Census Bureau (4). Patients were classified into SES quartiles based on the zip code median income. Use of AOMs was determined from the date of prescription of any of the following medications: phentermine, topiramate, lorcaserin (Belviq), phentermine/topiramate (Qsymia), and naltrexone/bupropion (Contrave). Patients were classified as "adherent" if they showed up for an office visit within 60 days of the date of the prescription; those patients who did not return for an office visit within this interval were classified as "nonadherent" because of the likelihood that prescriptions needed to be refilled at these missed visits.

### Statistical analyses

The primary objective for this study was to determine the effect of AOMs on long-term WR. A linear mixed model (treating participants as

a random effect) was used to examine AOMs, race, sex, time, and presence of comorbid conditions as fixed effects on weight change. Age and presurgery BMI were included as covariates. Seven time intervals were used in these analyses: before surgery and 1 to 2 years, 2 to 3 years, 3 to 4 years, 4 to 5 years, 5 to 6 years, and beyond 6 years after surgery.

Patients who had not yet achieved nadir weight ( $n=436$ ) were excluded from the following calculations. We calculated WL as the difference between the presurgical weight and the nadir weight for each participant ( $n=760$ ). We defined WR as the difference between the weight obtained at each subsequent office visit following the nadir date and the nadir weight in kilograms. WR was evaluated relative to amount of weight lost (WR/WL, expressed as a percentage) and relative to nadir (WR/nadir, expressed as a percentage) for each patient based on the recorded weights at each office visit after nadir. Hence, WR/WL and WR/nadir are both repeated measures for each participant.

The rate of WR was calculated based on both WR/WL and WR/nadir at each subsequent weight measurement relative to the time elapsed since nadir (reported as percentage per 30-day interval). Differences in continuous variables between categorical groups were assessed by ANOVA. Categorical outcomes were assessed by cross-tabulation and  $\chi^2$  distribution analysis. Multinomial logistic regressions were used to compare groups with more than two categorical outcomes across groups.

The 25%, 50%, and 75% values of the WR/nadir weight distribution based on the last observed weight were used to define thresholds and group patients into quartiles of low, moderate, and high rates of WR. We performed a Cox regression model to determine the proportional hazard ratio of WR at each of these three thresholds. Hence, event occurrence was defined as the time to first occurrence for a patient whose WR/nadir exceeded each specific cut-off threshold corresponding to the 25th, 50th, and 75th WR/nadir distribution (WR/nadir of 1.49%, 6.25%, and 14.29%, respectively). Race, sex, SES, and each comorbid condition were entered individually into the Cox regression as categorical predictors; age and WL were entered as continuous predictors. The final multivariable Cox regression included all the factors with  $P$  values  $<0.05$ . Because AOMs were prescribed intermittently, we further analyzed the rates of WR at each visit as "repeated exposures" using a generalized equation estimator with an independent correlation structure to correct within-participant correlation. The odds ratio (OR) for occurrence of an event was determined by binomial logistic regression analysis. We used specific WR rates as "events" based on the quartile distribution of all WR rates for the study population, as described above. All data analyses were performed using SPSS version 25 (IBM Corp., Armonk, New York).

## Results

A summary of the clinical characteristics of patients who achieved nadir weight and are at risk of WR after RYGB is presented in Table 1. Of the 760 in this cohort, 350 (46.1%) were documented users of AOMs. Of the AOM users, 119 (34.0%) were prescribed phentermine alone, 74 (21.1%) used topiramate alone, and 154 (44.0%) were prescribed a combination of phentermine and topiramate. Only three patients (0.9%) were prescribed lorcaserin and none were prescribed generic or brand-name bupropion/naltrexone or brand-name phentermine/topiramate. Liraglutide 3.0 was not an available option at the time. There were no

**TABLE 1** Characteristics of patients who achieved nadir weight stratified by AOM use

	No medication	Adherent	Nonadherent	Total	Sig
<i>N</i>	410 (53.9%)	157 (20.7%)	193 (25.4%)	760	
Age, y	47.0±0.5	44.2±0.8	45.2±0.9	45.9±0.4	0.007
Sex, %					
Female	76.1	91.1	81.9	80.7	0.000
Male	23.9	8.9	18.1	19.3	
Presurgical weight, kg	92.4±2.6	100.3±3.9	90.5±4.0	93.6±1.9	0.18
Presurgical BMI, kg/m <sup>2</sup>	46.8±0.4	46.5±0.7	47.2±0.7	47.8±0.3	0.77
Race, %					0.000
CA	44.6	39.5	65.1	54.6	
AA	24.4	40.1	36.8	30.8	
HA	10.5	20.4	18.7	14.6	
SES, %					0.009
1	23.2	33.8	30.4	27.2	
2	27.7	33.8	25.7	28.5	
3	21.9	18.8	19.4	20.6	
4	27.2	13.6	24.6	23.7	
T2D, %	54.1	62.4	56.0	56.3	NS
Dyslipidemia, %	46.3	48.4	28.0	42.1	NS
Hypertension, %	69.5	70.7	64.8	68.6	NS
OSA, %	36.1	35.0	37.3	36.2	NS
Osteoarthritis, %	10.7	8.9	12.4	10.8	NS

Data are mean ± SE. SES: 1, <\$47,297; 2, \$47,297-\$60,774; 3, \$60,775-\$76,924; 4, >\$76,924.

AA, African American; AOM, antiobesity medication; CA, Caucasian; HA, Hispanic; NS, not significant; OSA, obstructive sleep apnea; Sig, significance; SES, socioeconomic status; T2D, type 2 diabetes;

significant differences in presurgery BMI and prevalence of the comorbidities included in the analysis between the AOM users and nonusers. There were more AOM users among HA and AA patients than among CA patients. Relative to CA patients, the ORs for patients to be prescribed AOMs were 2.42 (CI: 1.74-3.36,  $P < 0.001$ ) for AA patients and 2.85 (CI 1.85-4.39,  $P < 0.001$ ) for HA patients. Patients in the lowest SES category were more likely to be prescribed AOMs (OR: 1.90, CI: 1.26-2.87,  $P = 0.002$ ).

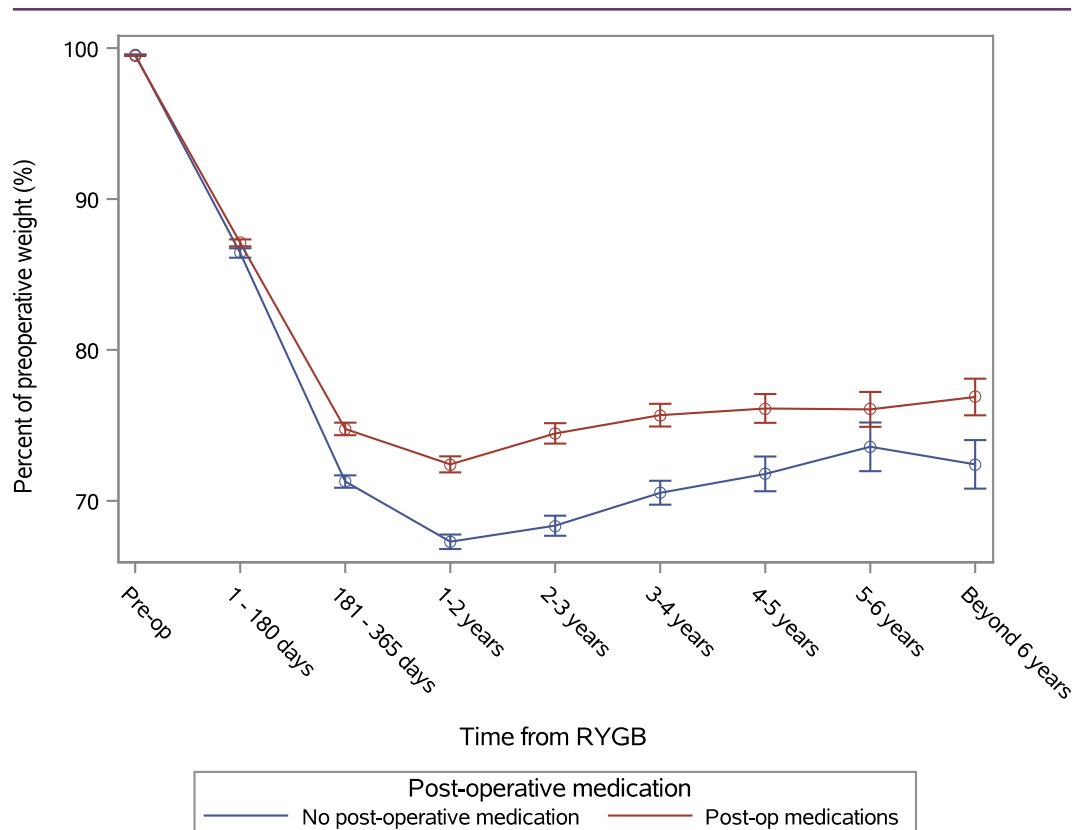
The weight trajectories for patients who used AOMs are compared with non-AOM users in Figure 1. In the mixed model analysis, patients who used AOMs had achieved less WL at nadir ( $P < 0.0001$ ) than patients who did not use AOMs after bariatric surgery. Figure 1 also suggests that users of AOMs had a smaller upward slope compared with nonusers, implying slower WR in the former group during the observation period up to 11 years. However, the interaction of time × AOM use was not statistically significant, suggesting that the pattern of WR was similar in the two groups. Therefore, although AOMs (phentermine and topiramate) were more likely to be prescribed in patients who had suboptimal WL, their effectiveness in mitigating WR could not be determined solely from weight trajectory of the current cohort.

To further evaluate the effect of AOMs on WR, we determined the increase in weight relative to nadir at the last available weight for each patient. These estimates of WR (percentage of nadir weight) were then classified by quartiles. Cut-off points for the 25th, 50th and 75th percentiles of WR were 1.5%, 6.25%, and 14.3% relative to the nadir, respectively. As a percentage of the amount of weight lost, WR was 1.8% ± 0.2%, 17.2% ± 0.8%, 30.3% ± 1.4%, and 41.1% ± 5.1%, respectively, for the four quartiles. Thus,

50% of the patients (upper two quartiles) regained at least one-third of the weight they had previously lost. The clinical characteristics of these quartiles of WR were published previously (3). Briefly, the quartiles were similar in age and sex distribution; significant differences were noted in race, presence of T2D, and use of AOMs. The upper two quartiles were more likely to include AA than CA patients (likelihood ratio: 1.553, CI: 1.023-2.358,  $P = 0.039$  in the third quartile and likelihood ratio: 2.154, CI: 1.37-3.385,  $P = 0.001$  in the fourth quartile). The quartile with the highest WR was also more likely to include patients with T2D (likelihood ratio: 1.689, CI: 1.114-2.571,  $P = 0.013$ ) and patients who were prescribed AOMs but were identified to be nonadherent (likelihood ratio relative to patients without AOM prescription: 1.683, CI: 1.041-2.557,  $P = 0.033$ ).

Because WR increases with time, differences between the quartiles could be explained by the duration of the observation period during which WR was assessed (the last office visit for each patient). Patients in the highest quartile of total WR were more likely to have undergone RYGB earlier (years after procedure: 4.3 ± 0.2, 3.1 ± 0.1, 4.3 ± 0.2, and 5.5 ± 0.2 years for the lowest to highest quartile, respectively;  $P < 0.0001$ ). Therefore, we normalized the WR/nadir values as monthly rates. The corresponding cut-off WR rates (percentage per 30 days) were 0.18%, 0.58%, and 1.22%.

We used three statistical models to evaluate the impact of AOMs on monthly WR rates for each of the quartile cut-off values shown. In the first model, a linear mixed model, adjusted for age, sex, race, and SES, was used to evaluate WR progression. Differences in WR between AOM users and nonusers were statistically significant only in the highest (most rapid) WR quartile. The results of the subgroup



**Figure 1** Trajectory of changes in body weight by use of antiobesity medication. Weights are shown as percentage of the immediate preoperative weight. Numbers of patients at preoperative stage, 1 to 180 days, 181 to 365 days, 1 to 2 years, 2 to 3 years, 3 to 4 years, 4 to 5 years, 5 to 6 years, and beyond 6 years: overall = 1,196, 1,183, 1,090, 1,078, 859, 763, 515, 373, 250; adherent = 159, 158, 155, 155, 142, 136, 122, 105, 87; nonadherent = 252, 250, 250, 259, 219, 203, 146, 98, 51; and none = 785, 775, 685, 673, 498, 424, 247, 170, 112. RYGB, Roux-en-Y gastric bypass surgery. [Color figure can be viewed at [wileyonlinelibrary.com](http://wileyonlinelibrary.com)]

of patients who regained weight relative to the nadir at a rate  $\geq 1.22\%$  per month (highest WR quartile) are presented in Figure 2. WR progression was smaller in the group of patients who were prescribed AOMs and were classified as adherent when compared with the nonadherent patients or nonusers of AOMs ( $P=0.012$ ). By the end of the observation period, WR relative to nadir was approximately 10% lower among adherent AOM users in comparison with nonadherent users.

In the second model, we evaluated whether AOMs can impact the occurrence of WR/nadir of at least 1.22% per month. The results of Cox regression analysis are presented in Figure 3, showing a proportional hazard ratio of 0.729 (CI: 0.556-0.957,  $P=0.023$ ) for the adherent AOM users compared with the nonusers of AOMs. Patients who were prescribed AOMs but classified as nonadherent had a proportional hazard ratio of 0.844 (CI: 0.659-1.081,  $P=0.18$ ). Similar analyses for the lower three quartiles of WR did not reveal statistically significant differences.

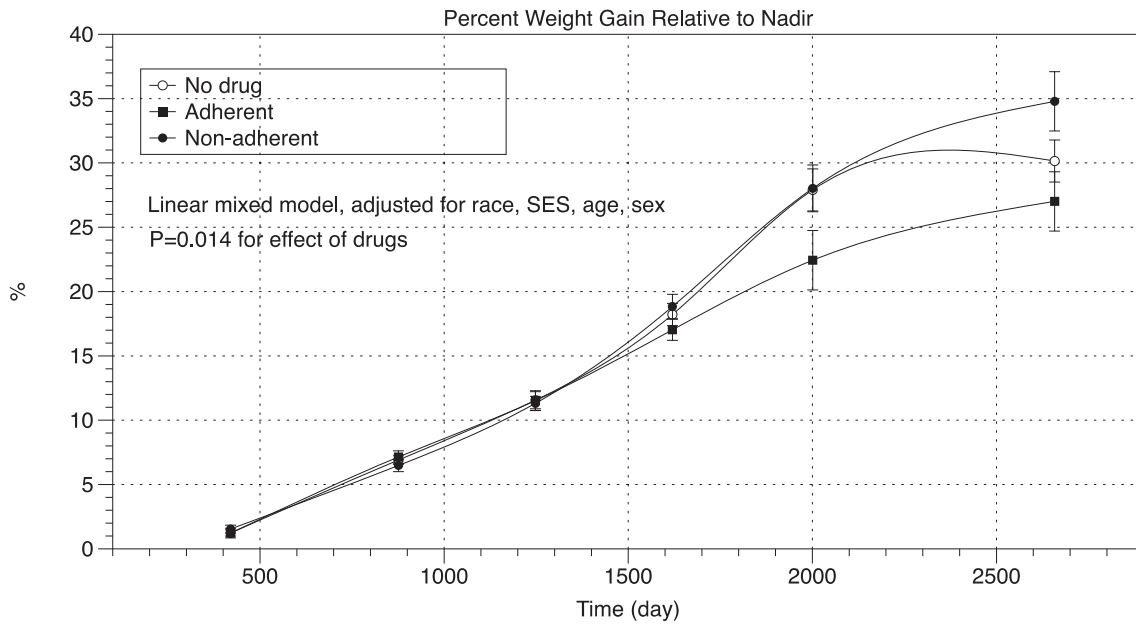
It is important to note that use of AOMs in this patient population was intermittent because patients were likely to discontinue the medications and resume them at subsequent times. The decision to prescribe and when to prescribe AOMs were variable among providers and patients. Thus, multiple exposures to AOMs occurred “randomly”

per patient during the observation interval. Therefore, to further evaluate the effectiveness of AOMs, we used the generalized equation estimator approach with an independent correlation structure to correct within-participant correlation. In a binary logistic model, adjusted for age, sex, race, and SES, the OR for occurrence of WR of  $\geq 1.22\%$  per month relative to nadir was 0.579 (CI: 0.371-0.877,  $P=0.01$ ) in the adherent AOM group and 0.872 (CI: 0.593-1.284,  $P=0.5$ ) compared with the non-AOM users. These results imply that AOMs effectively reduced the risk of recurrent bouts of rapid WR in our patient population.

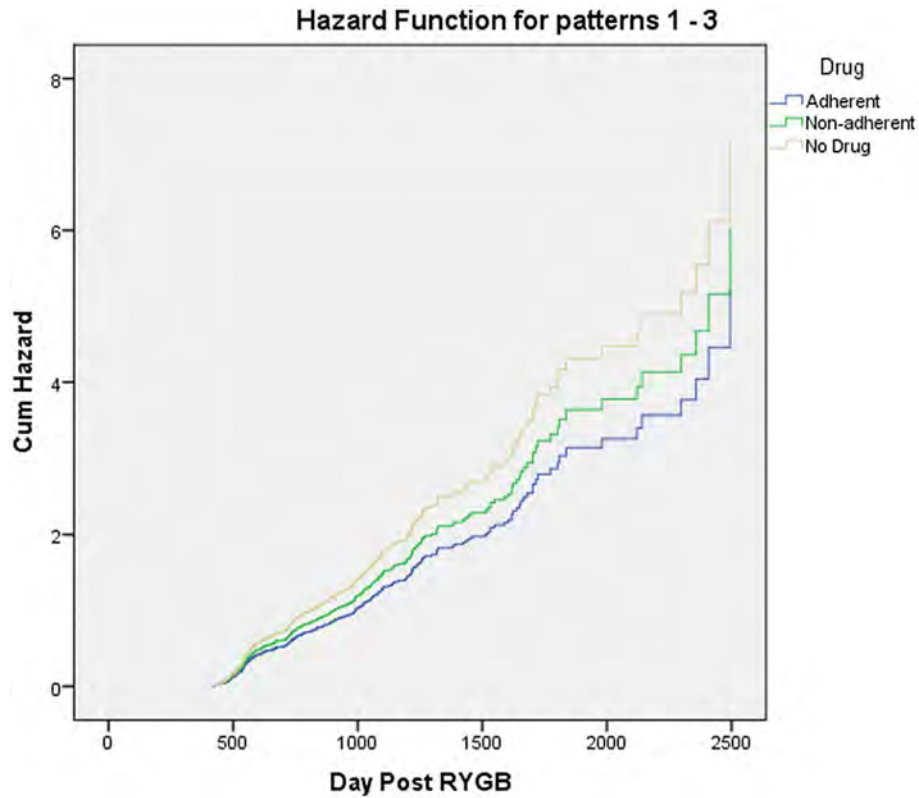
## Discussion

This large retrospective study of WR after RYGB suggests that the use of AOMs and adherence to those medications is effective in mitigating WR after RYGB. Our results relate specifically to the use of phentermine and topiramate, either individually or in combination. We were unable to compare the effectiveness of other AOMs because of the small numbers prescribed to this cohort at the time of analysis. The analytical approach in the current study focuses on the progression of body-weight changes throughout an 11-year observation period in an ethnically diverse patient population. Although it is conventional to evaluate the effectiveness of AOMs by the amount





**Figure 2** Trajectory of total weight regain in the highest quartile. Data are shown as percentage of nadir weight. Highest quartile is defined by a rate of weight regain equivalent to 1.22% of nadir weight per 30-day-interval. SES, socioeconomic status.



**Figure 3** Cox regression for weight regain relative to nadir normalized for a 30-day interval stratified by antiobesity medication use. Data are for the top quartile (weight regain  $\geq 1.22\%$  of nadir weight). RYGB, Roux-en-Y gastric bypass. [Color figure can be viewed at [wileyonlinelibrary.com](http://wileyonlinelibrary.com)]

of weight lost, this approach was not applicable in the current study. There were no specific clinical parameters that guided the providers' prescriptions of AOMs; and in most cases, the decision to take or withhold AOMs was effectively a random event. Therefore, to overcome this limitation, we used three independent statistical models, which consistently demonstrated that AOMs decrease cumulative WR by about 10% relative to nadir weight and reduce the odds of rapid WR after RYGB. As detailed elsewhere, rapid WR in our cohort is defined as a rate of increase in body weight of 1.22% per month relative to nadir weight (3). These results take into account that patients typically lost weight when taking AOMs and regained weight during intervals when the medications were not prescribed and that patients in the current study started AOMs at different stages and used them over variable and intermittent periods. Therefore, controlled prospective clinical trials are needed to further evaluate the impact of AOMs on WL parameters and long-term weight outcomes after bariatric surgery procedures.

Wider awareness of the clinical implications associated with obesity has increased the acceptance of surgical interventions. The beneficial effects of RYGB on T2D are clear, and studies with only 1 to 2 years of follow-up have purported that RYGB is associated with long-term weight stability. However, recent reports of WR after RYGB highlight the need for adjunct treatment strategies to maximize the long-term benefit and reduce the recurrence risk of comorbid conditions. Estimated proportions of patients who have "significant" WR have varied from 17% to 30% at 2 years from RYGB (5-8) to 59% in 1 small study with >20% WR at least 1 year from RYGB (9) to 79% by self-report (10). These estimates depend on the definition of *significant WR*, the duration of the study, and the method of reporting WR (11-14). Without a standard definition of WR, it is difficult to compare data from different studies. For example, in the Swedish Obese Subjects (SOS) study, long-term weight outcomes are reported as weight changes relative to the presurgical weight (15-18). This approach emphasizes the beneficial long-term outcomes of bariatric surgery because it continues to show significant WL 10 years following the surgical procedure. However, data presented as such do not provide clear and direct measures of the amount of WR. A discussion of the different ways of reporting WR and how they relate to clinical outcomes is presented by King et al (2). We have previously argued that because WR is the consequence of a specific physiological process characterized by a state of positive energy balance, it is better evaluated in terms of actual weight increase rather than by a decrease in previously achieved WL. Thus, we regard WR/nadir as a more clinically relevant parameter of the metabolic conditions associated with WR in the post-RYGB phase. Because total WR increases with time, we determined WR/nadir as a rate per 30 days to normalize for differences in observation intervals between groups. Further details characterizing WR in our patient population are presented elsewhere (3).

It is important to emphasize that the relapse of obesity is better defined by the recurrence of clinically significant comorbid conditions rather than by WR itself. Long-term observations, such as those from the SOS study, consistently document the beneficial impact of bariatric surgery on mortality, diabetes, and vascular disease (16,17,19,20). The relationship between WR and recurrence of specific comorbidities remains unclear. Although the SOS study has associated diabetes remission with the degree of WL at 2 and 10 years after surgery (21), it is difficult to evaluate the impact of WR from that study because of the specific way data are reported, as noted above. However, the potential for relapse is concerning and has prompted additional surgical

procedures ("revisional surgery") (22) aiming to increase malabsorption ("distalization") (23), increase the restriction at the gastro-jejunal anastomosis (24) (sclerotherapy) (25), and correct anatomical defects such as gastro-gastric fistulas (26). Unfortunately, position statements and guidelines related to the implementation of surgical revisions continue to rely on expert opinion (27) rather than on controlled prospective studies. Thus, nonsurgical interventions remain crucial for counteracting the growing problem of WR following bariatric surgery.

Interventions targeting disordered or maladaptive eating patterns such as night eating, grazing, and nibbling behaviors, which are widely reported among patients following bariatric surgery (6,28,29), have been effectively used to help mitigate WR (30). However, use of AOMs has been limited. One possible reason is that many patients are more likely to be followed up by bariatric surgeons who have limited experience in the use of anorexigenic pharmacotherapy. Additionally, guidelines for use of AOMs after bariatric surgery have not been established, thus leading to skepticism about their utility. Several possible physiological changes could potentially impact the effectiveness of AOMs after bariatric surgery. For example, changes in the regulation of satiety and the preexisting history of substantial WL after bariatric surgery could alter the effectiveness of AOMs. The current study further confirms that AOMs remain effective and are useful tools to help temper the brunt of WR among patients with history of RYGB, and potentially other bariatric surgery procedures. In our own experience, postsurgical AOM use in our clinic had been very limited prior to 2009 and had increased approximately fourfold by 2015, when >10% patients were prescribed phentermine, topiramate, or a combination of these two medications during postsurgery office visits.

Few other studies have demonstrated that AOMs remain effective after bariatric surgery (31-36). To our knowledge, compared with the prior studies cited, ours is the largest retrospective study to date and one that features an underserved ethnic patient population. It is important to note the unique setting of this retrospective study. As previously described in more detail elsewhere (3), race is an important determinant of WR after RYGB with AA patients being at high risk. In our center, we typically find that AA and HA patients are more likely to be prescribed AOMs than CA patients after RYGB, presumably because of their higher propensity for WR. Thus, it is possible that higher rates of WR among AA and HA patients could have influenced decisions to prescribe AOMs in our patient population. However, these prescriptions were not based on predetermined criteria or algorithms but were rather initiated by individual patient-physician interactions during routine office visits. Differences in AOM prescription practices between providers could further contribute to the variance in the clinical outcomes in the current study. However, despite these drawbacks, we are able to show that AOMs are important tools in the long-term management of patients with obesity and WR following RYGB and work as effectively as they do in medically managed patients with obesity. We also note that our previous findings of racial disparities of WR after RYGB may have been tempered by the higher rate of AOMs prescribed to AA and HA patients in our patient population.

There are few prospective trials investigating "rescue" pharmacotherapy with AOMs following bariatric surgery, with only six published to date with small numbers of patients (37-43). One of the studies used an AOM which has since been withdrawn from the market, fenfluramine (40), and two other trials used AOMs after the adjustable laparoscopic gastric band, which is rarely used today (41,42). The advent of larger randomized controlled clinical trials

evaluating the use of single and combination AOMs as rescue therapy for WR after bariatric surgery will be crucial to the development of treatment guidelines. The judicious use of multimodal medical and surgical treatment (43) for extreme obesity will further promote the advancement of the field of obesity medicine and mitigate the rising prevalence of this disease worldwide.

Strengths of this study are its large multiethnic patient population and its duration of 11 years. Details pertaining to factors that contribute to WR after RYGB have already been published. Its limitations include the retrospective nature of clinical observations, the lack of a unified protocol for use of AOMs, that the data pertain only two AOMs, and the randomness of decisions made by providers and patients to use or abstain from AOMs.

## Conclusion

Bariatric surgery is the most effective treatment strategy to combat obesity and achieve long-term resolution and/or improvement of most cardiometabolic dysfunction associated with it. However, as a chronic disease, obesity is subject to relapse years after bariatric surgery and it could require further medical interventions. Here we show that phentermine and topiramate could play a role in the management of weight relapse after RYGB. However, the full potential of these agents and newer AOMs to counter weight recidivism and prevent the recurrence of obesity-related comorbidities needs to be further explored in prospective clinical trials. Guidelines for initiating and monitoring the potential long-term use of AOMs after bariatric surgery need to be established. **O**

## Acknowledgments

The authors thank Ashley McCarthy for her helpful feedback.

**Funding agencies:** This work was supported in part by the NIH (P30DK046200). The funder had no role in the collection, management, or interpretation of the data; preparation, review, or approval of the manuscript; or decision to submit the manuscript for publication.

**Disclosure:** CMA reports receiving personal fees from Nutrisystem, Zafgen, Sanofi-Aventis, Orexigen, EnteroMedics, GI Dynamics, Scientific Intake, Gelesis, Novo Nordisk, SetPoint Health, Xeno Biosciences, Rhythm Pharmaceuticals, Eisai, and Takeda outside of the funded work. CMA reports receiving grant funding from Aspire Bariatrics, GI Dynamics, Orexigen, Takeda, the Vela Foundation, Gelesis, Energisis, Coherence Lab, and Novo Nordisk outside of the funded work. CMA reports past equity interest in ScienceSmart, LLC. All other authors declared no conflict of interest.

**Author contributions:** NWI and WAA had full access to all of the data in the study and take responsibility for the integrity of the data and the accuracy of the data analysis. NWI and WAA: concept and design. LY and NWI: acquisition, analysis, and interpretation of data. WAA, CMA, DTH, BC, and NWI: drafting of manuscript. All authors: critical revision of the manuscript for important intellectual content. NWI and WAA: statistical analysis. NWI: supervision.

## References

1. Yanos BR, Saules KK, Schuh LM, Sogg S. Predictors of lowest weight and long-term weight regain among Roux-en-Y gastric bypass patients. *Obes Surg* 2015;25:1364-1370.
2. King WC, Hinerman AS, Belle SH, Wahed AS, Courcoulas AP. Comparison of the performance of common measures of weight regain after bariatric surgery for association with clinical outcomes. *JAMA* 2018;320:1560-1569.
3. Thomas DD, Anderson WA, Apovian CM, et al. Weight recidivism after Roux-en-Y gastric bypass surgery: an 11-year experience in a multiethnic medical center. *Obesity (Silver Spring)* 2019;27:217-225.
4. US Census Bureau. 2012–2016 American Community Survey 5-Year Estimates. Accessed June 22, 2018. [https://factfinder.census.gov/faces/tableservices/jsf/pages/productview.xhtml?pid=ACS\\_16\\_5YR\\_S1903&prodType=table](https://factfinder.census.gov/faces/tableservices/jsf/pages/productview.xhtml?pid=ACS_16_5YR_S1903&prodType=table)
5. Bastos EC, Barbosa EM, Soriano GM, dos Santos EA, Vasconcelos SM. Determinants of weight regain after bariatric surgery. Article in Portuguese, English. *Arq Bras Cir Dig* 2013;26(suppl 1):26-32.
6. da Silva FB, Gomes DL, de Carvalho KM. Poor diet quality and postoperative time are independent risk factors for weight regain after Roux-en-Y gastric bypass. *Nutrition* 2016;32:1250-1253.
7. Shantavasinkul PC, Omotosho P, Corsino L, Portenier D, Torquati A. Predictors of weight regain in patients who underwent Roux-en-Y gastric bypass surgery. *Surg Obes Relat Dis* 2016;12:1640-1645.
8. Meguid MM, Glade MJ, Middleton FA. Weight regain after Roux-en-Y: a significant 20% complication related to PYY. *Nutrition* 2008;24:832-842.
9. Abu Dayyeh BK, Lautz DB, Thompson CC. Gastrojejunal stoma diameter predicts weight regain after Roux-en-Y gastric bypass. *Clin Gastroenterol Hepatol* 2011;9:228-233.
10. Odom J, Zalesin KC, Washington TL, et al. Behavioral predictors of weight regain after bariatric surgery. *Obes Surg* 2010;20:349-356.
11. Hawkins RB, Mehaffey JH, McMurry TL, et al. Clinical significance of failure to lose weight 10 years after Roux-en-Y gastric bypass. *Surg Obes Relat Dis* 2017;13:1710-1716.
12. Dakour Aridi HN, Wehbe MR, Shamseddine G, Alami RS, Safadi BY. Long-term outcomes of Roux-en-Y gastric bypass conversion of failed laparoscopic gastric band. *Obes Surg* 2017;27:1401-1408.
13. O'Brien PE, McPhail T, Chaston TB, Dixon JB. Systematic review of medium-term weight loss after bariatric operations. *Obes Surg* 2006;16:1032-1040.
14. Valezi AC, Mali Junior J, de Menezes MA, de Brito EM, de Souza SA. Weight loss outcome after silastic ring Roux-en-Y gastric bypass: 8 years of follow-up. *Obes Surg* 2010;20:1491-1495.
15. Zenténius E, Andersson-Assarsson JC, Carlsson LMS, Svensson PA, Larsson I. Self-reported weight-loss methods and weight change: ten-year analysis in the Swedish Obese Subjects study control group. *Obesity (Silver Spring)* 2018;26:1137-1143.
16. Kristensson FM, Andersson-Assarsson JC, Kanerva N, Peltonen M, Carlsson B, Carlsson LMS. Long-term effects of bariatric surgery in patients with obesity and chromosome 16 p11.2 microdeletion. *Surg Obes Relat Dis* 2017;13:1321-1325.
17. Sjöholm K, Pajunen P, Jacobson P, et al. Incidence and remission of type 2 diabetes in relation to degree of obesity at baseline and 2 year weight change: the Swedish Obese Subjects (SOS) study. *Diabetologia* 2015;58:1448-1453.
18. Sarzynski MA, Jacobson P, Rankinen T, et al. Associations of markers in 11 obesity candidate genes with maximal weight loss and weight regain in the SOS bariatric surgery cases. *Int J Obes (Lond)* 2011;35:676-683.
19. Sjöström L, Narbro K, Sjöström CD, et al. Effects of bariatric surgery on mortality in Swedish obese subjects. *N Engl J Med* 2007;357:741-752.
20. Carlsson LMS, Sjöholm K, Karlsson C, et al. Long-term incidence of microvascular disease after bariatric surgery or usual care in patients with obesity, stratified by baseline glycaemic status: a post-hoc analysis of participants from the Swedish Obese Subjects study. *Lancet Diabetes Endocrinol* 2017;5:271-279.
21. Sjöholm K, Sjöström E, Carlsson LM, Peltonen M. Weight change-adjusted effects of gastric bypass surgery on glucose metabolism: 2- and 10-year results from the Swedish Obese Subjects (SOS) study. *Diabetes Care* 2016;39:625-631.
22. Hjorth S, Näslund I, Andersson-Assarsson JC, et al. Reoperations after bariatric surgery in 26 years of follow-up of the Swedish Obese Subjects study. *JAMA Surg* 2019;154:319-326.
23. Himpens J, Coromina L, Verbrugge A, Cadiere GB. Outcomes of revisional procedures for insufficient weight loss or weight regain after Roux-en-Y gastric bypass. *Obes Surg* 2012;22:1746-1754.
24. Thompson CC, Jacobsen GR, Schroder GL, Horgan S. Stoma size critical to 12-month outcomes in endoscopic suturing for gastric bypass repair. *Surg Obes Relat Dis* 2012;8:282-287.
25. Abu Dayyeh BK, Jirapinyo P, Weitzner Z, et al. Endoscopic sclerotherapy for the treatment of weight regain after Roux-en-Y gastric bypass: outcomes, complications, and predictors of response in 575 procedures. *Gastrointest Endosc* 2012;76:275-282.
26. Chahine E, Kassis R, Dirani M, Joumaa S, Debs T, Chouillard E. Surgical management of gastrogastric fistula after Roux-en-Y gastric bypass: 10-year experience. *Obes Surg* 2018;28:939-944.
27. Mahawar KK, Himpens JM, Shikora SA, et al. The first consensus statement on revisional bariatric surgery using a modified Delphi approach. *Surg Endosc*. Published online June 19, 2019. doi:10.1007/s00464-019-06937-1
28. Kruseman M, Leimgruber A, Zumbach F, Golay A. Dietary, weight, and psychological changes among patients with obesity, 8 years after gastric bypass. *J Am Diet Assoc* 2010;110:527-534.
29. Conceição E, Mitchell JE, Vaz AR, et al. The presence of maladaptive eating behaviors after bariatric surgery in a cross sectional study: importance of picking or nibbling on weight regain. *Eat Behav* 2014;15:558-562.
30. Himes SM, Grothe KB, Clark MM, Swain JM, Collazo-Clavell ML, Sarr MG. Stop regain: a pilot psychological intervention for bariatric patients experiencing weight regain. *Obes Surg* 2015;25:922-927.
31. Toth AT, Gomez G, Shukla AP, et al. Weight loss medications in young adults after bariatric surgery for weight regain or inadequate weight loss: a multi-center study. *Children (Basel)* 2018;5:E116. doi:10.3390/children5090116
32. Nor Hanipah Z, Nasr EC, Bucak E, et al. Efficacy of adjuvant weight loss medication after bariatric surgery. *Surg Obes Relat Dis* 2018;14:93-98.
33. Schwartz J, Chaudhry UI, Suzo A, et al. Pharmacotherapy in conjunction with a diet and exercise program for the treatment of weight recidivism or weight loss plateau post-bariatric surgery: a retrospective review. *Obes Surg* 2016;26:452-458.
34. Kalarichian M, Turk M, Elliott J, Gourash W. Lifestyle management for enhancing outcomes after bariatric surgery. *Curr Diab Rep* 2014;14:540. doi:10.1007/s11892-014-0540-y

35. Howland RH. Therapies for obesity and medication-associated weight gain. *J Psychosoc Nurs Ment Health Serv* 2013;51:13-16.
36. Stanford FC, Alfaris N, Gomez G, et al. The utility of weight loss medications after bariatric surgery for weight regain or inadequate weight loss: a multi-center study. *Surg Obes Relat Dis* 2017;13:491-500.
37. Wharton S, Kuk JL, Luszczynski M, Kamran E, Christensen RAG. Liraglutide 3.0 mg for the management of insufficient weight loss or excessive weight regain post-bariatric surgery. *Clin Obes* 2019;9:e12323. doi:10.1111/cob.12323
38. Suliman M, Buckley A, Al Tikriti A, et al. Routine clinical use of liraglutide 3 mg for the treatment of obesity: outcomes in non-surgical and bariatric surgery patients. *Diabetes Obes Metab* 2019;21:1498-1501.
39. Miras AD, Pérez-Pevida B, Aldhwayan M, et al. Adjunctive liraglutide treatment in patients with persistent or recurrent type 2 diabetes after metabolic surgery (GRAVITAS): a randomised, double-blind, placebo-controlled trial. *Lancet Diabetes Endocrinol* 2019;7:549-559.
40. Jester L, Wittgrove AC, Clark W. Adjunctive use of appetite suppressant medications for improved weight management in bariatric surgical patients. *Obes Surg* 1996;6:412-415.
41. Zilberstein B, Pajecski D, Garcia de Brito AC, Gallafrio ST, Eshkenazy R, Andrade CG. Topiramate after adjustable gastric banding in patients with binge eating and difficulty losing weight. *Obes Surg* 2004;14:802-805.
42. Zoss I, Piec G, Horber FF. Impact of orlistat therapy on weight reduction in morbidly obese patients after implantation of the Swedish adjustable gastric band. *Obes Surg* 2002;12:113-117.
43. Sudlow A, le Roux CW, Pournaras DJ. Review of multimodal treatment for type 2 diabetes: combining metabolic surgery and pharmacotherapy. *Ther Adv Endocrinol Metab* 2019;10:2042018819875407. doi:10.1177/2042018819875407

# Two-year sustained weight loss and metabolic benefits with controlled-release phentermine/topiramate in obese and overweight adults (SEQUEL): a randomized, placebo-controlled, phase 3 extension study<sup>1–3</sup>

W Timothy Garvey, Donna H Ryan, Michelle Look, Kishore M Gadde, David B Allison, Craig A Peterson, Michael Schwiers, Wesley W Day, and Charles H Bowden

## ABSTRACT

**Background:** Obesity is a serious chronic disease. Controlled-release phentermine/topiramate (PHEN/TPM CR), as an adjunct to lifestyle modification, has previously shown significant weight loss compared with placebo in a 56-wk study in overweight and obese subjects with  $\geq 2$  weight-related comorbidities.

**Objective:** This study evaluated the long-term efficacy and safety of PHEN/TPM CR in overweight and obese subjects with cardiometabolic disease.

**Design:** This was a placebo-controlled, double-blind, 52-wk extension study; volunteers at selected sites continued with original randomly assigned treatment [placebo, 7.5 mg phentermine/46 mg controlled-release topiramate (7.5/46), or 15 mg phentermine/92 mg controlled-release topiramate (15/92)] to complete a total of 108 wk. All subjects participated in a lifestyle-modification program.

**Results:** Of 866 eligible subjects, 676 (78%) elected to continue in the extension. Overall, 84.0% of subjects completed the study, with similar completion rates between treatment groups. At week 108, PHEN/TPM CR was associated with significant, sustained weight loss (intent-to-treat with last observation carried forward;  $P < 0.0001$  compared with placebo); least-squares mean percentage changes from baseline in body weight were  $-1.8\%$ ,  $-9.3\%$ , and  $-10.5\%$  for placebo, 7.5/46, and 15/92, respectively. Significantly more PHEN/TPM CR-treated subjects at each dose achieved  $\geq 5\%$ ,  $\geq 10\%$ ,  $\geq 15\%$ , and  $\geq 20\%$  weight loss compared with placebo ( $P < 0.001$ ). PHEN/TPM CR improved cardiovascular and metabolic variables and decreased rates of incident diabetes in comparison with placebo. PHEN/TPM CR was well tolerated over 108 wk, with reduced rates of adverse events occurring between weeks 56 and 108 compared with rates between weeks 0 and 56.

**Conclusion:** PHEN/TPM CR in conjunction with lifestyle modification may provide a well-tolerated and effective option for the sustained treatment of obesity complicated by cardiometabolic disease. This trial was registered at [clinicaltrials.gov](http://clinicaltrials.gov) as NCT00796367. *Am J Clin Nutr* 2012;95:297–308.

## INTRODUCTION

Obesity is a global epidemic (1, 2). This chronic disease increases morbidity and mortality, in large part due to associated comorbidities, including T2D<sup>4</sup>, CVD, metabolic syndrome, liver

disease, and cancer (1–7). The first-line strategy for the treatment of obesity and prevention of cardiometabolic disease is achieving weight loss through lifestyle interventions, which consist of reductions in caloric intake (by 500–1000 calories/d), increases in physical activity, and changes in health behaviors (8). However, adherence to lifestyle changes can be challenging for a wide variety of reasons, such as a lack of readiness for change on the part of the patient, physical restrictions that limit activity, and a shortage of therapeutic venues that include a multidisciplinary health care team essential to treatment effectiveness. When lifestyle changes alone do not provide the desired weight loss, the addition of pharmacotherapy or bariatric surgery provides a viable option for patients meeting eligibility criteria. However, effective pharmacologic options are limited, and indication for bariatric surgery is limited to patients with a high BMI due to the inherent risks of invasive procedures (9, 10). Thus, it is imperative that effective, long-term pharmacologic strategies are identified that may be used in conjunction with lifestyle changes to combat the obesity epidemic.

<sup>1</sup> From the Departments of Nutrition Sciences and Medicine, UAB Diabetes Research and Training Center, University of Alabama at Birmingham, and the Birmingham VA Medical Center, Birmingham, AL (WTG); Pennington Biomedical Research Center, Baton Rouge, LA (DHR); San Diego Sports Medicine, San Diego, CA (ML); the Obesity Clinical Trials Program, Duke University Medical Center, Durham, NC (KMG); the Department of Biostatistics, UAB Nutrition and Obesity Research Center, University of Alabama at Birmingham, Birmingham, AL (DBA); Vivus Inc, Mountain View, CA (CAP, WWD, and CHB); and Medpace, Cincinnati, OH (MS).

<sup>2</sup> Vivus Inc provided funding and essential materials for this study.

<sup>3</sup> Address correspondence and requests for reprints to WT Garvey, Department of Nutrition Sciences, University of Alabama at Birmingham, Webb 232, 1675 University Boulevard, Birmingham, AL 35294-3360. E-mail: [garveyt@uab.edu](mailto:garveyt@uab.edu).

<sup>4</sup> Abbreviations used: AE, adverse event; bpm, beats per minute; C-SSRS, Columbia Suicide Severity Rating Scale; CVD, cardiovascular disease; Hb A<sub>1c</sub>, glycated hemoglobin; ITT, intent-to-treat; LOCF, last observation carried forward; LS, least-squares; PHEN/TPM CR, controlled-release phentermine/topiramate; SAE, serious adverse event; TEAE, treatment-emergent adverse event; T2D, type 2 diabetes; 7.5/46, 7.5 mg phentermine/46 mg controlled-release topiramate; 15/92, 15 mg phentermine/92 mg controlled-release topiramate.

Received August 11, 2011. Accepted for publication November 15, 2011.

First published online December 7, 2011; doi: 10.3945/ajcn.111.024927.

Currently, orlistat (Xenical; Genentech), a gastric and pancreatic lipase inhibitor, is the only approved agent for the long-term pharmacologic treatment of obesity in the United States (10). Phentermine (Apidex-P; Teva), a central norepinephrine-releasing drug, is approved for short-term (a few weeks) treatment of obesity as monotherapy (37.5 mg/d) (10, 11). Topiramate (Topamax; Janssen Pharmaceuticals), an anticonvulsant (200–400 mg/d) that is also approved for the prophylaxis of migraine headaches (100 mg/d), has shown weight-loss properties but is not currently approved as a therapy for obesity (10, 12–16). A low-dose combination of phentermine plus controlled-release topiramate (PHEN/TPM CR) as an adjunct to lifestyle modification was previously shown to reduce body weight through 56 wk of treatment in the CONQUER study (17). The SEQUEL study, an extension of the CONQUER study, was designed to assess the longer-term efficacy and safety of lifestyle intervention and 2 doses of PHEN/TPM CR for an additional 52 wk (ie, a total treatment duration of 108 wk).

## SUBJECTS AND METHODS

### Subjects

All subjects were eligible to enroll in the extension study if they completed the CONQUER study on treatment and complied with protocol requirements. Inclusion and exclusion criteria for CONQUER required subjects to have a BMI (in kg/m<sup>2</sup>) of  $\geq 27$  and  $\leq 45$  as well as  $\geq 2$  weight-related comorbidities, as previously described in detail (17). To continue into the SEQUEL extension study, female subjects of childbearing potential were required to continue contraception in the form of a double-barrier method, stable hormonal contraception plus single barrier, or tubal ligation. Exclusion criteria included having a BMI  $\leq 22$  at the completion of the CONQUER study, continuously not taking the study drug for  $>4$  wk at the completion of the CONQUER study, developing a condition during the CONQUER study that would interfere with compliance or attainment of study measures, or participating in another formal weight-loss program.

### Study design

SEQUEL was a double-blind, placebo-controlled, 52-wk extension of the CONQUER study. On completion of the 56-wk CONQUER study (17), sites that met the criteria described below were eligible to offer enrollment in SEQUEL. Participants in SEQUEL continued with the original treatment to which they were randomly assigned during CONQUER: lifestyle intervention plus placebo, lifestyle plus 7.5 mg phentermine/46 mg controlled-release topiramate, or lifestyle plus 15 mg phentermine/92 mg controlled-release topiramate, hereafter referred to as placebo, 7.5/46, and 15/92, respectively. Of the 93 CONQUER sites, 36 were selected for the extension study on the basis of their high initial enrollment numbers and rates of retention, and these sites remained blinded to assigned treatment through the end of SEQUEL. This study was conducted between December 2008 and June 2010 and was approved by institutional review boards at each site. All subjects provided written informed consent for participation in the SEQUEL extension. This trial was registered with clinicaltrials.gov as NCT00796367.

### Randomization and interventions

Subjects were randomly assigned by using a computer-generated algorithm and were stratified according to their sex and diabetic status. Study drugs and placebo were administered as capsules that were identical in size and appearance. Eligible subjects maintained their originally assigned once-daily treatment from the CONQUER study (2:1:2 randomization for placebo, 7.5/46, or 15/92) (17). Investigators and subjects remained blinded to treatment assignment. The screening visit for the extension study occurred at the final CONQUER visit, and study visits occurred at 4-wk intervals thereafter. All subjects continued to receive standardized diet and lifestyle-modification counseling based on the LEARN (Lifestyle, Exercise, Attitudes, Relationships, and Nutrition) program (18). Dose reductions or interruptions were allowed for subjects who experienced AEs or who had tolerability issues. Subjects discontinuing the study drug were encouraged to remain in the study, complete study assessments, and continue with the lifestyle counseling according to the LEARN program.

### Study endpoints

The CONQUER study had 2 predefined, coprimary endpoints, which were retained as the primary outcome measures in the SEQUEL extension study: mean percentage weight loss and percentage of subjects achieving  $\geq 5\%$  weight loss from baseline (week 0 of CONQUER) to week 108. Secondary endpoints included the following: weight loss in kilograms; percentage of subjects achieving  $\geq 10\%$ ,  $\geq 15\%$ , or  $\geq 20\%$  weight loss; and change in waist circumference from baseline to week 108. Other efficacy endpoints included changes from baseline to week 108 in blood pressure, serum lipid variables, glycemic measures, concomitant medications for weight-related comorbidities, and rate of progression to diabetes among subjects without diabetes at baseline. All subjects were assessed for diabetic status at baseline per the 2007 American Diabetes Association guidelines, as follows: fasting blood glucose  $\geq 126$  mg/dL or 2-h blood glucose  $\geq 200$  mg/dL after an oral-glucose-tolerance test (19). Hb A<sub>1c</sub> concentrations were also obtained to assess degree of hyperglycemia but were not used as a diagnostic criterion for diabetes at baseline (20). Subjects were considered to have progressed to T2D if their blood glucose was  $\geq 126$  mg/dL under fasting conditions during  $\geq 2$  consecutive measurements and/or  $\geq 200$  mg/dL at 2 h after an oral-glucose-tolerance test. Safety assessments included AEs, physical examination, clinical and laboratory measurements, vital signs, and electrocardiography. At each visit, depressive symptoms were assessed by using the 9-item Patient Health Questionnaire self-reported assessment for depressive symptoms, and the presence of suicidal ideation or behavior was assessed by using the C-SSRS, an 11-item, clinician-administered assessment.

### Statistical analysis

Analyses of change in weight, waist circumference, and other continuous efficacy measures were conducted in a modified ITT sample with the LOCF method to impute missing values. The modified ITT sample was defined as all subjects who received at least one study drug dose with at least one postbaseline measurement of body weight. ANCOVA was used to evaluate percentage weight loss, with treatment, sex, and diabetic status as



fixed effects and baseline weight as a covariate. LS means, corresponding SEs, 2-sided 95% CIs, and 2-sided *P* values for percentage weight loss within each treatment group were derived from the ANCOVA. Analyses of percentage of categorical weight loss were conducted by using logistic regression, with treatment, sex, and diabetic status as fixed effects and baseline weight as a covariate. For each treatment comparison, the estimated OR, SE, 95% Wald CI, and *P* value were determined. Multiple imputation was used as a sensitivity analysis to supplement the ITT-LOCF approach, and an analysis of subjects who completed the study while actively taking the study drug was also performed to understand the effect of treatment after 108 wk of exposure.

The annualized incidence rate of T2D was calculated as the number of newly diagnosed subjects divided by the number of subject-years of follow-up for each treatment group. The number of subject-years of follow-up was calculated as the sum of the number of days across all subjects from the randomization date in CONQUER to the onset date of T2D or to the date of completion or discontinuation from SEQUEL (for subjects who did not develop T2D) divided by 365.25.

Safety analyses were based on incidence of AEs, changes in laboratory evaluations, vital signs, electrocardiograms, physical examination findings, and results from the 9-item Patient Health Questionnaire and the C-SSRS during both the CONQUER and SEQUEL studies. TEAEs were defined as AEs occurring between week 0 of CONQUER and  $\leq 28$  d after the last dose of double-blind study drug in SEQUEL. Analysis of TEAEs was also performed from the start date of study drug in the SEQUEL study and  $\leq 28$  d after the last dose of study drug in the SEQUEL study. All other safety variables were measured between baseline (week 0 of CONQUER) and week 108 or early termination.

## RESULTS

### Disposition of study subjects and baseline characteristics

Of the 866 subjects who completed the CONQUER trial at eligible SEQUEL sites, 676 (78.1%) elected to enroll in SEQUEL and continue receiving their blinded treatment as an adjunct to lifestyle modification for an additional 52 wk (Figure 1). A greater proportion of subjects in the 15/92 treatment arm (85.5%) consented to continue with treatment than did subjects in the 7.5/46 treatment arm (79.4%), whereas the placebo group had the lowest proportion of subjects electing to continue in the protocol (69.4%). Overall, 84.0% (568/676) of subjects completed the extension study, including 86.3% (196/227) of those assigned to placebo, 82.5% (127/154) of those assigned to 7.5/46, and 83.1% (245/295) of those in the 15/92 group. Seven (3.1%) subjects in the placebo arm, 7 (4.5%) subjects in the 7.5/46 arm, and 13 (4.4%) in the 15/92 arm, discontinued the study drug due to an AE (Figure 1). Three subjects in the placebo arm and one subject in the 7.5/46 arm stopped treatment due to lack of efficacy, whereas no subjects in the 15/92 arm discontinued due to lack of efficacy. A higher number of subjects were lost to follow-up in the 15/92 group (20 subjects) than in either the placebo or 7.5/46 groups (4 subjects each).

Baseline demographic, anthropometric, and clinical characteristics, including comorbidities, were similar among subjects in all 3 treatment arms of the SEQUEL study, and in each of the

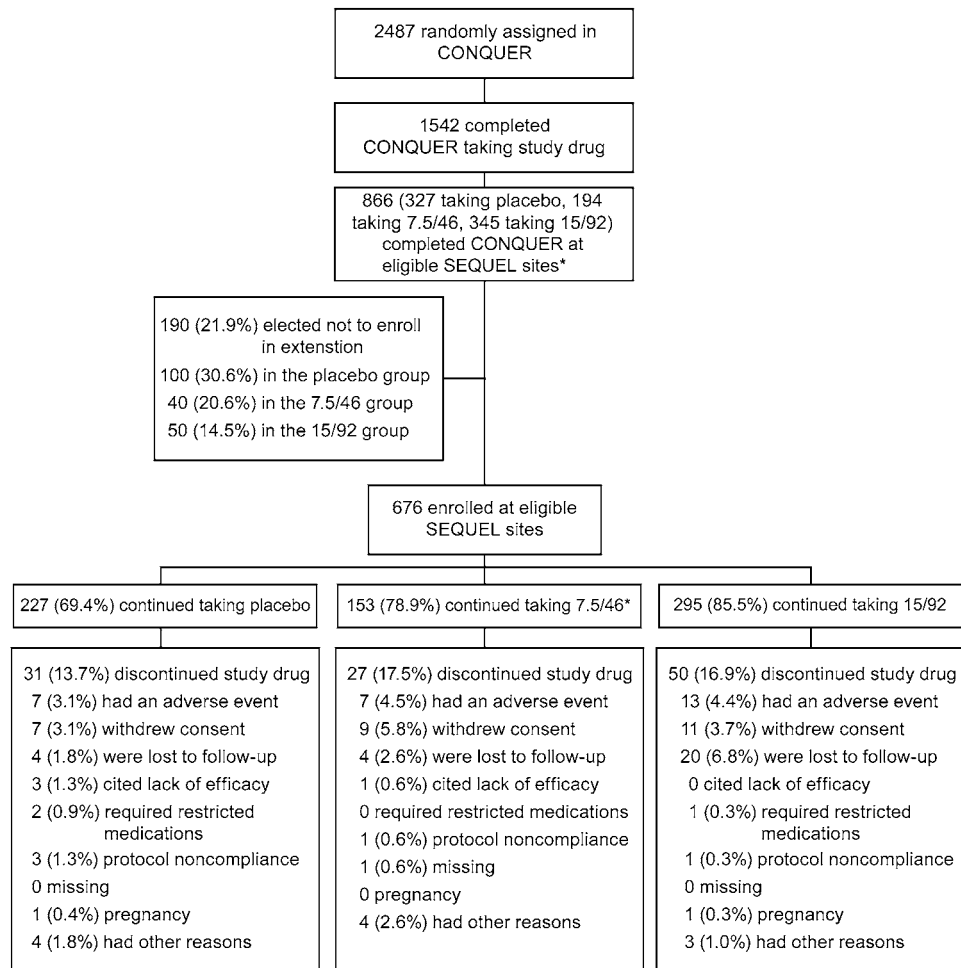
treatment arms the characteristics of the subjects in SEQUEL were similar to and representative of the larger CONQUER cohort (Table 1). Whereas the proportion of subjects with hypertension and dyslipidemia was similar between groups and between CONQUER and SEQUEL, a greater percentage of subjects enrolling in SEQUEL had T2D at baseline compared with the original CONQUER cohort (21.5% compared with 15.8%, respectively). In total, 451 (66.8%) subjects in SEQUEL met the American Heart Association and National Heart, Lung, and Blood Institute criteria (21, 22) for metabolic syndrome at baseline, including 152 (67.0%) in the placebo group, 107 (69.9%) in the 7.5/46 group, and 192 (65.1%) in the 15/92 group.

### Weight loss

Subjects in both PHEN/TPM CR arms showed significantly greater percentage weight loss than did those in the placebo arm, and the weight loss was sustained during 108 wk (Figure 2;  $P < 0.0001$  compared with placebo at all time points assessed). At week 108, the LS mean percentage changes from baseline in body weight in the ITT-LOCF analysis were significantly greater in the PHEN/TPM CR groups compared with placebo:  $-1.8\%$ ,  $-9.3\%$ , and  $-10.5\%$  for placebo, 7.5/46, and 15/92, respectively ( $P < 0.0001$  compared with placebo for all comparisons). For subjects who completed the study while still taking the study drug at week 108, the LS mean percentage changes from baseline in body weight were also significantly greater in the PHEN/TPM CR groups compared with placebo:  $-2.2\%$ ,  $-9.3\%$ , and  $-10.7\%$  for placebo, 7.5/46, and 15/92, respectively ( $P < 0.0001$  compared with placebo for all comparisons). Absolute LS mean weight loss using ITT-LOCF data were  $-2.1$ ,  $-9.6$ , and  $-10.9$  kg for the placebo, 7.5/46, and 15/92 groups, respectively ( $P < 0.0001$  compared with placebo for all comparisons). Greater proportions of subjects treated with each dose of PHEN/TPM CR experienced weight losses of  $\geq 5\%$ ,  $\geq 10\%$ ,  $\geq 15\%$ , and  $\geq 20\%$  when compared with placebo-treated subjects (Figure 3;  $P < 0.0001$  for all comparisons except for weight loss  $\geq 20\%$  for the 7.5/46 group,  $P = 0.0072$ ; ITT-LOCF). There were also significant reductions in waist circumference at Week 108 in subjects treated with PHEN/TPM CR, with mean reductions of  $-3.6$ ,  $-9.8$ , and  $-10.6$  cm for placebo, 7.5/46, and 15/92 treatment arms, respectively ( $P < 0.0001$  compared with placebo; ITT-LOCF).

An analysis of weight loss as a function of baseline BMI category ( $<30$ ,  $\geq 30$  and  $<35$ ,  $\geq 35$  and  $<40$ ,  $\geq 40$  and  $<45$ ) was performed (see Supplemental Figure 1 under "Supplemental data" in the online issue). PHEN/TPM CR was clearly effective in all BMI categories and produced greater weight loss than did placebo ( $P \leq 0.0061$ ). However, a significant treatment effect by baseline BMI category was observed ( $P = 0.0327$ ). Whereas the 7.5/46 and 15/92 doses were statistically similar in their effectiveness in the lower baseline BMI categories, the 15/92 group showed significantly greater percentage weight loss than did the 7.5/46 group in the most severely obese subjects (baseline BMI  $\geq 40$  and  $<45$ ;  $P = 0.0016$  compared with 7.5/46). Among all subjects with class II obesity or greater at baseline (ie, BMI  $\geq 35$ ) (8), LS mean percentage weight losses at week 108 were significantly greater for PHEN/TPM CR compared with placebo ( $P < 0.0001$ ; ITT-LOCF):  $-3.4\%$ ,  $-10.1\%$ , and  $-12.6\%$  for placebo, 7.5/46, and 15/92 treatment arms, respectively.





**FIGURE 1.** Trial profile. Standardized lifestyle intervention was used across all treatment groups. Of the 27 subjects who discontinued the study drug because of adverse events during the SEQUEL study, the event began during the CONQUER study for 3 subjects (one in each treatment group). For the remaining 24 subjects, the adverse event leading to discontinuation of the study drug began during the SEQUEL study. \*One subject in the 7.5/46 group enrolled in the study but discontinued before receiving the study drug. 7.5/46, 7.5 mg phentermine/46 mg controlled-release topiramate; 15/92, 15 mg phentermine/92 mg controlled-release topiramate.

In a prespecified subgroup analysis of weight loss in subjects with T2D at baseline, the PHEN/TPM CR-treated subjects also showed greater weight loss when compared with placebo-treated subjects. At week 108, subjects with T2D in the placebo group ( $n = 55$ ) lost 2.0% of their body weight, whereas subjects with T2D in both the 7.5/46 ( $n = 26$ ) and 15/92 ( $n = 64$ ) groups lost 9.0% of their body weight ( $P = 0.0003$  for 7.5/46 and  $P < 0.0001$  for 15/92 compared with placebo).

### Changes in weight-related comorbidities

Consistent with study entry criteria, enrolled subjects were generally affected by cardiometabolic disease. Many subjects were receiving medications to control blood pressure, lipid variables, and glucose concentrations, and all subjects were actively managed throughout the trial to control these comorbidities. Blood pressure in subjects with hypertension was generally well controlled with  $\geq 2$  antihypertensive medications, the most common of which were angiotensin-converting enzyme inhibitors, thiazide diuretics, and selective  $\beta$ -blockers. More than one-third of subjects with dyslipidemia were receiving

statins; specifically, 78 (34.4%), 58 (37.9%), and 93 (31.5%) subjects randomly assigned to the placebo, 7.5/46, and 15/92 subgroups, respectively, were taking statins. The second most common lipid-controlling treatment was fish oil or a specific omega-3 formulation. Subjects with diabetes ( $n = 145$ ) were required to be managed with a regimen of diet and exercise or metformin monotherapy; 38 (69.1%) subjects with T2D who were randomly assigned to placebo, 15 (57.7%) who were randomly assigned to 7.5/46, and 39 (60.9%) were randomly assigned to 15/92 used metformin during the SEQUEL study. Therefore, to assess effects of PHEN/TPM CR, changes in both cardiometabolic disease variables and medication requirements were assessed.

### Blood pressure

Both systolic and diastolic blood pressure decreased by 3–5 mm Hg at 108 wk compared with baseline in all treatment arms ( $P < 0.0001$  for all comparisons compared with baseline except for placebo compared with baseline for systolic blood pressure,  $P = 0.0002$ ; NS for PHEN/TPM CR groups compared with placebo; **Figure 4A**). Although the degree of blood pressure reduction did not differ significantly between treatment arms,

**TABLE 1**  
Baseline data by treatment group<sup>1</sup>

	Standardized lifestyle intervention across all treatment groups					
	Entire cohort (CONQUER study)			Long-term treatment (SEQUEL study)		
	PHEN/TPM CR			PHEN/TPM CR		
	Placebo (n = 994)	7.5/46 (n = 498)	15/92 (n = 995)	Placebo (n = 227)	7.5/46 (n = 153)	15/92 (n = 295)
Age (y)	51.2 ± 10.3 <sup>2</sup>	51.1 ± 10.4	51.0 ± 10.7	52.7 ± 9.8	52.2 ± 10.6	51.2 ± 10.4
Women [n (%)]	695 (69.9)	349 (70.1)	693 (69.6)	147 (64.8)	106 (69.3)	195 (66.1)
Race [n (%)]						
White	861 (86.6)	429 (86.1)	850 (85.4)	198 (87.2)	134 (87.6)	244 (82.7)
African	114 (11.5)	56 (11.2)	122 (12.3)	28 (12.3)	17 (11.1)	44 (14.9)
Asian	6 (0.6)	5 (1.0)	11 (1.1)	0	1 (0.7)	5 (1.7)
American Indian or Alaskan native	4 (0.4)	6 (1.2)	8 (0.8)	2 (0.9)	1 (0.7)	0
Native Hawaiian or other Pacific Islander	2 (0.2)	2 (0.4)	3 (0.3)	0	1 (0.7)	2 (0.7)
Other	12 (1.2)	5 (1.0)	8 (0.8)	1 (0.4)	0	3 (1.0)
Ethnicity [n (%)]						
Hispanic or Latino	128 (12.9)	70 (14.1)	130 (13.1)	42 (18.5)	25 (16.3)	56 (19.0)
Not Hispanic or Latino	866 (87.1)	428 (85.9)	865 (86.9)	185 (81.5)	128 (83.7)	239 (81.0)
Weight (kg) <sup>3</sup>	103.3 ± 18.1	102.6 ± 18.2	103.0 ± 17.6	101.1 ± 18.9	102.2 ± 18.4	101.9 ± 18.9
BMI (kg/m <sup>2</sup> ) <sup>3</sup>	36.7 ± 4.6	36.2 ± 4.4	36.6 ± 4.5	36.0 ± 4.8	36.1 ± 4.5	36.2 ± 4.7
Waist circumference (cm) <sup>3</sup>	113.4 ± 12.2	112.6 ± 12.5	113.2 ± 12.2	113.0 ± 12.5	112.9 ± 12.3	112.2 ± 12.3
Blood pressure (mm Hg) <sup>3</sup>						
Systolic	128.9 ± 13.5	128.3 ± 13.8	127.9 ± 13.4	128.5 ± 14.3	127.8 ± 11.4	127.3 ± 13.7
Diastolic	81.1 ± 9.2	80.6 ± 8.8	80.1 ± 9.1	79.9 ± 9.7	80.1 ± 8.8	80.1 ± 8.8
Heart rate (bpm) <sup>3</sup>	72.1 ± 9.9	72.1 ± 10.1	72.6 ± 10.1	70.6 ± 10.5	72.0 ± 9.6	73.0 ± 10.3
Total cholesterol (mg/dL) <sup>4</sup>	205.3 ± 41.7	201.6 ± 37.9	205.1 ± 40.4	203.5 ± 41.9	201.8 ± 35.8	201.9 ± 38.6
LDL cholesterol (mg/dL) <sup>5</sup>	123.8 ± 36.1	120.8 ± 33.8	123.7 ± 35.5	123.1 ± 36.6	121.7 ± 32.7	121.5 ± 35.4
HDL cholesterol (mg/dL) <sup>6</sup>	48.8 ± 13.8	48.5 ± 12.8	49.0 ± 13.7	49.5 ± 14.7	48.6 ± 13.3	48.7 ± 12.8
Triglycerides (mg/dL) <sup>7</sup>	163.6 ± 75.8	161.2 ± 75.4	162.0 ± 73.4	154.4 ± 66.7	157.2 ± 71.5	158.1 ± 72.0
Fasting glucose (mg/dL) <sup>8</sup>	106.5 ± 23.5	105.8 ± 20.7	105.9 ± 21.6	109.3 ± 24.4	110.7 ± 25.3	108.2 ± 24.1
Glycated hemoglobin (%) <sup>9</sup>	5.9 ± 0.8	5.8 ± 0.7	5.9 ± 0.8	6.0 ± 0.9	6.0 ± 0.9	6.0 ± 0.8
Subjects with [n (%)]						
Depression history	179 (18.0)	81 (16.3)	165 (16.6)	42 (18.5)	35 (22.9)	55 (18.6)
Hypertension <sup>10</sup>	524 (52.7)	261 (52.4)	520 (52.3)	120 (52.9)	71 (46.4)	154 (52.2)
Hypertriglyceridemia <sup>11</sup>	354 (35.6)	180 (36.1)	363 (36.5)	80 (35.2)	48 (31.4)	105 (35.6)
T2D <sup>12</sup>	159 (16.0)	68 (13.7)	166 (16.7)	55 (24.2)	26 (17.0)	64 (21.7)
Metabolic syndrome	698 (70.2)	353 (70.9)	679 (68.2)	152 (67.0)	107 (69.9)	192 (65.1)

<sup>1</sup> Baseline values for SEQUEL subjects were measured at the start of CONQUER. bpm, beats per minute; PHEN/TPM CR, controlled-release phentermine/topiramate; T2D, type 2 diabetes; 7.5/46, 7.5 mg phentermine/46 mg controlled-release topiramate; 15/92, 15 mg phentermine/92 mg controlled-release topiramate.

<sup>2</sup> Mean ± SD (all such values).

<sup>3</sup> Among CONQUER subjects, baseline weight, BMI, waist circumference, blood pressure, and heart rate values were missing for 2 subjects: one in the placebo group and one in the 15/92 group.

<sup>4</sup> Among CONQUER subjects at baseline, there were missing values for 2 subjects (one for placebo, one for 15/92).

<sup>5</sup> Among CONQUER subjects at baseline, there were missing values for 7 subjects (4 for placebo, 3 for 15/92).

<sup>6</sup> Among CONQUER subjects at baseline, there were missing values for 2 subjects (one for placebo, one for 15/92).

<sup>7</sup> Among CONQUER subjects at baseline, there were missing values for 2 subjects (one for placebo, one for 15/92).

<sup>8</sup> Among CONQUER subjects at baseline, there were missing values for 11 subjects (4 for placebo, 7 for 15/92).

<sup>9</sup> Among CONQUER subjects at baseline, there were missing values for 9 subjects (5 for placebo, 4 for 15/92).

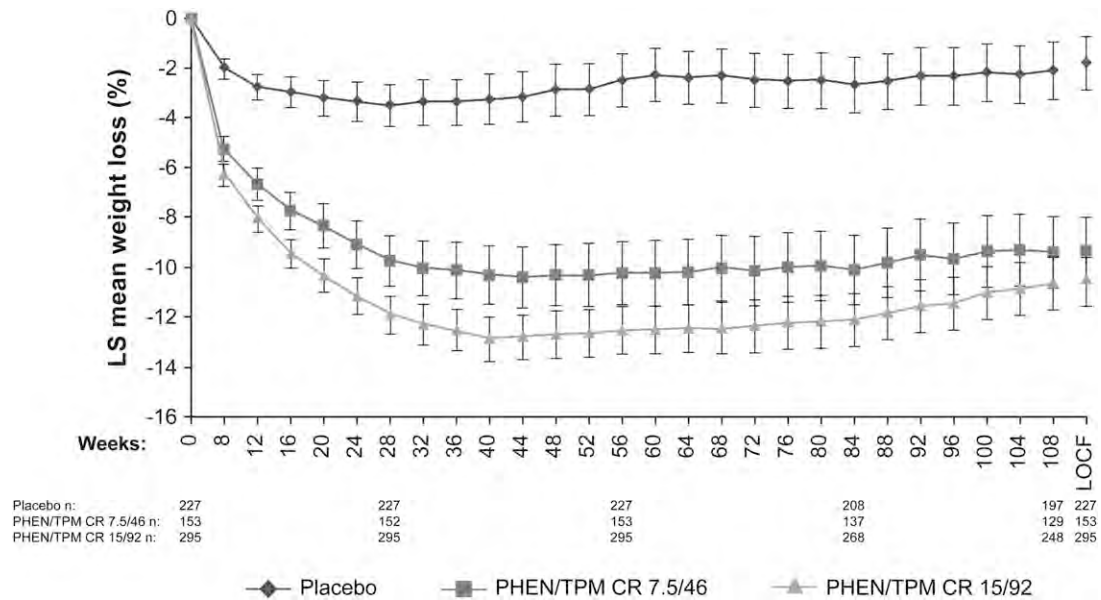
<sup>10</sup> Subjects with hypertension were those with systolic blood pressure ≥140 and ≤160 mm Hg (≥130 and ≤160 mm Hg if diabetic) or diastolic blood pressure ≥90 and ≤100 mm Hg (≥85 and ≤100 mm Hg if diabetic) or who were taking ≥2 antihypertensive medications and had blood pressure <140/90 mm Hg.

<sup>11</sup> Subjects with hypertriglyceridemia were those with fasting triglycerides between 200 and 400 mg/dL or who were taking ≥2 lipid-lowering medications and had fasting triglycerides of <200 mg/dL.

<sup>12</sup> Subjects with diabetes were those with an established diagnosis of T2D, managed with lifestyle measures, metformin therapy, or both.

subjects randomly assigned to placebo experienced a net increase in the number of antihypertensive medications used, whereas there was a net decrease in the number of medications in subjects receiving 7.5/46 or 15/92 (Figure 4B). Specifically, 7.5% (*n* = 17) of subjects in the placebo group experienced a decrease in concomitant antihypertensive medication use com-

pared with 13.1% (*n* = 20) in the 7.5/46 group and 15.6% (*n* = 46) in the 15/92 group. At the same time, more subjects receiving placebo experienced an increase in antihypertensive medication use than did subjects treated with PHEN/TPM CR: 11.0% (*n* = 25), 9.2% (*n* = 14), and 5.8% (*n* = 17) for the placebo, 7.5/46, and 15/92 groups, respectively.



**FIGURE 2.** Mean (95% CI) percentage weight loss from baseline to week 108. LS mean change in the overall study completor sample. Standardized lifestyle intervention was used across all treatment groups.  $P < 0.0001$  compared with placebo at all time points assessed. LOCF, last observation carried forward; LS, least-squares; PHEN/TPM CR 7.5/46, 7.5 mg phentermine/46 mg controlled-release topiramate; PHEN/TPM CR 15/92, 15 mg phentermine/92 mg controlled-release topiramate.

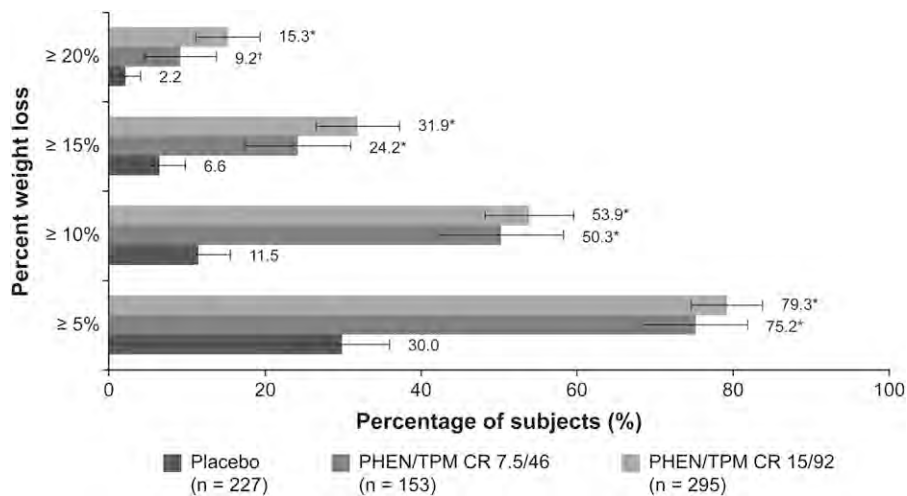
*Lipid variables*

Treatment with 7.5/46 and 15/92 led to progressively greater reductions in triglycerides and greater increases in HDL cholesterol than did placebo, despite the fact that the placebo group required a markedly greater net increase in the number of lipid-lowering medications used compared with the PHEN/TPM CR groups. LDL cholesterol decreased in all treatment arms, with the greatest reduction in the placebo group, whereas reduction in non-HDL cholesterol was similar in all groups (Figure 4, C and D). Similar to the changes seen in concomitant antihypertensive medication use, more subjects receiving PHEN/TPM CR had a decrease in lipid-lowering medications than did subjects receiving placebo: 3.1% ( $n = 7$ ), 5.9% ( $n = 9$ ), and 5.8% ( $n = 17$ ) for the placebo, 7.5/46, and 15/92 groups, respectively. Con-

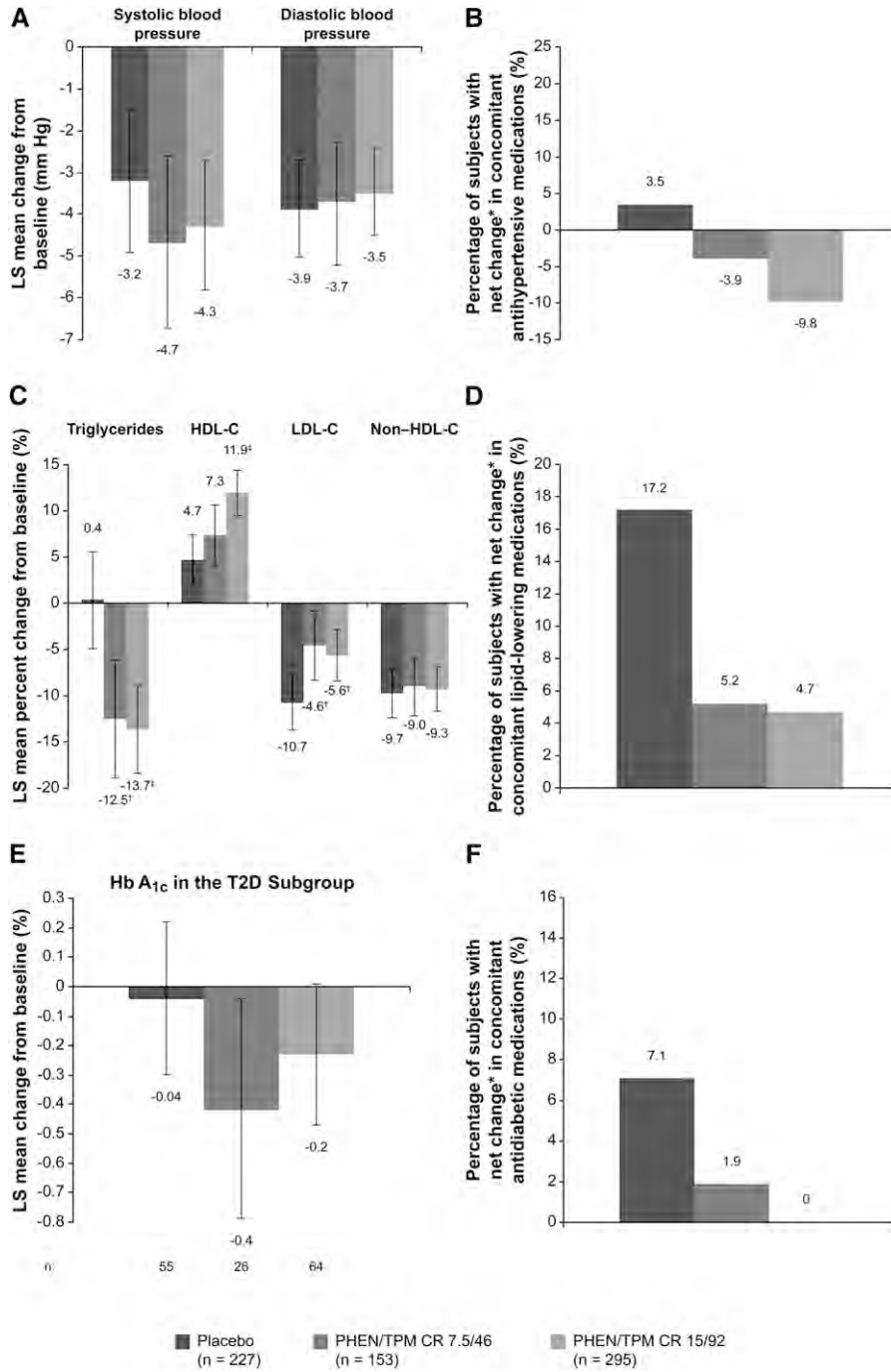
versely, 20.3% ( $n = 46$ ) of placebo-treated subjects increased lipid-lowering medication use compared with 11.1% ( $n = 17$ ) in the 7.5/46 group and 10.5% ( $n = 31$ ) in the 15/92 group.

*Glycemic variables*

PHEN/TPM CR treatment was associated with beneficial effects on glucose homeostasis at 108 wk (Table 2). When compared with placebo, treatment with PHEN/TPM CR reduced both fasting glucose and fasting insulin concentrations, which is indicative of an improvement in insulin sensitivity (23). In subjects without T2D at baseline, the favorable effects of weight loss on insulin sensitivity and glycemia were associated with decreased progression to T2D during the 2-y course of this study. The annualized incidence rates for progression to T2D



**FIGURE 3.** Percentages (and 95% CIs) of subjects achieving  $\geq 5\%$ ,  $\geq 10\%$ ,  $\geq 15\%$ , or  $\geq 20\%$  weight loss from baseline to week 108 (ITT-LOCF). Standardized lifestyle intervention was used across all treatment groups.  $*P < 0.0001$  compared with placebo;  $^{\dagger}P = 0.0072$  compared with placebo. ITT, intent-to-treat; LOCF, last observation carried forward; PHEN/TPM CR 7.5/46, 7.5 mg phentermine/46 mg controlled-release topiramate; PHEN/TPM CR 15/92, 15 mg phentermine/92 mg controlled-release topiramate.



**FIGURE 4.** Effects of PHEN/TPM CR on cardiometabolic variables. LS mean changes (95% CI) in (A) blood pressure, (B) antihypertensive medications, (C) lipid variables, (D) lipid-lowering medications, (E) Hb A<sub>1c</sub>, and (F) antidiabetic medications from baseline (week 0) to week 108 (ITT-LOCF). Changes in Hb A<sub>1c</sub> represent the T2D subgroup. Changes in concomitant medications represent the safety study. Standardized lifestyle intervention was used across all treatment groups. \*Percentage increase minus percentage decrease; *P* < 0.05 for between-group differences. <sup>†</sup>*P* < 0.01 compared with placebo; <sup>‡</sup>*P* < 0.0001 compared with placebo. Hb A<sub>1c</sub>, glycated hemoglobin; HDL-C, HDL cholesterol; ITT, intent-to-treat; LDL-C, LDL cholesterol; LOCF, last observation carried forward; LS, least-squares; PHEN/TPM CR 7.5/46, 7.5 mg phentermine/46 mg controlled-release topiramate; PHEN/TPM CR 15/92, 15 mg phentermine/92 mg controlled-release topiramate; T2D, type 2 diabetes.

among subjects without diabetes at baseline were 3.7%, 1.7%, and 0.9% in the placebo, 7.5/46, and 15/92 treatment groups, respectively. These data indicate a 54% reduction in the progression to T2D in subjects receiving 7.5/46 and a 76% reduction in subjects taking 15/92 compared with placebo (Figure 5).

When only subjects with T2D at baseline were considered, the initial mean Hb A<sub>1c</sub> at week 0 was similar in each of the 3

treatment groups (6.9% in subjects randomly assigned to placebo, 7.3% in the 7.5/46 treatment arm, and 6.9% in the 15/92 treatment arm). At 108 wk, Hb A<sub>1c</sub> did not substantially change from baseline in the placebo group (0%), whereas treatment with 7.5/46 and 15/92 led to reductions of 0.4% and 0.2%, respectively (Figure 4E). In these actively managed subjects, these reductions in Hb A<sub>1c</sub> were achieved without any net increase in

**TABLE 2**  
Effects on glucose homeostasis at week 108 (ITT-LOCF)<sup>1</sup>

	Standardized lifestyle intervention across all treatment groups		
	Placebo (n = 227)	PHEN/TPM CR	
		7.5/46 (n = 153)	15/92 (n = 295)
Fasting glucose (mg/dL)			
Baseline	109.3 ± 24.37 <sup>2</sup>	110.7 ± 25.28	108.2 ± 24.05
LS change at 108 wk	3.7 (0.8, 6.5) <sup>3</sup>	0.1 (-3.4, 3.7)	-1.2 (-3.8, 1.4)
P value vs placebo	N/A	0.0872	0.0048
Fasting insulin (μU/mL)			
Baseline	17.5 ± 12.01	16.8 ± 12.25	17.7 ± 14.61
LS change at 108 wk	-2.6 (-3.9, -1.3)	-5.3 (-6.9, -3.7)	-5.2 (-6.4, -4.0)
P value vs placebo	N/A	0.0051	0.0012
Hb A <sub>1c</sub> (%)			
Baseline	6.0 ± 0.90	6.0 ± 0.90	6.0 ± 0.85
LS change at 108 wk	0.2 (0.09, 0.2)	0.01 (-0.08, 0.1)	0.00 (-0.07, 0.07)
P value vs placebo	N/A	0.0042	0.0003

<sup>1</sup> Values represent changes from baseline (week 0) to week 108 (ITT-LOCF). Hb A<sub>1c</sub>, glycated hemoglobin; ITT, intent-to-treat; LOCF, last observation carried forward; LS, least-squares; N/A, not available; PHEN/TPM CR, controlled-release phentermine/topiramate; 7.5/46, 7.5 mg phentermine/46 mg controlled-release topiramate; 15/92, 15 mg phentermine/92 mg controlled-release topiramate.

<sup>2</sup> Mean ± SD (all such values).

<sup>3</sup> Mean; 95% CI in parentheses (all such values).

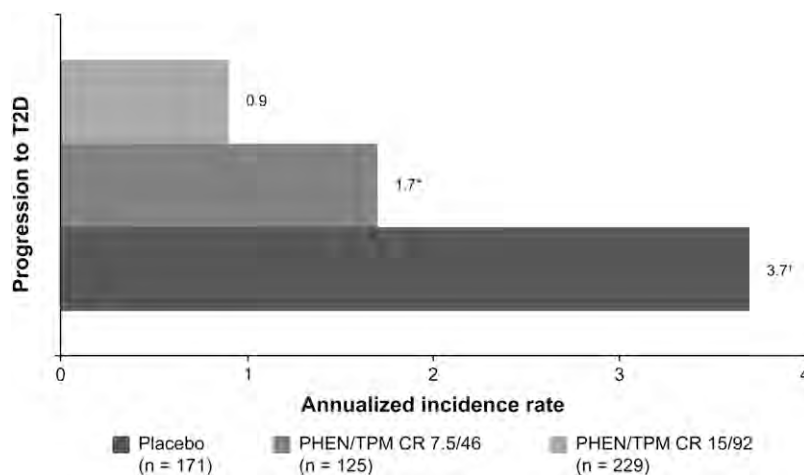
antidiabetic medications in the 15/92 group [3.1% (n = 9) experienced a decrease and 3.1% (n = 9) experienced an increase] and a small net increment in the 7.5/46 group [0.7% (n = 1) decreased and 2.6% (n = 4) increased use] compared with larger net increases in medications required in the placebo group [1.3% (n = 3) decreased and 8.4% (n = 19) increased use; Figure 4F].

Analysis of all primary and secondary variables by using multiple imputation instead of LOCF to accommodate for dropout yielded results consistent with those presented above (see Supplemental Tables 1 and 2 under “Supplemental data” in the online issue). Similar results were also observed in the set of subjects who completed the study while still taking the study drug (see Supplemental Tables 3 and 4 under “Supplemental data” in the online issue).

## Safety and tolerability

### AEs

PHEN/TPM CR was well tolerated over 108 wk, as shown by the TEAEs (Table 3). The most commonly reported TEAEs were upper respiratory tract infection, constipation, paraesthesia, sinusitis, and dry mouth. The type of TEAEs occurring between weeks 56 and 108 were similar to those reported in the overall CONQUER sample from weeks 0 to 56 (17). However, as delineated in Table 3, the incidence of individual TEAEs was markedly lower in the second year (weeks 56–108) than in the first year (weeks 0–56). The incidence of SAEs from weeks 0 to 108 was 6.2% for placebo, 5.9% for 7.5/46, and 8.1% for 15/92. The incidence of SAEs during the period of study extension



**FIGURE 5.** Annualized incidence rate for progression to T2D. Data represent subjects without T2D at baseline. Standardized lifestyle intervention was used across all treatment groups. \**P* = 0.1514 compared with placebo; <sup>†</sup>*P* = 0.0078 compared with placebo. PHEN/TPM CR 7.5/46, 7.5 mg phentermine/46 mg controlled-release topiramate; PHEN/TPM CR 15/92, 15 mg phentermine/92 mg controlled-release topiramate; T2D, type 2 diabetes.

**TABLE 3**  
All adverse events with frequency of  $\geq 5\%$  in any PHEN/TPM CR group<sup>1</sup>

	Standardized lifestyle intervention across all treatment groups					
	Weeks 0–56			Weeks 56–108		
	PHEN/TPM CR			PHEN/TPM CR		
	Placebo (n = 227)	7.5/46 (n = 153)	15/92 (n = 295)	Placebo (n = 227)	7.5/46 (n = 153)	15/92 (n = 295)
		<i>n</i> (%)		<i>n</i> (%)		
Constipation	16 (7.1)	25 (16.3)	62 (21.0)	7 (3.1)	11 (7.2)	12 (4.1)
Paraesthesia	6 (2.6)	21 (13.7)	62 (21.0)	0 (0.0)	1 (0.7)	10 (3.4)
Dry mouth	5 (2.2)	21 (13.7)	59 (20.0)	1 (0.4)	1 (0.7)	4 (1.4)
Upper respiratory tract infection	47 (20.7)	23 (15.0)	55 (18.6)	42 (18.5)	26 (17.0)	45 (15.3)
Nasopharyngitis	35 (15.4)	20 (13.1)	39 (13.2)	26 (11.5)	13 (8.5)	26 (8.8)
Dysgeusia	4 (1.8)	18 (11.8)	39 (13.2)	0 (0.0)	1 (0.7)	3 (1.0)
Sinusitis	19 (8.4)	17 (11.1)	39 (13.2)	18 (7.9)	12 (7.8)	28 (9.5)
Headache	21 (9.3)	8 (5.2)	28 (9.5)	6 (2.6)	4 (2.6)	12 (4.1)
Insomnia	15 (6.6)	12 (7.8)	24 (8.1)	8 (3.5)	9 (5.9)	11 (3.7)
Diarrhea	12 (5.3)	14 (9.2)	21 (7.1)	3 (1.3)	3 (2.0)	11 (3.7)
Back pain	19 (8.4)	11 (7.2)	21 (7.1)	7 (3.1)	9 (5.9)	15 (5.1)
Dizziness	6 (2.6)	9 (5.9)	20 (6.8)	2 (0.9)	2 (1.3)	1 (0.3)
Nausea	13 (5.7)	5 (3.3)	19 (6.4)	4 (1.8)	10 (6.5)	4 (1.4)
Bronchitis	8 (3.5)	9 (5.9)	17 (5.8)	7 (3.1)	8 (5.2)	10 (3.4)
Fatigue	11 (4.9)	7 (4.6)	17 (5.8)	2 (0.9)	2 (1.3)	4 (1.4)
Procedural pain	6 (2.6)	7 (4.6)	17 (5.8)	4 (1.8)	8 (5.2)	14 (4.7)
Arthralgia	20 (8.8)	13 (8.5)	13 (4.4)	14 (6.2)	7 (4.6)	16 (5.4)
Influenza	11 (4.9)	11 (7.2)	13 (4.4)	8 (3.5)	10 (6.5)	19 (6.4)
Urinary tract infection	11 (4.9)	8 (5.2)	13 (4.4)	13 (5.7)	14 (9.2)	18 (6.1)
Gastroenteritis	12 (5.3)	3 (2.0)	12 (4.1)	6 (2.6)	2 (1.3)	9 (3.1)

<sup>1</sup> Preferred terms were defined by the MedDRA Coding Dictionary, version 10.1 (26). PHEN/TPM CR, controlled-release phentermine/topiramate; 7.5/46, 7.5 mg phentermine/46 mg controlled-release topiramate; 15/92, 15 mg phentermine/92 mg controlled-release topiramate.

(weeks 56–108) was also similar across treatment groups: 4.0%, 2.6%, and 4.1% for placebo, 7.5/46, and 15/92, respectively—none of which was reported by investigators to be related to study treatment. The percentage of subjects discontinuing due to AEs by week 108 was also similar across treatment groups: 3.1%, 4.5%, and 4.4% of subjects in the placebo, 7.5/46, and 15/92 arms, respectively (Figure 1). There were no deaths in the extension study. During SEQUEL, there were 2 pregnancies, one carried to term in the 15/92 group and one resulting in miscarriage at ~6 wk gestation in the placebo group. The pregnancy that was carried to full term resulted in a healthy macrosomic infant with no observed teratogenic effects.

#### Physical examination and laboratory variables

The reductions in blood pressure at week 108 (Figure 4A) were accompanied by a mean increase in heart rate of 0.4 bpm in placebo subjects, 1.3 bpm in 7.5/46 subjects, and 1.7 bpm in 15/92 subjects; there were no AEs reported that were relevant to changes in heart rate, and there were no associated adverse clinical sequelae. No dose-related changes were observed in shift summaries of selected laboratory variables, and no subjects experienced an SAE or discontinued the study drug due to laboratory abnormalities. At week 108, there was a greater increase in serum bicarbonate with placebo than with PHEN/TPM CR. The mean changes in bicarbonate from baseline to week 108 were 2.2, 0.7, and 0.2 mEq/L for placebo, 7.5/46, and 15/92,

respectively (baseline mean bicarbonate concentration was 26.5 mEq/L in all 3 treatment groups). Although absolute changes were small, more subjects treated with PHEN/TPM CR experienced a decrease from baseline in serum bicarbonate of  $>5$  mEq/L at 2 consecutive visits during the 2-y study course than did those in the placebo group; this was observed in 4 subjects (1.8%) in the placebo-treated group, 20 (13.1%) in the 7.5/46-treated group, and 48 (16.3%) in the 15/92-treated group over 108 wk. When looking only at weeks 56–108, 7 (4.6%) subjects in the 7.5/46 group and 12 (4.1%) subjects in the 15/92 group were observed to have a  $>5$ -mEq/L decrease in serum bicarbonate from baseline compared with 0 (0%) in the placebo arm. The decreases in bicarbonate generally occurred during the first 3 mo of CONQUER, did not require clinical intervention, and were not progressive during the 2-y study, tending to normalize over time.

#### Psychiatric effects and suicidal behavior

There was no increase in serious suicidal ideation or suicidal behavior based on the C-SSRS questionnaire during the 108 wk of observation in subjects treated with PHEN/TPM CR. Six subjects responded “yes” to the C-SSRS categories of suicidal ideation and suicidality (3 placebo-treated subjects, 1 7.5/46-treated subject, and 2 15/92-treated subjects, but all were below the threshold for “serious” as defined by the instrument). There were 5 subjects with worsening suicidal ideation (2 in the placebo-, 1 in

the 7.5/46-, and 2 in the 15/92-treated groups). During the 2-y period, the incidence of reported anxiety-related AEs correlated with increasing dose: 3.1%, 6.5%, and 9.5% for placebo, 7.5/46, and 15/92 arms, respectively. Most anxiety events were mild in severity. Three subjects in the 15/92 group experienced a severe anxiety-related TEAE, with one subject discontinuing treatment. There were no anxiety-related SAEs. The occurrence of depression-related TEAEs was comparable in the placebo (7.9%) and 15/92 (8.1%) groups and occurred at a lower rate in the 7.5/46 group (3.9%).

## DISCUSSION

The previously published CONQUER study reported that treatment of overweight and obese adults with PHEN/TPM CR as an adjunct to lifestyle intervention promoted weight loss and reduced manifestations of cardiometabolic disease over 56 wk when compared with lifestyle intervention plus placebo (17). This extension study, SEQUEL, maintained the blinded treatment groups for an additional 52 wk and showed that these beneficial therapeutic effects were sustained during a 2-y period.

After 108 wk, the addition of PHEN/TPM CR to a standardized lifestyle modification led to substantial weight loss that coincides with the weight-loss target of 10% recommended by the National Heart, Lung, and Blood Institute for overweight and obese individuals (8). The percentage changes in body weight from baseline were  $-1.8\%$ ,  $-9.3\%$ , and  $-10.5\%$  in subjects treated with placebo, 7.5/46, and 15/92, respectively (ITT-LOCF); and 10% weight loss was achieved by  $>50\%$  of PHEN/TPM CR-treated subjects, whereas  $<12\%$  of subjects receiving placebo met this goal. Importantly, both doses of PHEN/TPM CR were significantly more effective than placebo regardless of baseline BMI and were similarly effective at baseline BMI values extending from  $<30$  to  $<40$ . In those subjects with class III obesity (BMI  $\geq 40$ ), the 15/92 dose produced an even more pronounced degree of weight loss, exceeding that observed with 7.5/46. These data are indicative of therapeutic efficacy for PHEN/TPM CR over a wide range of initial BMI, although higher doses might be more effective in cases of more severe obesity.

By design, subjects in the SEQUEL study were highly affected by cardiometabolic disease, and many were treated with numerous concomitant medications to control blood pressure, lipid variables, and glycemic variables, which were actively managed throughout the trial. PHEN/TPM CR improved these comorbidities and decreased the need for associated medications in comparison with the placebo group. For example, after 2 y of therapy, diastolic and systolic blood pressure showed equal reductions in the placebo and PHEN/TPM CR groups; however, this was accompanied by a net decrease in concomitant antihypertensive medication use in PHEN/TPM CR treatment groups, whereas antihypertensive medications were increased in the placebo group. Reducing the need for medications used to specifically control these comorbidities not only reduces the medication burden associated with cardiometabolic disease but could also improve subject compliance by decreasing their medication regimen complexity and reducing the overall treatment costs (24, 25).

When compared with placebo, PHEN/TPM CR-treated subjects exhibited lower fasting glucose and fasting insulin values compared with subjects receiving placebo, which is indicative of

an improvement in insulin sensitivity (23), and experienced greater reductions in waist circumference, a measure of central adiposity related to increased morbidity and mortality (21, 22, 27). Because insulin resistance and central adiposity are integral to the development of cardiometabolic disease, it appears that PHEN/TPM CR-induced weight loss is accompanied by favorable effects on pathophysiologic processes that could reduce risk of metabolic syndrome, T2D, and CVD (8, 21, 22). In support of this, we observed that, among subjects without T2D at baseline, treatment with PHEN/TPM CR reduced progression to T2D by 54% with the 7.5/46 dose and by 76% with the 15/92 dose when compared with the placebo intervention. Previous studies have shown that lifestyle-intervention programs reduce progression to T2D among high-risk individuals with impaired glucose tolerance, and the degree of protection correlated with the amount of weight loss (28–31). Along these same lines, incremental improvements in cardiometabolic disease risk factors have also been shown to correlate with an increasing degree of weight loss, together with associated reductions in morbidity and mortality (5, 32, 33).

Approximately 20% of subjects had T2D at study entry and had been treated with lifestyle modifications alone, single-agent metformin, or both. In the T2D subgroup, PHEN/TPM CR led to significant reductions in Hb A<sub>1c</sub> after 2 y compared with placebo. Improvements in fasting glucose, fasting insulin, and Hb A<sub>1c</sub> were experienced without any net change in concomitant anti-diabetic medications in subjects with T2D who were randomly assigned to 15/92 and a modest net increase in medications in those assigned to 7.5/46, whereas the placebo group experienced a substantial net increase in required antidiabetic medications to achieve guideline-dictated goals. Thus, weight loss associated with PHEN/TPM CR had a favorable impact on glycemic control in the subjects with T2D, without a need for added oral hypoglycemic agents.

Discontinuation rates during the extension study were similar between placebo and PHEN/TPM CR-treated subjects. The type of AEs reported during weeks 56–108 in the extension study were similar to those in the first 56 wk of the study; however, the incidence rates were lower in the second year of the study. In some subjects, PHEN/TPM CR treatment was associated with reductions in serum bicarbonate, particularly in the first 3 mo of the study, which is likely a manifestation of the carbonic anhydrase activity of topiramate. However, this effect was not progressive in these subjects, and serum bicarbonate tended to return toward normal during the remaining 2 y of the study without the need for clinical intervention. PHEN/TPM CR increased mean heart rate by 1.3–1.7 bpm over baseline; this increase was not accompanied by any related AE reporting and was accompanied by reductions in systolic and diastolic blood pressure. Rigorous assessments of suicidality were conducted by using the C-SSRS, which showed no increase in suicidal ideation associated with PHEN/TPM CR and no difference from placebo in AE reporting for incident depression. PHEN/TPM CR was associated with a dose-dependent increase in the incidence of anxiety. However, these anxiety-related TEAEs were mostly mild in nature and led to only one discontinuation of study drug. Finally, during the 108-wk trial, there were 2 pregnancies, with one pregnancy carried to term in a subject who was randomly assigned to 15/92, resulting in a healthy infant without any observed congenital malformations.



Limitations of this study were that not all CONQUER subjects were eligible to enroll into the SEQUEL extension because only high-enrolling centers were used. Furthermore, participation in the second-year extension study was optional. These aspects may have resulted in bias toward the inclusion of subjects with positive treatment outcomes, because one would expect that subjects who achieved satisfactory weight loss would be more likely to enroll for a second year. However, the baseline clinical characteristics of the subgroup entering the SEQUEL study were similar to those of the CONQUER cohort, with the exception of a greater percentage of subjects with T2D in SEQUEL. Another point pertains to the higher rate of subjects lost to follow-up in the 15/92 arm than in the placebo or 7.5/46 arms. Because the real reason for study discontinuation in these subjects is not known, this could result in an underestimation of important reasons for patients dropping out, including AEs or lack of efficacy. A third limitation of this study is that hyperglycemia, high blood pressure, and dyslipidemia were actively managed on the basis of national treatment guidelines, resulting in the confounding impact of medication changes on the secondary cardiometabolic variables. Actual treatment effects may have been different if related medications and doses were required to be fixed, thereby better isolating an effect of PHEN/TPM CR.

Medical options to promote sustained weight loss are limited. The lipase inhibitor orlistat is currently the only approved medication for chronic treatment of obesity in the United States (10). Bariatric surgery is an option for long-term weight loss but is generally limited to selected subjects with complicated or severe obesity because of the inherent risks of invasive surgical procedures and the requirements for long-term medical follow-up (9, 10, 34, 35). Results of this study suggest that PHEN/TPM CR together with lifestyle measures may be an additional therapeutic option for achieving long-term weight-loss in moderately to severely obese subjects.

In conclusion, PHEN/TPM CR used as an adjunct to lifestyle intervention for the treatment of obesity was well tolerated and produced significant, dose-related weight loss that was maintained during a 108-wk period. PHEN/TPM CR was also associated with sustained improvements in the clinical manifestations of weight-related cardiometabolic disease, including hyperglycemia, dyslipidemia, and elevated blood pressure, despite reduced use of concomitant medications. Importantly, these effects of PHEN/TPM CR led to a reduction in the rate of progression to T2D, with the greatest benefits seen in subjects receiving PHEN/TPM CR 15/92. Thus, PHEN/TPM CR may provide a well-tolerated, effective, and sustainable treatment option for obese subjects with cardiometabolic disease. Furthermore, the unmet clinical need for effective weight-loss medications, together with the favorable risk-benefit profile in the current study, suggests that PHEN/TPM CR in conjunction with a lifestyle-intervention program could be a valuable therapeutic approach to counteract increasing rates of obesity and its related complications.

We acknowledge and thank the SEQUEL subjects, investigators, and study coordinators; the Medpace team (study Contract Research Organization); The Lockwood Group (for manuscript development assistance); and Vivus Inc internal contributors.

The authors' responsibilities were as follows—KMG, DBA, DHR, MS, CAP, WWD, and CHB: designed the research; WTG, KMG, and ML: conducted the research; WTG, KMG, DBA, DHR, CAP, MS, WWD, and CHB: analyzed and interpreted data; WTG, DHR, ML, KMG, DBA, CAP, MS,

WWD, and CHB: drafted and edited the manuscript; and MS: had primary responsibility for final content and is the guarantor of the manuscript, having had full access to all of the data in the study, and takes responsibility for the integrity of the data and the accuracy of the data analysis. The external authors as well as those employed by the funding sponsor participated in protocol design, data analyses, interpretation, and preparation of the manuscript. WTG participated in clinical trials with Merck & Co, Inc; Amylin Pharmaceuticals; Vivus Inc; Abbott; and Daiichi-Sankyo. He has served as an advisor, consultant, and/or speaker for Abbott Nutrition, Daiichi-Sankyo, Johnson & Johnson, LipoScience, Tethys, and Vivus Inc. He is a scientific advisory board member for Daiichi-Sankyo and Tethys, and he holds stock in Bristol-Myers Squibb; Isis/Genzyme; Merck & Co, Inc; Pfizer Inc; Novartis Pharmaceuticals Corp; and Vivus Inc. DHR served as a consultant for Vivus but did not receive any payment for service. ML is a scientific advisory board member for Vivus Inc. KMG received research support from Forest Laboratories, the National Institute of Diabetes and Digestive and Kidney Diseases, and Vivus Inc and owns stock in Orexigen Therapeutics. DBA received grants, honoraria, donations, and consulting fees from numerous food, beverage, and pharmaceutical companies, as well as other commercial and nonprofit entities with interests in obesity, including but not limited to Arena Pharmaceuticals, Jason Pharmaceuticals Inc, Pfizer Inc, and Vivus Inc. He served as a board member for the Pfizer Inc VPO program. WWD, CHB, and CAP are employees of Vivus Inc. MS was employed as the lead statistician for Medpace Inc, the study Contract Research Organization, throughout the study design, execution, and analysis; he had no additional conflicts to disclose.

## REFERENCES

1. Flegal KM, Carroll MD, Ogden CL, Curtin LR. Prevalence and trends in obesity among US adults, 1999-2008. *JAMA* 2010;303:235-41.
2. Pi-Sunyer X. The medical risks of obesity. *Postgrad Med* 2009;121:21-33.
3. Delaet D, Schauer D. Obesity in adults. *Clin Evid (Online)* 2011. Available from: <http://clinicalevidence.bmj.com/ceweb/index.jsp> (cited 10 October 2011).
4. Després JP, Lemieux I. Abdominal obesity and metabolic syndrome. *Nature* 2006;444:881-7.
5. Flegal KM, Graubard BI, Williamson DF, Gail MH. Cause-specific excess deaths associated with underweight, overweight, and obesity. *JAMA* 2007;298:2028-37.
6. Klein S, Burke LE, Bray GA, Blair S, Allison DB, Pi-Sunyer X, Hong Y, Eckel RH; American Heart Association Council on Nutrition, Physical Activity, and Metabolism. Clinical implications of obesity with specific focus on cardiovascular disease: a statement for professionals from the American Heart Association Council on Nutrition, Physical Activity, and Metabolism: endorsed by the American College of Cardiology Foundation. *Circulation* 2004;110:2952-67.
7. Logue J, Murray HM, Welsh P, Shepherd J, Packard C, Macfarlane P, Cobbe S, Ford I, Sattar N. Obesity is associated with fatal coronary heart disease independently of traditional risk factors and deprivation. *Heart* 2011;97:564-8.
8. National Heart, Lung, and Blood Institute, NIH, US Department of Health and Human Services. Identification, evaluation, and treatment of overweight and obesity in adults. Washington, DC: National Heart, Lung, and Blood Institute, 2000. (NIH publication no. 00-4048.)
9. Colquitt JL, Picot J, Loveman E, Clegg AJ. Surgery for obesity. *Cochrane Database Syst Rev* 2009;CD003641.
10. Hussain SS, Bloom SR. The pharmacological treatment and management of obesity. *Postgrad Med* 2011;123:34-44.
11. Melnikova I, Wages D. Anti-obesity therapies. *Nat Rev Drug Discov* 2006;5:369-70.
12. Bray GA, Hollander P, Klein S, Kushner R, Levy B, Fitchet M, Perry BH. A 6-month randomized, placebo-controlled, dose-ranging trial of topiramate for weight loss in obesity. *Obes Res* 2003;11:722-33.
13. Rosenstock J, Hollander P, Gadde KM, Sun X, Strauss R, Leung A. A randomized, double-blind, placebo-controlled, multicenter study to assess the efficacy and safety of topiramate controlled release in the treatment of obese type 2 diabetic patients. *Diabetes Care* 2007;30:1480-6.

14. Tonstad S, Tykarski A, Weissgarten J, Ivleva A, Levy B, Kumar A, Fitchet M. Efficacy and safety of topiramate in the treatment of obese subjects with essential hypertension. *Am J Cardiol* 2005;96:243–51.
15. Toplak H, Hamann A, Moore R, Masson E, Gorska M, Vercausse F, Sun X, Fitchet M. Efficacy and safety of topiramate in combination with metformin in the treatment of obese subjects with type 2 diabetes: a randomized, double-blind, placebo-controlled study. *Int J Obes (Lond)* 2007;31:138–46.
16. Wilding J, Van Gaal L, Rissanen A, Vercausse F, Fitchet M. A randomized double-blind placebo-controlled study of the long-term efficacy and safety of topiramate in the treatment of obese subjects. *Int J Obes Relat Metab Disord* 2004;28:1399–410.
17. Gadde KM, Allison DB, Ryan DH, Peterson CA, Troupin B, Schwiens ML, Day WW. Effects of low-dose, controlled-release, phentermine plus topiramate combination on weight and associated comorbidities in overweight and obese adults (CONQUER): a randomised, placebo-controlled, phase 3 trial. *Lancet* 2011;377:1341–52.
18. Brownell K. The LEARN program for weight management. Dallas, TX: The Life Style Company, 2000.
19. American Diabetes Association. Standards of medical care in diabetes—2007. *Diabetes Care* 2007;30(suppl 1):S4–41.
20. American Diabetes Association. Standards of medical care in diabetes—2011. *Diabetes Care* 2011;34(suppl 1):S11–61.
21. Alberti KG, Eckel RH, Grundy SM, Zimmet PZ, Cleeman JI, Donato KA, Fruchart JC, James WP, Loria CM, Smith SC Jr; International Diabetes Federation Task Force on Epidemiology and Prevention; National Heart, Lung, and Blood Institute; American Heart Association; World Heart Federation; International Atherosclerosis Society; International Association for the Study of Obesity. Harmonizing the metabolic syndrome: a joint interim statement of the International Diabetes Federation Task Force on Epidemiology and Prevention; National Heart, Lung, and Blood Institute; American Heart Association; World Heart Federation; International Atherosclerosis Society; and International Association for the Study of Obesity. *Circulation* 2009;120:1640–5.
22. Grundy SM, Cleeman JI, Daniels SR, Donato KA, Eckel RH, Franklin BA, Gordon DJ, Krauss RM, Savage PJ, Smith SC Jr, et al; American Heart Association; National Heart, Lung, and Blood Institute. Diagnosis and management of the metabolic syndrome: an American Heart Association/National Heart, Lung, and Blood Institute Scientific Statement. *Circulation* 2005;112:2735–52.
23. Reaven GM. Banting lecture 1988. Role of insulin resistance in human disease. *Diabetes* 1988;37:1595–607.
24. Bangalore S, Kamalakkannan G, Parkar S, Messerli FH. Fixed-dose combinations improve medication compliance: a meta-analysis. *Am J Med* 2007;120:713–9.
25. Petrilla AA, Benner JS, Battleman DS, Tierce JC, Hazard EH. Evidence-based interventions to improve patient compliance with antihypertensive and lipid-lowering medications. *Int J Clin Pract* 2005; 59:1441–51.
26. Medical Dictionary for Regulatory Activities. Available from: <http://www.meddrmsso.com/> (cited 10 December 2010).
27. Leitzmann MF, Moore SC, Koster A, Harris TB, Park Y, Hollenbeck A, Schatzkin A. Waist circumference as compared with body-mass index in predicting mortality from specific causes. *PLoS ONE* 2011;6: e18582.
28. Knowler WC, Barrett-Connor E, Fowler SE, Hamman RF, Lachin JM, Walker EA, Nathan DM; Diabetes Prevention Program Research Group. Reduction in the incidence of type 2 diabetes with lifestyle intervention or metformin. *N Engl J Med* 2002;346:393–403.
29. Pan XR, Li GW, Hu YH, Wang JX, Yang WY, An ZX, Hu ZX, Lin J, Xiao JZ, Cao HB, et al. Effects of diet and exercise in preventing NIDDM in people with impaired glucose tolerance. The DaQing IGT and Diabetes Study. *Diabetes Care* 1997;20:537–44.
30. Tuomilehto J, Lindström J, Eriksson JG, Valle TT, Hämäläinen H, Ilanne-Parikka P, Keinänen-Kiukaanniemi S, Laakso M, Louheranta A, Rastas M, et al; Finnish Diabetes Prevention Study Group. Prevention of type 2 diabetes mellitus by changes in lifestyle among subjects with impaired glucose tolerance. *N Engl J Med* 2001;344:1343–50.
31. Lindström J, Louheranta A, Manninen M, Rastas M, Salminen V, Eriksson J, Uusitupa M, Tuomilehto J; Finnish Diabetes Prevention Study Group. The Finnish Diabetes Prevention Study (DPS): lifestyle intervention and 3-year results on diet and physical activity. *Diabetes Care* 2003;26:3230–6.
32. Wing RR, Lang W, Wadden TA, Safford M, Knowler WC, Bertoni AG, Hill JO, Brancati FL, Peters A, Wagenknecht L; Look AHEAD Research Group. Benefits of modest weight loss in improving cardiovascular risk factors in overweight and obese individuals with type 2 diabetes. *Diabetes Care* 2011;34:1481–6.
33. Tzotzas T, Evangelou P, Kiortsis DN. Obesity, weight loss and conditional cardiovascular risk factors. *Obes Rev* 2011;12:e282–9.
34. DeMaria EJ. Bariatric surgery for morbid obesity. *N Engl J Med* 2007; 356:2176–83.
35. International Diabetes Federation Consensus Panel. Bariatric surgical and procedural interventions in the treatment of obese patients with type 2 diabetes: a position statement from the International Diabetes Federation Taskforce on Epidemiology and Prevention. Available from: [http://www.sicob.org/00\\_materiale/IDF\\_Position\\_Statement.pdf](http://www.sicob.org/00_materiale/IDF_Position_Statement.pdf) (cited 10 October 2011).



November 30, 2020

Ms. Kimberly Anderson, Esq.  
State Medical Board of Ohio  
30 East Broad Street  
3<sup>rd</sup> Floor  
Columbus, OH 43215

RE: Rules: 4731-11-04 and 4731-11-04.1

*Submitted electronically via: Kimberly.Anderson@med.ohio.gov*

Dear Ms. Anderson:

Cleveland Clinic is a not-for-profit, integrated healthcare system dedicated to patient-centered care, teaching and research. With a footprint in Northeast Ohio, Florida and Nevada, Cleveland Clinic Health System operates 18 hospitals with approximately 4,900 staffed beds, 21 outpatient Family Health Centers, 11 ambulatory surgery centers and numerous physician offices. Cleveland Clinic employs over 3,400 salaried physicians and scientists. Last year, our system cared for 2.4 million unique patients, including 10 million outpatient visits and 309,000 hospital admissions and observations. Below are our comments in respect to the above captioned rule.

Cleveland Clinic has been caring for patients struggling with obesity for many years. Every day, Cleveland Clinic sees nearly 14,000 unique patients who suffer with obesity (BMI >30 kg/m<sup>2</sup>). Of those, 1,500 have a BMI over 35 kg/m<sup>2</sup> and 1,000 have a BMI at or above 40kg/m<sup>2</sup>. To support these patients, Cleveland Clinic employs more than 40 physicians who are specifically licensed in obesity medicine and who are certified by the American Board of Obesity Medicine. Finally, Cleveland Clinic established a fellowship in obesity medicine that will begin in 2021. Today there are 17 medical subspecialty programs in obesity medicine and more than 4,000 certified ABOM in the United States. Cleveland Clinic also employs more than 10 advanced practice providers (APPs) whose practice is dedicated to seeing patients with obesity and who are licensed by the Ohio State Medical Board to prescribe anti-obesity medications.

Cleveland Clinic appreciates the recent meeting with representatives from the State Medical Board on November 23, 2020 to discuss the proposed amendments to rule OAC 4731-11-04 and 4731-11-04.1. This is an important step towards the improving the appropriate treatments for patients with obesity. As a follow-up to our discussion last week, we offer below general comments on the Board's regulation of anti—obesity medications, as well as specific comments on the proposed rule changes.

First and foremost we want to emphasize that obesity is a chronic disease and is associated with more than 200 other medical comorbidities including diabetes, fatty liver disease, sleep apnea, hypertension, along with an increased mortality. Historically, the disease of obesity was thought to be a lifestyle

choice, a behavior problem that exists in weak individuals who don't have the coping mechanisms or willpower to resist high-calorie foods and are too lazy to pursue routine exercise. It made sense at that time for physicians to recommend that everyone "restrict" food intake and to treat "overeating" with appetite suppressants, as if all patients with obesity have a problem with hunger. The belief was that patients should be able to lose weight and keep it off with behavioral changes. However, in the scientific world, this belief is not commonly accepted. We understand the disease of obesity as the failure of normal weight and energy regulatory mechanisms and that appetite is tightly regulated through metabolic adaptation. The cornerstone for treatment of obesity is behavioral modification and lifestyle changes, including physical activity, sleep and stress. We know it is difficult to maintain weight loss with lifestyle intervention alone, and many regain their lost weight, in part due to adaptive physiologic responses (e.g. a decrease in metabolism and an increased appetite) that occur with weight loss.

Anti-obesity medications (AOM) are not "diet pills" or "appetite suppressants" and are often required as adjuvant therapy for weight loss induction and maintenance; these medications have the potential to augment further weight loss when combined with a lifestyle intervention and are paramount for long-term success (Wadden TA et al *NEJM* 2005; LeRoux et al. *Lancet*, 2017). The most commonly prescribed AOM not only in our practice, but in the United States is Phentermine. Phentermine is not only effective, it is also inexpensive, safe, and has a very low potential of addiction. Limiting the use of Phentermine to three months is simply not a current standard of practice for the chronic disease management of obesity and thus clearly not in the best interests of patients. This is especially detrimental to those of low socioeconomic status and others whose insurance does not cover AOMs, who could benefit from the long-term use of this affordable and effective medication. Over the last two decades, as more knowledge of the disease of obesity is understood, the management of obesity has shifted away from using AOMs for short-term weight loss and adapted a chronic disease management model which incorporates combination therapies of behavioral, pharmacological and surgical interventions to achieve sustainable weight loss in the setting of metabolic adaptation. Obesity as a medical specialty is growing exponentially nationwide and its care has shifted since these rules were written many years ago.

Lastly, the emergence of the COVID-19 pandemic has presented an unprecedented challenge to our healthcare system. Many institutions have rapidly changed their healthcare delivery models by quickly adopting robust telemedicine offerings to patients. Telemedicine is a growing segment of medical care with the potential to improve access by removing geographic barriers and extending care to home. This is accomplished by using new technologies via a modality that patients are already using in their personal lives. Telemedicine has the potential to decrease costs and increase access while maintaining quality of care. The federal government and the Medical Board recently relaxed standards for prescribing controlled substances, so providers are now able to prescribe Phentermine (and other anti-obesity medications) via telemedicine. We urge the Board to make permanent the option to prescribe anti-obesity medications via telemedicine, which would greatly benefit the care of patients suffering with obesity.

Below we have included comments on specific sections of each of the rules.

**4731-11-04** (Rule Title) Controlled substances: utilization of ~~short-term anorexiant~~ for weight reduction ~~sympathomimetics~~ for overweight and obesity.

### Cleveland Clinic Comments

We suggest that the title of the rule should be changed to read Controlled substances: utilization of sympathomimetics for overweight and obesity.

### **4731-11-04** Controlled substances: utilization of short term anorexiant for weight reduction

#### Proposed Language

4731-11-04(C)(1) The physician shall personally meet face-to-face or via telemedicine with the patient, at a minimum, every thirty days when controlled substances are being utilized for weight reduction, and shall record in the patient record information demonstrating the patient's continuing efforts to lose weight, the patient's dedication to the treatment program and response to treatment, and the presence or absence of contraindications, adverse effects, and indicators of possible substance abuse that would necessitate cessation of treatment utilizing controlled substances.

### Cleveland Clinic comments

We suggest that the Medical Board allow patients to meet with their physicians via telemedicine as patients oftentimes find it difficult to come to the office because they are struggling to get time off of work or they face challenges with transportation. It should be noted that patients with severe obesity may be reluctant to come to hospitals as they may be challenged with mobility, the lack of an appropriate physical environment (e.g. waiting room chairs, exam tables, etc.) in clinics, or stigmatizing encounters. Providing patients with the option of telemedicine will alleviate these concerns and remove a substantial barrier to their success while still maintaining the important patient-physician relationship.

#### Proposed Language

**4731-11-04(C)(2)** The controlled substance ~~short term anorexiant~~ is prescribed strictly in accordance with the F.D.A. approved labeling. If the F.D.A. approved labeling of the controlled substance short term anorexiant being utilized for weight loss states that it is indicated for use for "a few weeks," the total course of treatment using that controlled substance shall be closely monitored for the first three months of treatment not exceed twelve weeks. That time period includes any interruption in treatment that may be permitted under paragraph (C)(3) of this rule.

Cleveland Clinic Comments: We suggest the above modifications be made to the current language. There are a number of studies (please see relevant studies cited at the end of this document) that demonstrate that addiction to these anti-obesity medications is low and their efficacy in treatment is high. Further, studies also show that patients who are able to stay on the medications are able to maintain their weight loss. The requirement that patients only use these for short-term treatment of their obesity is not a standard of care and would continue to be a substantial barrier to care for those patients who actually respond well to the medications. Stopping an effective obesity treatment is counterintuitive. We don't do this in other chronic diseases, therefore we should not consider short term treatment models for obesity.

#### Proposed Language

**4731-11-04 (C)(3)** ~~A physician shall not initiate a course of treatment utilizing a controlled substance short term anorexiant for purposes of weight reduction if the patient has received any controlled substance for purposes of weight reduction within the past six months. However, the physician may resume utilizing a controlled substance short term anorexiant following an interruption of treatment of more than seven days if the interruption resulted from one or more of the following:~~

~~(a) Illness of or injury to the patient justifying a temporary cessation of treatment; or~~

~~(b) Unavailability of the physician; or~~

~~(c) Unavailability of the patient, if the patient has notified the physician of the cause of the patient's unavailability~~

**4731-11-04 (C)(4)** After initiating treatment, the physician may elect to switch to another anti-obesity medication based on sound medical judgment, ~~but the total course of treatment for any short term anorexiant combination of controlled substances each of which is indicated for "a few weeks" shall not exceed twelve weeks.~~

#### Cleveland Clinic Comments

As mentioned previously, we believe that references to short-term use of the anti-obesity medications should be modified because studies have demonstrated the long-term safety and efficacy of the medications. The anti-obesity medication called Qsymia which is a combination of Phentermine and Topiramate is approved for chronic treatment of obesity therefore it does not seem logical for Phentermine monotherapy to be restricted.

#### Proposed Language

**4731-11-04 (5)** The physician shall not initiate or shall discontinue utilizing all controlled substance ~~short term anorexiant~~s for purposes of weight reduction immediately upon ascertaining or having reason to believe:

(5)(c)

~~(e) That the patient has failed to lose weight while under treatment with a controlled substance or controlled substances over a period of thirty days during the current course of treatment, which determination shall be made by weighing the patient at least every thirtieth day, except that a patient who has never before received treatment for obesity utilizing any controlled substance who fails to lose weight during the first thirty days of the first such treatment attempt may be treated for an additional thirty days;~~

#### Cleveland Clinic Comments

We are concerned that the rule requires patients to be removed from an anti-obesity medication if they do not lose weight. We suggest that this language be removed because in our experience, there may be several other variables (e.g. changes in lifestyle factors including sleep, physical activity, stress and diet, the presence of medications that cause weight gain or the weight trajectory of the patient prior to initiation of an anti-obesity medication) that may confound the weight outcome. For example, some patients prior to starting an anti-obesity medication are rapidly gaining weight and the medication may lead to weight stabilization. In this instance, we believe patients should be allowed to remain on the medication so that they can begin their treatment and move towards weight loss.

**4731-11-04.1** Controlled substances: utilization for chronic weight management

#### Cleveland Clinic Comments

It should be noted that there are several anti-obesity medications (orlistat, naltrexone-bupropion, phentermine-topiramate XR, liraglutide) currently used to treat the chronic disease of obesity. Almost all of these are not controlled substances and therefore should be either described separately or excluded from this rule. These medications should be considered much like any other medication used to treat chronic diseases, for example, anti-hypertensive medications or diabetes medications.

Similar to our comments above, and especially because of what we have learned during the COVID-19 pandemic in terms of the successful use of telemedicine, we believe the Medical Board should include telemedicine as an option for patients to support their weight loss journey.

#### Proposed Language

**4731-11-04.1(B)(1)** The physician shall meet face-to-face with the patient for the initial visit and at least every thirty days either face-to face or telemedicine during the first three months of treatment. If the F.D.A. approved labeling for the controlled substance ~~anorexiat~~ anti-obesity medication requires induction of treatment at one dose and an increase to a higher dose after a stated period of less than thirty days, the physician may give the patient a prescription for the higher dose at the initial visit and the first thirty day period then starts from the date the prescription for the higher dose may be filled.

#### Other Cleveland Clinic Comments – Phentermine Designation

We believe that the Medical Board should designate Phentermine as a chronic weight loss medication. We understand the concern of its addiction potential, but there have been no studies that support this statement. Below we have provided our reasoning and supporting research for our position.

Clinical guidelines support long-term use

The 2015 Endocrine Society has clinical guidelines on the pharmacologic management of obesity stating that there is minimal evidence of any serious, long-term side effects with Phentermine and that it is reasonable for clinicians to prescribe Phentermine long-term for the treatment of obesity. The guidelines include safety recommendations for long-term prescribing. The review article below also describes the off-label use of phentermine in clinical practice.

#### References

Apovian CM, Aronne LJ, Bessenen DH et al. Pharmacological Management of Obesity: An Endocrine Society Clinical Practice Guideline. *J Clin Endocrinol Metab*, February 2015, 100(2):342–362 Available at: <https://academic.oup.com/jcem/article/100/2/342/2813109>

Hendricks EJ. Off-label drugs for weight management. <https://www.dovepress.com/off-label-drugs-for-weight-management-peer-reviewed-article-DMSO> Available at: <https://www.dovepress.com/off-label-drugs-for-weight-management-peer-reviewedarticle-DMSO>

Phentermine has demonstrated safety in long-term use

In a 28 week, randomized, controlled trial comparing phentermine/topiramate extended release (Qsymia®) compared to phentermine 15mg daily or topiramate, the 15mg phentermine for 6 months led to 7% weight loss and was safe. This is the same dose available in Qsymia® formulation with is FDA approved for long-term use. Due to the high cost of Qsymia®, it would benefit patients to have phentermine available for long-term use.

#### References

Aronne LJ, Wadden TA, Peterson C et al. Evaluation of Phentermine and Topiramate versus Phentermine/Topiramate Extended-Release in Obese Adults. *Obesity* (2013) 21, 2163–2171. doi:10.1002/oby.20584 Available at: <https://onlinelibrary.wiley.com/doi/full/10.1002/oby.20584> Qsymia® prescribing information Available at: <https://dailymed.nlm.nih.gov/dailymed/drugInfo.cfm?setid=40dd5602-53da-45ac-bb4b->



Studies demonstrate long-term safety and efficacy

A retrospective study from an electronic medical record of 13,972 adults comparing those with longer term use to those with short-term use (<3 months) demonstrated that long-term users of phentermine experienced more weight loss: patients using continuously for >12 months experienced 7.4% weight loss, and at 24 months it was much greater than the short-term group. Composite cardiovascular death (CVD) or death outcome was rare (0.3%, 41 deaths) with no significant difference between groups comparing short term, vs long-term use. Patients using phentermine for longer periods experienced greater weight loss that was sustained while staying on the medication.

Reference

Lewis KH, Fischer H, Ard J. et al. Safety and Effectiveness of Longer-Term Phentermine Use: Clinical Outcomes from an Electronic Health Record Cohort. *Obesity* (2019) 27, 591-602. doi:10.1002/oby.22430. Available at: <https://onlinelibrary.wiley.com/doi/abs/10.1002/oby.22430>

Phentermine has demonstrated that it has very low addictive potential.

In the Rule 4731-11-04, one of the current parameters is usage beyond 12 weeks. In the following study, 269 patients were treated for 1.1-21.1 years and the study showed that phentermine did not induce drug cravings or withdrawal symptoms.

Reference

Hendricks EJ, Srisurapanont M, Schmidt SL et al. Addiction potential of phentermine prescribed during long-term treatment of obesity. *International Journal of Obesity* (2013) 38: 292-8.

Thank you for conducting a thoughtful process that allows us to provide input on such important issues and for your consideration of this information. Please do not hesitate to contact us if you need additional information.

Sincerely,



Barto Burguera, M.D. Ph.D  
Chairman Endocrinology & Metabolism Institute  
Professor of Medicine, Cleveland Clinic Lerner College of Medicine



Marcio L. Griebeler, M.D.  
Director, Obesity EMI Programs

Diana Isaacs, PharmD, BCPS, BCACP, BC-ADM, CDE  
Clinical Pharmacy Specialist



W. Scott Butsch, M.D. MSc. FTOS  
Director of Obesity Medicine, Bariatric and Metabolic Institut

11/23/2020

## STATE MEDICAL BOARD OF OHIO

Jill Phalen Reardon

Director of External Affairs

State Medical Board of Ohio

30East Broad Street, 3<sup>rd</sup> Floor

Columbus Ohio 43215

O: 614 466 0781

C:614 551 9957

Jill.Reardon@med.ohio.gov

Dear Sirs,

I would like to take an opportunity to comment on the upcoming review for Rule 4731-11-04 and its restrictive nature regarding the long-term use of certain anti-obesity medications such as phentermine, diethylpropion and phendimetrazine.

Since June of 2013, Obesity has been regarded as a multi-faceted chronic disease in need of chronic treatment regimens including diet, exercise, pharmacology and surgery. National organizations such as the Obesity Medicine Association have long advocated for long term use of pharmacotherapy as adjunctive treatment of obesity as part of a comprehensive obesity management program that includes a thorough medical evaluation and lifestyle changes. **The data is quite clear that combination treatments of diet exercise and pharmacotherapy are more successful than either diet and exercise or pharmacotherapy alone.**

Currently the medication options for treatment of obesity include FDA approved anti-obesity medications such as phentermine, diethylpropion, phendimetrazine, orlistat, Qsymia, contrave and saxenda. As a chronic disease with a high relapse rate when therapy is discontinued, (similar to what is seen in hypertension or hyperlipidemia) obesity requires long term therapies to maintain successful treatment. The current evidence points to issues with “set point” where the hypothalamus protects the current weight even if it is not a healthy one. Thus, weight loss leads to metabolic adaptation to drive the individual back to an unhealthy weight. These homeostatic mechanisms underline the need to utilize chronic therapies to maintain progress towards a healthy weight. (NEJM 10/27/2011 sumithran)

Due to expansion in the understanding of the mechanisms related to appetite regulation and energy homeostasis, across the country the use of anti-obesity medications has changed since their original FDA labeling. The original labeling of short-term appetite suppressant for 12 weeks based on short term studies from 50yrs ago reflect a time where obesity was more poorly understood and not today's knowledge base. The newer generation of anti-obesity medications with their emphasis on long term management reflect that fact.

There are several facts to consider: several of the older medications have been on the US market for more than 50 years with no evidence of harm when prescribed appropriately by trained practitioners whether used short or long term. This is evidenced across the country where these tools are used under physician judgement with consent for off- label use and risk benefit conversations with patients in the context of a comprehensive program. Additionally, newer data suggest better efficacy when medications such as phentermine are used long term up to 2 years. One study showed patients on phentermine for 2 years continuously lost 7.4 percent more weight than those only using medication for 3 months with no increase in adverse outcomes (Obesity March 21, 2019).

Currently Ohio has an obesity rate of 34% by 2019 data and there are concerns that this rate will approach 40% possibly by end of 2020. We know that COVID has an increased mortality in the obese population. We also know that weight loss of 5-10% is recognized in decreasing the health risks for obesity. As an Ohio native, I would advocate that limiting access to potential tools for the treatment of this disease is worrisome for doing more harm than good.

I realize that there are concerns for addiction or addictive behaviors with this class of medication but that appears to be overinflated. Registries in ERs historically have not demonstrated any evidence for high addictive behaviors with this class of medications. In fact, one study published in the International Journal of Obesity did not find any phentermine abuse or psychological addiction even when individuals were on higher than commonly recommended doses and treatment durations of up to 21 years. (International Journal of Obesity (2014) 38,292-298).

Since overweight and obesity are chronic medical conditions, there should be no time limitations on the use of existing pharmacotherapy for obesity. This is under the assumption that the patients have been monitored as recommended by the FDA for the first twelve weeks, evaluated for efficacy and side effect profiles of the therapy. Additionally, continued monitoring is warranted that is individualized to patient's needs, disease state and comorbid conditions. Continued assessments of medications and dosages for their appropriateness for the patient's current level of risk associated with the patient's therapy plan is critical for optimum treatment.

In summary, I urge the state medical board to allow patients with overweight and obesity the opportunity for the same long term treatment options as other chronic diseases. Allowing obesity medicine specialists to utilize phentermine and other short term obesity drugs for long term treatment of this chronic disease would be extremely beneficial step toward the goal of combating obesity here in Ohio. This approach would be more in line with the current knowledge base for the disease of obesity rather than using antiquated rules assigned to a presumed cosmetic issue from the 1950s-1960s. That just makes common sense.

RESPECTFULLY,

BRUCE BARKER MD  
DIPLOMATE AMERICAN BOARD OF OBESITY MEDICINE  
DIPLOMATE AMERICAN BOARD OF FAMILY MEDICINE  
801 OHIOHEALTH BLVD SUITE 160  
DELAWARE OHIO 43015



December 17, 2020

Kimberly Anderson, General Counsel  
State Medical Board of Ohio  
30 E. Broad Street, 3<sup>rd</sup> Floor  
Columbus, Ohio

Dear Ms. Anderson:

The Ohio Association of Physician Assistants (OAPA) would like to ONCE AGAIN address rules OAC 4731-11-02, 4731-11-03, 4731-11-04, 4731-11-04.1, 4731-11-07 and 4731-11-11 which the Medical Board is proposing to continue without any changes; and further OAPA would like to submit suggested amendments to 4731-11-04.1.

In 2018, the 132<sup>nd</sup> General Assembly passed Senate Bill 259 which expands the authority of physician assistants to prescribe drugs and therapeutic devices by eliminating the State Medical Board's authority to adopt a physician assistant formulary, which in turn expands the supervising physician's authority and decision-making process in granting physician-delegated prescriptive privileges to physician assistants. OAPA recognizes Senate Bill 259 does not eliminate the Board's statutory authority to adopt rules in accordance with ORC 4730.39 governing physician-delegated prescriptive authority, provided any rules adopted are consistent with the intent and spirit of the statutes. OAPA believes a physician assistant has the authority to prescribe any drugs or therapeutic devices that are within the supervising physician scope of practice in accordance with ORC 4730.41 and 4730.42. Further, OAPA believes the Board should not have authority to promulgate rules that would restrict a supervising physician from delegating to a physician assistant the responsibility of **prescribing, administering and/or monitoring the therapeutic efficacy of** any drug or therapeutic device the supervising physician is authorized to prescribe within their scope of practice that have not been specifically restricted by federal law

OAPA could not find any federal rules and regulations that restricts a physician assistant from prescribing stimulants or anorexiant for either short-term weight reduction or chronic weight management. Nor could OAPA find any pharmaceutical manufacturers suggestion that only a physician shall be allowed to prescribe anorexiant for the same.

OAC 4730-2-07 (A)(3) currently states that physician assistants and supervising physicians must follow the requirements set in all sections of OAC 4731-11. OAPA understands that multiple sections of OAC 4730 of the physician assistant rules have been proposed to be amended to comply with the recent changes made in Senate Bill 259 and are currently being reviewed by the Common Sense Initiative Office, however; the requirements set forth in OAC 4730-2-07 to comply with OAC 4731-11 have not been proposed to be either amended or eliminated.

Constituent Chapter of the American Academy of Physician Assistants

1700 Reed Road, Suite N • Columbus, OH 43220 • PH: 800.292.4997 • FX: 614.824.2103 • oapa@ohioapa.com • www.ohioapa.com



Therefore, OAPA is suggesting the following amendments to OAC 4731-11-04.1:

**4731-11-04.1 Controlled substances: utilization for chronic weight management.**

(A) A PROVIDER (PHYSICIAN, PHYSICIAN ASSISTANT AND/OR APRN) ~~physician~~ shall determine whether to utilize a controlled substance anorexiant for purposes of chronic weight management as an adjunct to a reduced calorie diet and increased physical activity. The determination shall be made in compliance with the provisions of this rule.

(1) Before initiating treatment utilizing any controlled substance anorexiant, the PROVIDER shall complete all of the following requirements:

(a) Obtain a thorough history;

(b) Perform a physical examination of the patient;

(c) Determine the patient's BMI;

(d) Review the patient's attempts to lose weight in the past for indications that the patient has made a substantial good faith effort to lose weight in a regimen for weight reduction based on caloric restriction, nutritional counseling, intensive behavioral therapy, and exercise without the utilization of controlled substance anorexiant. The review shall include available records from the PROVIDER'S ~~physician's~~ own prior treatment of the patient, prior treatment provided by another PROVIDER ~~physician~~ prior participation in a weight-loss program, or prior treatment by a dietitian;

(e) Rule out the existence of any recognized contraindications to the use of the controlled substance anorexiant to be utilized;

(f) Assess and document the patient's freedom from signs of drug or alcohol abuse;

(g) Access OARRS and document in the patient's record the receipt and assessment of the information received; and

(h) Develop and record in the patient record a treatment plan that includes, at a minimum, a diet and exercise program for weight loss.

(2) The PROVIDER ~~physician~~ shall not initiate treatment utilizing a controlled substance anorexiant upon ascertaining or having reason to believe any one or more of the following:

(a) The patient has a history of, or shows a propensity for, alcohol or drug abuse, or has made any false or misleading statement to the PROVIDER ~~physician or physician assistant~~ relating to the patient's use of drugs or alcohol;

(b) The patient has consumed or disposed of any controlled substance other than in strict compliance with the treating PROVIDER'S ~~physician's~~ directions; or

(c) The PROVIDER ~~physician~~ knows or should know the patient is pregnant.

(3) The PROVIDER ~~physician~~ shall not initiate treatment utilizing a controlled substance anorexiant if any of the following conditions exist:

(a) The patient has an initial BMI of less than thirty, unless the patient has an initial BMI of at least twenty-seven with comorbid factors.

(b) The review of the patient's attempts to lose weight in the past indicates that the patient has not made a substantial good faith effort to lose weight in a regimen for weight reduction based on caloric restriction, nutritional counseling, intensive behavioral therapy, and exercise without the utilization of controlled substance anorexiant. The review shall include available records from the PROVIDER'S own

prior treatment of the patient, prior treatment provided by another PROVIDER, prior participation in a weight-loss program, or prior treatment by a dietitian.

(4) The PROVIDER ~~physician~~ shall prescribe the controlled substance anorexiant strictly in accordance with the F.D.A. approved labeling;

(5) Throughout the course of treatment with any controlled substance anorexiant the PROVIDER ~~physician~~ shall comply with rule 4731-11-11 of the Administrative Code. ~~and the physician assistant shall comply with rule 4730-2-10 of the Administrative Code.~~

(B) A PROVIDER ~~physician~~ shall provide treatment utilizing a controlled substance anorexiant for weight management in compliance with paragraph (A) of this rule and the following:

(1) The PROVIDER ~~physician~~ shall meet face-to-face with the patient for the initial visit and at least every thirty days during the first three months of treatment. If the F.D.A. approved labeling for the controlled substance anorexiant requires induction of treatment at one dose and an increase to a higher dose after a stated period of less than thirty days, the PROVIDER ~~physician~~ may give the patient a prescription for the higher dose at the initial visit and the first thirty day period then starts from the date the prescription for the higher dose may be filled.

~~(2) Following the initial visit and two follow-up visits, the treatment may be continued under one of the following means:~~

~~(a) The physician may authorize refills for the controlled substance anorexiant up to five times within six months after the initial prescription date;~~

~~(b) The treatment may be provided by a physician assistant in compliance with this rule, the supervisory plan or policies of the healthcare facility, and the physician assistant formulary adopted by the board.~~

~~(3) When treatment for chronic weight management is provided by a physician assistant, the following requirements apply:~~

~~(a) The supervising physician shall personally review the medical records of each patient to whom the physician assistant has prescribed a controlled substance anorexiant following each visit; and~~

~~(b) A physician assistant shall not initiate utilization of a different controlled substance anorexiant but may recommend such change for the supervising physician's initiation.~~

~~(4) (2) A PROVIDER ~~physician~~ shall discontinue utilizing any controlled substance anorexiant immediately upon ascertaining or having reason to believe:~~

~~(a) That the patient has repeatedly failed to comply with the PROVIDER'S ~~physician's~~ treatment recommendations; or~~

~~(b) That the patient is pregnant.~~

(C) A violation of any provision of this rule, as determined by the board, shall constitute the following as applicable:

(1) For a PROVIDER ~~physician~~:

(a) "Failure to maintain minimal standards applicable to the selection or administration of drugs," as that clause is used in division (B)(2) of section 4731.22 of the Revised Code;

(b) "Selling, giving away, personally furnishing, prescribing, or administering drugs for other than legal and legitimate therapeutic purposes," as that clause is used in division (B)(3) of section 4731.22 of the Revised Code; and



(c) "A departure from, or the failure to conform to, minimal standards of care of similar practitioners under the same or similar circumstances, whether or not actual injury to a patient is established," as that clause is used in division (B)(6) of section 4731.22 of the Revised Code.

(2) For a physician assistant:

(a) "A departure from, or failure to conform to, minimal standards of care of similar physician assistants under the same or similar circumstances, regardless of whether actual injury to a patient is established," as that clause is used in division (B)(19) of section 4730.25 of the Revised Code;

(b) "Failure to comply with the requirements of this chapter, Chapter 4731. of the Revised Code, or any rules by the board," as that clause is used in division (B)(2) of section 4730.25 of the Revised Code; and

(c) "Violating or attempting to violate, directly or indirectly, or assisting in or abetting the violation of, or conspiring to violate, any provision of this chapter, Chapter 4731. of the Revised Code, or the rules adopted by the board," as that clause is used in division (B)(3) of section 4730.25 of the Revised Code.

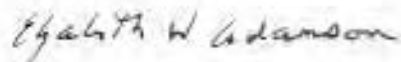
*Note: OAPA has not suggested inserting the terms "physician assistant" in every section of OAC 4731-11 because the requirements set forth in OAC 4730-2-07 clearly imply that every standard of care a physician shall be held to when prescribing controlled substances, a physician assistant should be held to the same standards. And, as physician assistant is currently included in OAC 4731-11-04.1 (A) (2) (a) and (5), (B)(2)(a)(b) and (3)(a)(b); OAPA believes it is necessary to **amend by deleting** these subsections as to keep the language consistent throughout all sections of OAC 4731-11.*

The passage of Senate Bill 259 has greatly expanded Physician Assistant scope of practice and prescriptive authority to be equivalent to and consistent with their supervising physician scope of practice. There are no citation in either ORC 4730 or OAC 4730 that specifically requires a supervising physician to **"personally review the medical records of each patient to whom the physician assistant has prescribed a controlled substance anorexiant following each visit"**, or for any other particular type of patient care service, condition, diagnosis, drugs and therapeutic devices or treatment. The responsibilities of the supervising physician are clearly delineated in ORC 4730.21. OAPA believes the language in OAC 4731-11-04.1 requiring a physician to "personally review each medical record for each visit" is overly restrictive and inconsistent with the intent of ORC 4730.21. OAPA also believes the current language in OAC 4731-11-04.1 has already caused confusion amongst some physicians and administrators that have questioned if physician assistants are not mentioned in the other sections of OAC 4731-11 are they excluded from being able to be delegated the authority to prescribe stimulants and/or anorexiants as described in OAC 4731-11-03 and OAC 4731-11-04.

In conclusion, OAPA believes to achieve clarity with our regulatory terminology in Ohio, future consideration should be the utilization of more generic term such as practitioner, prescriber, provider or prescribing provider when crafting new language for Ohio statutes or rules governing the prescriptive authority and/or scope of practice for physicians, physician assistants and advanced practice registered nurses. The Medical Board's request for review OAC 4731-11 has clearly evoked the need to consider making these changes.

If it has not been done already, OAPA respectfully requests this proposed rule be reviewed by the Physician Assistant Policy Committee of the Medical Board so they may make recommendations to the board in accordance with ORC 4730.06 (A) (2). OAPA greatly appreciate the opportunity to comment on these proposed rules. If you have any questions or need further information, please do not hesitate to contact us.

Sincerely,

A handwritten signature in cursive script that reads "Elizabeth W. Adamson".

Elizabeth W. Adamson  
Executive Director

**From:** [Reardon, Jill](#)  
**To:** [Anderson, Kimberly](#); [Soin, Amol](#)  
**Subject:** FW: Interested party meeting regarding proposed weight loss rules  
**Date:** Monday, November 30, 2020 2:50:02 PM

---

fyi

---

**From:** Chris Gallagher <chris@potomaccurrents.com>  
**Sent:** Monday, November 30, 2020 2:49 PM  
**To:** Reardon, Jill <Jill.Reardon@med.ohio.gov>  
**Cc:** Joe Nadglowski <jnadglowski@obesityaction.org>  
**Subject:** Re: Interested party meeting regarding proposed weight loss rules

Afternoon Jill,

Please see the following comments from the Obesity Action Coalition regarding the Medical Board's proposed rules surrounding obesity pharmacotherapy:

-----

On behalf of the more than 70,000 members of the Obesity Action Coalition (OAC), a national non-profit organization dedicated to giving a voice to the individual affected by the disease of obesity, we are pleased to provide the following comments regarding the State Medical Board of Ohio's review of the prescribing restrictions for anti-obesity agents outlined under rule:

4731-11-04, OAC, Controlled Substances: Utilization of short term anorexiant for weight reduction

4731-11-04.1, OAC, Controlled substances: Utilization for chronic weight management

The OAC is extremely appreciative of Dr. Soin for his time last week to allow the Medical Board to learn additional information regarding the impact that these regulations will have on obesity medicine specialists and the patients they treat. Dr. Soin asked several important and thoughtful questions of the attendees on the call last week and we are thankful for his deep interest in affording stakeholders sufficient time to educate the Board regarding how obesity care has evolved over the last decade.

While the OAC is thankful that the Board continues to review these regulations, we remain deeply concerned that the Board could be willing to continue a discriminatory approach toward prescribing rules associated with anti-obesity medications – especially given the tremendous advances that have been made this decade in understanding both the science and physiology surrounding obesity. Even more troubling is that the Board is poised to affirm this approach despite growing evidence that the link between obesity and even overweight places affected individuals at significant risk of severe outcomes, such as death and hospitalization should they contract COVID-19.

Throughout the past decade, the Food and Drug Administration has approved a number of anti-

obesity medications and many more agents are progressing through the development process. Some of these new treatment tools employ combinations of older drugs, including phentermine. Despite this progress, patients continue to face discriminatory hurdles to care – barriers that are based more on historical misconceptions than evidence-based science. Preconceptions that those who are affected by obesity came to it through character flaw, lack of willpower, poor lifestyle choices or all of the above.

Those who are affected by obesity deserve both respect and access to the full continuum of care for this complex and chronic disease — in the same fashion that others currently enjoy who struggle with chronic disease states such as high cholesterol, heart disease or diabetes. We are hopeful that the Board will work with both healthcare professionals and patients to better understand the significant changes that have occurred in the obesity treatment landscape since these rules were last substantively amended more than a decade ago. It is critical that the Medical Board shift its view from acute care management of obesity to one that embraces a chronic care philosophy needed to address the complexity of the chronic disease of obesity.

Again, thank you for this opportunity to provide feedback regarding this issue. We urge the State Medical Board to rescind these bias and discriminatory prescribing rules. Failure to do so could be devastating — especially during this deadly pandemic.

Christopher Gallagher

Washington Representative

Obesity Action Coalition

[www.obesityaction.org](http://www.obesityaction.org)

The Obesity Action Coalition (OAC) is a more than 70,000 member-strong 501(c)(3) National non-profit organization dedicated to giving a voice to the individual affected by the disease of obesity and helping individuals along their journey toward better health through education, advocacy and support. Our core focuses are to raise awareness and improve access to the prevention and treatment of obesity, provide evidence-based education on obesity and its treatments, fight to eliminate weight bias and discrimination, elevate the conversation of weight and its impact on health and offer a community of support for the individual affected.

On Nov 23, 2020, at 5:12 PM, [Jill.Reardon@med.ohio.gov](mailto:Jill.Reardon@med.ohio.gov) wrote:

Thank you so much for your attendance at our meeting on the Medical Board's proposed weight loss rules. Your input as experts in the area of weight loss are

invaluable.

We will review the previous input you may have given the board on these rules and continue to accept any additional comments by email until close of business on Monday, November 30, 2020. Additionally, the rules are currently pending at the Common Sense Initiative and after the rules complete that process, there will be two more opportunities for public comment during the the JCARR process. As was mentioned by Dr. Soin, this subject will be discussed at our next Medical Board meeting to be held on December 9<sup>th</sup>, during the Policy Committee. Here is the link to find the time of the meetings and the agendas: [Medical Board of Ohio list of Board meetings and agendas](#). The Medical Board has a You Tube channel that will show the hearing live as well. For your reference here is the link to the You Tube channel: [Ohio Medical Board of Ohio You Tube Channel](#).

If you would like to be included on a list to receive notification of rule filings, please send an e-mail to [Judith.Rodriguez@med.ohio.gov](mailto:Judith.Rodriguez@med.ohio.gov) to add your name and e-mail address to that list.

Again, thank you again for your time and input and best wishes for a Happy Thanksgiving.

Jill

Jill Phalen Reardon  
Director of External Affairs  
State Medical Board of Ohio  
30 East Broad Street, 3rd Floor  
Columbus, Ohio 43215  
o: 614 466 0781  
c: 614 551 9957  
[Jill.Reardon@med.ohio.gov](mailto:Jill.Reardon@med.ohio.gov)  
w: [med.ohio.gov](http://med.ohio.gov)

<image017.png>

[<image018.jpg>](#) [<image019.png>](#) [<image020.png>](#)

Jill Phalen Reardon  
Director of External Affairs  
State Medical Board of Ohio  
30 East Broad Street, 3rd Floor  
Columbus, Ohio 43215  
o: 614 466 0781  
c: 614 551 9957  
[Jill.Reardon@med.ohio.gov](mailto:Jill.Reardon@med.ohio.gov)

w: [med.ohio.gov](http://med.ohio.gov)

<image021.png>

[<image022.jpg>](#) [<image023.png>](#) [<image024.png>](#)

Confidentiality Notice: This message is intended for use only by the individual or entity to whom or which it is addressed and may contain information that is privileged, confidential and/or otherwise exempt from disclosure under applicable law. If the reader of this message is not the intended recipient, or the employee or agent responsible for delivering the message to the intended recipient, you are hereby notified that any dissemination, distribution or copying of this communication is strictly prohibited. If you have received this communication in error, please notify me immediately by telephone.

Chris Gallagher  
Washington Policy Advisor  
ASMBS, OAC, TOS, OMA and SCAI  
[chris@potomaccurrents.com](mailto:chris@potomaccurrents.com)  
571-235-6475



**From:** [Reardon, Jill](#)  
**To:** [Anderson, Kimberly](#)  
**Cc:** [Soin, Amol](#)  
**Subject:** FW: Interested party meeting regarding proposed weight loss rules  
**Date:** Monday, November 30, 2020 3:32:31 PM  
**Attachments:** [Lewis et al-2019-Obesity.pdf](#)  
[image001.png](#)  
[image003.png](#)  
[image004.png](#)  
[image005.png](#)  
[image007.png](#)  
[image008.png](#)

---

fyi

---

**From:** Ted Kyle <ted.kyle@conscienhealth.org>  
**Sent:** Monday, November 30, 2020 3:31 PM  
**To:** Reardon, Jill <Jill.Reardon@med.ohio.gov>  
**Cc:** Chris Gallagher <chris@potomaccurrents.com>; GRIEBEM@ccf.org; Butsch, Winfield <BUTSCHW@ccf.org>; Anderson, Stan <stanand1@sbcglobal.net>; JJohns@amcno.org; Jennifer Hayhurst (jhayhurst@osma.org) <jhayhurst@osma.org>; Cjnorthup@premierhealth.com; Blair Barnhart-Kinkle <barnhab@ccf.org>; Michael Evans (EVANSM10@ccf.org) <EVANSM10@ccf.org>  
**Subject:** Re: Interested party meeting regarding proposed weight loss rules

Here is the article on longer term phentermine use that I mentioned on our call last week.

Perhaps the most important thing to bear in mind is that obesity is a complex, chronic disease that requires long-term care. Back in the 1950s, when phentermine was first approved, people thought that weight loss was the answer to obesity. Now obesity care specialists understand that long-term weight management is essential. Discontinuing an anti-obesity medicine after a person loses weight is like discontinuing a medicine for hypertension after a person's blood pressure goes down. In both cases a person's condition returns to its former state.

Thus in the late 1990s, FDA updated its guidance on meds for obesity to reflect the need for long-term therapy. All new obesity drugs, including the combination of phentermine and topiramate (Qsymia) are studied and approved for use in this way.

Because phentermine is so old and inexpensive, this is not how it has been labeled. But it is a mainstay for obesity medicine, because it is both effective and very inexpensive. By restricting its use to short-short term applications, Ohio regulations are preventing patients in Ohio from getting the most cost effective care possible. The only other alternative is newer and much more expensive drugs.

I ask that you include, by reference here (<https://conscienhealth.org/2019/03/older-than-dirt-phentermine-works/>), my commentary on this subject with these comments.

Thank you for your attention to this subject and for welcoming my input as a pharmacist and patient advocate.

Ted Kyle

On Mon, Nov 23, 2020 at 5:13 PM [Jill.Reardon@med.ohio.gov](mailto:Jill.Reardon@med.ohio.gov) <[Jill.Reardon@med.ohio.gov](mailto:Jill.Reardon@med.ohio.gov)> wrote:

Thank you so much for your attendance at our meeting on the Medical Board's proposed weight loss rules. Your input as experts in the area of weight loss are invaluable.

We will review the previous input you may have given the board on these rules and continue to accept any additional comments by email until close of business on Monday, November 30, 2020. Additionally, the rules are currently pending at the Common Sense Initiative and after the rules complete that process, there will be two more opportunities for public comment during the the JCARR process. As was mentioned by Dr. Soin, this subject will be discussed at our next Medical Board meeting to be held on December 9<sup>th</sup>, during the Policy Committee. Here is the link to find the time of the meetings and the agendas: [Medical Board of Ohio list of Board meetings and agendas](#). The Medical Board has a You Tube channel that will show the hearing live as well. For your reference here is the link to the You Tube channel: [Ohio Medical Board of Ohio You Tube Channel](#).

If you would like to be included on a list to receive notification of rule filings, please send an e-mail to [Judith.Rodriguez@med.ohio.gov](mailto:Judith.Rodriguez@med.ohio.gov) to add your name and e-mail address to that list.

Again, thank you again for your time and input and best wishes for a Happy Thanksgiving.

Jill

Jill Phalen Reardon  
Director of External Affairs  
State Medical Board of Ohio  
30 East Broad Street, 3rd Floor  
Columbus, Ohio 43215  
o: 614 466 0781  
c: 614 551 9957  
[Jill.Reardon@med.ohio.gov](mailto:Jill.Reardon@med.ohio.gov)  
w: [med.ohio.gov](http://med.ohio.gov)



Jill Phalen Reardon  
Director of External Affairs  
State Medical Board of Ohio  
30 East Broad Street, 3rd Floor  
Columbus, Ohio 43215  
o: 614 466 0781  
c: 614 551 9957  
[Jill.Reardon@med.ohio.gov](mailto:Jill.Reardon@med.ohio.gov)  
w: [med.ohio.gov](http://med.ohio.gov)



Confidentiality Notice: This message is intended for use only by the individual or entity to whom or which it is addressed and may contain information that is privileged, confidential and/or otherwise exempt from disclosure under applicable law. If the reader of this message is not the intended recipient, or the employee or agent responsible for delivering the message to the intended recipient, you are hereby notified that any dissemination, distribution or copying of this communication is strictly prohibited. If you have received this communication in error, please notify me immediately by telephone.

--

Ted Kyle, RPh, MBA  
ConscienHealth  
2270 Country Club Dr, Pittsburgh, PA 15241-2337  
[Ted.Kyle@ConscienHealth.org](mailto:Ted.Kyle@ConscienHealth.org) +1.412.206.9303  
Administrative Assistant: [Peggy.Stegmaier@conscienhealth.org](mailto:Peggy.Stegmaier@conscienhealth.org)  
<http://facebook.com/ConscienHealth> <http://twitter.com/ConscienHealth>  
Subscribe to free health & obesity updates: <http://conscienhealth.org/subscribe/>

**CAUTION:** This is an external email and may not be safe. If the email looks suspicious, please do not click links or open attachments and forward the email to [csc@ohio.gov](mailto:csc@ohio.gov) or click the Phish Alert Button if available.

**From:** [Reardon, Jill](#)  
**To:** [Anderson, Kimberly](#); [Soin, Amol](#)  
**Subject:** FW: Ohio Anti-Obesity Treatment rules  
**Date:** Thursday, December 10, 2020 12:58:20 PM

---

fyi

---

**From:** Fitch, Angela Kay, M.D. <AFITCH@mgm.harvard.edu>  
**Sent:** Wednesday, December 9, 2020 6:51 PM  
**To:** Reardon, Jill <Jill.Reardon@med.ohio.gov>  
**Subject:** Ohio Anti-Obesity Treatment rules

Jill,

Please let me know if I can be of service in the future and I thank you and Dr Soin for seriously considering a change in phentermine prescribing laws in Ohio.

I was formerly at the University of Cincinnati as you may recall in my first message to you and one of the reasons I left to come to Massachusetts General Hospital was to be able to treat obesity in an adequate fashion that I was not able to do in Ohio.

Thank you again for your consideration and if I can be of service as an outside of Ohio now expert I am happy to help. With the obesity and COVID-19 pandemics intersecting it is more important than ever to treat obesity seriously and have access to medication that can do that. You may also want to hear from patients and we can also provide that testimony if it is helpful.

Happy Holidays!  
Stay well!

Angela

Angela Fitch, MD, FACP, FOMA  
Associate Director MGH Weight Center  
Assistant in Medicine MGH  
Assistant Professor of Medicine Harvard Medical School  
Vice President Obesity Medicine Association

MGH Weight Center  
50 Staniford Street  
Boston, MA 02493  
Office: 617.726.4400  
Cell: 952.237.5489

The information in this e-mail is intended only for the person to whom it is addressed. If you believe

this e-mail was sent to you in error and the e-mail contains patient information, please contact the Mass General Brigham Compliance HelpLine at <http://www.massgeneralbrigham.org/complianceline>. If the e-mail was sent to you in error but does not contain patient information, please contact the sender and properly dispose of the e-mail.

**CAUTION:** This is an external email and may not be safe. If the email looks suspicious, please do not click links or open attachments and forward the email to [csc@ohio.gov](mailto:csc@ohio.gov) or click the Phish Alert Button if available.



# Common Sense Initiative

Mike DeWine, Governor  
Jon Husted, Lt. Governor

Carrie Kuruc, Director

## Business Impact Analysis

Agency, Board, or Commission Name: State Medical Board of Ohio

Rule Contact Name and Contact Information:

Judy Rodriguez, Public Services Manager – Judith.rodriguez@med.ohio.gov

Regulation/Package Title (a general description of the rules' substantive content):

Controlled Substance Rules

Rule Number(s): 4731-11-02, 4731-11-03, 4731-11-04, 4731-11-04.1, 4731-11-07, 4731-11-

11

Date of Submission for CSI Review: 10/5/20

Public Comment Period End Date: 10/19/20

Rule Type/Number of Rules:

New/\_\_\_ rules

No Change/ 2 rules (FYR? yes\_\_\_)

Amended/ 4 rules (FYR? yes)

Rescinded/\_\_\_ rules (FYR? \_\_\_)

The Common Sense Initiative is established in R.C. 107.61 to eliminate excessive and duplicative rules and regulations that stand in the way of job creation. Under the Common Sense Initiative, agencies must balance the critical objectives of regulations that have an adverse impact on business with the costs of compliance by the regulated parties. Agencies should promote transparency, responsiveness, predictability, and flexibility while developing regulations that are fair and easy to follow. Agencies should prioritize compliance over punishment, and to that end, should utilize plain language in the development of regulations.

77 SOUTH HIGH STREET | 30TH FLOOR | COLUMBUS, OHIO 43215-6117

CSIPublicComments@governor.ohio.gov

### **Reason for Submission-**

1. **R.C. 106.03 and 106.031 require agencies, when reviewing a rule, to determine whether the rule has an adverse impact on businesses as defined by R.C. 107.52. If the agency determines that it does, it must complete a business impact analysis and submit the rule for CSI review.**

**Which adverse impact(s) to businesses has the agency determined the rule(s) create?**

**The rule(s):**

- a.  **Requires a license, permit, or any other prior authorization to engage in or operate a line of business.**
- b.  **Imposes a criminal penalty, a civil penalty, or another sanction, or creates a cause of action for failure to comply with its terms.**
- c.  **Requires specific expenditures or the report of information as a condition of compliance.**
- d.  **Is likely to directly reduce the revenue or increase the expenses of the lines of business to which it will apply or applies.**

### **Regulatory Intent**

2. **Please briefly describe the draft regulation in plain language.  
*Please include the key provisions of the regulation as well as any proposed amendments.***

Rule 4731-11-02 General provisions-No change

The rule provides general information regarding controlled substance prescribing for physicians.

Rule 4731-11-03-Utilization of anabolic steroids, schedule II controlled substances-Amend

The rule outlines the utilization of anabolic steroids and schedule II controlled substances. The rule is proposed to be amended to remove the reference to the rescinded intractable pain rules and to reference chronic pain as defined in Rule 4731-11-01, OAC and to correct a typographical error.

Rule 4731-11-04 Controlled substances: Utilization of short term anorexiant for weight reduction-Amend

77 SOUTH HIGH STREET | 30TH FLOOR | COLUMBUS, OHIO 43215-6117

[CSIPublicComments@governor.ohio.gov](mailto:CSIPublicComments@governor.ohio.gov)



The rule sets forth the requirements for physicians to prescribe short-term anorexiants for weight loss. The rule is proposed to be amended to correct the spelling of dietitian in Section 4731-11-04(B)(1), OAC.

Rule 4731-11-04.1 Controlled substances: utilization for chronic weight management-Amend

The rule sets forth the requirements for physicians and physician assistants in the utilization of controlled substances for chronic weight management. The rule is proposed to be amended to remove reference to the discontinued physician assistant formulary in Section 4731-11-04.1(B)(2)(b).

Rule 4731-11-07 Research utilizing controlled substances-No change

The rule outlines the research programs which are not impacted by the rules.

Rule 4731-11-11 Standards and procedures for review of “Ohio Automated Rx Reporting System” (OARRS)-Amend

The rule sets forth the standards and procedures to be followed by physicians prior to prescribing controlled substances and the red flags of abuse for physicians to monitor when prescribing controlled substances. The rule is proposed to be amended to update the reference to the Pharmacy Board rule for reported drugs in paragraph (A)(5) and to correct a typographical error.

**3. Please list the Ohio statute(s) that authorize the agency, board or commission to adopt the rule(s) and the statute(s) that amplify that authority.**

Statutory authority: 4731.295, 4731.281, 4731.05

Amplifying statutes: 4731.281, 4731.296, 4731.295, 4731.294, 4731.293, 4731.292, 4731.291, 4731.282

**4. Does the regulation implement a federal requirement? Is the proposed regulation being adopted or amended to enable the state to obtain or maintain approval to administer and enforce a federal law or to participate in a federal program? If yes, please briefly explain the source and substance of the federal requirement.**

No. Although the Controlled Substance Act establishes the schedule for controlled drugs, the rules are not required by the federal law.

**5. If the regulation includes provisions not specifically required by the federal government, please explain the rationale for exceeding the federal requirement.**

Not applicable.

77 SOUTH HIGH STREET | 30TH FLOOR | COLUMBUS, OHIO 43215-6117

[CSIPublicComments@governor.ohio.gov](mailto:CSIPublicComments@governor.ohio.gov)

**6. What is the public purpose for this regulation (i.e., why does the Agency feel that there needs to be any regulation in this area at all)?**

The rules provide specific guidance to physicians in the prescribing of controlled substances, which are prescription drugs which can lead to addiction.

**7. How will the Agency measure the success of this regulation in terms of outputs and/or outcomes?**

The success of these regulations will be measured by physicians prescribing controlled substances in accordance with the rules; the rules being written in plain, understandable language; licensee compliance with the rules; and minimal questions from the licensees about the proposed rules.

**8. Are any of the proposed rules contained in this rule package being submitted pursuant to R.C. 101.352, 101.353, 106.032, 121.93, or 121.931?**

*If yes, please specify the rule number(s), the specific R.C. section requiring this submission, and a detailed explanation.*

No.

**Development of the Regulation**

**9. Please list the stakeholders included by the Agency in the development or initial review of the draft regulation.**

*If applicable, please include the date and medium by which the stakeholders were initially contacted.*

Interested parties that have requested notification of proposed rule changes, including Ohio State Medical Association, Ohio Association of Physician Assistants, Physician Assistant Policy Committee and the Pharmacy Board.

**10. What input was provided by the stakeholders, and how did that input affect the draft regulation being proposed by the Agency?**

**Comments on Rule 4731-11-02: None**

**Comments on Rule 4731-11-03: None**

**Comments on Rule 4731-11-04 and 4731-11-04.1:**

- Trace Curry, M.D. Eliminate the 12-week limit:

77 SOUTH HIGH STREET | 30TH FLOOR | COLUMBUS, OHIO 43215-6117

[CSIPublicComments@governor.ohio.gov](mailto:CSIPublicComments@governor.ohio.gov)

- Derrick Cetin, D.O.Current rule emphasizes when NOT to use rather than when to use. If patient just 1 day late for filling script, must be off for 6 months, they gain back weight. Should be able to use the short acting medications such as phentermine long term to treat obesity as it should be as a chronic disease
- Luke Selby, M.D., Chris Gallagher, Megan Skinner, APRN and Maria Schroff, M.D. Urges the Board to work with both patients and the healthcare community to better understand how Ohio's overly restrictive and dated prescribing restrictions are impeding so many Ohioans from accessing the full continuum of care for obesity — in the same fashion that others currently enjoy who struggle with chronic disease such as high cholesterol, heart disease or diabetes.
- Neal Nesbett, M.D.Re-submission of 2013 letter as OSMA position has not changed. Rule is out-dated, particularly 3 months limitation and having see patient every 3 months
- Beth Adamson, OAPA:Comments are applicable to 4731-11-04 and 4731-11-04.1. Supervising physician should be authorize PA to prescribe any drug within physician's normal practice and without requiring physician to review each chart after the PA sees the patient. Recommends use of a more inclusive term such as "practitioner" or "prescriber"
- Donna Leitzel, patient Rule imposes extraordinary restrictions on use of weight loss drugs
- Ross Henchen, M.D., Cheryl Milani, MMS, PA-C, Alana Mercer, MSHS, PA-C:The rules are overly restrictive. Let PAs prescribe weight loss drugs; consider rescinding the rules completely and let physicians use medical judgment.
- Latyonya Fore, NP:Recommends removal of the verbiage “short term anorexiant for purposes of weight reduction” and replacing it with “anti-obesity medication for the purpose of treating overweight and obesity. Allow long-term use of "short-term" drugs. In 4731-11-04.1, allow PAs to prescribe and change medications as do APRNs.
- Barto Burguera M.D., Ph.D.:The rule should allow telemedicine visits for both 4731-11-04 and 4731-11-04.1. For 4731-11-04, drop the 12 weeks maximum, require closer monitoring for 12 weeks, but allow long term use. Should not require discontinuation based on failure to loose weight. Medical Board should designate phentermine to be a chronic weight loss drug. The letter Incudes references to several studies.
- Karen Schultz, CNS:Should amend both 4731-11-04 and 4731-11-04.1 to allow continuous treatment as phentermine is safe.
- Scott W. Butsch, M.D.Obesity is a chronic disease and the rules prevent appropriate treatment.
- Kay Mavko, R.D.Please correct spelling of dietitian. For both 4731-11-04 and 4731-11-04.1, add requirements for “nutritionally adequate calorie restricted diet” , “nutritional counseling and intensive behavioral therapy” and exercise program for weight loss.

77 SOUTH HIGH STREET | 30TH FLOOR | COLUMBUS, OHIO 43215-6117

[CSIPublicComments@governor.ohio.gov](mailto:CSIPublicComments@governor.ohio.gov)

- Stan Anderson, M.D. Obesity needs on-going treatment, OARRS should take care of "doctor shopping" concerns, easier to prescribe morphine than Schedule 4 weight loss drug, chronic weight management drugs too expensive for many patients
- Sandra Thornhill, P.A. Should rescind the rule, have a rule for obesity treatment instead. Limits patient's ability to lose any significant amount of weight. Rule limits PA practice and is contradictive to "new process of prescribing."
- Ethan Lazarus, M.D. Should allow long-term use of phentermine. Ohio physician who treats obesity according to standard of care violates the Ohio rule.
- Steven Schierholt, Executive Director, Board of Pharmacy: Supports continuing the rules are currently written.
- The Board's Physician Assistant Policy Committee recommended two changes to rule 4731-11-04.1:
  - (1) Remove reference to PA formulary in Rule 4731-11-04.1(B)(2)(b);
  - (2) Modify requirement for supervising physician to have a discussion with the physician assistant rather than personally reviewing the medical records in paragraph (B)(3)(a) of Rule 4731-11-04.1.

**Comments on Rule 4731-11-07: None**

**Comments on Rule 4731-11-11:**

- The Board of Pharmacy recommended changing paragraph (A)(5) to update the rule reference defining "reported drugs".

The Board reviewed the comments at its Policy Committee meetings in September, October and November of 2019. The Board determined to accept the following changes:

4731-11-04: update spelling of dietitian;

4731-11-04.1: remove the reference to the discontinued physician assistant formulary;

4731-11-11: update the Pharmacy Board rule reference in paragraph (A)(5).

**11. What scientific data was used to develop the rule or the measurable outcomes of the rule? How does this data support the regulation being proposed?**

The Medical Board, which includes nine physicians, utilized its medical expertise in developing these rules.

**12. What alternative regulations (or specific provisions within the regulation) did the Agency consider, and why did it determine that these alternatives were not appropriate? If none, why didn't the Agency consider regulatory alternatives?**

No alternative regulation was considered other than the amendments discussed above. The Board continues to have concerns regarding the safety of prescribing controlled substance medication and works closely with the Board of Pharmacy on this issue.

**13. Did the Agency specifically consider a performance-based regulation? Please explain.**

*Performance-based regulations define the required outcome, but don't dictate the process the regulated stakeholders must use to achieve compliance.*

The proposed rules are performance based.

**14. What measures did the Agency take to ensure that this regulation does not duplicate an existing Ohio regulation?**

The Medical Board is the only state agency that licenses physicians.

**15. Please describe the Agency's plan for implementation of the regulation, including any measures to ensure that the regulation is applied consistently and predictably for the regulated community.**

The rule will be posted on the Medical Board's website. Medical Board staff members are available by telephone and e-mail to answer questions.

**Adverse Impact to Business**

**16. Provide a summary of the estimated cost of compliance with the rule. Specifically, please do the following:**

**a. Identify the scope of the impacted business community; and**

The business community impacted is composed of physician licensees regulated by the Medical Board.

**b. Identify the nature of all adverse impact (e.g., fees, fines, employer time for compliance,); and**

The rules require periodic examinations for patients being prescribed controlled substance medications.

**c. Quantify the expected adverse impact from the regulation.**

*The adverse impact can be quantified in terms of dollars, hours to comply, or other factors; and may be estimated for the entire regulated population or for a*

77 SOUTH HIGH STREET | 30TH FLOOR | COLUMBUS, OHIO 43215-6117

[CSIPublicComments@governor.ohio.gov](mailto:CSIPublicComments@governor.ohio.gov)

*“representative business.” Please include the source for your information/estimated impact.*

There may be additional time for physicians treating patients with controlled substances for weight loss. However, these rules have been in place for many years, and there are no amendments requiring additional physician time.

**17. Why did the Agency determine that the regulatory intent justifies the adverse impact to the regulated business community?**

Controlled substances pose health and safety risks to patients and it is important to have comprehensive standards for the prescribing of these drugs.

**Regulatory Flexibility**

**18. Does the regulation provide any exemptions or alternative means of compliance for small businesses? Please explain.**

No. The regulation is applied equally for all physicians and physician assistants.

**19. How will the agency apply Ohio Revised Code section 119.14 (waiver of fines and penalties for paperwork violations and first-time offenders) into implementation of the regulation?**

Violations of these rules could result in disciplinary action , including fines. Any disciplinary action is imposed pursuant to Chapter 119 and the Medical Board’s laws and rules. Due process requires equal application of the laws and rules to all licensees.

**20. What resources are available to assist small businesses with compliance of the regulation?**

Board staff is available to answer questions regarding the rule. The rules are posted and are available on the Board’s website.

4731-11-02

**General provisions.**

- (A) A physician shall not utilize a controlled substance other than in accordance with all of the provisions of this chapter of the Administrative Code.
- (B) A physician shall not utilize a controlled substance without taking into account the drug's potential for abuse, the possibility the drug may lead to dependence, the possibility the patient will obtain the drug for a nontherapeutic use or to distribute to others, and the possibility of an illicit market for the drug.
- (C) A physician shall complete and maintain accurate medical records reflecting the physician's examination, evaluation, and treatment of all the physician's patients. Patient medical records shall accurately reflect the utilization of any controlled substances in the treatment of a patient and shall indicate the diagnosis and purpose for which the controlled substance is utilized, and any additional information upon which the diagnosis is based.
- (D) A physician shall obey all applicable provisions of sections 3719.06, 3719.07, 3719.08 and 3719.13 of the Revised Code and the rules promulgated thereunder, all prescription issuance rules adopted under Chapter 4729. of the Revised Code, and all applicable provisions of federal law governing the possession, distribution, or use of controlled substances.
- (E) Violations of this rule:
  - (1) A violation of any provision of this rule, as determined by the board, shall constitute any or all of the following: "failure to maintain minimal standards applicable to the selection or administration of drugs," as that clause is used in division (B)(2) of section 4731.22 of the Revised Code; and "a departure from, or the failure to conform to, minimal standards of care of similar physicians under the same or similar circumstances, whether or not actual injury to a patient is established," as that clause is used in division (B)(6) of section 4731.22 of the Revised Code.
  - (2) A violation of paragraph (C) of this rule shall further constitute "selling, prescribing, giving away, or administering drugs for other than legal and legitimate therapeutic purposes," as that clause is used in division (B)(3) of section 4731.22 of the Revised Code.



4731-11-03

**Utilization of anabolic steroids, schedule II controlled substance cocaine hydrochloride, and schedule II controlled substance stimulants.**

(A) A physician shall not:

- (1) Utilize anabolic steroids, growth hormones, testosterone or its analogs, human chorionic gonadotropin ("HCG"), or other hormones for the purpose of enhancing athletic ability.
- (2) Utilize the schedule II controlled substance cocaine hydrochloride for a purpose other than one of the following:
  - (a) As a topical anesthetic in situations in which it is properly indicated; or
  - (b) For in-office diagnostic testing for pupillary disorders.
- (3) Utilize a schedule II controlled substance stimulant in any of the following circumstances:
  - (a) For purposes of weight reduction or control;
  - (b) When the physician knows or has reason to believe that a recognized contra-indication to its use exists; or
  - (c) In the treatment of a patient who the physician knows or should know is pregnant, except if the following criteria are met:
    - (i) After the physician's medical assessment the physician and patient determine that the benefits of treating the patient with a schedule II controlled substance stimulant outweigh the risks, and
    - (ii) The basis for the determination is documented in the patient record.

(B) Utilizing a schedule II controlled ~~subtanees~~substance stimulant:

- (1) Before initiating treatment utilizing a schedule II controlled substance stimulant, the physician shall perform all of the following:
  - (a) Obtain a thorough history;

- (b) Perform an appropriate physical examination of the patient; and
  - (c) Rule out the existence of any recognized contra-indications to the use of the controlled ~~substances~~substance stimulant to be utilized.
- (2) A physician may utilize a schedule II controlled substance stimulant only for one of the following purposes:
- (a) The treatment of narcolepsy, idiopathic hypersomnia, and hypersomnias due to medical conditions known to cause excessive sleepiness;
  - (b) The treatment of abnormal behavioral syndrome (attention deficit disorder, hyperkinetic syndrome), and/or related disorders;
  - (c) The treatment of drug-induced or trauma-induced brain dysfunction;
  - (d) The differential diagnostic psychiatric evaluation of depression;
  - (e) The treatment of depression shown to be refractory to other therapeutic modalities, including pharmacologic approaches, such as antidepressants;
  - (f) As adjunctive therapy in the treatment of the following:
    - (i) Chronic severe pain;
    - (ii) Closed head injuries;
    - (iii) Cancer-related fatigue;
    - (iv) Fatigue experienced during the terminal stages of disease;
    - (v) Depression experienced during the terminal stages of disease; or
    - (vi) ~~Intractable~~Chronic pain, as defined in rule ~~4731-21-01~~4731-11-01 of the Administrative Code.
  - (g) The treatment of binge eating disorder.

- (3) Upon ascertaining or having reason to believe that the patient has a history of or shows a propensity for alcohol or drug abuse, or that the patient has consumed or disposed of any controlled substance other than in strict compliance with the treating physician's directions, the physician shall perform both of the following:
    - (a) Reappraise the desirability of continued utilization of schedule II controlled substance stimulants and shall document in the patient record the factors weighed in deciding to continue their use; and
    - (b) Actively monitor such patient for signs and symptoms of drug abuse and drug dependency.
- (C) A violation of any provision of this rule, as determined by the board, shall constitute any or all of the following:
- (1) "Failure to maintain minimal standards applicable to the selection or administration of drugs," as that clause is used in division (B)(2) of section 4731.22 of the Revised Code;
  - (2) "Selling, giving away, personally furnishing, prescribing, or administering drugs for other than legal and legitimate therapeutic purposes," as that clause is used in division (B)(3) of section 4731.22 of the Revised Code;
  - (3) "A departure from, or the failure to conform to, minimal standards of care of similar practitioners under the same or similar circumstances, whether or not actual injury to a patient is established," as that clause is used in division (B)(6) of section 4731.22 of the Revised Code.

4731-11-04

**Controlled substances: Utilization of short term anorexiant for weight reduction.**

- (A) A physician shall utilize a schedule III or IV controlled substance short term anorexiant for purposes of weight reduction only if it has an F.D.A. approved indication for this purpose and then only in accordance with all of the provisions of this rule.
- (B) Before initiating treatment for weight reduction utilizing any schedule III or IV controlled substance short term anorexiant, the physician shall complete all of the following requirements:
- (1) The physician shall review the physician's own records of prior treatment or review the records of prior treatment by another treating physician, ~~dietician~~dietitian, or weight-loss program to determine the patient's past efforts to lose weight in a treatment program utilizing a regimen of weight reduction based on caloric restriction, nutritional counseling, intensive behavioral therapy, and exercise, without the utilization of controlled substances, and that the treatment has been ineffective.
  - (2) The physician shall complete and document the findings of all of the following:
    - (a) Obtain a thorough history;
    - (b) Perform an appropriate physical examination of the patient;
    - (c) Determine the patient's BMI;
    - (d) Rule out the existence of any recognized contraindications to the use of the controlled substance to be utilized;
    - (e) Assess and document the patient's freedom from signs of drug or alcohol abuse, and the presence or absence of contraindications and adverse side effects.
    - (f) Access OARRS for the patient's prescription history during the preceding twelve month period and document in the patient's record the receipt and assessment of the report received; and
    - (g) Develop and record in the patient record a treatment plan that includes, at a minimum, a diet and exercise program for weight loss.

- (3) The physician shall not initiate treatment utilizing a controlled substance short term anorexiant upon ascertaining or having reason to believe any one or more of the following:
- (a) The patient has a history of or shows a propensity for alcohol or drug abuse, or has made any false or misleading statement to the physician related to the patient's use of drugs or alcohol;
  - (b) The patient has consumed or disposed of any controlled substance other than in strict compliance with the treating physician's directions;
  - (c) The physician knows or should know the patient is pregnant;
  - (d) The patient has a BMI of less than thirty, unless the patient has a BMI of at least twenty seven with comorbid factors;
  - (e) The review of the physician's own records of prior treatment or review of records of prior treatment provided by another physician, ~~dietician~~dietitian, or weight-loss program indicate that the patient made less than a substantial good faith effort to lose weight in a treatment program utilizing a regimen of weight reduction based on caloric restriction, nutritional counseling, intensive behavioral therapy, and exercise without the utilization of controlled substances.
- (C) A physician may utilize a schedule III or IV controlled substance short term anorexiant, that bears appropriate F.D.A. approved labeling for weight loss, in the treatment of obesity as an adjunct, in a regimen of weight reduction based on caloric restriction, provided that:
- (1) The physician shall personally meet face-to-face with the patient, at a minimum, every thirty days when controlled substances are being utilized for weight reduction, and shall record in the patient record information demonstrating the patient's continuing efforts to lose weight, the patient's dedication to the treatment program and response to treatment, and the presence or absence of contraindications, adverse effects, and indicators of possible substance abuse that would necessitate cessation of treatment utilizing controlled substances.
  - (2) The controlled substance short term anorexiant is prescribed strictly in accordance with the F.D.A. approved labeling. If the F.D.A. approved labeling of the controlled substance short term anorexiant being utilized for weight loss states that it is indicated for use for "a few weeks," the total course of treatment using that controlled substance shall not exceed twelve

weeks. That time period includes any interruption in treatment that may be permitted under paragraph (C)(3) of this rule.

- (3) A physician shall not initiate a course of treatment utilizing a controlled substance short term anorexiant for purposes of weight reduction if the patient has received any controlled substance for purposes of weight reduction within the past six months. However, the physician may resume utilizing a controlled substance short term anorexiant following an interruption of treatment of more than seven days if the interruption resulted from one or more of the following:
  - (a) Illness of or injury to the patient justifying a temporary cessation of treatment; or
  - (b) Unavailability of the physician; or
  - (c) Unavailability of the patient, if the patient has notified the physician of the cause of the patient's unavailability.
- (4) After initiating treatment, the physician may elect to switch to a different controlled substance short term anorexiant for weight loss based on sound medical judgment, but the total course of treatment for any short term anorexiant combination of controlled substances each of which is indicated for "a few weeks" shall not exceed twelve weeks.
- (5) The physician shall not initiate or shall discontinue utilizing all controlled substance short term anorexiant for purposes of weight reduction immediately upon ascertaining or having reason to believe:
  - (a) That the patient has a history of or shows a propensity for alcohol or drug abuse, or has made any false or misleading statement to the physician relating to the patient's use of drugs or alcohol;
  - (b) That the patient has consumed or disposed of any controlled substance other than in strict compliance with the treating physician's directions;
  - (c) That the patient has failed to lose weight while under treatment with a controlled substance or controlled substances over a period of thirty days during the current course of treatment, which determination shall be made by weighing the patient at least every thirtieth day, except that a patient who has never before received treatment for obesity utilizing

any controlled substance who fails to lose weight during the first thirty days of the first such treatment attempt may be treated for an additional thirty days;

(d) That the patient has repeatedly failed to comply with the physician's treatment recommendations; or

(e) That the physician knows or should know the patient is pregnant.

(D) A violation of any provision of this rule, as determined by the board, shall constitute the following:

(1) "Failure to maintain minimal standards applicable to the selection or administration of drugs," as that clause is used in division (B)(2) of section 4731.22 of the Revised Code;

(2) "Selling, giving away, personally furnishing, prescribing, or administering drugs for other than legal and legitimate therapeutic purposes," as that clause is used in division (B)(3) of section 4731.22 of the Revised Code; and

(3) "A departure from, or the failure to conform to, minimal standards of care of similar practitioners under the same or similar circumstances, whether or not actual injury to a patient is established," as that clause is used in division (B)(6) of section 4731.22 of the Revised Code.



4731-11-04.1

**Controlled substances: utilization for chronic weight management.**

(A) A physician shall determine whether to utilize a controlled substance anorexiant for purposes of chronic weight management as an adjunct to a reduced calorie diet and increased physical activity. The determination shall be made in compliance with the provisions of this rule.

(1) Before initiating treatment utilizing any controlled substance anorexiant, the physician shall complete all of the following requirements:

(a) Obtain a thorough history;

(b) Perform a physical examination of the patient;

(c) Determine the patient's BMI;

(d) Review the patient's attempts to lose weight in the past for indications that the patient has made a substantial good faith effort to lose weight in a regimen for weight reduction based on caloric restriction, nutritional counseling, intensive behavioral therapy, and exercise without the utilization of controlled substance anorexiant. The review shall include available records from the physician's own prior treatment of the patient, prior treatment provided by another physician, prior participation in a weight-loss program, or prior treatment by a dietitian;

(e) Rule out the existence of any recognized contraindications to the use of the controlled substance anorexiant to be utilized;

(f) Assess and document the patient's freedom from signs of drug or alcohol abuse;

(g) Access OARRS and document in the patient's record the receipt and assessment of the information received; and

(h) Develop and record in the patient record a treatment plan that includes, at a minimum, a diet and exercise program for weight loss.

(2) The physician shall not initiate treatment utilizing a controlled substance anorexiant upon ascertaining or having reason to believe any one or more of the following:

- (a) The patient has a history of, or shows a propensity for, alcohol or drug abuse, or has made any false or misleading statement to the physician or physician assistant relating to the patient's use of drugs or alcohol;
    - (b) The patient has consumed or disposed of any controlled substance other than in strict compliance with the treating physician's directions; or
    - (c) The physician knows or should know the patient is pregnant.
  - (3) The physician shall not initiate treatment utilizing a controlled substance anorexiant if any of the following conditions exist:
    - (a) The patient has an initial BMI of less than thirty, unless the patient has an initial BMI of at least twenty seven with comorbid factors.
    - (b) The review of the patient's attempts to lose weight in the past indicates that the patient has not made a substantial good faith effort to lose weight in a regimen for weight reduction based on caloric restriction, nutritional counseling, intensive behavioral therapy, and exercise without the utilization of controlled substance anorexiant. The review shall include available records from the physician's own prior treatment of the patient, prior treatment provided by another physician, prior participation in a weight-loss program, or prior treatment by a dietitian.
  - (4) The physician shall prescribe the controlled substance anorexiant strictly in accordance with the F.D.A. approved labeling;
  - (5) Throughout the course of treatment with any controlled substance anorexiant the physician shall comply with rule 4731-11-11 of the Administrative Code and the physician assistant shall comply with rule 4730-2-10 of the Administrative Code.
- (B) A physician shall provide treatment utilizing a controlled substance anorexiant for weight management in compliance with paragraph (A) of this rule and the following:
- (1) The physician shall meet face-to-face with the patient for the initial visit and at least every thirty days during the first three months of treatment. If the F.D.A. approved labeling for the controlled substance anorexiant requires induction of treatment at one dose and an increase to a higher dose after a stated period of less than thirty days, the physician may give the patient a prescription for

the higher dose at the initial visit and the first thirty day period then starts from the date the prescription for the higher dose may be filled.

(2) Following the initial visit and two follow-up visits, the treatment may be continued under one of the following means:

(a) The physician may authorize refills for the controlled substance anorexiant up to five times within six months after the initial prescription date;

(b) The treatment may be provided by a physician assistant in compliance with this rule, the supervisory plan or policies of the healthcare facility, ~~and the physician assistant formulary adopted by the board.~~

(3) When treatment for chronic weight management is provided by a physician assistant, the following requirements apply:

(a) The supervising physician shall personally review the medical records of each patient to whom the physician assistant has prescribed a controlled substance anorexiant following each visit; and

(b) A physician assistant shall not initiate utilization of a different controlled substance anorexiant, but may recommend such change for the supervising physician's initiation.

(4) A physician shall discontinue utilizing any controlled substance anorexiant immediately upon ascertaining or having reason to believe:

(a) That the patient has repeatedly failed to comply with the physician's treatment recommendations; or

(b) That the patient is pregnant.

(C) A violation of any provision of this rule, as determined by the board, shall constitute the following as applicable:

(1) For a physician:

(a) "Failure to maintain minimal standards applicable to the selection or administration of drugs," as that clause is used in division (B)(2) of

section 4731.22 of the Revised Code;

- (b) "Selling, giving away, personally furnishing, prescribing, or administering drugs for other than legal and legitimate therapeutic purposes," as that clause is used in division (B)(3) of section 4731.22 of the Revised Code; and
- (c) "A departure from, or the failure to conform to, minimal standards of care of similar practitioners under the same or similar circumstances, whether or not actual injury to a patient is established," as that clause is used in division (B)(6) of section 4731.22 of the Revised Code.

(2) For a physician assistant:

- (a) "A departure from, or failure to conform to, minimal standards of care of similar physician assistants under the same or similar circumstances, regardless of whether actual injury to a patient is established," as that clause is used in division (B)(19) of section 4730.25 of the Revised Code;
- (b) "Failure to comply with the requirements of this chapter, Chapter 4731. of the Revised Code, or any rules adopted by the board," as that clause is used in division (B)(2) of section 4730.25 of the Revised Code; and
- (c) "Violating or attempting to violate, directly or indirectly, or assisting in or abetting the violation of, or conspiring to violate, any provision of this chapter, Chapter 4731. of the Revised Code, or the rules adopted by the board," as that clause is used in division (B)(3) of section 4730.25 of the Revised Code.

4731-11-07

**Research utilizing controlled substances.**

The provisions of this chapter of the Administrative Code shall not apply to or in any way prohibit research conducted under the auspices of an accredited medical school, or research which meets both of the following conditions:

- (A) The U.S. food and drug administration has approved an investigational new drug ("IND") application for the research or has notified the researchers that the proposed study is exempt from the "IND" regulations; and
- (B) The research is conducted in conformance with the approval granted by either of the following:
  - (1) An institutional review board of a hospital or medical center accredited by the "Joint Commission," "Healthcare Facilities Accreditation Program" or other accrediting body approved by the board; or
  - (2) An institutional review board accredited by the association for the accreditation of human research protection programs.

4731-11-11

**Standards and procedures for review of "Ohio Automated Rx Reporting System" (OARRS).**

(A) For purposes of this rule:

- (1) "Delegate" means an authorized representative who is registered with the Ohio board of pharmacy to obtain an OARRS report on behalf of a physician;
- (2) "OARRS" means the "Ohio Automated Rx Reporting System" drug database established and maintained pursuant to section 4729.75 of the Revised Code.
- (3) "OARRS report" means a report of information related to a specified patient generated by the drug database established and maintained pursuant to section 4729.75 of the Revised Code.
- (4) "Personally furnish" means the distribution of drugs by a prescriber to the prescriber's patients for use outside the prescriber's practice setting.
- (5) "Reported drugs" means all the drugs listed in rule ~~4729-37-02~~[4729:8-2-01](#) of the Administrative Code that are required to be reported to the drug database established and maintained pursuant to section 4729.75 of the Revised Code, including controlled substances in schedules II, III, IV, and V.

(B) Standards of care:

- (1) The accepted and prevailing minimal standards of care require that when prescribing or personally furnishing a reported drug, a physician shall take into account all of the following:
  - (a) The potential for abuse of the reported drug;
  - (b) The possibility that use of the reported drug may lead to dependence;
  - (c) The possibility the patient will obtain the reported drug for a nontherapeutic use or distribute it to other persons; and
  - (d) The potential existence of an illicit market for the reported drug.
- (2) In considering whether a prescription for or the personally furnishing of a reported drug is appropriate for the patient, the physician shall use sound clinical judgment and obtain and review an OARRS report consistent with the provisions of this rule.

- (C) A physician shall obtain and review an OARRS report to help determine if it is appropriate to prescribe or personally furnish an opioid analgesic, benzodiazepine, or reported drug to a patient as provided in this paragraph and paragraph (F) of this rule:
- (1) A physician shall obtain and review an OARRS report before prescribing or personally furnishing an opiate analgesic or benzodiazepine to a patient, unless an exception listed in paragraph (G) of this rule is applicable.
  - (2) A physician shall obtain and review an OARRS report when a patient's course of treatment with a reported drug other than an opioid analgesic or benzodiazepine has lasted more than ninety days, unless an exception listed in paragraph (G) of this rule is applicable.
  - (3) A physician shall obtain and review an OARRS report when any of the following red flags pertain to the patient:
    - (a) Selling prescription drugs;
    - (b) Forging or altering a prescription;
    - (c) Stealing or borrowing reported drugs;
    - (d) Increasing the dosage of reported drugs in amounts that exceed the prescribed amount;
    - (e) Suffering an overdose, intentional or unintentional;
    - (f) Having a drug screen result that is inconsistent with the treatment plan or refusing to participate in a drug screen;
    - (g) Having been arrested, convicted, or received diversion or intervention in lieu of conviction for a drug related offense while under the physician's care;
    - (h) Receiving reported drugs from multiple prescribers, without clinical basis;
    - (i) Traveling with a group of other patients to the physician's office where all or most of the patients request controlled substance prescriptions;



- (j) Traveling an extended distance or from out of state to the physician's office;
  - (k) Having a family member, friend, law enforcement officer, or health care professional express concern related to the patient's use of illegal or reported drugs;
  - (l) A known history of chemical abuse or dependency;
  - (m) Appearing impaired or overly sedated during an office visit or exam;
  - (n) Requesting reported drugs by street name, color, or identifying marks;
  - (o) Frequently requesting early refills of reported drugs;
  - (p) Frequently losing prescriptions for reported drugs;
  - (q) A history of illegal drug use;
  - (r) Sharing reported drugs with another person; or
  - (s) Recurring visits to non-coordinated sites of care, such as emergency departments, urgent care facilities, or walk-in clinics to obtain reported drugs.
- (D) A physician who decides to utilize an opioid analgesic, benzodiazepine, or other reported drug in any of the circumstances within paragraphs (C)(2) and (C)(3) of this rule, shall take the following steps prior to issuing a prescription for or personally furnishing the opioid analgesic, benzodiazepine, or other reported drug:
- (1) Review and document in the patient record the reasons why the physician believes or has reason to believe that the patient may be abusing or diverting drugs;
  - (2) Review and document in the patient's record the patient's progress toward treatment objectives over the course of treatment;
  - (3) Review and document in the patient record the functional status of the patient, including activities for daily living, adverse effects, analgesia, and aberrant behavior over the course of treatment;

(4) Consider using a patient treatment agreement including more frequent and periodic reviews of OARRS reports and that may also include more frequent office visits, different treatment options, drug screens, use of one pharmacy, use of one provider for the prescription or personally furnishing of reported drugs, and consequences for non-compliance with the terms of the agreement. The patient treatment agreement shall be maintained as part of the patient record; and

(5) Consider consulting with or referring the patient to a substance abuse specialist.

(E) Frequency for follow-up OARRS reports:

(1) For a patient whose treatment with an opioid analgesic or benzodiazepine lasts more than ninety days, a physician shall obtain and review and OARRS report for the patient at least every ninety days during the course of treatment, unless an exception listed in paragraph (G) of this rule is applicable.

(2) For a patient who is treated with a reported drug other than an opioid analgesic or benzodiazepine for a period lasting more than ninety days, the physician shall obtain and review and OARRS report for the patient at least annually following the initial OARRS report obtained and reviewed pursuant to paragraph (C)(2) of this rule until the course of treatment utilizing the reported drug has ended, unless an exception in paragraph (G) of this rule is applicable.

(F) When a physician or their delegate requests an OARRS report in compliance with this rule, a physician shall document receipt and review of the OARRS report in the patient record, as follows:

(1) Initial reports requested shall cover at least the twelve months immediately preceding the date of the request:

(2) Subsequent reports requested shall, at a minimum, cover the period from the date of the last report to present;

(3) If the physician practices primarily in a county of this state that adjoins another state, the physician or their delegate shall also request a report of any information available in the drug database that pertains to prescriptions issued or drugs furnished to the patient in the state adjoining that county; and

(4) If an OARRS report regarding the patient is not available, the physician shall

document in the patient's record the reason that the report is not available and any efforts made in follow-up to obtain the requested information.

- (G) A physician shall not be required to review and assess an OARRS report when prescribing or personally furnishing an opioid analgesic, benzodiazepine, or other reported drug under the following circumstances, unless a physician believes or has reason to believe that a patient may be abusing or diverting reported drugs:
- (1) The reported drug is prescribed or personally furnished to a hospice patient in a hospice care program as those terms are defined in section 3712.01 of the Revised Code, or any other patient diagnosed as terminally ill;
  - (2) The reported drug is prescribed for administration in a hospital, nursing home, or residential care facility;
  - (3) The reported drug is prescribed or personally furnished in an amount indicated for a period not to exceed seven days;
  - (4) The reported drug is prescribed or personally furnished for the treatment of cancer or another condition associated with cancer; and
  - (5) The reported drug is prescribed or personally furnished to treat acute pain resulting from a surgical or other invasive procedure or a delivery.

# Safety and Effectiveness of Longer-Term Phentermine Use: Clinical Outcomes from an Electronic Health Record Cohort

Kristina H. Lewis<sup>1,2</sup>, Heidi Fischer<sup>3</sup>, Jany Ard<sup>1</sup>, Lee Barton<sup>3</sup>, Daniel H. Bessessen<sup>4</sup>, Matthew F. Daley<sup>5</sup>, Jay Desai<sup>6</sup>, Stephanie L. Fitzpatrick<sup>7</sup>, Michael Horber<sup>8</sup>, Corinna Koebnick<sup>3</sup>, Caryn Oshiro<sup>9</sup>, Aya Yamamoto<sup>3</sup>, Deborah R. Young<sup>3</sup>, and David E. Arterburn<sup>10</sup>

**Objective:** The aim of this work was to study weight loss and risk of cardiovascular disease (CVD) or death associated with longer-term phentermine use.

**Methods:** Using electronic health record data, 13,972 adults were identified with a first phentermine fill in 2010 to 2015, creating exposure categories according to a patient's duration of use (referent:  $\leq 3$  months). Multivariable linear models were used to compare percent weight loss across categories at 6, 12, and 24 months, and Cox proportional hazards models were used to compare risk of composite CVD or death, up to 3 years after starting phentermine.

**Results:** The cohort was 84% female and 45% white, with a mean (SD) baseline age 43.5 (10.7) years and BMI of 37.8 (7.2) kg/m<sup>2</sup>. In multivariable models, longer-term users of phentermine experienced more weight loss; patients using continuously for  $> 12$  months lost 7.4% more than the referent group at 24 months ( $P < 0.001$ ). The composite CVD or death outcome was rare (0.3%, 41 events), with no significant difference in hazard ratios between groups.

**Conclusions:** Greater weight loss without increased risk of incident CVD or death was observed in patients using phentermine monotherapy for longer than 3 months. Despite the limitations of the observational design, this study supports the effectiveness and safety of longer-term phentermine use for low-risk individuals.

*Obesity* (2019) 27, 591-602. doi:10.1002/oby.22430

## Introduction

Lifestyle interventions remain the cornerstone of treatment for patients with obesity, typically yielding a peak weight loss of 5% to 10% after 6 months (1). However, up to one-third of patients do not respond to such programs (2,3), and weight regain is common following intervention cessation (4,5). Pharmacotherapy can increase the proportion of individuals who respond to lifestyle interventions as well as the duration and magnitude of response (6). Clinically significant durable weight loss has been demonstrated in placebo-controlled trials of antioesity medications (7-14), but broader use of medications

remains limited because of concerns about cost, efficacy, and adverse events (15). The most commonly used weight-loss medication in the United States is phentermine (16,17), a sympathomimetic amine that acts by inhibiting appetite and that was originally approved for weight loss in 1959 (18,19). Most studies examining phentermine monotherapy have limited treatment duration to less than 12 weeks (20), aligning with a package insert that recommends that the medication be used as "a short-term adjunct (a few weeks)" to lifestyle-based programs (21). Concerns about longer-term phentermine use include increased risk

<sup>1</sup> Department of Epidemiology and Prevention, Division of Public Health Sciences, Wake Forest School of Medicine, Winston-Salem, North Carolina, USA. Correspondence: Kristina H. Lewis (khlewis@wakehealth.edu) <sup>2</sup> Department of Implementation Science, Division of Public Health Sciences, Wake Forest School of Medicine, Winston-Salem, North Carolina, USA. <sup>3</sup> Department of Research and Evaluation, Kaiser Permanente Southern California, Pasadena, California, USA <sup>4</sup> Diabetes & Endocrinology Division, Denver Health Medical Center, Denver, Colorado, USA <sup>5</sup> Institute for Health Research, Kaiser Permanente Colorado, Aurora, Colorado, USA <sup>6</sup> HealthPartners Institute, Bloomington, Minnesota, USA <sup>7</sup> Kaiser Permanente Center for Health Research, Portland, Oregon, USA <sup>8</sup> Mid-Atlantic Permanente Research Institute, Kaiser Permanente Mid-Atlantic States, Rockville, Maryland, USA <sup>9</sup> Center for Health Research, Kaiser Permanente Hawaii, Honolulu, Hawaii, USA <sup>10</sup> Kaiser Permanente Washington Health Research Institute, Seattle, Washington, USA.

**Funding agencies:** This work was supported by Patient-Centered Outcomes Research Institute (PCORI) as part of the Patient Outcomes Research to Advance Learning (PORTAL) project (PCORI CD RN 1306-04681).  
**Disclosure:** The authors declared no conflicts of interest.  
**Author contributions:** Study concept and design: KHL, DEA, and JA; acquisition, analysis, and interpretation of data: all authors; drafting of manuscript: KHL and HF; critical revision of manuscript: all authors; statistical analysis plan: HF, KHL, and DEA; graphical support: CK; supervision: KHL, DEA, and DRY.  
**Received:** 9 November 2018; **Accepted:** 9 January 2019; **Published online 22 March 2019.** doi:10.1002/oby.22430

of cardiovascular disease (CVD) (6,17) and potential for addiction (22).

Weight-loss treatment approaches are evolving to favor long-term therapy, aligning with the new chronic disease model of obesity. Newer antiobesity medications have, accordingly, been approved by the Food and Drug Administration (FDA) for long-term use (i.e., more than 12 months) (20). If phentermine monotherapy, which is widely available and low cost, was found to be safe and effective for long-term use, the impact for obesity treatment could be significant.

Using data from electronic health records (EHRs), we studied whether adults prescribed phentermine for longer than 12 weeks experienced differential weight loss, change in blood pressure (BP) or heart rate (HR), or increased risk of incident CVD or death compared with adults prescribed phentermine in an on-label short-term episode. Our primary hypothesis was that longer-term users would experience greater weight loss without increased risk of CVD or death.

## Methods

### Study design, health care systems, and data sources

The data sources for this retrospective cohort study were EHRs abstracted from the Patient Outcomes Research to Advance Learning (PORTAL) cohort, a collaborative data effort across several integrated health insurance and care-delivery systems in the United States as part of the National Patient-Centered Clinical Research Network (PCORnet) initiative (23,24). Data elements included membership status, demographics, vital signs, health care use, laboratory values, and pharmacy dispensing. This cohort included data from Kaiser Permanente (Southern California, Colorado, Northwest, Washington state, Hawaii, and Mid-Atlantic States [Maryland, Virginia, District of Columbia]) and from Denver Health and HealthPartners (Minnesota). The study was approved by the Kaiser Permanente Southern California Institutional Review Board, with other sites ceding primary review.

### Study population

We identified adult health plan members 18 to 64 years old with a “first” phentermine fill (dose  $\leq 37.5$  mg/d) between January 1, 2010, and September 30, 2015. To find likely incident users, we limited selection to patients with at least 12 months of continuous baseline enrollment, during which there were no prior phentermine prescriptions (25). We chose the study end date to coincide with the *International Classification of Diseases, Ninth Revision to Tenth Revision* transition, after which changes in diagnosis coding could have led to systematic differences in detection of outcomes and covariates.

We required patients to have BMI  $\geq 27$  kg/m<sup>2</sup> within 3 months prior to their first phentermine fill. We excluded those with history of bariatric surgery or cancer diagnosis (other than nonmelanoma skin cancer). We also excluded anyone with baseline year evidence of pregnancy, use of other weight-loss medications, palliative care encounters, or diagnosis and/or procedure codes for any cardiovascular outcomes of interest, including myocardial infarction, stroke, angina, coronary artery bypass grafting, or carotid artery procedures (Figure 1). Weight, BP, and HR analyses were limited to individuals with at least one relevant measurement before and after initiating phentermine.

## Exposure

Our exposure of interest was a patient’s pattern of phentermine use in follow-up, characterized based on duration and persistence of use. For each individual, we first created episodes of phentermine use and mapped them across follow-up time (26-28). See Supporting Information Figure S1 for details on how episodes were created.

Individuals with one phentermine treatment episode lasting  $\leq 112$  days and no subsequent use during follow-up were treated as our referent or “short-term” use group, reflecting FDA-approved use of the medication. This episode duration ( $\leq 112$  days) was based on multiplying the on-label duration of 90 days by a factor of 1.25 to account for days in the episode when a patient was between fills (28). Patients with a single phentermine treatment episode lasting  $> 112$  and up to 365 days, but with no subsequent treatment episodes, were labeled “medium-term continuous” users. Patients with a single continuous episode lasting  $> 365$  days were labeled “long-term continuous” users.

In clinical practice, patients often take phentermine intermittently over time. To separately capture these individuals and allow for follow-up beyond the first treatment episode, we created two additional groups. Persons with two or more separate treatment episodes in which no episode exceeded 112 days were termed “short-term intermittent” users. Those with two or more episodes in which at least one episode exceeded 112 days were termed “medium-term intermittent” users.

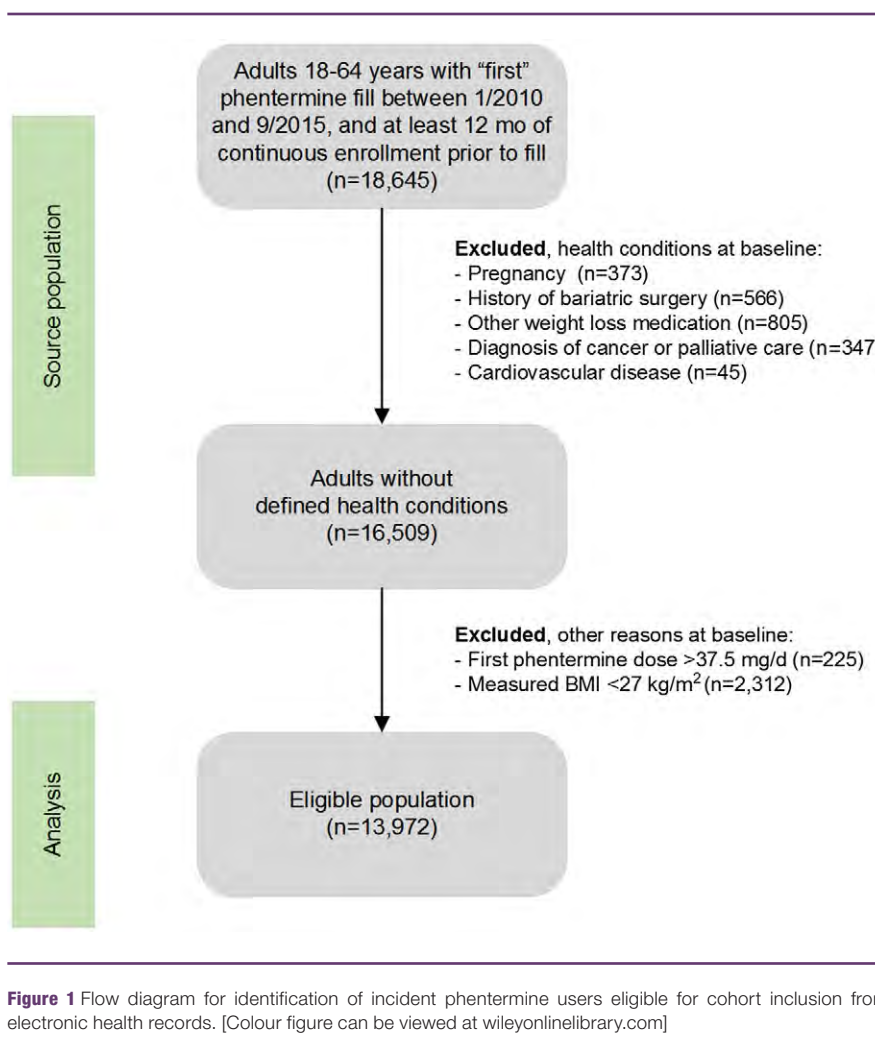
We treated phentermine use as a time-varying exposure. A patient’s inclusion in a particular exposure category was dependent on his or her exposure pattern up to the time point of interest, meaning that patients could change exposure categories over time. For example, at the 6-month mark, we could not yet classify anyone as being in the long-term continuous group because less than a year of phentermine exposure had elapsed. Therefore, these individuals were included in our medium-term continuous group for 6-month analyses, only separating out as a distinct group after 12 months of continuous exposure to phentermine.

## Outcomes

Our outcome for drug effectiveness was percent change in weight from baseline, measured at 6, 12, and 24 months after initial phentermine dispensing. We abstracted all weights recorded in the outpatient setting. We selected baseline weight (kilograms) as the nearest measure on or within 90 days prior to the index date. Because we were working with clinical data, follow-up did not occur precisely at 6, 12, or 24 months for most individuals. We accepted weights for each follow-up point based on a variable window that enlarged as follow-up time progressed. For our 6-month outcome, we accepted the nearest weight measure within  $-30$  to  $+90$  days; at 12 months, we accepted the nearest weight measure within  $-90$  to  $+90$  days; and at 24 months, we accepted the nearest weight measure within  $-180$  to  $+180$  days.

We examined changes in systolic BP (SBP), diastolic BP (DBP) (mmHg), and HR (beats per minute [bpm]) from baseline as intermediate outcomes for cardiovascular risk because of the sympathomimetic effect of phentermine. We derived change in HR, SBP, and DBP from outpatient measures, selecting the nearest measure per window per patient for analysis. Additional rules used for cleaning vital sign data are available in Supporting Information Table S1.

Our distal outcome measure for cardiovascular risk was a composite measure of incident myocardial infarction, stroke, angina, coronary artery



bypass grafting, carotid artery intervention, or death. We abstracted all relevant *International Classification of Diseases, Ninth Revision* diagnosis or procedure and Current Procedural Terminology procedure codes (Supporting Information Table S2) and used a previously published method to assign incident events (29). Information about date of death came from a combination of EHR, administrative, and state mortality databases (30).

### Covariates

All models included EHR-derived covariates for sex, race or ethnicity (non-Hispanic white, non-Hispanic black, Hispanic, Asian, other), age group (18-34, 35-49, 50-64), baseline BMI category (27-29.9, 30-34.9, 35-39.9, 40-49.9, or  $\geq 50$ ), hypertension, diabetes, smoking status, health care system, calendar year of phentermine initiation, and average daily dose category of phentermine (37.5 mg/d or <37.5 mg/d). BP and HR models were adjusted for baseline tertile of each measure.

We used demographic information from geographic information systems to create a covariate for area-level measure of poverty (percent of households in census block below poverty level: <5%, 5% to <10%, 10% to <20% or  $\geq 20\%$ ) (31). We assigned the rare patients missing

phentermine dose ( $n = 39$ ) or poverty ( $n = 538$ ) the modal values for their region.

### Statistical analysis

We built separate multivariable linear models at 6, 12, and 24 months of follow-up to examine the outcomes of percent change in weight and change in SBP, DBP, and HR. In weight analyses, we limited inclusion in the referent group to patients with at least one refill because patients with a single fill were likely intolerant to phentermine. Their inclusion would have biased weight loss results in favor of longer-term users.

We used Cox proportional hazards models with phentermine treated as a time-varying covariate to examine the composite outcome of incident CVD or death in a time-to-event fashion up to 3 years after the index date. Patients achieving any one of the submeasures composing our composite outcome were considered to have the outcome at that time.

Patients were not included in multivariable linear models if any of the following occurred before a time point of interest: health insurance plan disenrollment, > 18 months since any clinical care or encounters

**TABLE 1** Characteristics of phentermine users according to final exposure categorization<sup>a</sup>

	On-label users		Off-label users			Total (N = 13,972)
	Short-term referent (n = 6,764)	Short-term intermittent (n = 2,938)	Medium-term continuous (n = 1,703)	Medium-term intermittent (n = 2,423)	Long-term continuous (n = 144)	
<b>Sex<sup>b</sup></b>						
Female	5,611 (83.1%)	2,523 (85.8%)	1,402 (82.3%)	2,047 (84.3%)	116 (80.6%)	11,699 (83.7%)
<b>Race/ethnicity<sup>c</sup></b>						
Non-Hispanic white	3,007 (44.5%)	1,093 (37.2%)	894 (52.5%)	1,181 (48.6%)	80 (55.6%)	6,255 (44.8%)
Non-Hispanic black	1,370 (20.3%)	786 (26.7%)	253 (14.9%)	446 (18.4%)	19 (13.2%)	2,874 (20.6%)
Hispanic	1,749 (25.9%)	764 (26.0%)	367 (21.6%)	564 (23.2%)	27 (18.8%)	3,471 (24.8%)
Asian	305 (4.5%)	137 (4.7%)	101 (5.9%)	107 (4.4%)	12 (8.3%)	662 (4.7%)
Other	324 (4.8%)	162 (5.5%)	88 (5.2%)	130 (5.4%)	6 (4.2%)	710 (5.1%)
<b>Age (y)<sup>c</sup></b>	43.7 (10.9)	42.3 (10.6)	44.3 (10.4)	43.7 (10.5)	46.5 (10.0)	43.5 (10.7)
<b>BMI (kg/m<sup>2</sup>)<sup>c</sup></b>						
Mean (SD)	38.0 (7.5)	37.0 (6.9)	38.4 (7.0)	37.6 (6.8)	37.5 (7.1)	37.8 (7.2)
27-29.9	687 (10.2%)	381 (13%)	118 (6.9%)	234 (9.6%)	14 (9.7%)	1,434 (10.3%)
30-34.9	1,977 (29.3%)	979 (33.3%)	477 (28%)	738 (30.4%)	45 (31.3%)	4,216 (30.2%)
35-39.9	1,890 (28.0%)	773 (26.3%)	519 (30.5%)	735 (30.3%)	46 (31.9%)	3,963 (28.4%)
40-49.9	1,733 (25.7%)	673 (22.9%)	472 (27.7%)	593 (24.4%)	30 (20.8%)	3,501 (25.1%)
≥ 50.0	468 (6.9%)	136 (4.6%)	117 (6.9%)	128 (5.3%)	9 (6.3%)	858 (6.1%)
<b>Hypertension diagnosis<sup>d</sup></b>	1,443 (21.4%)	578 (19.6%)	357 (21%)	476 (19.6%)	35 (24.3%)	2,889 (20.7%)
<b>Diabetes diagnosis<sup>c,d</sup></b>	824 (12.2%)	299 (10.2%)	224 (13.2%)	253 (10.4%)	24 (16.7%)	1,624 (11.6%)
<b>Smoking status<sup>c,e</sup></b>						
Never users	4,211 (62.3%)	1,870 (63.6%)	1,035 (60.8%)	1,469 (60.5%)	69 (47.9%)	8,654 (61.9%)
Ever users	2,298 (34%)	944 (32.1%)	612 (35.9%)	849 (35%)	65 (45.1%)	4,768 (34.1%)
Missing/unknown	246 (3.6%)	128 (4.4%)	56 (3.3%)	110 (4.5%)	10 (6.9%)	550 (3.9%)
<b>Area families below poverty level<sup>f</sup></b>						
Missing <sup>e,g</sup>	234 (3.5%)	146 (5%)	56 (3.3%)	93 (3.8%)	9 (6.3%)	538 (3.9%)
< 5%	1,568 (23.2%)	686 (23.3%)	445 (26%)	612 (25.2%)	38 (26.4%)	3,349 (24%)
5-< 10%	1,779 (26.3%)	769 (26.1%)	448 (26.2%)	656 (27%)	37 (25.7%)	3,682 (26.4%)
10-< 20%	1,812 (26.8%)	798 (27.1%)	443 (25.9%)	629 (25.9%)	35 (24.3%)	3,717 (26.6%)
≥ 20%	1,362 (20.2%)	543 (18.5%)	318 (18.6%)	438 (18%)	25 (17.4%)	2,686 (19.2%)
<b>Follow-up duration (y)<sup>c</sup></b>	1.6 (1.1)	2.2 (0.9)	1.6 (1.0)	2.4 (0.8)	2.3 (0.8)	1.9 (1.0)
<b>Median percent of follow-up on phentermine</b>	9%	16%	33%	42%	75%	19%
<b>Daily phentermine dose<sup>c</sup></b>						
< 37.5 mg	3,688 (54.6%)	1,528 (51.9%)	1,120 (65.8%)	1,526 (62.9%)	89 (61.8%)	7,951 (56.9%)
37.5 mg	3,053 (45.2%)	1,404 (47.7%)	580 (34.1%)	892 (36.7%)	53 (36.8%)	5,982 (42.8%)
Missing <sup>g</sup>	14 (0.2%)	10 (0.3%)	3 (0.2%)	10 (0.4%)	2 (1.4%)	39 (0.3%)

Data given as n (%) for categorical variables and mean (SD) for continuous variables.

<sup>a</sup>On-label short-term users (referent) had a single phentermine use episode ≤ 112 days. Short-term intermittent users rotated on and off phentermine but never remained on the drug for longer than 112 days. Off-label user groups defined as follows: medium-term continuous users had a single phentermine treatment episode lasting > 112 but ≤ 365 days; medium-term intermittent users had multiple treatment episodes in which at least one exceeded 112 days; and long-term continuous users had a single episode lasting > 365 days. Note that “n” in each column corresponds to final exposure assignment at end of follow-up. Because of the time-varying nature of the exposure, relative size of groups and distribution of characteristics may differ between time points in early follow-up (e.g., at 6 and 12 months).

<sup>b</sup>P = 0.004 for  $\chi^2$  test.

<sup>c</sup>P < 0.001 for difference across groups using  $\chi^2$  test for categorical and Kruskal-Wallis test for continuous variables.

<sup>d</sup>Defined as one relevant inpatient or two outpatient *International Classification of Diseases, Ninth Revision* codes in year prior to index phentermine prescription.

<sup>e</sup>Tobacco “ever users” includes current and historical smokers.

<sup>f</sup>Using geographic information systems measures mapping to 2010 census block group socioeconomic status data, categories go from highest to lowest SES vertically.

<sup>g</sup>For analyses, patients missing either the area-level poverty measure or daily phentermine dose had these values set to modal value for patients in their region. A sensitivity analysis was conducted excluding these patients entirely from analyses and results did not change.



**TABLE 2** Difference in percent weight loss over follow-up: results from multivariable linear models using time-varying exposure<sup>a</sup>

	6 months		12 months		24 months	
	Parameter estimate (95% CI)	n (% of enrolled with weight data available) <sup>b</sup>	Parameter estimate (95% CI)	n (% of enrolled with weight data available) <sup>b</sup>	Parameter estimate (95% CI)	n (% of enrolled with weight data available) <sup>b</sup>
Intercept <sup>c</sup>	-2.68 (-3.28 to -2.08) <sup>d,e</sup>		-1.38 (-2.08 to -0.67) <sup>f</sup>		-0.16 (-1.07 to 0.75)	
Short-term <sup>c</sup>	Referent	2,555 (66%)	Referent	2,074 (78%)	Referent	1,323 (90%)
Short-term intermittent <sup>c</sup>	-1.75 (-2.13 to -1.37) <sup>d,g</sup>	1,450 (73%)	-1.36 (-1.80 to -0.93) <sup>g</sup>	1,743 (82%)	-0.26 (-0.83 to 0.32) <sup>g</sup>	1,545 (92%)
Medium-term continuous <sup>c</sup>	-5.07 (-5.40 to -4.73) <sup>d,g</sup>	2,352 (74%)	-4.66 (-5.13 to -4.19) <sup>g</sup>	1,371 (78%)	-1.71 (-2.46 to -0.96) <sup>g</sup>	613 (89%)
Medium-term intermittent <sup>c</sup>	-4.22 (-5.11 to -3.33) <sup>d,g</sup>	179 (78%)	-5.63 (-6.13 to -5.13) <sup>g</sup>	1,178 (86%)	-3.48 (-4.07 to -2.88) <sup>g</sup>	1,368 (93%)
Long-term continuous <sup>c</sup>	n/a		n/a		-7.36 (-8.96 to -5.76) <sup>g</sup>	98 (89%)

<sup>a</sup>Separate models built for each time point, all adjusted for gender, race and ethnicity, smoking, diabetes, hypertension, baseline BMI, average medication strength, year of original prescription, and site.  
<sup>b</sup>n (%) by exposure category within each time point references those with a weight measure versus total number assigned to that exposure category at that time point.  
<sup>c</sup>Short-term users (referent) had a single phentermine use episode ≤ 112 days; short-term intermittent users rotated on and off phentermine but never remained on the drug for longer than 112 days. Off-label user groups were defined as follows: medium-term continuous users had a single phentermine treatment episode lasting > 112 but ≤ 365 days; medium-term intermittent users had multiple treatment episodes in which at least one exceeded 112 days; and long-term continuous users had a single episode lasting > 365 days.  
<sup>d</sup>Parameter estimates for intercept approximate percent weight loss of referent group when all covariates are set to their referent value, and parameter estimates for comparison groups should be interpreted as difference in percent weight loss compared with referent group.  
<sup>e</sup>p < 0.0001 for comparing intercept to zero.  
<sup>f</sup>p < 0.001 for comparing intercept to zero.  
<sup>g</sup>p < 0.0001 for comparing percent weight loss in comparison groups to referent group.  
n/a, not applicable.

in their health system, incident pregnancies, bariatric procedures, prescription of any weight-loss medication besides phentermine, prescription for phentermine >37.5 mg/d, CVD outcome (e.g., myocardial infarction), or death. Patients were censored at these times in the Cox model.

### Sensitivity analyses

Unmeasured patient characteristics or differential response to phentermine could predict greater medication persistence and more weight loss. Therefore, we conducted two sensitivity analyses to assess whether patients who used phentermine for longer did so because the medication was working better for them. In the first sensitivity analysis, we treated phentermine use over follow-up as a fixed exposure, allowing patients to populate their final exposure categories artificially early. We then conducted weight-loss analysis using these fixed exposure categories, beginning at 3 months, when phentermine duration should have been relatively equal between categories.

Second, we conducted a separate “responders-only” sensitivity analysis. In this analysis, we limited inclusion in the cohort to patients who achieved  $\geq 3\%$  weight loss by 3 months. Our goal with this analysis was to reduce the potential impact of phentermine nonresponders on lower weight loss in the referent group. The responder analysis was also conducted in two ways, treating phentermine as both time varying and fixed.

To test the sensitivity of our weight findings to varying acceptable time windows for follow-up measures, we reran models using acceptable windows of  $-/+90$  days,  $+90$  days,  $-/+60$  days,  $+60$  days,  $-30/+90$  days, and  $-30/+60$  days at each time point (6, 12, and 24 months).

To examine whether a higher-risk subgroup of patients might be more likely to experience adverse effects, we repeated HR and BP analyses on the subset of individuals with baseline hypertension diagnoses.

## Results

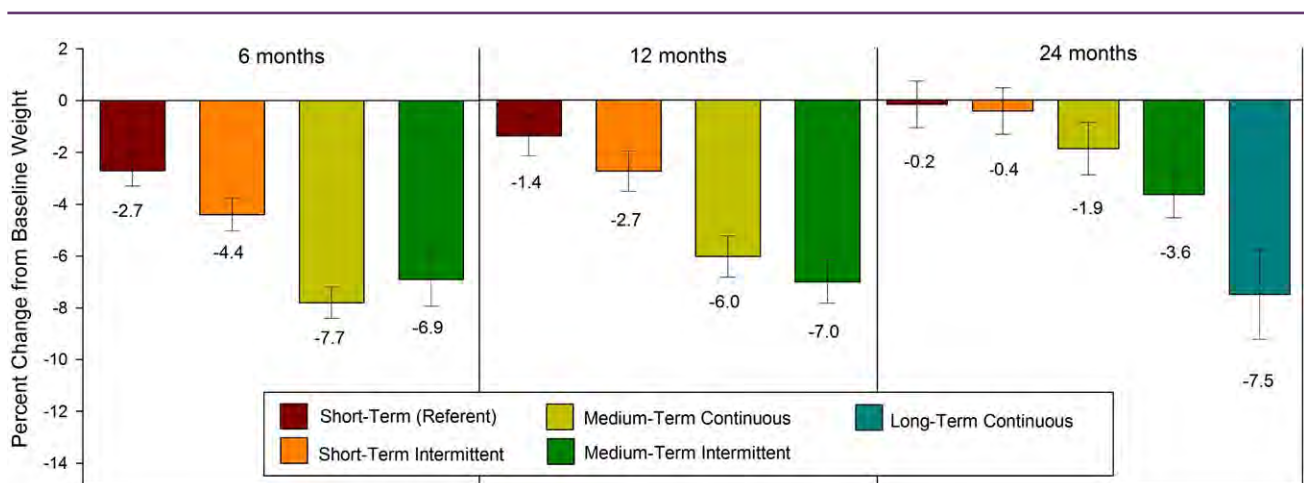
### Study population

We identified 13,972 incident phentermine users (Figure 1). Most were women (84%), and the mean (SD) baseline age was 43.5 (10.7) years; just under half (45%) were non-Hispanic white (Table 1). Baseline BMI was 37.8 (7.2) kg/m<sup>2</sup>, 21% carried a diagnosis of hypertension at baseline, and 12% had a diagnosis of diabetes. Phentermine use groups differed by baseline characteristics, with on-label users slightly more likely to be minorities, younger, not diabetic, and never smokers compared with off-label groups. Off-label groups included a higher proportion of patients taking a lower daily dose of phentermine.

### Weight loss

At 6, 12, and 24 months after phentermine initiation, weight loss was greater among off-label and intermittent short-term users than our referent short-term single episode users (Table 2). The mean weight change for short-term single episode (referent) phentermine use can be approximated by examining the intercept values for models at each time point (Table 2, Figure 2). By 6 months after drug initiation (or  $\sim 3$  months after discontinuing phentermine), short-term users averaged 2.7% (95% CI: 2.1%-3.3%) total weight loss. By 12 months, their weight loss was 1.4% (95% CI: 0.7%-2.1%), and by 24 months, the weight change in this group was not different from zero.

The magnitude of difference in weight loss between comparison groups and the referent group varied with duration of follow-up (Table 2, Figure 2). At 6 months, short-term intermittent users lost 1.8% (95% CI: 1.4%-2.1%) additional body weight relative to short-term single episode (referent) users, while medium-term continuous users lost 5.1% (95% CI: 4.7%-5.4%) more. At 12 months, the medium-term intermittent group lost 5.6% (95% CI: 5.1%-6.1%) more weight than short-term single episode users. At 24 months after phentermine initiation,



**Figure 2** Estimated percent weight loss at 6 months and 1 and 2 years after phentermine initiation; results from multivariable linear models. Estimates at each time point are from separate multivariable linear models, and  $n$  (%) by group over follow-up is presented in Table 2. Note that because real clinical follow-up does not occur at exact 6-month intervals, weights were drawn from an acceptable time window of outpatient visits around each time point of interest, as outlined in *Methods*. Estimates for the referent group (on-label continuous) were based on the y-intercept of multivariable models in the case in which all covariates are set to referent. Estimates for comparison groups were generated by summing the intercept weight loss and the additional change in weight by group at each time point. Error bars represent 95% CI for each estimate.

**TABLE 3** Difference in percent weight loss over follow-up: results from multivariable linear models using time-varying exposure among early phentermine responders<sup>a</sup>

	6 months		12 months		24 months	
	Parameter estimate (95% CI)	n (% of enrolled with weight data available) <sup>b</sup>	Parameter estimate (95% CI)	n (% of enrolled with weight data available) <sup>b</sup>	Parameter estimate (95% CI)	n (% of enrolled with weight data available) <sup>b</sup>
Intercept <sup>c</sup>	-6.26 (-7.09 to -5.43) <sup>d,e</sup>		-4.07 (-5.20 to -2.94) <sup>e</sup>		-3.01 (-4.53 to -1.48) <sup>f</sup>	
Short-term <sup>c</sup>	Referent	767 (70%)	Referent	604 (82%)	Referent	364 (94%)
Short-term intermittent <sup>c</sup>	-1.54 (-2.12 to -0.97) <sup>d,g</sup>	565 (78%)	-1.75 (-2.49 to -1.02) <sup>g</sup>	604 (84%)	-0.07 (-1.16 to 1.02) <sup>g</sup>	495 (93%)
Medium-term continuous <sup>c</sup>	-3.35 (-3.82 to -2.88) <sup>d,g</sup>	1,574 (78%)	-3.64 (-4.33 to -2.95) <sup>g</sup>	848 (80%)	-0.54 (-1.71 to 0.64) <sup>g</sup>	364 (89%)
Medium-term intermittent <sup>c</sup>	-2.25 (-3.34 to -1.15) <sup>d,g</sup>	103 (82%)	-4.21 (-4.93 to -3.48) <sup>g</sup>	744 (90%)	-2.47 (-3.49 to -1.46) <sup>g</sup>	788 (94%)
Long-term continuous <sup>c</sup>	n/a		n/a		-7.68 (-10.02 to -5.34) <sup>g</sup>	52 (91%)

<sup>a</sup>Separate models built for each time point, all adjusted for gender, race and ethnicity, smoking, diabetes, hypertension, baseline BMI, average medication strength, year of original prescription, and site. Models include only patients who had documented weight loss of  $\geq 3\%$  by 3 months after starting phentermine.

<sup>b</sup>n (%) by exposure category within each time point references those with a weight measure versus total number assigned to that exposure category at that time point.

<sup>c</sup>Short-term users (referent) had a single phentermine use episode  $\leq 112$  days; short-term intermittent users rotated on and off phentermine but never remained on drug for longer than 112 days. Off-label user groups were defined as follows: medium-term continuous users had a single phentermine treatment episode lasting  $> 112$  but  $\leq 365$  days; medium-term intermittent users had multiple treatment episodes in which at least one exceeded 112 days; and long-term continuous users had a single episode lasting  $> 365$  days.

<sup>d</sup>Parameter estimates for intercept approximate percent weight loss of referent group when all covariates are set to their referent value, and parameter estimates for comparison groups should be interpreted as difference in percent weight loss compared with referent group.

<sup>e</sup> $P < 0.0001$  for comparing intercept to zero.

<sup>f</sup> $P < 0.001$  for comparing intercept to zero.

<sup>g</sup> $P < 0.0001$  for comparing percent weight loss in comparison groups with referent group.

n/a, not applicable.

long-term continuous (>12 months) users lost 7.4% (95% CI: 5.8%-9.0%) more weight than short-term single episode users.

When we examined weight change at 3 months using final assigned exposure categories rather than time-varying exposure, individuals in the off-label and intermittent use categories already had greater weight loss than those in the referent group (Supporting Information Table S3). In these models, short-term users had lost 3.5% (95% CI: 3.1%-4.0%) body weight at 3 months, with additional weight loss by group as follows: short-term intermittent, 0.4% (95% CI: 0.1%-0.7%); medium-term continuous, 2.6% (95% CI: 2.3%-2.9%); medium-term intermittent, 3.0% (95% CI: 2.7%-3.3%); and long-term continuous, 3.4% (95% CI: 2.6%-4.3%). Referent and between-group patterns for weight loss at 6, 12, and 24 months in this sensitivity analysis using fixed phentermine use groups were otherwise similar to our main findings.

Our responders-only analysis for weight loss included 4,340 individuals who experienced ≥3% weight loss by 3 months, representing 62% of the 7,043 patients who had weight data available at that time point. In multivariable models treating phentermine as a time-varying exposure among responders, referent group weight loss was greater than in our main analyses, as follows: 6.3% (95% CI: 5.4%-7.1%) at 6 months, 4.1% (95% CI: 2.9%-5.2%) at 12 months, and 3.0% (95% CI: 1.5%-4.5%) at 24 months (Table 3, Figure 3). Despite selecting for individuals with more initial success, weight loss in our comparison groups was still greater than the referent group at all time points in follow-up. Comparison groups displayed a similar magnitude of difference as observed in our main analysis (Table 3) but with greater overall weight loss for all groups (Figure 3). The sensitivity analysis for responders using end-group assignments and examining early (3 month) weight loss between groups showed slightly greater early weight loss among comparison groups compared with the referent group; however, between-group differences at this early time point were attenuated (Supporting Information Table S4).

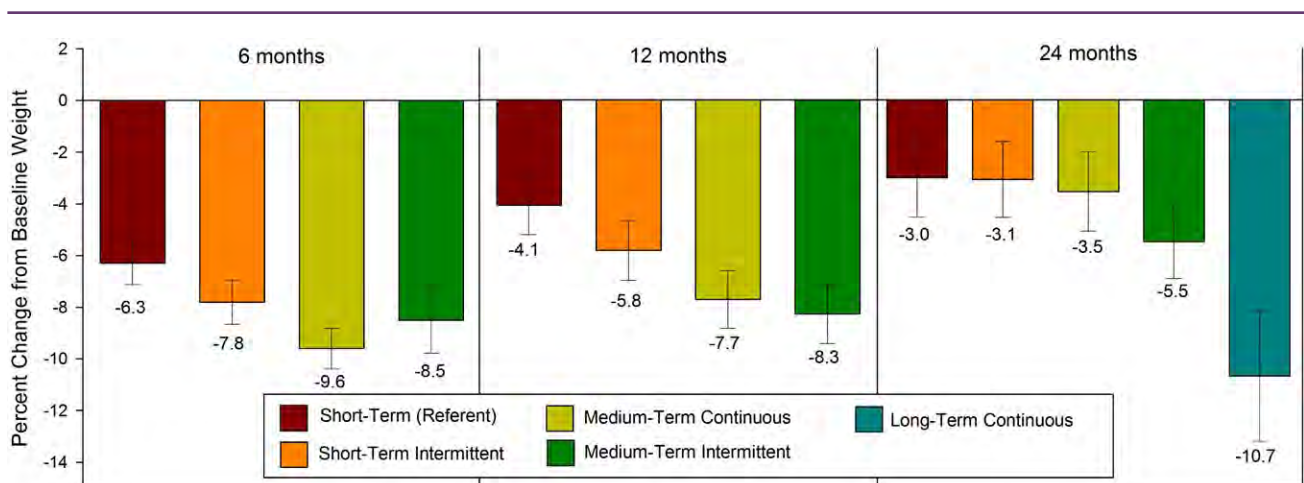
Varying the time window for acceptable EHR weight measures did not appreciably change referent or between-group results compared with our main analysis despite a large amount of variability in missingness that occurred as a result of requiring narrower or wider time windows around each point (Supporting Information Table S5). Related to missingness, the reader will note that the number of patients in each exposure category varies over follow-up. In part, this is due to the time-varying nature of our exposure; however, additional reasons for missingness are summarized in Supporting Information Table S6.

### Changes in BP and HR

At baseline, mean (SD) HR was 79 (12) bpm, and mean (SD) BP was 122 (12)/74 (9). Patients in the short-term single episode (referent) group had no significant change in HR at 6, 12, or 24 months (Table 4). The greatest relative HR increase among medium-term continuous users was at 6 months and was 1.6 (95% CI: 1.0-2.2) bpm higher than the referent group; among medium-term intermittent users, at 12 months, it was 1.1 (95% CI: 0.3-1.9) bpm higher than the referent group. Comparison group changes in HR did not differ from the referent group at 24 months.

SBP in the referent group was stable at 6 and 12 months, but at 24 months, it had increased by 1.8 (0.5-3.2) mmHg, relative to baseline. There was no between-group difference in SBP change at 6 months; however, the comparison groups on the whole had slightly lower BP than the referent group at 12 and 24 months, again with variability in magnitude of difference by group. For example, at 24 months, patients in the long-term continuous user group experienced SBP Δ-3.3 (-0.8 to -5.9) mmHg relative to the on-label users.

DBP in the referent (short-term) group was stable relative to baseline at 6, 12, and 24 months, and there were no significant between-group differences in DBP over follow-up.



**Figure 3** Estimated percent weight loss at 6 months and 1 and 2 years after phentermine initiation among responders; results from multivariable linear models. Models include only phentermine responders, patients who had lost ≥3% body weight by 3 months after initiating medication. Estimates at each time point are from separate multivariable linear models, and *n* (%) by group over follow-up is presented in Table 2. Note that because real clinical follow-up does not occur at exact 6-month intervals, weights were drawn from an acceptable time window of outpatient visits around each time point of interest, as outlined in *Methods*. Estimates for the referent group (on-label continuous) were based on the y-intercept of multivariable models in the case in which all covariates are set to referent. Estimates for comparison groups were generated by summing the intercept weight loss and the additional change in weight by group at each time point. Error bars represent 95% CI for each estimate.

**TABLE 4** Change in heart rate (HR) and blood pressure (BP) over follow-up: results from multivariable linear models using time-varying exposure<sup>a</sup>

	Heart rate results					
	6 months		12 months		24 months	
	Parameter estimate ΔHR (bpm) (95% CI)	n (%) enrolled with VS data <sup>b</sup>	Parameter estimate ΔHR (bpm) (95% CI)	n (%) enrolled with VS data <sup>b</sup>	Parameter estimate ΔHR (bpm) (95% CI)	n (%) enrolled with VS data <sup>b</sup>
Intercept <sup>c</sup>	1.01 (-0.13 to 2.16) <sup>d</sup>	n/a	0.64 (-0.51 to 1.80)	n/a	0.55 (-0.77 to 1.86)	n/a
Short-term <sup>c</sup>	Ref	4,268 (68%)	Ref	3,672 (79%)	Ref	2,534 (91%)
Short-term intermittent <sup>c</sup>	0.81 (0.08 to 1.53) <sup>d,e</sup>	1,439 (74%)	0.27 (-0.43 to 0.96) <sup>f</sup>	1,723 (83%)	0.13 (-0.65 to 0.91)	1,533 (93%)
Medium-term continuous <sup>c</sup>	1.61 (0.99 to 2.24) <sup>d,e</sup>	2,353 (75%)	1.16 (0.40 to 1.92) <sup>f</sup>	1,362 (79%)	-0.19 (-1.28 to 0.90)	610 (90%)
Medium-term intermittent <sup>c</sup>	-0.77 (-2.57 to 1.04) <sup>d,e</sup>	181 (80%)	1.09 (0.28 to 1.90) <sup>f</sup>	1,184 (88%)	0.67 (-0.14 to 1.49)	1,360 (95%)
Long-term continuous <sup>c</sup>	n/a		n/a		2.64 (0.15 to 5.14)	96 (90%)

	Blood pressure results					
	6 months		12 months		24 months	
	Parameter estimate (95% CI)	n (%) enrolled with VS data <sup>b</sup>	Parameter estimate (95% CI)	n (%) enrolled with VS data <sup>b</sup>	Parameter estimate (95% CI)	n (%) enrolled with VS data <sup>b</sup>
Intercept <sup>c</sup>	-0.99 (-2.13 to 0.14) <sup>d</sup>	n/a	-0.19 (-1.37 to 0.99)	n/a	1.83 (0.48 to 3.19) <sup>g</sup>	n/a
Short-term <sup>c</sup>	Ref	4,377 (68%)	Ref	3,742 (79%)	Referent	2,592 (92%)
Short-term intermittent <sup>c</sup>	-0.78 (-1.49 to -0.06) <sup>d</sup>	1,468 (75%)	-0.41 (-1.11 to 0.30) <sup>h</sup>	1,759 (83%)	0.2 (-0.60 to 1.00) <sup>i</sup>	1,560 (94%)
Medium-term continuous <sup>c</sup>	0.08 (-0.46 to 0.61) <sup>d</sup>	2,402 (76%)	0.21 (-0.31 to 0.73)	1,395 (80%)	0.4 (-0.18 to 0.98)	622 (90%)
Medium-term intermittent <sup>c</sup>	-0.5 (-1.12 to 0.12) <sup>d</sup>	183 (80%)	-1.11 (-1.88 to -0.33) <sup>h</sup>	1,200 (88%)	-0.94 (-2.05 to 0.17) <sup>j</sup>	1,383 (95%)
Long-term continuous <sup>c</sup>	0.36 (-0.11 to 0.82) <sup>d</sup>		-0.39 (-0.95 to 0.18)		-0.12 (-0.93 to 0.69)	
	-1.18 (-2.98 to 0.61) <sup>d</sup>		-0.92 (-1.74 to -0.09) <sup>h</sup>		-0.41 (-1.25 to 0.43) <sup>j</sup>	
	-0.81 (-2.16 to 0.53) <sup>d</sup>		-0.19 (-0.79 to 0.41)		0.12 (-0.49 to 0.73)	
	n/a		n/a		-3.31 (-5.85 to -0.76) <sup>j</sup>	99 (91%)
					-0.69 (-2.54 to 1.16)	

<sup>a</sup>Separate models built for each time point, all adjusted for gender, race and ethnicity, smoking, diabetes, hypertension, baseline HR or BP tertile, average medication strength, year of original prescription, and site.  
<sup>b</sup>n (%) by exposure category within each time point references those with a HR measure versus total number assigned to that exposure category at that time point.  
<sup>c</sup>Short-term users (referent) had a single phentermine use episode ≤ 112 days; short-term intermittent users rotated on and off phentermine but never remained on the drug for longer than 112 days. Off-label user groups were defined as follows: medium-term continuous users had a single phentermine treatment episode lasting > 112 but ≤ 365 days; medium-term intermittent users had multiple treatment episodes in which at least one exceeded 112 days; and long-term continuous users had a single episode lasting > 365 days.  
<sup>d</sup>Parameter estimates for intercept approximate change from baseline in BP or HR of referent group when all covariates are set to their referent value, and parameter estimates for comparison groups should be interpreted as difference in BP or HR compared with referent group.  
<sup>e</sup>p < 0.0001 for comparing HR and BP change in comparison groups with referent group.  
<sup>f</sup>p = 0.005 for comparing HR change in comparison groups with referent group.  
<sup>g</sup>p = 0.008 for comparing SBP change in comparison groups with referent group.  
<sup>h</sup>p = 0.02 for comparing SBP change in comparison groups with referent group.  
<sup>i</sup>p = 0.03 for comparing SBP change in comparison groups with referent group.  
 VS, vital signs; n/a, not applicable.



**TABLE 5** Results from multivariable Cox models<sup>a</sup>: hazard ratio for composite outcome of incident myocardial infarction, stroke, CVD intervention, or death up to 3 years after phentermine initiation

	Hazard ratio	CI <sup>b</sup>
Short-term (referent)	Reference	
Short-term intermittent	0.74	0.29-1.91
Medium-term intermittent	0.50	0.14-1.74
Medium & long-term continuous combined <sup>c</sup>	1.58	0.69-3.63

<sup>a</sup>Models include phentermine exposure as time-varying covariate as well as gender, race and ethnicity, smoking, diabetes, hypertension, baseline BMI, average medication strength, year of original prescription, and site.

<sup>b</sup> $P = 0.30$  for examining differences between groups.

<sup>c</sup>There were no events in long-term continuous subgroup; therefore, to allow this group to contribute person-time to the models, it was grouped with the medium-term continuous exposure category.

Among patients with baseline hypertension, BP increased more over time than in our main cohort (Supporting Information Table S7), but there were no 6- or 12-month differences by phentermine exposure category. By 24 months, SBP in longer-term phentermine use groups for hypertensive patients was lower than among short-term hypertensive users. Between-group comparisons for  $\Delta$ HRR among patients with hypertension were similar to our main analysis.

## Incident CVD or death

Up to 3 years after the index date, incidence of composite adverse outcomes was low. Forty-one people out of 13,972 (0.3%) experienced an event (for group-specific event rates, see Supporting Information Table S8). Because there were no qualifying CVD or death events in the long-term continuous user group, these individuals were grouped with the medium-term continuous users for analysis. Multivariable Cox regression models treating phentermine use as a time-varying covariate found no significant difference in risk of incident CVD or death between groups (Table 5).

## Discussion

In this large cohort study, a longer duration of phentermine use was associated with clinically significant greater weight loss up to 2 years after initiating medication, with no observed increase in risk for incident cardiovascular events or death over 3 years of follow-up. Discontinuation of phentermine consistently resulted in weight regain.

There are few prior studies examining long-term use of phentermine, particularly as monotherapy for obesity (6,20,22,32). However, in 2012, a new brand-named drug, Phentermine/Topiramate-CR, earned FDA approval for long-term ( $\geq 12$  months) use as a weight-loss medication. Randomized trial data from patients taking this medication for 24 months showed sustained 9% to 11% weight loss without increased cardiovascular risk (33,34). While these findings suggested possible safety and effectiveness of using phentermine monotherapy for longer than 12 weeks, Phentermine/Topiramate-CR has a lower daily phentermine dose than is typical of monotherapy, necessitating additional studies on this topic to inform clinical care.

Experts now recognize obesity as a chronic disease, best treated with comprehensive intensive lifestyle intervention and long-term follow-up, using tools such as pharmacotherapy and bariatric surgery to supplement lifestyle change as needed (35). There is a need for longer-term effective, safe, and affordable pharmacotherapy that can be used as an adjunct to lifestyle change advice. Longer-term use of phentermine in the United States indeed appears to be a pervasive practice (36); 30% of our cohort was made up of individuals with at least one phentermine episode lasting  $> 12$  weeks.

Our findings show that patients prescribed phentermine for  $\leq 3$  months, as is currently directed by labeling, did not experience durable clinically significant weight loss. In contrast, patients using phentermine off-label for longer periods generally experienced greater weight loss that was sustained so long as they remained on medication. For example, medium-term users (those on phentermine for up to 12 months) averaged significantly greater weight loss than the referent group at 12 months but had regained nearly 70% by 24 months.

Findings from our analysis of phentermine responders, patients with at least 3% weight loss by 3 months after medication initiation, underscore the importance of not continuing to prescribe a medication to patients who do not appear to experience clinical benefit (Figure 2, Figure 3). Patients who responded early across all groups reached clinically significant levels of weight loss ( $\geq 5\%$  on average) by 6 months and generally had more durable weight loss. This finding aligns with similar observations from the literature on diet-induced weight loss, in which early response tends to predict greater overall weight-loss success (2,37).

We observed a slight increase in average HR among phentermine users that normalized after discontinuation. This finding is consistent with the drug's mechanism of action, and the magnitude of increase is similar to prior studies of phentermine-containing medications (33). The relative decrease in SBP associated with longer-term phentermine use, despite the sympathomimetic effect of the drug, may be attributable to greater weight loss, resulting in a net-lowering effect. We observed this relative BP lowering even among patients with baseline hypertension. We cannot exclude the occurrence of rare hypertensive events resulting in emergency department visits because our analyses relied on outpatient information.

Importantly, we did not observe an increase in risk of CVD or death related to the duration of phentermine use up to 3 years after initiating medication. Additional study of these rare outcomes is needed, including research with a larger higher-risk population of long-term users and greater duration of follow-up. Our overall low rate of the composite outcome (0.3% of all patients experienced an event) may be related to the patient population in this study; 85% were women, and we excluded individuals with prevalent CVD. However, our findings are consistent with those from placebo-controlled trials of Phentermine/Topiramate-CR, in which 7 of 2,581 (0.3%) of active drug patients experienced a similar composite outcome (34) and provide some reassurance about the relative safety of phentermine prescribing in low-risk individuals.

Our study has several important limitations. First, we cannot interpret the relationship between duration of phentermine use and percent weight loss as causal. Our referent group likely includes patients who discontinued phentermine because of ineffectiveness, and, conversely,

our comparison groups contained people who remained on medication precisely because it was effective for them. Our sensitivity analyses support this suspicion; differences in weight loss favored longer-term users even at the 3-month mark when phentermine duration was approximately equal between groups. We tried to mitigate this bias by limiting our weight analyses to patients with at least one refill and by conducting a responders-only analysis; however, the possibility for residual confounding and/or reverse causality remains.

Duration of follow-up differed between exposure categories and was systematically greater for longer-term phentermine users. This could have led to an ascertainment bias between categories, but it is not clear in which direction our results would be biased.

We did not address provider- or health-system-level variables, and it is possible that these factors differed systematically between groups in a way that favored longer-term phentermine users. For example, if physicians willing to prescribe phentermine for longer durations are more likely to be obesity specialists (36), or if this pattern of prescribing is more likely to be associated with participation in a comprehensive weight-management program, such differences could confound the relationship between phentermine use duration and weight loss.

Our data should be interpreted with regard to dispensing of phentermine and may not fully indicate whether patients reliably took the medication. Similarly, it is possible that some patients had phentermine or other weight-loss medications filled outside of our systems, going undetected in our data. Although we adjusted for daily dose of phentermine and censored for doses exceeding 37.5 mg/d, we did not specifically study appropriate dosing for longer-term use of this medication. Similarly, we did not examine coadministered medications that could have led to weight loss or gain or changing BP or HR as a side effect (e.g., topiramate, metoprolol). We did censor for incident use of any FDA-approved weight-loss medications in follow-up.

As with any EHR-based study, there was loss to follow-up in our cohort over time, with missingness possibly not at random. We did find that a large portion of the missingness (e.g., 32% at 24 months) was due to patients prescribed phentermine in later years reaching the end of the study period (September 30, 2015), which is unlikely to be a source of bias. On a related note, the number of patients in our “long-term continuous” use group was quite small relative to the other groups; therefore, additional study with a larger group of patients using phentermine for  $\geq 12$  months would help to bolster our findings.

Finally, we did not attempt to characterize other possible adverse outcomes of phentermine use such as anxiety, sleep disturbance, or addiction. A clinical trial with regular standardized outcome assessments at predetermined intervals would be important to accurately describe the risk of such events.

## Conclusion

**Recommendations to limit phentermine use to less than 3 months do not align with current concepts of pharmacological treatment for patients with obesity.** Our results show that longer-term phentermine users experienced greater weight loss without apparent increases in cardiovascular risk. Given the chronicity of obesity and the paucity of

good long-term treatment options for this condition, these data provide reassurance that longer-term phentermine monotherapy is a reasonable treatment option in low-risk individuals. Still, there is a need for randomized controlled trials to definitively establish the safety and effectiveness of protracted phentermine monotherapy. **O**

## Acknowledgments

We thank Dr. Sengwee Toh of the Department of Population Medicine at Harvard Pilgrim Healthcare Institute/Harvard Medical School for providing his input and expertise on pharmacoepidemiologic methods for this paper. Additionally, we thank the analysts in each PORTAL region for their time and effort in extracting the EHR data used in this study.

© 2019 The Obesity Society

## References

- Jensen MD, Ryan DH, Donato KA, et al. Guidelines (2013) for managing overweight and obesity in adults. *Obesity* 2014;22:S1-S410.
- Miller CK, Nagaraja HN, Weinhold KR. Early weight-loss success identifies nonresponders after a lifestyle intervention in a worksite diabetes prevention trial. *J Acad Nutr Diet* 2015;115:1464-1471.
- Wadden TA, West DS, Neiberg RH, et al. One-year weight losses in the Look AHEAD study: factors associated with success. *Obesity (Silver Spring)* 2009;17:713-722.
- Barte JC, ter Bogt NC, Bogers RP, et al. Maintenance of weight loss after lifestyle interventions for overweight and obesity, a systematic review. *Obes Rev* 2010;11:899-906.
- Soleymani T, Daniel S, Garvey WT. Weight maintenance: challenges, tools and strategies for primary care physicians. *Obes Rev* 2016;17:81-93.
- Apovian CM, Aronne LJ, Bessesen DH, et al. Pharmacological management of obesity: an Endocrine Society clinical practice guideline. *J Clin Endocrinol Metab* 2015;100:342-362.
- Apovian CM, Aronne L, Rubino D, et al. A randomized, phase 3 trial of naltrexone SR/bupropion SR on weight and obesity-related risk factors (COR-II). *Obesity (Silver Spring)* 2013;21:935-943.
- Gadde KM, Allison DB, Ryan DH, et al. Effects of low-dose, controlled-release, phentermine plus topiramate combination on weight and associated comorbidities in overweight and obese adults (CONQUER): a randomised, placebo-controlled, phase 3 trial. *Lancet* 2011;377:1341-1352.
- Pi-Sunyer X, Astrup A, Fujioka K, et al. Controlled trial of 3.0 mg of liraglutide in weight management. *N Engl J Med* 2015;373:11-22.
- Smith SR, Weissman NJ, Anderson CM, et al. Multicenter, placebo-controlled trial of lorcaserin for weight management. *N Engl J Med* 2010;363:245-256.
- Astrup A, Carraro R, Finer N, et al. Safety, tolerability and sustained weight loss over 2 years with the once-daily human GLP-1 analog, liraglutide. *Int J Obes (Lond)* 2012;36:843-854.
- Fidler MC, Sanchez M, Raether B, et al. A one-year randomized trial of lorcaserin for weight loss in obese and overweight adults: the BLOSSOM trial. *J Clin Endocrinol Metab* 2011;96:3067-3077.
- Greenway FL, Fujioka K, Plodkowski RA, et al. Effect of naltrexone plus bupropion on weight loss in overweight and obese adults (COR-I): a multicentre, randomised, double-blind, placebo-controlled, phase 3 trial. *Lancet* 2010;376:595-605.
- Torgerson JS, Hauptman J, Boldrin MN, Sjostrom L. XENical in the prevention of diabetes in obese subjects (XENDOS) study: a randomized study of orlistat as an adjunct to lifestyle changes for the prevention of type 2 diabetes in obese patients. *Diabetes Care* 2004;27:155-161.
- LeBlanc ESPC, Webber EM, Redmond N, Rushkin M, O'Connor EA. Behavioral and pharmacotherapy weight loss interventions to prevent obesity-related morbidity and mortality in adults: updated evidence report and systematic review for the US Preventive Services Task Force. *JAMA* 2018;320:1172-1191.
- Xia Y, Kelton CM, Guo JJ, Bian B, Heaton PC. Treatment of obesity: pharmacotherapy trends in the United States from 1999 to 2010. *Obesity (Silver Spring)* 2015;23:1721-1728.
- Bray GA, Heisel WE, Afshin A, et al. The science of obesity management: an Endocrine Society scientific statement. *Endocr Rev* 2018;39:79-132.
- Patel D. Pharmacotherapy for the management of obesity. *Metabolism* 2015;64:1376-1385.
- Colman E. Anorectics on trial: a half century of federal regulation of prescription appetite suppressants. *Ann Intern Med* 2005;143:380-385.
- Velazquez A, Apovian CM. Updates on obesity pharmacotherapy. *Ann N Y Acad Sci* 2018;1411:106-119.
- Adipex-P (phentermine hydrochloride) [package insert]. Sellersville, PA: Teva Pharmaceuticals USA; 2012. [https://www.accessdata.fda.gov/drugsatfda\\_docs/label/2012/085128s0651bl.pdf](https://www.accessdata.fda.gov/drugsatfda_docs/label/2012/085128s0651bl.pdf).



22. Hendricks EJ, Srisurapanont M, Schmidt SL, et al. Addiction potential of phentermine prescribed during long-term treatment of obesity. *Int J Obes (Lond)* 2014;38:292-298.
23. Young DR, Waitzfelder BA, Arterburn D, et al. The Patient Outcomes Research to Advance Learning (PORTAL) network adult overweight and obesity cohort: development and description. *JMIR Res Protoc* 2016;5:e87. doi:10.2196/resprot.5589
24. McGlynn EA, Lieu TA, Durham ML, et al. Developing a data infrastructure for a learning health system: the PORTAL network. *J Am Med Inform Assoc* 2014;21:596-601.
25. Johnson ES, Bartman BA, Briesacher BA, et al. The incident user design in comparative effectiveness research. *Pharmacoepidemiol Drug Saf* 2013;22:1-6.
26. Food and Drug Administration. Guidance for Industry and FDA Staff: Best Practices for Conducting and Reporting Pharmacoepidemiologic Safety Studies Using Electronic Healthcare Data. Silver Spring, MD: Food and Drug Administration; 2013.
27. Parker MM, Moffet HH, Adams A, Karter AJ. An algorithm to identify medication nonpersistence using electronic pharmacy databases. *J Am Med Inform Assoc* 2015;22:957-961.
28. Andrade SE, Kahler KH, Frech F, Chan KA. Methods for evaluation of medication adherence and persistence using automated databases. *Pharmacoepidemiol Drug Saf* 2006;15:565-574; discussion 575-577.
29. Fisher DPJE, Haneuse S, Arterburn D, et al. Association between bariatric surgery and macrovascular disease outcomes in patients with type 2 diabetes and severe obesity. *JAMA* 2018;320:1570-1582.
30. Arterburn D, Johnson ES, Butler MG, Fisher D, Bayliss EA. Predicting 90-day mortality after bariatric surgery: an independent, external validation of the OS-MRS prognostic risk score. *Surg Obes Relat Dis* 2014;10:774-779.
31. Krieger N, Chen JT, Waterman PD, Rehkopf DH, Subramanian SV. Race/ethnicity, gender, and monitoring socioeconomic gradients in health: a comparison of area-based socioeconomic measures—the public health disparities geocoding project. *Am J Public Health* 2003;93:1655-1671.
32. Allison DB, Gadde KM, Garvey WT, et al. Controlled-release phentermine/topiramate in severely obese adults: a randomized controlled trial (EQUIP). *Obesity (Silver Spring)* 2012;20:330-342.
33. Garvey WT, Ryan DH, Look M, et al. Two-year sustained weight loss and metabolic benefits with controlled-release phentermine/topiramate in obese and overweight adults (SEQUEL): a randomized, placebo-controlled, phase 3 extension study. *Am J Clin Nutr* 2012;95:297-308.
34. Jordan J, Astrup A, Engeli S, Narkiewicz K, Day WW, Finer N. Cardiovascular effects of phentermine and topiramate: a new drug combination for the treatment of obesity. *J Hypertens* 2014;32:1178-1188.
35. Bray GA, Kim KK, Wilding JPH; World Obesity Federation. Obesity: a chronic relapsing progressive disease process. A position statement of the World Obesity Federation. *Obes Rev* 2017;18:715-723.
36. Hendricks EJ, Rothman RB, Greenway FL. How physician obesity specialists use drugs to treat obesity. *Obesity (Silver Spring)* 2009;17:1730-1735.
37. Fabricatore AN, Wadden TA, Moore RH, Butryn ML, Heymsfield SB, Nguyen AM. Predictors of attrition and weight loss success: results from a randomized controlled trial. *Behav Res Ther* 2009;47:685-691.



**MEMORANDUM**

TO: Mark Bechtel, M.D., President  
Members, State Medical Board of Ohio

FROM: Kimberly C. Anderson, Chief Legal Counsel

RE: Initial Circulation of Rules

DATE: December 30, 2020 (UPDATED 1/7/21)

---

Several sets of rules are due for their five-year rule review in 2021. Technical changes have been proposed, including some required by recent legislation.

4731-11-08 Prescribing to Self and Family: Proposed no change;

4731-14-01 Pronouncement of Death: Edits to reflect statutory changes;

4731-23-01 Definitions: Proposed no change;

4731-23-02 Delegation of Medical Tasks Changes needed for sections dealing with DODD statutes which have been repealed. I have reached out to DODD for comments;

4731-23-03 Delegation of Medical Tasks: Prohibitions Proposed no change;

4731-23-04 Violations Proposed no change;

4731-26-01 Definitions Updated to add and delete license types to reflect statutory changes; updated language change to “license” from “certificate”;

4731-26-02 Prohibitions Updated statutory authority and amplifying statutes;

4731-26-03 Violations; Miscellaneous Updated to add and delete license types to reflect statutory changes; updated statutory authority and amplifying statutes

**Requested action: Approve rules for initial circulation to interested parties.**

---

## 4731-11-08. Utilizing controlled substances for self and family members

- (A) Accepted and prevailing standards of care presuppose a professional relationship between a patient and physician when the physician is utilizing controlled substances. By definition, a physician may never have such a relationship with himself or herself. Thus, a physician may not self-prescribe or self-administer controlled substances. This paragraph does not prohibit a physician from obtaining a schedule V controlled substance for personal use in conformance with state and federal laws, in the same manner that a non-physician may obtain a schedule V controlled substance.
- (B) Accepted and prevailing standards of care require that a physician maintain detached professional judgment when utilizing controlled substances in the treatment of family members. A physician shall utilize controlled substances when treating a family member only in an emergency situation which shall be documented in the patient's record.
- (C) For purposes of this rule, "family member" means a spouse, parent, child, sibling or other individual in relation to whom a physician's personal or emotional involvement may render that physician unable to exercise detached professional judgment in reaching diagnostic or therapeutic decisions.

**Cite as Ohio Admin. Code 4731-11-08**

**History.** Five Year Review (FYR) Dates: 08/17/2016 and 08/17/2021

Promulgated Under: [119.03](#)

Statutory Authority: [4731.05](#)

Rule Amplifies: [4731.22](#)

Prior Effective Dates: 11/11/98, 3/15/01, 9/30/08

**Prior History:** (Effective: 09/30/2008

R.C. 119.032 review dates: 06/06/2008 and 09/30/2013

Promulgated Under: 119.03

Statutory Authority: 4731.05, 4731.052

Rule Amplifies: 4731.22, 4731.052

Prior Effective Dates: 11/11/98; 3/15/01 )

## **4731-14-01 Pronouncement of death.**

(A) Only an individual holding one of the following current certificates or licenses may pronounce a person dead:

(1) A certificate to practice medicine and surgery or osteopathic medicine and surgery issued under section 4731.14 or ~~4731.29~~ of the Revised Code;

(2) A training certificate issued under section 4731.291 of the Revised Code;

(3) A clinical research faculty certificate issued under section 4731.293 of the Revised Code;

(4) A special activities certificate issued under section 4731.294 of the Revised Code;

(5) A certificate of authority to practice as a certified nurse practitioner or clinical nurse specialist issued under section 4723.42 of the Revised Code, when the holder acts in compliance with section 4723.36 of the Revised Code;

(6) A license to practice as a registered nurse issued under section 4723.09 of the Revised Code, when the holder acts in compliance with section 4723.36 of the Revised Code.

(7) A license to practice as a physician assistant issued under section 4730.12 of the Revised Code, when the holder acts in compliance with section 4730.202 of the Revised Code;

(8) A certificate of conceded eminence issued under section 4731.297 of the Revised Code;

(9) A certificate to practice podiatric medicine and surgery issued under section 4731.56, ~~4731.57~~, or ~~4731.571~~ of the Revised Code.

(B) A physician holding a current certificate to practice medicine or surgery or osteopathic medicine and surgery issued under section 4731.14 or ~~4731.29~~ of the Revised Code may pronounce a person dead without personally examining the body of the deceased only if a competent observer has recited the facts of the deceased's present medical condition to the physician and the physician is satisfied that death has occurred.

(C) For purposes of this rule a competent observer shall mean one of the following:

(1) A licensed practical nurse holding a current license issued under Chapter 4723. of the Revised Code;

(2) An EMT-Basic holding a current certificate issued under section 4765.30 of the Revised Code;

(3) An EMT-intermediate holding a current certificate issued under section 4765.30 of the Revised Code;

(4) A EMT - paramedic holding a current certificate issued under section 4765.30 of the Revised Code;

(5) A chiropractor holding a current certificate issued under Chapter 4734. of the Revised Code;

(6) An individual authorized to pronounce a person dead under paragraph (A) of this rule;

(7) A coroner's investigator as referenced in section [313.05](#) of the Revised Code.

Replaces: 4731-14-01

Effective: 6/30/2016

Five Year Review (FYR) Dates: 06/30/2021

Promulgated Under: [119.03](#)

Statutory Authority: [4731.05](#), [4731.053](#)

Rule

Amplifies: [4723.36](#), [4730.202](#), [4731.053](#), [4731.291](#), [4731.293](#), [4731.294](#), [4731.297](#), [4731.34](#), [4731.51](#)

Prior Effective Dates: 5/10/90, 5/31/02, 2/28/04, 6/30/07

## **4731-23-01 Definitions.**

As used in Chapter 4731-23 of the Administrative Code:

- (A) "Administer" means the direct application of a drug, whether by injection, inhalation, ingestion, or any other means to a person.
- (B) "Delegate" means to transfer authority for the performance of a medical task to an unlicensed person.
- (C) "On-site supervision" means that the physical presence of the physician is required in the same location (e.g., the physician's office suite) as the unlicensed person to whom the medical task has been delegated while the medical task is being performed. "On-site supervision" does not require the physician's presence in the same room.
- (D) "Physician" means an individual authorized by Chapter 4731. of the Revised Code to practice medicine and surgery, osteopathic medicine and surgery, or podiatric medicine and surgery.
- (E) "Task" includes, but is not limited to, a routine medical service not requiring the special skills of a licensed provider.
- (F) "Unlicensed person" means an individual who is not licensed or otherwise specifically authorized by the Revised Code to perform the delegated medical task.
- (G) "Drug" means the same as in division (E) of section [4729.01](#) of the Revised Code.

Effective: 11/30/2016

Five Year Review (FYR) Dates: 08/16/2016 and 11/30/2021

Promulgated Under: [119.03](#)

Statutory Authority: [4731.05](#), [4731.053](#)

Rule Amplifies: [4731.053](#), [4731.22](#), [4731.34](#)

Prior Effective Dates: 9/30/01

## **4731-23-02 Delegation of medical tasks.**

(A) A physician shall not delegate the performance of a medical task unless that physician has complied with all of the requirements of this chapter of the Administrative Code and the delegation otherwise conforms to minimal standards of care of similar physicians under the same or similar circumstances.

(B) Prior to a physician's delegation of the performance of a medical task, that physician shall determine each of the following:

- (1) That the task is within that physician's authority;
- (2) That the task is indicated for the patient;
- (3) The appropriate level of supervision;
- (4) That no law prohibits the delegation;
- (5) That the person to whom the task will be delegated is competent to perform that task; and,
- (6) That the task itself is one that should be appropriately delegated when considering the following factors:
  - (a) That the task can be performed without requiring the exercise of judgment based on medical knowledge;
  - (b) That results of the task are reasonably predictable;
  - (c) That the task can safely be performed according to exact, unchanging directions;
  - (d) That the task can be performed without a need for complex observations or critical decisions;
  - (e) That the task can be performed without repeated medical assessments; and,
  - (f) That the task, if performed improperly, would not present life threatening consequences or the danger of immediate and serious harm to the patient.

(C) When a physician delegates the administration of drugs, that physician shall provide on-site supervision, except in the following situations:

- (1) When the physician has transferred responsibility for the on-site supervision of the unlicensed person who is administering the drug to another physician and that physician has knowingly accepted that responsibility on a patient-by-patient basis; or
- (2) In the routine administration of a topical drug, such as a medicated shampoo.
- (3) When delegation occurs pursuant to section [5126.36](#) of the Revised Code within the programs and services offered by a county board of developmental disabilities. Statute is repealed. Check with DODD.



(4) When delegation occurs pursuant to section [5123.42](#) of the Revised Code. Is statute still applicable? Check with DODD.

(5) When written policies and procedures have been adopted for the distribution of drugs by an unlicensed person to individuals incarcerated in state correctional institutions as defined in division (A) of section 2796.01 of the Revised Code, other correctional facilities including county and municipal jails, workhouses, minimum security jails, halfway houses, community residential centers, regional jails and multi-county jails, or any other detention facility as defined in division (F) of section [2921.01](#) of the Revised Code.

(D) This chapter of the Administrative Code shall not apply if the rules contained herein:

(1) Prevent an individual from engaging in an activity performed for a handicapped child as a service needed to meet the educational needs of the child, as identified in the individualized education program developed for the child under Chapter 3323. of the Revised Code;

(2) Prevent delegation from occurring pursuant to section [5126.36](#) of the Revised Code within the programs and services offered by a county board of developmental disabilities; Statute is repealed. Check with DODD.

(3) Conflict with any provision of the Revised Code that specifically authorizes an individual to perform a particular task;

(4) Conflict with any rule adopted pursuant to the Revised Code that is in effect on the effective date of this section, as long as the rule remains in effect, specifically authorizing an individual to perform a particular task;

(5) Prohibit a perfusionist from administering drugs intravenously while practicing as a perfusionist.

Effective: 11/30/2016

Five Year Review (FYR) Dates: 08/16/2016 and 11/30/2021

Promulgated Under: [119.03](#)

Statutory Authority: [4731.05](#), [4731.053](#)

Rule Amplifies: [4731.22](#), [4731.053](#), [4731.34](#)

Prior Effective Dates: 9/30/01, 5/31/02

## **4731-23-03 Delegation of medical tasks; Prohibitions.**

(A) A physician shall not delegate the practice of medicine as defined in section [4731.34](#) of the Revised Code unless specifically authorized to do so in the Revised Code or by an administrative rule adopted pursuant to the Revised Code and which became effective prior to April 10, 2001. Nothing in this chapter of the Administrative Code shall prohibit the performance of emergency medical tasks.

(B) A physician shall not delegate a task to an unlicensed person if the task is beyond that person's competence. In a hospital, as defined in section [3727.01](#) of the Revised Code, or an ambulatory care center affiliated with the hospital (if the center meets the same credentialing, quality assurance, and utilization review standards as the hospital) wherein unlicensed persons are employed or otherwise authorized by the governing authority of the institution to perform specific medical tasks, one factor the physician shall take into account is the policies by which the employer or the governing authority of the institution seeks to ensure that competent persons will be performing the delegated tasks.

(C) A physician shall not delegate a medical task that is not within the authority of that physician or is beyond the physician's training, expertise, or normal course of practice.

(D) A physician shall not transfer his or her responsibility for supervising an unlicensed person in the performance of a delegated medical task, except to another physician who has knowingly accepted that responsibility.

(E) A physician shall not authorize or permit an unlicensed person to whom a medical task is delegated to delegate the performance of that task to another person.

(F) Except as provided in divisions (D)(4) to (D)(8) of section [4731.053](#) of the Revised Code, a physician shall not delegate to an unlicensed person the administration of anesthesia, controlled substances, or drugs administered intravenously.

(G) The supervising physician retains responsibility for the manner in which the delegated task is carried out.

Five Year Review (FYR) Dates: 08/17/2016 and 08/17/2021

Promulgated Under: [119.03](#)

Statutory Authority: [4731.05](#), [4731.053](#)

Rule Amplifies: [4731.22](#), [4731.34](#)

Prior Effective Dates: 9/30/01, 5/31/02

## **4731-23-04 Violations.**

(A) A violation of any provision of any rule in this chapter of the Administrative Code, as determined by the board, shall constitute "a departure from, or the failure to conform to, minimal standards of care of similar practitioners under the same or similar circumstances, whether or not actual injury to a patient is established," as that clause is used in division (B)(6) of section [4731.22](#) of the Revised Code.

(B) A violation of any provision of any rule in this chapter of the Administrative Code that pertains to the administration of drugs, as determined by the board, shall constitute "failure to maintain minimal standards applicable to the selection or administration of drugs," as that clause is used in division (B)(2) of section [4731.22](#) of the Revised Code.

Five Year Review (FYR) Dates: 08/17/2016 and 08/17/2021

Promulgated Under: [119.03](#)

Statutory Authority: [4731.05](#), [4731.053](#)

Rule Amplifies: [4731.22](#), [4731.34](#)

Prior Effective Dates: 9/30/01

## **4731-26-01 Definitions.**

For purposes of Chapter 4731-26 of the Administrative Code:

(A) "Licensee" means any of the following:

(1) An individual holding a license certificate to practice as a physician assistant under Chapter 4730. of the Revised Code;

(2) An individual holding a license certificate to practice medicine and surgery, osteopathic medicine and surgery, or podiatric medicine and surgery under Chapter 4731. of the Revised Code;

(3) An individual holding a license certificate to practice a limited branch of medicine under Chapter 4731. of the Revised Code;

4) An individual holding a license to practice dietetics under Chapter 4759 of the Revised Code

(5) An individual holding a license certificate of registration as an anesthesiologist assistant under Chapter 4760. of the Revised Code;

(6) An individual holding a license or limited permit to practice respiratory care under Chapter 4761 of the Revised Code

~~(5)~~(7) An individual holding a license certificate to practice as an acupuncturist ~~or an oriental medicine practitioner~~ under Chapter 4762. of the Revised Code;

~~(6)~~(8) An individual holding a license certificate to practice as a radiologist assistant under Chapter 4774. of the Revised Code; or

~~(7)~~(9) An individual holding a license to practice as a genetic counselor under Chapter 4778. of the Revised Code.

(B) "Health care services" means examination, consultation, health care, treatment, or other services provided by a licensee under the legal authority conferred by a license, certificate, permit or registration issued by the board.

(C) "Patient" means a person for whom the licensee has provided health care services, whether provided by mutual consent or implied consent, or provided without consent pursuant to a court order. Once a licensee-patient relationship is established, a person remains a patient until the relationship is terminated. Patient includes any of the following:

(1) A person who is receiving or has received health care services from the licensee without termination of the licensee-patient relationship; or

(2) A person who meets the criteria of a key third party, as that term is defined in paragraph (D) of this rule.

(D) "Key third party" means an individual closely involved in the patient's decision-making regarding health care services, including but not limited to, the patient's spouse or partner, parents, child, sibling, or guardian. For purposes of this chapter, an individual's status as a key

third party ceases upon the termination of the licensee-patient relationship or upon termination of the individual's relationship with the patient.

(E) "Chaperone" means a third person who, with the patient's consent, is present during a medical examination.

(F) "Former patient" means one of the following:

(1) A person for whom the licensee has not rendered health care services since the licensee-patient relationship was terminated; or

(2) A person who has otherwise been admitted, discharged, or referred to another licensee for care subsequent to receipt of health care services by a licensee in an emergency setting or on an episodic basis, and such action has been recorded in the person's medical record or chart.

(G) "Intimate examination" means an examination of the pelvic area, genitals, rectum, breast, or prostate.

(H) "Sexual misconduct" means conduct that exploits the licensee-patient relationship in a sexual way, whether verbal or physical, and may include the expression of thoughts, feelings, or gestures that are sexual or that reasonably may be construed by a patient as sexual. Sexual misconduct includes sexual impropriety, sexual contact, or sexual interaction as follows:

(1) "Sexual impropriety" means conduct by the licensee that is seductive, sexually suggestive, disrespectful of patient privacy, or sexually demeaning to a patient, including but not limited to, the following:

(a) Neglecting to employ disrobing or draping practices respecting the patient's privacy;

(b) Subjecting a patient to an intimate examination in the presence of a third party, other than a chaperone, without the patient's consent or in the event such consent has been withdrawn;

(c) Making comments that are not clinically relevant about or to the patient, including but not limited to, making sexual comments about a patient's body or underclothing, making sexualized or sexually demeaning comments to a patient, criticizing the patient's sexual orientation, or making comments about potential sexual performance;

(d) Soliciting a date or romantic relationship with a patient;

(e) Participation by the licensee in conversation regarding the sexual problems, sexual preferences, or sexual fantasies of the licensee;

(f) Requesting details of the patient's sexual history, sexual problems, sexual preferences, or sexual fantasies when not clinically indicated for the type of health care services; and

(g) Failing to offer the patient the opportunity to have a third person or chaperone in the examining room during an intimate examination and/or failing to provide a third person or chaperone in the examining room during an intimate examination upon the request of the patient.

(2) "Sexual contact" includes, but is not limited to, the following:

(a) Touching a breast or any body part that has sexual connotation for the licensee or patient, for any purpose other than appropriate health care services, or where the patient has refused or has withdrawn consent; and

(b) Examining or touching of the patient's genitals without the use of gloves.

(3) "Sexual interaction" means conduct between a licensee and patient, whether or not initiated by, consented to, or participated in by a patient, that is sexual or may be reasonably interpreted as sexual, including but not limited to, the following:

(a) Sexual intercourse, genital to genital contact;

(b) Oral to genital contact;

(c) Oral to anal contact, genital to anal contact;

(d) Kissing in a romantic or sexual manner;

(e) Encouraging the patient to masturbate in the presence of the licensee or masturbation by the licensee while the patient is present;

(f) Offering to provide health care services, such as drugs, in exchange for sexual favors; and

(g) Performing an intimate examination without clinical justification.

(h) Conduct that is sexually demeaning to a patient or which demonstrates a lack of respect for the patient's privacy.

(4) Conduct described in paragraphs (H)(1)(a), (H)(1)(b), (H)(1)(g), and (H)(2)(b) of this rule does not constitute sexual misconduct when all of the following criteria are met:

(a) The conduct occurred during the rendering of health care services in an emergency setting;

(b) The health care services rendered were clinically necessary;

(c) The patient was unconscious or otherwise unable to consent to health care services; and

(d) The patient's clinical condition required immediate action and the licensee's violation of the provisions of paragraph (H)(1)(a), (H)(1)(b), (H)(1)(g), or (H)(2)(b) of this rule, as applicable, was due to circumstances not within the licensee's control.

(I) "Emergency setting" means an emergency department.

(J) "Board" means the state medical board of Ohio.

(K) "Conduct" includes, but is not limited to the following:

(1) Behaviors, gestures, or expressions, whether verbal or physical; or

(2) The creation, receipt, exchange, saving, or sending of images or communications, whether verbal or written, via a telecommunications device.

Effective: 6/30/2016

Five Year Review (FYR) Dates: 03/15/2016 and 06/30/2021

Promulgated Under: [119.03](#)

Statutory Authority: [4730.07](#), [4731.05](#), [4759.05](#), [4760.19](#), [4761.03](#), [4762.19](#), [4774.11](#), [4778.12](#)

Rule Amplifies: [4730.25](#), [4731.22](#), [4759.07](#), [4760.13](#), [4761.09](#), [4762.13](#), [4774.13](#), [4778.14](#)

Prior Effective Dates: 11/30/06, 11/30/10



## **4731-26-02 Prohibitions.**

Sexual misconduct, as that term is defined in paragraph (H) of rule [4731-26-01](#) of the Administrative Code, between a licensee and a patient is never diagnostic or therapeutic.

(A) A licensee shall not engage in sexual misconduct with a patient or key third party, as that term is defined in paragraph (C) of rule [4731-26-01](#) of the Administrative Code.

(B) Conduct included within the definition of sexual misconduct occurring between a licensee and a former patient constitutes sexual misconduct and is prohibited if it meets any of the following criteria:

(1) The conduct occurred within ninety days after the licensee-patient relationship was terminated;

(2) The conduct occurred between a psychiatrist and a person to whom the psychiatrist formerly provided psychiatric or mental health services, and the conduct is in violation of the code of ethics of the "American Psychiatric Association"; or

(3) The board determines that the conduct constitutes sexual misconduct upon consideration of the following factors:

(a) The duration of the licensee-patient relationship;

(b) The nature of the health care services provided;

(c) The lapse of time since the licensee-patient relationship ended;

(d) The extent to which the former patient confided personal or private information to the licensee;

(e) The degree of emotional dependence that the former patient has or had on the licensee; and

(f) The extent to which the licensee used or exploited the trust, knowledge, emotions, or influence derived from the previous licensee-patient relationship.

Replaces: 4731-26-02

Five Year Review (FYR) Dates: 03/15/2016 and 03/15/2021

Promulgated Under: [119.03](#)

Statutory Authority: [4730.07](#), [4731.05](#), [4759.05](#), [4760.19](#), [4761.03](#), [4762.19](#), [4774.11](#), [4778.12](#)

Rule Amplifies: [4730.25](#), [4731.22](#), [4759.07](#), [4760.13](#), [4761.09](#), [4762.13](#), [4774.13](#), [4778.14](#)

Prior Effective Dates: 11/30/06, 11/30/10

## **4731-26-03 Violations, miscellaneous.**

(A) Except as provided in paragraph (C) of this rule, a violation of rule [4731-26-02](#) of the Administrative Code, as determined by the board, shall constitute the following:

(1) For a physician, ~~or massage therapist, or cosmetic therapist~~, "a departure from, or the failure to conform to, minimal standards of care of similar practitioners under the same or similar circumstances, whether or not actual injury to a patient is established," as that clause is used in division (B)(6) of section [4731.22](#) of the Revised Code.

(2) For a physician assistant, "a departure from, or failure to conform to, minimal standards of care of similar physician assistants under the same or similar circumstances, regardless of whether actual injury to a patient is established, as that clause is used in division (B)(19) of section [4730.25](#) of the Revised Code.

(3) For a dietitian, "a departure from, or failure to conform to, minimal standards of care of similar practitioners under the same or similar circumstances, whether or not actual injury to a patient is established" as that clause is used in division (A)(11) of section 4759.07 of the Revised Code.

~~(3)~~ (4) For an anesthesiologist assistant, "a departure from, or failure to conform to, minimal standards of care of similar practitioners under the same or similar circumstances whether or not actual injury to the patient is established," as that clause is used in division (B)(4) of section [4760.13](#) of the Revised Code.

(5) For a respiratory care professional or limited permit holder, "a departure from, or a failure to conform to, minimal standards of care of similar practitioners under the same or similar circumstances, whether or not actual injury to a patient is established", as that clause is used in division (A)(10) of section 4761.09 of the Revised Code.

~~(6) For an acupuncturist or oriental medicine practitioner,~~ a "departure from, or failure to conform to, minimal standards of care of similar practitioners under the same or similar circumstances whether or not actual injury to the patient is established," as that clause is used in division (B)(4) of section [4762.13](#) of the Revised Code.

(7) For a radiologist assistant, a "departure from, or failure to conform to, minimal standards of care of similar practitioners under the same or similar circumstances whether or not actual injury to the patient is established," as that clause is used in division (B)(4) of section [4774.13](#) of the Revised Code.

(8) For a genetic counselor, a "departure from, or failure to conform to, minimal standards of care of similar practitioners under the same or similar circumstances whether or not actual injury to the patient is established," as that clause is used in division (B)(4) of section [4778.14](#) of the Revised Code.

(B) Where the alleged conduct does not in itself constitute sexual misconduct, as defined in paragraph (H) of rule [4731-26-01](#) of the Administrative Code, the board may consider expert testimony or other evidence in making its determination as to whether the conduct of the licensee constitutes sexual misconduct.

(C) Nothing in this rule shall limit the board's authority to investigate and take action under section [4730.25](#), [4731.22](#), [4759.07](#), [4760.13](#), [4761.09](#), [4762.13](#), [4774.13](#) or 4778. 14 of the Revised Code.

Effective: 6/30/2016

Five Year Review (FYR) Dates: 03/15/2016 and 06/30/2021

Promulgated Under: [119.03](#)

Statutory Authority: [4730.07](#), [4731.05](#), [4759.05](#), [4760.19](#), [4761.03](#), [4762.19](#), [4774.11](#), [4778.12](#)

Rule Amplifies: [4730.25](#), [4731.22](#), [4759.07](#), [4760.13](#), [4761.09](#), [4762.13](#), [4774.13](#), [4778.14](#)

Prior Effective Dates: 11/30/06, 11/30/10



---

**MEMORANDUM**

TO: Mark Bechtel, M.D., President  
Members, State Medical Board of Ohio

FROM: Kimberly C. Anderson, Chief Legal Counsel

RE: CME Rules

DATE: December 30, 2020; Updated January 5, 2021

---

Sixteen rules were filed in the package related to physician continuing medical education. The public hearing was held on December 4, 2020, and the Hearing Examiner's report is attached. The JCARR meeting was held on December 7, 2020. No comments were received. JCARR jurisdiction was scheduled to end on January 3, 2021.

HB 442 was recently adopted by the General Assembly. It will become effective 90 days after signature by Governor DeWine, likely in early April.

Section 4745.04(C)(2) is being amended to increase the number of CME credits which may be earned through providing volunteer health care services. Currently up to three credits may be earned and the new legislation permits physicians to earn up to ten hours. The legislation also adds language regarding the calculation so that physicians may earn continuing medical education at the rate of one credit hour for every five hours spent providing healthcare services as a volunteer. A copy of the relevant portion of the legislation is attached.

In addition, the continuing medical education requirement for holders of a clinical research faculty license has been eliminated.

These changes will require an amendment to rules 4731-10-02(A)(6), (F) and 4731-10-08(D). I have placed these rules in TBR status so that they may be refiled with the amendments.

The following amendments are recommended:

**4731-10-02 Requisite Hours of Continuing Medical Education for License Renewal or Reinstatement**

(A)(6) Pursuant to section 4745.04 of the Revised Code, providing health care services in Ohio, as a volunteer, to indigent and uninsured persons, ~~up to a maximum of three hours per registration period.~~

~~(F) During a clinical research registration period, every holder of a clinical research faculty~~

---

~~certificate shall be required to complete seventy-five hours of CME pursuant to the requirements of section 4731.293 of the Revised Code. Such hours must meet the criteria established in paragraph (A)(1) of this rule. If a holder of a clinical research faculty certificate has not completed the requisite hours of CME, a holder is not eligible for certificate renewal until such time as the requisite hours have been completed. Any CME undertaken after the end of a clinical research registration period and utilized for purposes of renewing a suspended certificate cannot also be utilized to meet the CME requirement of the current clinical research registration period.~~

**4731-10-08 Evidence of Continuing Medical Education**

(D) Licensees seeking to receive credit pursuant to paragraph (A)(~~36~~) of rule 4731-10-02 of the Administrative Code shall maintain a log of their qualifying activities. The log shall indicate the dates the health care services were provided, the number of hours spent providing health care services on those dates, and the location where the health care services were provided.

**Requested motion:** I move to amend rules 4731-10-02 and 4731-10-08 as set forth in the December 30, 2020 memorandum from Ms. Anderson and to adopt the rules in this package at a later date.

RECEIVED:  
December 30, 2020

**SUMMARY OF THE DECEMBER 4, 2020 PUBLIC HEARING  
REGARDING PROPOSED CHANGES TO THE OHIO ADMINISTRATIVE CODE**

Pursuant to Section 119.03, Ohio Revised Code, a public hearing was held on December 4, 2020, to hear comments concerning proposed changes to the administrative rules of the State Medical Board of Ohio (“Board”). R. Gregory Porter, Hearing Examiner, presided.

**PURPOSE OF THE HEARING**

**The following changes are proposed:**

<b>Rule No.</b>	<b>Title</b>	<b>Proposed Action</b>
4731-10-01	Definitions	Rescind
4731-10-01	Definitions	Adopt new rule
4731-10-02	Requisite Hours of Continuing Medical Education for License Renewal or Reinstatement	Rescind
4731-10-02	Requisite Hours of Continuing Medical Education for License Renewal or Reinstatement	Adopt new rule
4731-10-03	CME Waiver	Rescind
4731-10-03	CME Waiver	Adopt New Rule
4731-10-04	Continuing Medical Education Requirements for Restoration of a License	Rescind
4731-10-04	Continuing Medical Education Requirements for Restoration of a License	Adopt new rule
4731-10-05	Out of State Licensees	Rescind
4731-10-06	Licensure After Cutoff for Preparation of Registration Notices	Rescind
4731-10-07	Internships, Residencies, and Fellowships	Rescind
4731-10-08	Evidence of Continuing Medical Education	Rescind
4731-10-08	Evidence of Continuing Medical Education	Adopt new rule
4731-10-09	Continuing Medical Education Requirement for Mid-Term Licensees	Rescind
4731-10-10	Continuing Medical Education Requirements Following License Restoration	Rescind
4731-10-11	Telemedicine Certificates	Rescind

### **PROCEDURAL MATTERS**

1. The record was held open until 5:00 p.m. on December 4, 2020, for the purpose of receiving written comments concerning the proposed changes to the Ohio Administrative Code. No comments were received.
2. The hearing examiner marked Exhibits 1, 2, and 3 post hearing.
3. Due to the ongoing Covid-19 emergency, the hearing was conducted via videoconferencing software.

### **TESTIMONY HEARD**

Kimberly Anderson, Chief Legal Counsel for the Board

### **EXHIBITS EXAMINED**

Exhibit 1: Copy of the rules originally filed in Package 189167 with JCARR, Secretary of State, and the Legislative Services Commission via the Electronic Rule-Filing System on October 30, 2020 and a copy of the confirmation of filing. Also included are copies of the confirmation of the revised filings on November 3 and November 24, 2020.

Exhibit 2: Copy of the Notice of Public Hearing for the rules in Package 189167 showing it was filed on October 30, 2020. Also attached are the revised Notices of Public Hearing showing that it was filed November 3, 2020 and November 24, 2020.

Exhibit 3: Copies of the address portion of e-mails sent to persons and organizations pursuant to their standing request to be notified when the Medical Board proposes rules.

### **SUMMARY OF EVIDENCE**

1. Kimberly Anderson, Chief Legal Counsel for the Board, identified Exhibits 1 through 3. She further testified with respect to the notice that the Board provided to the public and interested parties regarding the proposed rule changes, and with respect to other procedural matters. (Hearing Transcript at 6-8)
2. No comments were received concerning the proposed changes to the Board's administrative rules.



### CONCLUSION

The requirements of Chapter 119, Ohio Revised Code, have been satisfied. The Board may proceed to take action regarding the proposed rescission of rules 4731-10-01, 4731-10-02, 4731-10-03, 4731-10-04, 4731-10-05, 4731-10-06, 4731-10-07, 4731-10-08, 4731-10-09, 4731-10-10, and 4731-10-11; and the proposed adoption of new rules 4731-10-01, 4731-10-02, 4731-10-03, 4731-10-04, and 4731-10-08.



---

R. Gregory Porter  
Hearing Examiner

registered ~~sanitarian~~environmental health specialist shall use 5370  
the title "~~registered sanitarian~~" "registered environmental 5371  
health specialist" or the abbreviation "~~R.S.~~" "R.E.H.S." after 5372  
the person's name, or represent self as a registered 5373  
~~sanitarian~~environmental health specialist. Whoever violates this 5374  
section is guilty of a misdemeanor of the fourth degree. 5375

**Sec. 4745.04.** (A) As used in this section: 5376

(1) "Indigent and uninsured person" and "volunteer" have 5377  
the same meanings as in section 2305.234 of the Revised Code. 5378

(2) "Licensing agency that licenses health care 5379  
professionals" means all of the following: 5380

(a) The state dental board established under Chapter 4715. 5381  
of the Revised Code; 5382

(b) The board of nursing established under Chapter 4723. 5383  
of the Revised Code; 5384

(c) The state vision professionals board established under 5385  
Chapter 4725. of the Revised Code; 5386

(d) The state board of pharmacy established under Chapter 5387  
4729. of the Revised Code; 5388

(e) The state medical board established under Chapter 5389  
4731. of the Revised Code; 5390

(f) The state board of psychology established under 5391  
Chapter 4732. of the Revised Code; 5392

(g) The state chiropractic board established under Chapter 5393  
4734. of the Revised Code; 5394

(h) The Ohio occupational therapy, physical therapy, and 5395  
athletic trainers board established under Chapter 4755. of the 5396

Revised Code;	5397
(i) The counselor, social worker, and marriage and family therapist board established under Chapter 4757. of the Revised Code;	5398 5399 5400
(j) The chemical dependency professionals board established under Chapter 4758. of the Revised Code;	5401 5402
(k) The state board of emergency medical services established under Chapter 4765. of the Revised Code;	5403 5404
(l) The state speech and hearing professionals board established under Chapter 4744. of the Revised Code;	5405 5406
(m) Any other licensing agency that considers its licensees to be health care professionals.	5407 5408
(B) Notwithstanding any provision of the Revised Code to the contrary, a licensing agency that licenses health care professionals shall apply toward the satisfaction of a portion of a licensee's continuing education requirement the provision of health care services if all of the following apply:	5409 5410 5411 5412 5413
(1) The licensing agency that licenses health care professionals requires a licensee to complete continuing education as a condition of having a license renewed by the agency.	5414 5415 5416 5417
(2) The licensee provides the health care services to an indigent and uninsured person.	5418 5419
(3) The licensee provides the health care services as a volunteer.	5420 5421
(4) The licensee satisfies the requirements of section 2305.234 of the Revised Code to qualify for the immunity from	5422 5423

liability granted under that section. 5424

(5) The health care services provided are within the scope 5425  
of authority of the licensee renewing the license. 5426

(C) (1) Except as provided in division (C) (2) of this 5427  
section, a licensing agency that licenses health care 5428  
professionals shall permit a licensee to satisfy up to one-third 5429  
of the licensee's continuing education requirement by providing 5430  
health care services as a volunteer. A licensing agency that 5431  
licenses health care professionals shall permit a licensee to 5432  
earn continuing education credits at the rate of one credit hour 5433  
for each sixty minutes spent providing health care services as a 5434  
volunteer. 5435

(2) In the case of a person holding a license to practice 5436  
medicine and surgery, osteopathic medicine and surgery, or 5437  
podiatric medicine and surgery, the state medical board shall 5438  
permit the person to satisfy not more than ~~three-ten~~ hours of 5439  
the person's continuing education requirement by providing 5440  
health care services as a volunteer. The board shall permit a 5441  
licensee to earn continuing education credits at the rate of one 5442  
credit hour for every five hours spent providing health care 5443  
services as a volunteer. 5444

(D) A licensing agency that licenses health care 5445  
professionals shall adopt rules as necessary to implement this 5446  
section. The rules shall be adopted in accordance with Chapter 5447  
119. of the Revised Code. 5448

(E) Continuing education credit received under this 5449  
section for providing health care services is not compensation 5450  
or any other form of remuneration for purposes of section 5451  
2305.234 of the Revised Code and does not make the provider of 5452

those services ineligible for the immunity from liability 5453  
granted under that section. 5454

Sec. 4762.011. On and after the effective date of this 5455  
section, this chapter no longer applies to oriental medicine 5456  
practitioners. 5457

**Sec. 5107.541.** A county department of job and family 5458  
services may contract with the chief administrator of a 5459  
nonpublic school or with any school district board of education 5460  
that has adopted a resolution under section 3319.089 of the 5461  
Revised Code to provide for a participant of the work experience 5462  
program who has a minor child enrolled in the nonpublic school 5463  
or a public school in the district to be assigned under the work 5464  
experience program to volunteer or work for compensation at the 5465  
school in which the child is enrolled. Unless it is not possible 5466  
or practical, a contract shall provide for a participant to 5467  
volunteer or work at the school as a classroom aide. If that is 5468  
impossible or impractical, the contract may provide for the 5469  
participant to volunteer to work in another position at the 5470  
school. A contract may provide for the nonpublic school or board 5471  
of education to receive funding to pay for coordinating, 5472  
training, and supervising participants volunteering or working 5473  
in schools. 5474

~~Notwithstanding section 3319.088 of the Revised Code, a A~~ 5475  
participant volunteering or working as a classroom aide under 5476  
this section is not required to obtain an educational aide- 5477  
~~permit or paraprofessional license. The participant shall not be~~ 5478  
considered an employee of a political subdivision for purposes 5479  
of Chapter 2744. of the Revised Code and is not entitled to any 5480  
immunity or defense available under that chapter, the common law 5481  
of this state, or section 9.86 of the Revised Code. 5482

4731-10-02

**Requisite hours of continuing medical education for license renewal or reinstatement.**

(A) During a registration period, a licensee shall be required to complete fifty hours of CME. A licensee must complete a minimum of one hour of CME, approved by the board, on the topic of a licensee's duty to report misconduct under section 4731.224 of the Revised Code. The remainder shall be completed by participating in the following:

- (1) Educational activities recognized by the American medical association as category 1 pursuant to its CME categorization system, and
  - (a) Are certified for category 1 CME credit by the Ohio state medical association
  - (b) Are certified for category 1 CME credit by an institution or organization accredited by the Ohio State Medical Association or the Accreditation Council for Continuing Medical Education; or
  - (c) Have been awarded category 1 CME credit directly by the American medical association.
- (2) Educational activities recognized by the American osteopathic association as category 1 pursuant to its CME categorization system, and
  - (a) Are certified for category 1 CME credit by the Ohio osteopathic association
  - (b) Are certified for category 1 CME credit by an institution or organization accredited by the Ohio osteopathic association or the American osteopathic association; or
  - (c) Have been awarded category 1 CME credit directly by the American osteopathic association
- (3) Educational activities certified for category 1 CME credit by the Ohio foot and ankle medical association
- (4) Educational activities certified for continuing education contact hours by a provider approved by the council on podiatric medical education
- (5) Internships, residencies, or fellowships accredited by the accreditation council for graduate medical education, the American osteopathic association, or the council on podiatric medical education. Credit shall be earned at a rate of one hour of CME for each week of participation.

- 
- (6) Pursuant to section 4745.04 of the Revised Code, providing health care services in Ohio, as a volunteer, to indigent and uninsured persons, up to a maximum of three hours per registration period.
- (B) If a licensee has not completed the requisite hours of CME, a licensee is not eligible for license renewal or license reinstatement until such time as the requisite hours have been completed. Any CME undertaken after the end of a registration period and utilized for purposes of renewing or reinstating a suspended license cannot also be utilized to meet the CME requirement of the current registration period.
- (C) Licensees who are not working in the medical profession or who are retired from practice but wish to renew or reinstate their licenses shall meet the CME requirements of section 4731.282 of the Revised Code and this chapter of the Administrative Code.
- (D) Licensees residing or practicing out of the state who wish to renew or reinstate their licenses must meet the CME requirements of section 4731.282 of the Revised Code and this chapter of the Administrative Code even though not currently residing or practicing in Ohio.
- (E) During a volunteer registration period, every holder of a volunteer's certificate shall be required to complete one hundred fifty hours of CME pursuant to the requirements of section 4731.295 of the Revised Code. Seventy-five hours must meet the criteria established in paragraph (A)(1) of this rule. If a holder of a volunteer's certificate has not completed the requisite hours of CME, a holder is not eligible for certificate renewal until such time as the requisite hours have been completed. Any CME undertaken after the end of a volunteer registration period and utilized for purposes of renewing a suspended certificate cannot also be utilized to meet the CME requirement of the current volunteer registration period.
- (F) During a clinical research registration period, every holder of a clinical research faculty certificate shall be required to complete seventy-five hours of CME pursuant to the requirements of section 4731.293 of the Revised Code. Such hours must meet the criteria established in paragraph (A)(1) of this rule. If a holder of a clinical research faculty certificate has not completed the requisite hours of CME, a holder is not eligible for certificate renewal until such time as the requisite hours have been completed. Any CME undertaken after the end of a clinical research registration period and utilized for purposes of renewing a suspended certificate cannot also be utilized to meet the CME requirement of the current clinical research registration period.
- (G) During a conceded eminence registration period, every holder of a certificate of conceded eminence shall be required to complete fifty hours of CME pursuant to the requirements of section 4731.297. Such hours must meet the criteria established in



paragraph (A)(1) of this rule. If a holder of a certificate of conceded eminence has not completed the requisite hours of CME, a holder is not eligible for certificate renewal until such time as the requisite hours have been completed. Any CME undertaken after the end of a conceded eminence registration period and utilized for purposes of renewing a suspended certificate cannot also be utilized to meet the CME requirement of the current conceded eminence registration period.

Replaces: 4731-10-02, 4731-10-05, 4731-10-07

Effective:

Five Year Review (FYR) Dates:

---

Certification

---

Date

Promulgated Under: 119.03  
Statutory Authority: 4731.05, 4745.04  
Rule Amplifies: 4731.282, 4731.291, 4731.293, 4731.295, 4731.297,  
4745.04  
Prior Effective Dates: 03/10/1998 (Emer.), 06/08/1998, 02/28/2003,  
05/31/2018

4731-10-08

**Evidence of continuing medical education.**

- (A) Each licensee or certificate holder applying for license renewal or license reinstatement shall certify completion of the requisite hours of CME pursuant to the rules in this chapter.
- (B) The board may select applications for verification that all CME requirements have been met. Licensees and certificate holders whose applications are selected shall submit additional documentation of compliance with CME requirements as the board may require. Failure to submit the additional documents shall constitute a violation of section 4731.282 of the Revised Code and section 4731.22 of the Revised Code.
- (C) Licensees and certificate holders have a continuing obligation to maintain detailed records of CME hours completed. The licensee or certificate holder shall obtain verification of completion of CME activities. At a minimum, verification shall include a description of the CME activity, the date of attendance or completion, and the number of hours completed. Records of all CME undertaken shall be retained by the licensee or certificate holder for two years after the end of the CME period and shall be made available to the board upon request.
- (D) Licensees seeking to receive credit pursuant to paragraph (A)(36) of rule 4731-10-02 of the Administrative Code shall maintain a log of their qualifying activities. The log shall indicate the dates the health care services were provided, the number of hours spent providing health care services on those dates, and the location where the health care services were provided.
- (E) Notwithstanding the provisions of paragraph (C) of this rule, licensees and certificate holders shall not destroy or otherwise make unavailable written documentation of CME activity after the board has requested verification of CME pursuant to this rule or section 4731.22 of the Revised Code. Upon verification that all CME requirements have been met, the applicant or licensee or certificate holder may destroy the requested records.
- (F) Nothing in this rule shall limit the board's authority to investigate and take action under section 4731.22 of the Revised Code.

Replaces: 4731-10-08

Effective:

Five Year Review (FYR) Dates:

---

Certification

---

Date

Promulgated Under: 119.03  
Statutory Authority: 4745.04, 4731.282, 4731.05  
Rule Amplifies: 4731.22, 4745.04, 4731.282  
Prior Effective Dates: 05/16/1983, 10/31/1996, 03/10/1998 (Emer.),  
06/08/1998, 02/28/2003, 05/31/2018



---

MEMORANDUM

TO: Dr. Bechtel, MD – Board President  
Board Members – State Medical Board of Ohio  
Stephanie Loucka, Executive Director of the State Medical Board of Ohio

FROM: Chelsea Wonski, Legislative Director

DATE: 1/13/2021

RE: Legislative Update

---

- Summary of lame duck
  - Senate Bill 310 is the capital appropriations bill. The language in the as passed version included amendments that waive supervision agreement requirements for physician assistants and advanced practice registered nurses allowing those individuals the ability to work with physicians other than those with which they hold a supervision agreement. Additionally, the bill allows retired medical professionals to practice temporarily without reinstatement of their license during the pandemic. The language included a provision that excludes those whose licenses had been previously suspended or revoked or were surrendered to avoid disciplinary action. These provisions will be effective until May 1, 2021 unless they are extended.
  - House Bill 263 places limits on the Boards ability to deny a license based on a prior criminal conviction. The new law requires the Board to create an inclusive list of criminal offenses that would prevent an applicant from becoming licensed. There are also new reporting requirements to the department of administrative services.
  - House Bill 442, which applies to certified public accounts, had an amendment added late in the legislative process which removes oriental medical practitioners and cosmetic therapists from under the regulatory authority of the Medical Board. The amendment also reduced the education hour requirements for massage therapists and increased the number of volunteer hours that may be applied as continuing education credit for physicians.
- Legislative outreach initiatives



---

MEMORANDUM

TO: Dr. Bechtel, MD – Board President  
Board Members – State Medical Board of Ohio  
Stephanie Loucka, Executive Director of the State Medical Board of Ohio

FROM: Nathan T. Smith, Senior Legal and Policy Counsel and Chelsea Wonski, Legislative Director

DATE: January 7, 2020

RE: Senate Bill 310 Implementation

---

Senate Bill 310 was passed and subsequently signed by Governor DeWine on December 29, 2020. Several uncodified sections respond to the COVID-19 pandemic and the resulting strain on the health care providers. There is an emergency clause attached to this bill making it effective immediately upon Governor DeWine's signature until the May 1, 2021 end date stated in the legislation. This memo seeks to explain the impact of these uncodified sections and identify implementation issues.

**I. Temporary Relaxation of Physician Assistant and Advanced Practice Nurse Supervision while practicing within a hospital or other health care facility**

**Physician Assistants:**

- During the period beginning on December 29, 2020 and ending May 1, 2021, a physician assistant may practice under the direction, control, and supervision of a physician or podiatrist with whom the physician assistant has not entered into a supervision agreement.
  - The physician assistant may perform services authorized by a physician or podiatrist and by the hospital or other health care facility within which the physician assistant is practicing.

**Impact:**

For physician assistants that are employed by or under contract with a hospital or other health care facility, they may practice under the direction, control, and supervision of any physician or podiatrist in that setting regardless of whether they have a supervision agreement with that physician or podiatrist. Also, these PAs may perform services within their scope of practice, if authorized by the physician or podiatrist and the hospital or health care facility, regardless if those services are authorized in any existing supervision agreement to which they are a party.

**For physicians and podiatrists practicing in a hospital or other health care facility,** they may (1) supervise a PA (employed by or under contract with a hospital or other health care facility) that they do not have a supervision agreement with and (2) authorize that PA to perform services that are within their scope of practice if those services are also authorized by the hospital or health care facility.

**For the Medical Board:** Investigation and enforcement of certain statutory violations by physicians, podiatrists, and PAs related to supervising and practicing only within the confines of a supervision

---

agreement will have to be suspended for the four (4) month period that this ~~unmodified~~ law will be effective.

**Questions:**

- (1) Who from the hospital or health care facility authorizes the services a PA is allowed to perform, and on what basis?
- (2) How is this authorization recorded and communicated to supervising physicians, PAs, patients, and in the event of an adverse consequence to the Medical Board?

**Advanced Practice Nurses:**

There is also a section that provides similar relaxation of Advanced Practice Nurse Supervision under a standard care arrangement with a physician or podiatrist. The impact and questions related to this section are similar to those surrounding PAs, but are a Nursing Board issue.

**II. Temporary expansion of EMT scope of practice regarding administering COVID-19 tests**

- During the period beginning on December 29, 2020 and ending May 1, 2021, and notwithstanding any conflicting provision of the Revised Code, an emergency medical technician-basic, emergency medical technician-intermediate, and emergency medical technician- paramedic who has received proper training may administer a test for COVID-19 and collect and label test specimens.

**III. Temporary allowance of practice of a Licensed Practice Nurse at the direction of a Respiratory Care Professional**

- During the period beginning on December 29, 2020 and ending May 1, 2021, and notwithstanding any conflicting provision of the Revised Code, a licensed practical nurse may perform nursing care as identified in division (F) of section 4723.01 of the Revised Code at the direction of a respiratory care professional, and a respiratory care professional may provide that direction.

**IV. Temporary Licenses for inactive health professionals**

- A health care professional who meets both of the following conditions may practice during the period beginning on the effective date of this section and ending May 1, 2021:
  1. In the five-year period immediately preceding the effective date of this section, the professional held a license or certificate to practice issued by a licensing board.
  2. During the five-year period described in the language, the professional's license or certificate expired or became inactive, which may have occurred because the professional retired from practice.
- The health care professional shall be deemed to be practicing under a temporary license as if it were issued by the professional's respective licensing board and shall not be required to reactivate, restore, or renew the professional's prior license or certificate in order to practice under this section.
- The following health care professionals are eligible to practice under the provisions of HB 442:
  1. Licensed practical nurses, registered nurses, and advanced practice registered nurses;



2. Pharmacists;
  3. Physician assistants;
  4. Physicians, including podiatrists;
  5. Respiratory care professionals;
  6. Emergency medical technicians-basic, emergency medical technicians-intermediate, and emergency medical technicians-paramedic.
- A health care professional who meets the previous conditions is not authorized to practice under this section if either of the following applies:
    1. The respective licensing board had revoked or suspended the professional's prior license or certificate.
    2. The professional surrendered the professional's prior license or certificate in an effort to avoid disciplinary or other adverse action.

**Impact:**

This legislation allows a physician, podiatrist, physician assistant, or respiratory care professional who meets the requirements to practice in Ohio on a temporary license until May 1, 2021 without having to reactivate, restore, or renew the medical professional's prior license or certificate. The requirements are:

- (1) The practitioner must have previously held a license with the State Medical Board of Ohio in the last 5 years (12/29/15 - 12/29/2020) and let that license expire during that time period to utilize this provision. The reason for the expiration of the license may be retirement but is not mandated.
- (2) Practitioners who have had their license revoked or suspended or who had surrendered their license to avoid disciplinary or other adverse action are disqualified from utilizing this provision to practice temporarily in Ohio.

**Questions:**

- (1) How will the Medical Board become aware of or track these expired practitioners practicing on a temporary license? There is no obligation to report to or register with the Medical Board imposed by this uncodified section.
- (2) Is the practice of these expired practitioners practicing on a temporary license limited to a hospital or other health care facility who could achieve that reporting? The text of the uncodified section does not seem to limit it to that.
- (3) If the Medical Board becomes aware of a practitioner practicing under this temporary license who is statutorily disqualified due to previous discipline by the State Medical Board, how can that practitioner be stopped from practicing? The uncodified section does not provide an enforcement mechanism. Could summary suspension be utilized?



---

MEMORANDUM

TO: Dr. Bechtel, MD – Board President  
Board Members – State Medical Board of Ohio  
Stephanie Loucka, Executive Director of the State Medical Board of Ohio

FROM: Chelsea Wonski, Legislative Director

DATE: January 7, 2020

RE: House Bill 442

---

Bill Number/ Sponsor(s): Rep. Bill Roemer (R-38) and Rep. Thomas West (D-49)

Date Introduced: 12/9/2019

Date of final passage: 12/22/2020

Effective Date: 3/22/2021

Summary:

- The original intent of the bill was to address concern regarding the experience and education requirements for certified public accountants
- The bill was amended in the Senate committee to include changes to the licensing authority of several state licensing boards
- Changes impacting the Medical Board include the following:
  - Eliminates the license for cosmetic therapists, currently under the purview of the Medical Board.
  - Allows the Medical Board the authority to recognize accrediting organizations for purposes of physician assistant education programs. Current law specifies that programs must be accredited by the Accreditation Review Commission on Education for the Physician Assistant.
  - Eliminates the license for oriental medicine practitioners.
  - Authorizes a physician to satisfy up to ten hours of the physician's continuing education requirement by providing volunteer health care services. Currently, physicians may obtain three hours of CME for volunteer hours.
    - Additionally, the language sets the conversion rate for volunteer hours as one credit hour of continuing education for every five hours spent volunteering. The current ratio is 1:1.
  - Codifies in Ohio law a 600-hour education requirement to qualify for a license to practice massage therapy. Currently, massage therapists are required in OAC rule 4731-1-16 to complete 750 education hours to qualify for licensure.

- Eliminates the following for clinical research faculty certificates: (1) qualification requirements other than proof of appointment to academic staff of medical school (MD, DO, DPM) and licensure in another state or country; (2) initial certificate and renewal fees; and (3) continuing medical education requirements.
- Eliminates the qualification requirements other than proof of program acceptance and holding a current, unrestricted license to practice medicine in another country for visiting clinical professional development certificates and eliminates the associated fee.
- Eliminates the fee for visiting podiatric faculty certificates.



---

MEMORANDUM

TO: Dr. Bechtel, MD – Board President  
Board Members – State Medical Board of Ohio  
Stephanie Loucka, Executive Director of the State Medical Board of Ohio

FROM: Chelsea Wonski, Legislative Director

DATE: January 7, 2021

RE: House Bill 263

---

Bill Number/ Sponsor(s): Rep Kyle Koehler (R- 79)

Date Introduced: 5/28/2019

Date of final passage: 12/22/2020

Effective Date: 3/31/2021

Summary:

**Establishment of List of Disqualifying Offenses (R.C. 9.79(B))**

- Within 180 days of the effective date of this section, each licensing authority shall establish and publish on its website a list of specific criminal offenses for which a conviction, judicial finding of guilt or plea of guilty may disqualify an individual from obtaining a license.
- The licensing authority must identify each disqualifying offense by name or by the Revised Code section number and include only those criminal offenses that are directly related to the duties and responsibilities of the occupation.
- The licensing authority may include in the list an existing or former municipal ordinance or law of this or any other state or the United States that is substantially equivalent to any section or offense included in the adopted list.

**Restrictions on Use of Criminal Information in Making Licensing Decisions (R.C. 9.79(C)(1))**

- A licensing authority shall not refuse to issue an initial license to an individual based on any of the following:
  - Solely or in part on a conviction of, judicial finding of guilt of, or plea of guilty to an offense that is not included on the adopted list of disqualifying offenses.

- A criminal charge that does not result in a conviction, judicial finding of guilt, or plea of guilty
- A nonspecific qualification such as "moral turpitude" or lack of "moral character";
- A disqualifying offense included on the adopted list of disqualifying offenses if consideration of that offense occurs after the time periods allowed in R.C. 9.79(D).

**Use of Adopted List of Disqualifying Offenses in Making Licensing Decisions (R.C. 9.79 (C)(2) and (D))**

- A licensing authority may take a conviction, judicial finding of guilt, or plea of guilty into consideration if the individual was convicted of, found guilty pursuant to a judicial finding of, or pleaded guilty to a disqualifying offense that is included in the adopted list. R.C. 9.79(C)(2).

**Standard and Factors in Licensing Authority Consideration of a Disqualifying Offense (R.C. 9.79(D)(1):**

- In considering a conviction of, judicial finding of guilt of, or plea of guilty to a disqualifying offense in determining whether to refuse to issue an initial license, the licensing authority shall consider all of the following factors using a preponderance of the evidence standard to determine whether the conviction, judicial finding of guilt, or plea of guilty to the offense disqualifies the individual from receiving the license:
  - The nature and seriousness of the offense for which the individual was convicted, found guilty pursuant to a judicial finding, or pleaded guilty;
  - The passage of time since the individual committed the offense;
  - The relationship of the offense to the ability, capacity, and fitness required to perform the duties and discharge the responsibilities of the occupation
  - Any evidence of mitigating rehabilitation or treatment undertaken by the individual, including whether the individual has been issued a certificate of qualification for employment (R.C. 2953.25) or a certificate of achievement and employability (R.C. 2961.22).
  - Whether the denial of a license is reasonably necessary to ensure public safety

**Time Limits on Use of Disqualifying Offenses (R.C. 9.79(D)(2)):**

- A licensing authority may take a disqualifying offense into account only during the following time periods:
  - For a conviction of, judicial finding of guilt of, or plea of guilty to a disqualifying offense that is an offense of violence or a sexually oriented offense, any time.
  - For a conviction of, judicial finding of guilt of, or plea of guilty to a disqualifying offense that does not involve a breach of fiduciary duty and that is not an offense of violence or a sexually oriented offense, whichever of the following is later, provided the individual was not convicted of, found guilty pursuant to a judicial finding of, and did not enter a plea of guilty to any other offense during the applicable period:
    1. Five years from the date of conviction, judicial finding of guilt, or plea of guilty;
    2. Five years from the date of the release from incarceration;
    3. The time period specified in division (D)(3) of this section
  - For a conviction of, judicial finding of guilt of, or plea of guilty to a disqualifying offense that involves a breach of fiduciary duty and that is not an offense of violence or a sexually oriented offense, whichever of the following is later, provided the individual was not convicted of, found guilty pursuant to a judicial finding of, and did not enter a plea of guilty to any other offense during the applicable period:
    1. Ten years from the date of conviction, judicial finding of guilt, or plea of guilty;
    2. Ten years from the date of the release from incarceration;
    3. The time period specified in division (D)(4) of this section.

Divisions (D)(3) and (D)(4) extend the time limits for which the licensing authority may take the offense into account when an individual is subject to community control, parole, or post-release control.

**Requirements for Notification by Licensing Authority Refusing to Issue an Initial License for Reason of Disqualifying Offense (R.C. 9.79(E))**

- If a licensing authority refuses to issue an initial license to an individual, the licensing authority shall notify the individual in writing of all the following:
  - The grounds and reasons for the refusal, including an explanation of the licensing authority's application of the factors in division (D) to the evidence the licensing authority used to reach the decision;
  - The individual's right to a hearing regarding the licensing authority's decision R.C. 119.06;
  - The earliest date the individual may reapply for a license;
  - Notice that evidence of rehabilitation may be considered on reapplication

**Burden of Proof in an Administrative Hearing (R.C. 9.79(F))**

In an administrative hearing or civil action reviewing a licensing authority's refusal to issue an initial license under this section, the licensing authority has the burden of proof on the question of whether the individual's conviction of, judicial finding of guilt of, or plea of guilty to an offense directly relates to the licensed occupation.

**Ability to Consider Licensure Discipline in Deciding Whether to Issue a License (R.C. 9.79(J))**

Nothing in this language prohibits a licensing authority from considering either of the following when making a determination of whether to issue a license to an individual: (1) Past disciplinary action taken by the licensing authority against the individual; (2) Past disciplinary action taken against the individual by an authority in another state that issues a license that is substantially similar to the license for which the individual applies.

**Relevant Miscellaneous provisions in R.C. 9.79:**

- A licensing authority that is authorized by law to limit or otherwise place restrictions on a license may do so to comply with the terms and conditions of a community control sanction, post-release control sanction, or an intervention plan established in accordance with section 2951.041 of the Revised Code (R.C. 9.79(G))
- Each licensing authority shall adopt any rules that it determines are necessary to implement this section (R.C. 9.79(H))
- Under R.C. 9.79(I)(2), the following relevant exclusion from the requirements of R.C. 9.79 applies: Any position for which federal law requires disqualification from licensure or employment based on a conviction of, judicial finding of guilt of, or plea of guilty to an offense.
- If a licensing authority issues a license to an individual after considering a conviction of, judicial finding of guilt of, or plea of guilty to an offense under division (D) of this section, the licensing authority shall not refuse to renew the individual's license based on that conviction, judicial finding of guilt, or plea of guilty. (R.C. 9.79(K))

### **Applying R.C. 9.79 to the Medical Board chapters of the Ohio Revised Code:**

Consistent with the requirements and procedures for evaluating criminal convictions in R.C. 9.79, the new law does the following in Chapters 4730, 4731, 4759, 4760, 4761, 4762, 4774, and 4778 of the Ohio Revised Code :

- (1) Removes good moral character requirements
- (2) Removes Medical Board discretion in examining the criminal records check of an applicant in deciding whether to grant a license.
- (3) Adds provisions that state that the Medical Board shall not refuse to issue a license because of a conviction “unless the refusal is in accordance with section 9.79 of the Revised Code.”
- (4) Removes requirement of no criminal record to qualify for expedited licensure under R.C. 4731.299.

### **Annual Reporting requirements (R.C. 9.78(F))**

- Requires a state licensing authority to provide an annual report to the director of administrative services including the following regarding each license type of the licensing authority:
  - The number of applications received for the license
  - The number of those applications that resulted in a license being granted
  - The number of those applications that resulted in a license being denied
  - A list of criminal offenses reported by individuals who were granted a license
  - A list of criminal offenses reported by individuals who were denied a license
  - A list of all requests by individuals who have been convicted of a criminal offense who have requested the licensing authority to determine whether the individual’s criminal conviction disqualifies the individual from obtaining a license that includes the following information:
    1. The number of requests for which the licensing authority determined that an individual’s criminal conviction disqualified the individual from obtaining a license and a list of those offenses
    2. The number of requests for which the licensing authority determine that an individual’s criminal conviction did not disqualify them from obtaining a license and a list of those offenses
  - For each disqualifying offense included on the list adopted R.C. 9.79(B), the number of individuals who were convicted of, found guilty pursuant to a judicial finding of, or pleaded guilty to that disqualifying offense who were issued a license and the number of individuals who were denied a license.
  - Any other information that the director may require
  - The first report is to be submitted to the director of administrative services by June 30, 2021 and must include the required information for January 1, 2016, to December 31, 2020, if available. Annual reports shall be submitted each year by the 30<sup>th</sup> day of June.



**From:** [Erin Hennessey](#)  
**To:** [Anderson, Kimberly](#)  
**Subject:** Re: Light and laser based therapy proposals  
**Date:** Monday, October 17, 2022 11:43:59 AM

---

Ms. Anderson,

I will pass the information along. Thank you for your quick response!

Erin

> On Oct 17, 2022, at 10:58 AM, Kimberly.Anderson@med.ohio.gov wrote:

>

> If they can get them to us in the next few days, we can accept late comments.

>

> Kimberly Anderson

> Chief Legal Counsel

> State Medical Board of Ohio

> 30 East Broad Street, 3rd Floor

> Columbus, Ohio 43215

> o: 614-466-7207

> c: 614-230-9077

> Kimberly.Anderson@med.ohio.gov

>

>

>

>

>

>

> Confidentiality Notice: This message is intended for use only by the individual or entity to whom or which it is addressed and may contain information that is privileged, confidential and/or otherwise exempt from disclosure under applicable law. If the reader of this message is not the intended recipient, or the employee or agent responsible for delivering the message to the intended recipient, you are hereby notified that any dissemination, distribution or copying of this communication is strictly prohibited. If you have received this communication in error, please notify me immediately by telephone.

>

>

> -----Original Message-----

> From: Erin Hennessey <emhenny@gmail.com>

> Sent: Monday, October 17, 2022 10:53 AM

> To: Anderson, Kimberly <Kimberly.Anderson@med.ohio.gov>

> Subject: Light and laser based therapy proposals

>

> Good morning, Kimberly!

>

> There are many folks just seeing the proposed rules on light and laser this, will you still accept comments?

>

> Erin

>

> Sent from my iPhone

>

>

>

>

> CAUTION: This is an external email and may not be safe. If the email looks suspicious, please do not click links

or open attachments and forward the email to [csc@ohio.gov](mailto:csc@ohio.gov) <<mailto:csc@ohio.gov>> or click the Phish Alert Button if available.

>

>

>

>



**MEMORANDUM**

TO: Betty Montgomery, President  
Members, State Medical Board of Ohio

FROM: Kimberly C. Anderson, Chief Legal Counsel

RE: Proposed Initial Circulation, Mental or Physical Impairment, Rule 4731-28-01, OAC

DATE: November 1, 2022

---

Rule 4731-28-01, OAC, which contains definitions related to mental or physical impairment is due for the five year rule review. The rule needs to be updated to add the references for the statutes related to the inability to practice due to mental or physical illness for dietitians and respiratory care professionals. Please see the proposed updated rule.

**Requested Action:** Approve sending proposed amended rule to interested parties for initial circulation.

---

4731-28-01

**Mental or physical impairment.**

For the purposes of division (B)(4) of section 4730.25 of the Revised Code, division (B)(19) of section 4731.22 of the Revised Code, [division \(A\)\(14\) of section 4759.07 of the Revised Code](#), division (B)(5) of section 4760.13 of the Revised Code, [division \(A\)\(14\) of section 4761.09 of the Revised Code](#), division (B)(5) of section 4762.13 of the Revised Code, division (B)(5) of section 4774.13 of the Revised Code, and division (B)(5) of section 4778.14 of the Revised Code, the following definitions apply:

- (A) "Mental illness" includes, but is not limited to, mental disorder; and
- (B) "Inability to practice according to acceptable and prevailing standards of care by reason of mental illness or physical illness, including, but not limited to, physical deterioration that adversely affects cognitive, motor, or perceptive skills", includes inability to practice in accordance with such standards without appropriate treatment, monitoring, or supervision.



---

**MEMORANDUM**

TO: Betty Montgomery, President  
Members, State Medical Board of Ohio

FROM: Kimberly C. Anderson, Chief Legal Counsel

RE: Controlled Substance Prescribing Rules (Rules 4731-11-03, 4731-11-04, 4731-11-04.1,  
OAC)

DATE: November 2, 2022

---

The proposed amendments to Rules 4731-11-03 and 4731-11-04 and proposed rescission of Rule 4731-11-04.1 were filed with CSI on September 22, 2022, with a public comment period ending on October 14, 2022. The Business Impact Analysis and proposed rules are attached for your review. Several comments were received.

**4731-11-03**

Kinsey Jolliff, Dr. Joan Papp, and Dr. Neera Gupta expressed concerns regarding Section (B)(2)(e) regarding the adjunctive use of stimulants in the treatment of chronic pain and requested a call to discuss. On October 25, 2022, Dr. Schottenstein, Aaron Mabe and I met with Mr. Jolliff, Dr. Papp, and Dr. Gupta to discuss their concerns. Dr. Schottenstein provided a copy of the Status Report on Role of Stimulants in Chronic Pain Management, which is attached for your review. A follow up comment and an article from the Journal of Substance Abuse Treatment on Associations Between Prescription and Illicit Stimulant and Opioid Use in the United States were provided for the Board's review and are attached. The updated comment states the following:

We recommend removal of section (B)(2)(e) based on lack of current scientific evidence that stimulants are an effective treatment modality for chronic pain and that neither the primary nor adjunctive use of stimulants in the treatment of chronic pain are recognized by FDA as approved indications. Conversely, the risks of stimulant addiction are well described in the current literature; according to an analysis of the most recent NSDUH report (attached) 30% of patients report misusing their prescribed stimulants while only 12% of patients prescribed opioids reported misuse. In light of current trends of increasing stimulant deaths in the U.S., unnecessary exposure to this addictive, non-proven therapy should be avoided at all costs. The opioid epidemic began similarly, in large part due to recommendations to prescribe opioids for chronic pain without supporting scientific evidence. If stimulants are allowed to be prescribed in the same manner, it is very likely that the current stimulant crisis will worsen and unnecessarily claim thousands of lives.

**Recommendation: The language in this portion of the rule is not new language. Rule 4731-11-03 has permitted the prescribing of stimulants for adjunctive use in the treatment of chronic pain for**

---

many years. The updated language is a clean-up to reference changes in terminology from intractable pain to chronic pain. The Board should consider the comments made and the accompanying literature and determine whether the requested change should be made to the rule.

**4731-11-04**

1. Barto Burguera, M.D., W. Scott Butsch, M.D., Marcio Griebeler, M.D., and Diana Isaacs, PharmD, of the Cleveland Clinic provided the following comments:

- (a) Amend Rule 4731-11-04(C) to modify the language to reflect the fact that weight reduction based on caloric restrictions is not always the chosen intervention, and that comprehensive lifestyle interventions include making healthy changes in diet, physical activity, sleep and circadian rhythm and stress are often the chosen course of treatment.

The recommended change is as follows:

A prescriber may utilize a schedule III or IV controlled substance that bears appropriate FDA approved labeling for weight loss, in the treatment of obesity as an adjunct, ~~in a regimen of weight reduction based on caloric restriction~~ to a lifestyle intervention, provided that: . . .

**Recommendation: The Board should consider this comment and determine whether the rule should be amended to reflect this comment.**

- (b) Amend 4731-11-04(C)(2) to follow the prescribing pattern that is currently used for Vyvanse where three prescriptions can be issued at one time.

**Recommendation: The language of 4731-11-04(C)(2) reflects the statutory limitation on personal furnishing of controlled substances.**

- (c) Amend 4731-11-04 (C)(4)(a) so that patients can use heartrate and blood pressure monitors at home to assess the presence of uncommon side effects.

The recommended change is as follows:

The prescriber shall assess the patient at least once every three months and shall obtain the patient's weight, blood pressure, and heart rate. ~~heart and lungs.~~ The findings shall be entered in the patient's record.

**Recommendation: The Board should consider this comment and determine whether the rule should be amended to reflect this comment.**

2. Ms. Hoffman indicated that she is in favor of the removal of the 12-week restriction on phentermine.

**Recommendation: No change recommended.**

3. Cameron Mcnamee of the Ohio Board of Pharmacy recommended changing the "shall" to "may" in the first sentence of Rule 4731-11-04(C)(2).

**Recommendation: This change should be made.**

4. Steven Carp, M.D.: Comment recommended removal of the prescribing limitation for phentermine.

**Recommendation: The draft rule removes the prescribing limitation for phentermine, so no change needed.**

**Requested Action:** Review the comments received and determine whether the rules should be amended.





# Common Sense Initiative

**Mike DeWine**, Governor  
**Jon Husted**, Lt. Governor

**Sean McCullough**, Director

## Business Impact Analysis

**Agency, Board, or Commission Name:** State Medical Board of Ohio

**Rule Contact Name and Contact Information:**

**Kimberly Anderson** [Kimberly.Anderson@med.ohio.gov](mailto:Kimberly.Anderson@med.ohio.gov); (614) 466-7207

**Regulation/Package Title (a general description of the rules' substantive content):**

**Controlled Substance Rules**

**Rule Number(s):** 4731-11-03, 4731-11-04, 4731-11-04.1

**Date of Submission for CSI Review:** 9/22/22

**Public Comment Period End Date:** 10/14/22

**Rule Type/Number of Rules:**

New/ 1 rules

No Change/      rules (FYR?     )

Amended/ 1 rules (FYR? y)

Rescinded/ 2 rules (FYR? y)

The Common Sense Initiative is established in R.C. 107.61 to eliminate excessive and duplicative rules and regulations that stand in the way of job creation. Under the Common Sense Initiative, agencies must balance the critical objectives of regulations that have an adverse impact on business with the costs of compliance by the regulated parties. Agencies should promote transparency, responsiveness, predictability, and flexibility while developing regulations that are fair and easy to follow. Agencies should prioritize compliance over punishment, and to that end, should utilize plain language in the development of regulations.

77 SOUTH HIGH STREET | 30TH FLOOR | COLUMBUS, OHIO 43215-6117

[CSIPublicComments@governor.ohio.gov](mailto:CSIPublicComments@governor.ohio.gov)

### **Reason for Submission**

- 1. R.C. 106.03 and 106.031 require agencies, when reviewing a rule, to determine whether the rule has an adverse impact on businesses as defined by R.C. 107.52. If the agency determines that it does, it must complete a business impact analysis and submit the rule for CSI review.**

**Which adverse impact(s) to businesses has the agency determined the rule(s) create?**

**The rule(s):**

- Requires a license, permit, or any other prior authorization to engage in or operate a line of business.**
- Imposes a criminal penalty, a civil penalty, or another sanction, or creates a cause of action for failure to comply with its terms.**
- Requires specific expenditures or the report of information as a condition of compliance.**
- Is likely to directly reduce the revenue or increase the expenses of the lines of business to which it will apply or applies.**

### **Regulatory Intent**

- 2. Please briefly describe the draft regulation in plain language.**

*Please include the key provisions of the regulation as well as any proposed amendments.*

Rule 4731-11-03: Utilization of anabolic steroids, Schedule II controlled substances. The rule outlines the utilization of anabolic steroids and schedule II controlled substances. The rule is proposed to be amended to do the following:

- Correct a typographical error in paragraph (B);
- Add the requirement of a mental status examination of the patient to (B)(1)(b);
- Correct a typographical error in (B)(1)(c);
- Update the language of attention deficit hyperactivity disorder and delete reference to abnormal behavioral syndrome and hyperkinetic syndrome in (B)(2)(b);
- Updates the language in (B)(2)(c) regarding certain neurocognitive disorders;

77 SOUTH HIGH STREET | 30TH FLOOR | COLUMBUS, OHIO 43215-6117

[CSIPublicComments@governor.ohio.gov](mailto:CSIPublicComments@governor.ohio.gov)

- Deletes the differential diagnostic psychiatric evaluation of depression as a condition for which Schedule II controlled substance could be prescribed in paragraph (B)(2)(d); and
- Updates paragraph (B)(2)(e) reference the definition of chronic pain in Rule 4731-11-01.

Rule 4731-11-04 Controlled Substances: Utilization of short term anorexiant for weight reduction-Rescind/New: The rule sets forth the requirements for physicians to prescribe short-term anorexiant for weight loss.

Rule 4731-11-04.1 Controlled Substances: Utilization for Chronic Weight Management-Rescind  
The rule sets forth the requirements for physicians and physician assistants in the utilization of controlled substances for chronic weight management.

A new rule 4731-11-04 is proposed to address controlled substances for the treatment of obesity. The new rule will set forth requirements for the utilization of schedule III or IV controlled substances that are FDA approved for the treatment of obesity.

**3. Please list the Ohio statute(s) that authorize the agency, board or commission to adopt the rule(s) and the statute(s) that amplify that authority.**

4731-11-03: Authorized by 4731.05, Amplifies 4731.22

4731-11-04: Authorized by 4731.05; Amplifies 4731.22

**4. Does the regulation implement a federal requirement? Is the proposed regulation being adopted or amended to enable the state to obtain or maintain approval to administer and enforce a federal law or to participate in a federal program? If yes, please briefly explain the source and substance of the federal requirement.**

No. Although the Controlled Substance Act establishes the schedule for controlled drugs, the rules are not required by the federal law.

**5. If the regulation includes provisions not specifically required by the federal government, please explain the rationale for exceeding the federal requirement.**

Not applicable.

**6. What is the public purpose for this regulation (i.e., why does the Agency feel that there needs to be any regulation in this area at all)?**

The rules provide guidance to physicians in the prescribing of controlled substances for the treatment of specific medical conditions.

77 SOUTH HIGH STREET | 30TH FLOOR | COLUMBUS, OHIO 43215-6117

[CSIPublicComments@governor.ohio.gov](mailto:CSIPublicComments@governor.ohio.gov)

**7. How will the Agency measure the success of this regulation in terms of outputs and/or outcomes?**

The success of these regulations will be measured by physicians prescribing controlled substances in accordance with the rules; the rules being written in plain, understandable language; licensee compliance with the rules; and minimal questions from licensees about the proposed rule requirements.

**8. Are any of the proposed rules contained in this rule package being submitted pursuant to R.C. 101.352, 101.353, 106.032, 121.93, or 121.931?**

*If yes, please specify the rule number(s), the specific R.C. section requiring this submission, and a detailed explanation.*

No.

**Development of the Regulation**

**9. Please list the stakeholders included by the Agency in the development or initial review of the draft regulation.**

*If applicable, please include the date and medium by which the stakeholders were initially contacted.*

The rules were circulated to interested parties, including but not limited to the Ohio State Medical Association, Ohio Association of Physician Assistants, the Pharmacy Board, the Physician Assistant Policy Committee of the State Medical Board, and the Ohio Osteopathic Association, the Ohio Hospital Association and the Academy of Medicine of Cleveland and Northern Ohio. In addition, in November 2020, a virtual meeting was held with Dr. Soin, a member of the State Medical Board and physicians specializing in the treatment of obesity to obtain comments regarding Rules 4731-11-04 and 4731-11-04.1. The State Medical Board made initial draft changes based on the feedback from the virtual meeting, and circulated the draft rules to the interested parties.

**10. What input was provided by the stakeholders, and how did that input affect the draft regulation being proposed by the Agency?** A spreadsheet outlining the comments received in the most recent circulation is attached.

The Board fully reviewed the comments received for rule 4731-11-03, as follows:

- John Smith, J.D., Government Relations Coordinator had questions regarding the meaning of the term, mental status examination in section (B)(1)(b). Specifically, he questioned whether there was a standard mental status examination for patients that may be prescribed a stimulant and whether comprehensive neuropsych testing was required.

77 SOUTH HIGH STREET | 30TH FLOOR | COLUMBUS, OHIO 43215-6117

[CSIPublicComments@governor.ohio.gov](mailto:CSIPublicComments@governor.ohio.gov)

**The Board determined to make no change. A mental status examination is the psychological equivalent of the physical examination, including the clinician’s observations and impressions of the patient at the time of the interview. Neuropsych testing is not required.**

- Lee Reynolds, MD. Of 4KidHelp provided a comment that telehealth should be available for patients with ADD/ADHD being treated with stimulants.

**The Board determined to make no change because the proposed rules on telehealth as authorized by HB 122 will address this issue.**

- Kinsey Jolliff, Principal, Government Relations for The MetroHealth System provided the following recommendations:
  - Add a section requiring a 30-day follow up for the first 90 days and then every 90 days to be consistent with requirements for Schedule III and IV anorexiant since Schedule II drugs have a higher potential for addiction.

**The Board determined to make no change because the degree of follow-up should be based on clinician judgment.**

- Questions why Schedule II stimulants may not be used for weight reduction or control but may be used in paragraph (B)(2)(f) for binge eating disorder.

**The Board determined not to make this change because the language in paragraph (B)(2)(f) is based on FDA approval of Vyvanse for the indication of binge eating disorder. Schedule II stimulants are not used for weight reduction or control due to a perceived increased risk of addiction and diversion when prescribed for that indication.**

- Concerned with allowing Schedule II stimulant in (B)(2)(e) for the treatment of chronic pain. Use of stimulants for treatment of chronic pain is outdated.

**The Board determined not to make a change here because stimulants are not recommended for primary treatment of pain but may be helpful for the physical and mental health function in patients who are being treated for pain.**

The Board fully reviewed the comments and is proposing the following changes to proposed rule 4731-11-04:

- 4731-11-04(B)(1) Delete “caloric restriction” because it is duplicative with nutritional counseling.
- 4731-11-04(B)(3)(d): Add the following as comorbid risk factors with the BMI of 27: insulin resistance, metabolic syndrome, prediabetes.

77 SOUTH HIGH STREET | 30TH FLOOR | COLUMBUS, OHIO 43215-6117

[CSIPublicComments@governor.ohio.gov](mailto:CSIPublicComments@governor.ohio.gov)

- 4731-11-04(B)(3)(f) Delete language prohibiting initiation of treatment with a controlled substance if the patient was unsuccessful in previous attempts to lose weight. **The Board agreed to this change but recommended adding language requiring documentation of the rationale for initiation or re-initiation of treatment with controlled substances.**
- 4731-11-04(C)(1): Delete the requirement for an assessment every thirty days for the first three months of utilization of controlled substances for weight reduction.
- 4731-11-04(C)(2) Delete the requirement to limit prescriptions to 30 days. Language regarding personally furnishing needs updated to accurately reflect the language of Section 4729.291 of the Revised Code which places restrictions on the aggregate and individual amounts of controlled substances that can be personally furnished. **The Board agreed to make this change with the following updated language:**

The prescriber shall ~~not personally furnish or prescribe more than a 30-day supply of~~ controlled substances, ~~at one time,~~ for weight reduction or chronic weight management only in accordance with section 4729.291 of the revised code. For any controlled substance that is personally furnished to or for patients, taken as a whole, the prescriber shall not exceed a total of two thousand five hundred dosage units in any thirty-day period and for an individual patient, shall not in any seventy-two hour period, personally furnish an amount that exceeds the amount necessary for that patient's use in a seventy-two hour period. Dosage unit means any of the following:

- (a) A single pill, capsule, ampule, or tablet;
- (b) In the case of a liquid solution, one milliliter;
- (c) In the case of a cream, lotion, or gel, one gram; or
- (d) Any other form of administration available as a single unit.

- 4731-11-04(C)(4)(a) Several comments recommended the addition of language that would allow the assessments to be conducted via telemedicine. **Rules 4731-11-09 and 4731-37-01 will specifically address telemedicine, but a change is recommended to replace the word, “check” with “obtain” to allow the patient’s weight, blood pressure, pulse, heart, and lung assessment to be completed through remote monitoring.**
- 4731-11-04(C)(4)(b) Several comments recommended the elimination of the requirement to continue to lose weight or to maintain a goal weight as these concepts are not consistent with the treatment of obesity as a chronic, progressive disease. **The Board agreed to amend with the following language:**

For the continuation of Schedule III or IV controlled substances designated as FDA short term use controlled substances beyond three months, the patient must

77 SOUTH HIGH STREET | 30TH FLOOR | COLUMBUS, OHIO 43215-6117

[CSIPublicComments@governor.ohio.gov](mailto:CSIPublicComments@governor.ohio.gov)

maintain a 5% weight reduction ~~continue to lose weight during the active weight reduction treatment or maintain goal weight.~~ The prescriber shall document the patient's weight loss or maintenance in the record.

- 4731-11-04(C)(5)(c) Several comments recommended modification of this language to eliminate the thirty day timeframe and to eliminate weighing the patient at least every thirty days. **The Board agreed to the following revised language:**

~~That the patient has not responded by achieving less than 5% weight reduction after three months failed to lose weight while under treatment with a controlled substance or controlled substances for weight reduction over a period of thirty days during the current course of treatment, which determination shall be made by weighing the patient at least every thirtieth day, except that a patient who has never before received treatment for obesity utilizing any controlled substance who fails to lose weight during the first thirty days of the first such treatment attempt may be treated for an additional thirty days;~~

The proposed changes to Rule 4731-11-04 were also provided to the Board of Pharmacy and there were no objections.

**11. What scientific data was used to develop the rule or the measurable outcomes of the rule? How does this data support the regulation being proposed?**

The Medical Board, which includes nine physicians, utilized its medical expertise in developing these rules. In addition, the Board reviewed journal articles and medical studies provided by the interested parties to make the proposed changes to Rule 4731-11-04.

**12. What alternative regulations (or specific provisions within the regulation) did the Agency consider, and why did it determine that these alternatives were not appropriate? If none, why didn't the Agency consider regulatory alternatives?**

The Board considered and adopted much of the alternative language suggested by the interested parties.

**13. Did the Agency specifically consider a performance-based regulation? Please explain. *Performance-based regulations define the required outcome, but don't dictate the process the regulated stakeholders must use to achieve compliance.***

77 SOUTH HIGH STREET | 30TH FLOOR | COLUMBUS, OHIO 43215-6117

[CSIPublicComments@governor.ohio.gov](mailto:CSIPublicComments@governor.ohio.gov)



The proposed rules are performance based.

**14. What measures did the Agency take to ensure that this regulation does not duplicate an existing Ohio regulation?**

The Medical Board is the only state agency that licenses physicians.

**15. Please describe the Agency’s plan for implementation of the regulation, including any measures to ensure that the regulation is applied consistently and predictably for the regulated community.**

The rule will be posted on the Medical Board’s website. Medical Board staff members are available by telephone and e-mail to answer questions.

**Adverse Impact to Business**

**16. Provide a summary of the estimated cost of compliance with the rule. Specifically, please do the following:**

**a. Identify the scope of the impacted business community; and**

The impacted business community is composed of physician and physician assistant licensees regulated by the Medical Board.

**b. Identify the nature of all adverse impact (e.g., fees, fines, employer time for compliance); and**

The rules requires periodic examinations for patients being prescribed controlled substance medications.

**c. Quantify the expected adverse impact from the regulation.**

*The adverse impact can be quantified in terms of dollars, hours to comply, or other factors; and may be estimated for the entire regulated population or for a “representative business.” Please include the source for your information/estimated impact.*

There may be additional time for physicians treating patients with controlled substances for weight loss.

**17. Why did the Agency determine that the regulatory intent justifies the adverse impact to the regulated business community?**

Controlled substances pose health and safety risks to patients and it is important to have comprehensive standards for the prescribing of these drugs.

**Regulatory Flexibility**

**18. Does the regulation provide any exemptions or alternative means of compliance for small businesses? Please explain.**

77 SOUTH HIGH STREET | 30TH FLOOR | COLUMBUS, OHIO 43215-6117

[CSIPublicComments@governor.ohio.gov](mailto:CSIPublicComments@governor.ohio.gov)



No. The regulation is applied equally for all physicians and physician assistants.

**19. How will the agency apply Ohio Revised Code section 119.14 (waiver of fines and penalties for paperwork violations and first-time offenders) into implementation of the regulation?**

Violations of these rules could result in disciplinary action, including fines. Any disciplinary action is imposed pursuant to Chapter 119 and the Medical Board's laws and rules. Due process requires equal application of the laws and rules to all licensees.

**20. What resources are available to assist small businesses with compliance of the regulation?**

The proposed rules will be available on the Board's website. The Board staff is available to answer questions regarding the rules.

Name	Organization	Summary of comment	Recommendation
Ethan Lazarus, MD	Obesity Medicine Association	Obesity has been recognized as a chronic disease by the AMA since 2013 and should be treated the same as other diseases such as hypertension and Type 2 diabetes. The rule draft is a step in the right direction, but has concerns. <b>4731-11-04(B)(3)(d)</b> : BMI is a population-based measurement and should not be strictly enforced with the individual patient. The language as drafted does not make allowance for on-label use of medication in children, like Saxenda, which is based on BMI percentile, not BMI. Recommends adding language "or the benefits of weight loss treatment for the patient would significantly outweigh any risks of the medication being used" or "pursuant to guidance from package inserts." <b>4731-11-04(B)(3)(f)</b> :The language is castigatory, blaming the patient for the disease of obesity and should be removed. Past poor performance does not indicate that the patient can't do well moving forward. Under this language, the patient gets one shot at treating obesity and if they don't do well, cannot be treated again. <b>4731-11-04(C)(3)</b> :Some patients with the most severe obesity do not lose 5% or more body weight within the first three months. Qsymia package insert states that it can be continued if at 3 months the patient has lost 3% or more. Recommends adding language that in the event 5% weight loss is not achieved within 3 months, the provider should document pros and cons of continuing medication to see if 5% can be achieved at 6 months. <b>4731-11-04(C)(4)(b)</b> : Recommends striking this language because it is inconsistent with the disease of obesity as a chronic progressive disease. Also, the concept of "goal weight" is a myth and should be retired. <b>4731-11-04(C)(5)</b> -Recommends clarifying that weight loss program would be discontinued if the patient made a false or misleading statement regarding the patient's use of other stimulants, whether prescription or illicit. <b>4731-11-04(C)(5)(c)</b> : Recommends striking this language. <b>4731-11-04(C)(5)(f)</b> : Recommends striking this language because it is duplicative.	Delete language in 4731-11-04(B)(3)(f). Modify language in 4731-11-04(C)(4)(b) to eliminate the requirement to continue to lose weight or to maintain a goal weight. Recommend requiring patient to maintain a 5% weight reduction. Recommend modification of language in 4731-11-04(C)(5)(c) that the patient has "not responded by achieving less than 5%weight reduction after three months while under treatment with a controlled substance or controlled substances.
Joe Nadglowski	Obesity Action Coalition	<b>4731-11-04(C)(1)</b> : Monthly assessment is not necessary. Patients with chronic diseases like obesity are typically assessed every 2-3 months. <b>4731-11-04(C)(3)</b> :Recommend changing language to encourage the patient to maintain 5% weight reduction. With a growing understanding of obesity, it is difficult to mandate that patients must continue to lose weight or achieve their goal weight to continue on anti-obesity medication. This is treating obesity different than other chronic diseases, such as high blood pressure or high cholesterol. <b>4731-11-04(C)(4)(a)</b> : Agree with the assessment at least every three months, but telemedicine should be an option. <b>4731-11-04(B)(3)(f)</b> : Language is castigatory and stigmatizing and should be removed. Past poor performance is not an indication that the patient can't do well moving forward.	Change 4731-11-04(C)(1) that assessment is once in the first 3 months. 4731-11-04(C)(4)(a) assessments may be able to be completed via telemedicine pursuant to Rules 4731-37-01 and 4731-11-09. See above regarding deletion of language in 4731-11-04(B)(3)(f).
Kristin Englund, MD, MLS	Academy of Medicine of Cleveland and Northern Ohio	<b>4731-11-04(C)(1)</b> : Monthly assessments are not necessary. Recommend that the prescriber follow up with the patient once in the first three months of treatment. <b>4731-11-04(C)(2)</b> :Phentermine should not be restricted to a 30 day prescription. <b>4731-11-04(C)(4)(a)</b> : Patients do not need to be seen monthly while on phentermine. Patient may use heart rate and blood pressure monitors at home and alert provider if concerns arise. <b>4731-11-04(C)(5)(c)</b> : Patients do not need to be weighed by the physician every 30 days. Each patient responds differently to medication and should be assessed on an individual basis by the provider. Care can be delivered through telemedicine.	Change 4731-11-04(C)(1) that assessment is once in the first 3 months. Delete "or prescribe" in 4731-11-04(C)(2). 4731-11-04(C)(4)(a) assessments may be able to be completed via telemedicine pursuant to Rules 4731-37-01 and 4731-11-09. See above regarding deletion of language in 4731-11-04(B)(3). Modify language in 4731-11-04(C)(5)(c) to eliminate requirement for weighing patient every thirty days.
Sergio J. Bardaro, MD	Ohio/Kentucky Chapter of American Society of Bariatric and Metabolic Surgery	<b>4731-11-04(C)(1)</b> : Monthly assessment is not necessary. Typical follow up is every 2-3 months. <b>4731-11-04(C)(2)</b> : Eliminate the word "prescribe" so that the 30 day limitation applies only to personally furnishing of phentermine. <b>4731-11-04(C)(4)(a)</b> : Add language that telemedicine may be used to assess the patient in lieu of a face-to-face encounter when clinically appropriate. <b>4731-11-04(C)(4)(b)</b> :Recommend changing language to read, "For the continuation of Schedule III or IV controlled substances designated for the treatment of obesity beyond three months, the patient must maintain a 5% weight reduction." It is difficult to mandate that patients must continue to lose weight or achieve their goal weight. <b>4731-11-04(B)(3)(f)</b> : The language "indicate that the patient made less than a substantial good faith effort to lose weight in a treatment program" is castigatory and stigmatizing and should be removed. Under this language, the patient has one chance to treat obesity and if they don't do well, are barred from being treated again.	Recommend making all suggested changes.
Bernard Lenchitz	University of Cincinnati	Supports the proposed rule that eliminates the 12 week restriction on phentermine.	

Bruce Barker, MD	Ohio Health Weight Management	<p><b>4731-11-04(B)(1):</b> Recommends removal of caloric restriction. It is redundant with nutritional counseling. <b>4731-11-04(B)(3)(d):</b> See Dr. Lazarus comment, above. <b>4731-11-04(B)(3)(f):</b> Language is derogatory and weight biased, blaming the patient for the disease of obesity. Past poor performance does not indicate patient cannot do well moving forward. <b>4731-11-04(C)(3):</b> See Dr. Lazarus comment, above. <b>4731-11-04(B)(3)(d):</b> comorbid risk factors with BMI of 27 should also include insulin resistance, metabolic syndrome, prediabetes. <b>4731-11-04(C)(4)(b):</b> See Dr. Lazarus comment, above. <b>4731-11-04(C)(5):</b> See Dr. Lazarus comment, above. <b>4731-11-04(C)(5)(c):</b> No other drug class prohibits pursuing further treatment on the basis of a treatment failure. The process of determining the most effective tool strategy often takes time and multiple trials. Combination therapies are commonly required. This statement should be removed in its entirety. <b>4731-11-04(C)(5)(f):</b> This statement is duplicative. Sent a separate comment to proposed telehealth rules and indicates that follow up visits for treating chronic obesity can be done via telehealth.</p>	Recommend removal of "caloric restriction" in 4731-11-04(B)(1). Obtain Board feedback on adding insulin resistance, metabolic syndrome and prediabetes to the co-morbid conditions in paragraph (B)(3)(d).
Barto Burguera, MD, PH.D, Diana Issaacs, PharmD, Marcio Griebeler, MD, W. Scott Butsch, MD, Roy Kim, MD	Cleveland Clinic	<p><b>4731-11-04(B)(3)(e): Recommend deletion of the reference to caloric restrict as duplicative as the concept is embedded in nutritional counseling and intensive behavioral therapy.</b> <b>4731-11-04(C)(1):</b> Monthly assessments are not necessary and the language should be changed so that the prescriber shall assess the patient once in the first three months of utilization of controlled substances. <b>4731-11-04(C)(2):</b> Strike the words, "prescribe". Anti-obesity medication are commonly prescribed with a 30 day prescription with two refills. <b>4731-11-04(C)(4)(a):</b> See Dr. Englund comments, above. <b>4731-11-04(C)(4)(b):</b> Disagree with the statement, "the patients must continue to lose weight" and "maintain goal weight" as it fails to recognize the multifactorial nature of weight loss. Recommend changing the language to, "For the continuation of Schedule III or IV controlled substances designated as FDA short term use controlled substances beyond three months, the patient must maintain a 5% weight reduction. <b>4731-11-04(C)(5)(c):</b> Concerned that the patient may be removed from Anti Obesity Medication if they do not lose weight. There are other variables that cause weight gain and some patients are rapidly gaining weight prior to starting an AOM and the AOM may lead to weight stabilization. Recommend the deletion of this language.</p>	Recommend acceptance of all suggested changes.
Angela Fitch, MD	Harvard Medical School, Massachusetts General Hospital Weight Center, Obesity Medicine Association	Comments substantially similar to those from Cleveland Clinic, above.	Recommend acceptance of all suggested changes.
Jennifer Hayhurst	Ohio State Medical Association	Comments substantially similar to those from Obesity Action Coalition, above.	See Obesity Action Coalition, above.
Kinsey Jolliff	MetroHealth System	<p><b>4731-11-03:</b> Recommend adding a section requiring 30 day follow up for first 90 days and then every 90 days to be consistent with rules for Schedule II and IV anorexiant. Schedule II medications in this rule have a higher potential for addiction and no follow up is proposed. Is there inconsistency with 4731-11-03(A)(3)(a) and (B)(2)(f)? <b>4731-11-03(B)(2)(e):</b> Concerned with indications for schedule II stimulant for chronic pain is long outdated and a schedule II stimulant should not have a primary role as adjunctive therapy for chronic pain treatment. <b>4731-11-04(C)(2):</b> Need clarification on the personally furnishing limits.</p>	Changes to 4731-11-03 not recommended. Recommend clarification of language so that it matches 4729.291.



4731-11-03

**Utilization of anabolic steroids, schedule II controlled substance cocaine hydrochloride, and schedule II controlled substance stimulants.**

(A) A physician shall not:

- (1) Utilize anabolic steroids, growth hormones, testosterone or its analogs, human chorionic gonadotropin ("HCG"), or other hormones for the purpose of enhancing athletic ability.
- (2) Utilize the schedule II controlled substance cocaine hydrochloride for a purpose other than one of the following:
  - (a) As a topical anesthetic in situations in which it is properly indicated; or
  - (b) For in-office diagnostic testing for pupillary disorders.
- (3) Utilize a schedule II controlled substance stimulant in any of the following circumstances:
  - (a) For purposes of weight reduction or control;
  - (b) When the physician knows or has reason to believe that a recognized contra-indication to its use exists; or
  - (c) In the treatment of a patient who the physician knows or should know is pregnant, except if the following criteria are met:
    - (i) After the physician's medical assessment the physician and patient determine that the benefits of treating the patient with a schedule II controlled substance stimulant outweigh the risks, and
    - (ii) The basis for the determination is documented in the patient record.

(B) Utilizing a schedule II controlled ~~substance~~ substance stimulant:

- (1) Before initiating treatment utilizing a schedule II controlled substance stimulant, the physician shall perform all of the following:
  - (a) Obtain a thorough history;

- (b) Perform an appropriate physical examination and mental status examination of the patient; and
  - (c) Rule out the existence of any recognized contra-indications to the use of the controlled ~~substance~~substance stimulant to be utilized.
- (2) A physician may utilize a schedule II controlled substance stimulant only for one of the following purposes:
- (a) The treatment of narcolepsy, idiopathic hypersomnia, and hypersomnias due to medical conditions known to cause excessive sleepiness;
  - (b) The treatment of ~~abnormal behavioral syndrome~~ (attention deficit hyperactivity disorder; ~~hyperkinetic syndrome~~); and/or related disorders;
  - (c) The treatment of major or mild neurocognitive disorder due to traumatic brain injury or substance/medication-induced major or mild neurocognitive disorder; ~~drug-induced or trauma-induced brain dysfunction~~;
  - ~~(d) The differential diagnostic psychiatric evaluation of depression;~~
  - ~~(e)~~(d) The treatment of depression shown to be refractory to other therapeutic modalities, including pharmacologic approaches, such as antidepressants;
  - ~~(f)~~(e) As adjunctive therapy in the treatment of chronic pain, as defined in rule 4731-11-01 of the administrative code, ~~the following~~:
    - ~~(i) Chronic severe pain;~~
    - ~~(ii) Closed head injuries;~~
    - ~~(iii) Cancer-related fatigue;~~
    - ~~(iv) Fatigue experienced during the terminal stages of disease;~~
    - ~~(v) Depression experienced during the terminal stages of disease; or~~
    - ~~(vi) Intractable pain, as defined in rule 4731-21-01 of the Administrative Code.~~

~~(g)~~(f) The treatment of binge eating disorder.

- (3) Upon ascertaining or having reason to believe that the patient has a history of or shows a propensity for alcohol or drug abuse, or that the patient has consumed or disposed of any controlled substance other than in strict compliance with the treating physician's directions, the physician shall perform both of the following;
    - (a) Reappraise the desirability of continued utilization of schedule II controlled substance stimulants and shall document in the patient record the factors weighed in deciding to continue their use; and
    - (b) Actively monitor such patient for signs and symptoms of drug abuse and drug dependency.
- (C) A violation of any provision of this rule, as determined by the board, shall constitute any or all of the following:
- (1) "Failure to maintain minimal standards applicable to the selection or administration of drugs," as that clause is used in division (B)(2) of section 4731.22 of the Revised Code;
  - (2) "Selling, giving away, personally furnishing, prescribing, or administering drugs for other than legal and legitimate therapeutic purposes," as that clause is used in division (B)(3) of section 4731.22 of the Revised Code;
  - (3) "A departure from, or the failure to conform to, minimal standards of care of similar practitioners under the same or similar circumstances, whether or not actual injury to a patient is established," as that clause is used in division (B)(6) of section 4731.22 of the Revised Code.

**\*\*\* DRAFT - NOT YET FILED \*\*\***

4731-11-04

**Controlled substances: Utilization of short term anorexiant  
for weight reduction.**

TO BE RESCINDED

- (A) A physician shall utilize a schedule III or IV controlled substance short term anorexiant for purposes of weight reduction only if it has an F.D.A. approved indication for this purpose and then only in accordance with all of the provisions of this rule.
- (B) Before initiating treatment for weight reduction utilizing any schedule III or IV controlled substance short term anorexiant, the physician shall complete all of the following requirements:
- (1) The physician shall review the physician's own records of prior treatment or review the records of prior treatment by another treating physician, dietician, or weight-loss program to determine the patient's past efforts to lose weight in a treatment program utilizing a regimen of weight reduction based on caloric restriction, nutritional counseling, intensive behavioral therapy, and exercise, without the utilization of controlled substances, and that the treatment has been ineffective.
  - (2) The physician shall complete and document the findings of all of the following:
    - (a) Obtain a thorough history;
    - (b) Perform an appropriate physical examination of the patient;
    - (c) Determine the patient's BMI;
    - (d) Rule out the existence of any recognized contraindications to the use of the controlled substance to be utilized;
    - (e) Assess and document the patient's freedom from signs of drug or alcohol abuse, and the presence or absence of contraindications and adverse side effects.
    - (f) Access OARRS for the patient's prescription history during the preceding twelve month period and document in the patient's record the receipt and assessment of the report received; and
    - (g) Develop and record in the patient record a treatment plan that includes, at a minimum, a diet and exercise program for weight loss.



- (3) The physician shall not initiate treatment utilizing a controlled substance short term anorexiant upon ascertaining or having reason to believe any one or more of the following:
  - (a) The patient has a history of or shows a propensity for alcohol or drug abuse, or has made any false or misleading statement to the physician related to the patient's use of drugs or alcohol;
  - (b) The patient has consumed or disposed of any controlled substance other than in strict compliance with the treating physician's directions;
  - (c) The physician knows or should know the patient is pregnant;
  - (d) The patient has a BMI of less than thirty, unless the patient has a BMI of at least twenty seven with comorbid factors;
  - (e) The review of the physician's own records of prior treatment or review of records of prior treatment provided by another physician, dietician, or weight-loss program indicate that the patient made less than a substantial good faith effort to lose weight in a treatment program utilizing a regimen of weight reduction based on caloric restriction, nutritional counseling, intensive behavioral therapy, and exercise without the utilization of controlled substances.
  
- (C) A physician may utilize a schedule III or IV controlled substance short term anorexiant, that bears appropriate F.D.A. approved labeling for weight loss, in the treatment of obesity as an adjunct, in a regimen of weight reduction based on caloric restriction, provided that:
  - (1) The physician shall personally meet face-to-face with the patient, at a minimum, every thirty days when controlled substances are being utilized for weight reduction, and shall record in the patient record information demonstrating the patient's continuing efforts to lose weight, the patient's dedication to the treatment program and response to treatment, and the presence or absence of contraindications, adverse effects, and indicators of possible substance abuse that would necessitate cessation of treatment utilizing controlled substances.
  - (2) The controlled substance short term anorexiant is prescribed strictly in accordance with the F.D.A. approved labeling. If the F.D.A. approved labeling of the controlled substance short term anorexiant being utilized for weight loss states that it is indicated for use for "a few weeks," the total course of treatment using that controlled substance shall not exceed twelve

**\*\*\* DRAFT - NOT YET FILED \*\*\***

4731-11-04

3

weeks. That time period includes any interruption in treatment that may be permitted under paragraph (C)(3) of this rule.

- (3) A physician shall not initiate a course of treatment utilizing a controlled substance short term anorexiant for purposes of weight reduction if the patient has received any controlled substance for purposes of weight reduction within the past six months. However, the physician may resume utilizing a controlled substance short term anorexiant following an interruption of treatment of more than seven days if the interruption resulted from one or more of the following:
  - (a) Illness of or injury to the patient justifying a temporary cessation of treatment; or
  - (b) Unavailability of the physician; or
  - (c) Unavailability of the patient, if the patient has notified the physician of the cause of the patient's unavailability.
- (4) After initiating treatment, the physician may elect to switch to a different controlled substance short term anorexiant for weight loss based on sound medical judgment, but the total course of treatment for any short term anorexiant combination of controlled substances each of which is indicated for "a few weeks" shall not exceed twelve weeks.
- (5) The physician shall not initiate or shall discontinue utilizing all controlled substance short term anorexiants for purposes of weight reduction immediately upon ascertaining or having reason to believe:
  - (a) That the patient has a history of or shows a propensity for alcohol or drug abuse, or has made any false or misleading statement to the physician relating to the patient's use of drugs or alcohol;
  - (b) That the patient has consumed or disposed of any controlled substance other than in strict compliance with the treating physician's directions;
  - (c) That the patient has failed to lose weight while under treatment with a controlled substance or controlled substances over a period of thirty days during the current course of treatment, which determination shall be made by weighing the patient at least every thirtieth day, except that a patient who has never before received treatment for obesity utilizing

**\*\*\* DRAFT - NOT YET FILED \*\*\***

4731-11-04

4

any controlled substance who fails to lose weight during the first thirty days of the first such treatment attempt may be treated for an additional thirty days;

(d) That the patient has repeatedly failed to comply with the physician's treatment recommendations; or

(e) That the physician knows or should know the patient is pregnant.

(D) A violation of any provision of this rule, as determined by the board, shall constitute the following:

(1) "Failure to maintain minimal standards applicable to the selection or administration of drugs," as that clause is used in division (B)(2) of section 4731.22 of the Revised Code;

(2) "Selling, giving away, personally furnishing, prescribing, or administering drugs for other than legal and legitimate therapeutic purposes," as that clause is used in division (B)(3) of section 4731.22 of the Revised Code; and

(3) "A departure from, or the failure to conform to, minimal standards of care of similar practitioners under the same or similar circumstances, whether or not actual injury to a patient is established," as that clause is used in division (B)(6) of section 4731.22 of the Revised Code.

4731-11-04

**Controlled substances for the treatment of obesity.**

(A) A prescriber may utilize a schedule III or IV controlled substance for the treatment of obesity only if it has an F.D.A approved indication for this purpose and then only in accordance with all of the provisions of this rule.

(B) Before initiating treatment for obesity utilizing any schedule III or IV controlled substance, the prescriber shall complete all of the following requirements:

(1) The prescriber shall review the prescriber's own records of prior treatment or review the records of prior treatment by another treating physician, prescriber, dietitian, or weight-loss program to determine the patient's past efforts to lose weight in a treatment program utilizing a regimen of weight reduction based on nutritional counseling, intensive behavioral therapy, and exercise, without the utilization of controlled substances, and that the treatment has been ineffective

(2) The prescriber shall complete and document the findings of all of the following:

(a) Obtain a thorough history;

(b) Perform an appropriate examination of the patient;

(c) Determine the patient's BMI;

(d) Rule out the existence of any recognized contraindications to the use of the controlled substance to be utilized;

(e) Assess and document the patient's freedom from signs of drug or alcohol abuse, and the presence or absence of contraindications and adverse side effects.

(f) Access OARRS for the patient's prescription history during the preceding twelve month period and document in the patient's record the receipt and assessment of the report received; and

(g) Develop and record in the patient record a treatment plan that includes, at a minimum, a diet and exercise program for weight loss.

(3) The prescriber shall not initiate treatment utilizing a controlled substance for the treatment of obesity upon ascertaining or having reason to believe any one or more of the following:

(a) The patient has a history of or shows a propensity for alcohol or drug abuse, or has made any false or misleading statement to the prescriber physician related to the patient's use of drugs or alcohol;

(b) The patient has consumed or disposed of any controlled substance other

than in strict compliance with the treating prescriber's directions;

(c) The prescriber knows or should know the patient is pregnant;

(d) The patient has a BMI of less than thirty, unless the patient has a BMI of at least twenty seven with comorbid factors, including Type 2 diabetes, cardio vascular disease, hypertension, hyperlipidemia, obstructive sleep apnea, nonalcoholic fatty liver disease, osteoarthritis, insulin resistance, metabolic syndrome, pre-diabetes, or major depression;

(e) The patient has any condition that would contraindicate the use of the controlled substance to be utilized;

(f) The prescriber shall document in the patient's record the rationale for initiation or re-initiation of treatment utilizing a controlled substance for chronic obesity.

(C) A prescriber may utilize a schedule III or IV controlled substance that bears appropriate F.D.A. approved labeling for weight loss, in the treatment of obesity as an adjunct, in a regimen of weight reduction based on caloric restriction, provided that:

(1) The prescriber shall assess the patient, at a minimum, once in the first three months of utilization of controlled substances for weight reduction, and shall record in the patient record information demonstrating the patient's continuing efforts to lose weight, the patient's dedication to the treatment program and response to treatment, and the presence or absence of contraindications, adverse effects, and indicators of possible substance abuse that would necessitate cessation of treatment utilizing controlled substances.

(2) The prescriber shall personally furnish controlled substances for weight reduction or chronic weight management. For any controlled substance that is personally furnished, the prescriber shall not exceed a total of two thousand five hundred dosage units in any thirty-day period and shall not in any seventy-two hour period, personally furnish an amount that exceeds the amount necessary for the patient's use in a seventy-two hour period. Dosage unit means any of the following:

(a) A single pill, capsule, ampule, or tablet;

(b) In the case of a liquid solution, one milliliter;

(c) In the case of a cream, lotion or gel, one gram; or

(d) Any other form of administration available as a single unit.

(3) The prescriber shall not personally furnish or prescribe additional controlled

substances to treat obesity for a patient who has not achieved a weight loss of at least 5% of the patient's initial weight, during the initial three months of treatment using controlled substances to treat obesity.

(4) The prescriber may personally furnish or prescribe controlled substances to treat obesity when the prescriber observes and records that the patient significantly benefits from the controlled substances and has no serious adverse effects related to the drug regimen. A patient significantly benefits from the controlled substances when weight is reduced or when weight loss is maintained and any existing co-morbidity is reduced.

(a) The prescriber shall assess the patient at least once every three months and shall obtain the patient's weight, blood pressure, pulse, heart and lungs. The findings shall be entered in the patient's record.

(b) For the continuation of Schedule III or IV controlled substances designated as FDA short term use controlled substances beyond three months, the patient must maintain a 5% weight reduction. The prescriber shall document the patient's weight loss or maintenance in the record.

(c) The prescriber shall document the patient's progress with the treatment plan.

(d) The prescriber shall access OARRS in accordance with rules 4731-11-11 and 4730-2-10 of the Administrative Code.

(5) The prescriber shall discontinue utilizing all controlled substances for purposes of weight reduction immediately upon ascertaining or having reason to believe:

(a) That the patient has made any false or misleading statement to the prescriber relating to the patient's use of drugs or alcohol;

(b) That the patient has consumed or disposed of any controlled substance other than in strict compliance with the treating physician's directions;

(c) That the patient has not responded by achieving less than 5% weight reduction after three months while under treatment with a controlled substance or controlled substances;

(d) That the patient has repeatedly failed to comply with the prescriber's treatment recommendations;

(e) That the patient demonstrates any signs that the controlled substance is not safe for or well tolerated by the patient; or

(f) That the prescriber knows or should know the patient is pregnant.

(D) A violation of any provision of this rule, as determined by the board, shall constitute the following:

(1) For a physician:

(a) "Failure to maintain minimal standards applicable to the selection or administration of drugs," as that clause is used in division (B)(2) of section 4731.22 of the Revised Code;

(b) "Selling, giving away, personally furnishing, prescribing, or administering drugs for other than legal and legitimate therapeutic purposes," as that clause is used in division (B)(3) of section 4731.22 of the Revised Code; and

(c) "A departure from, or the failure to conform to, minimal standards of care of similar practitioners under the same or similar circumstances, whether or not actual injury to a patient is established," as that clause is used in division (B)(6) of section 4731.22 of the Revised Code.

(2) For a physician assistant:

(a) "A departure from, or failure to conform to, minimal standards of care of similar physician assistants under the same or similar circumstances, regardless of whether actual injury to a patient is established," as that clause is used in division (B)(19) of section 4730.25 of the Revised Code;

(b) "Failure to comply with the requirements of this chapter, Chapter 4731. of the Revised Code, or any rules adopted by the board," as that clause is used in division (B)(2) of section 4730.25 of the Revised Code; and

(c) "Violating or attempting to violate, directly or indirectly, or assisting in or abetting the violation of, or conspiring to violate, any provision of this chapter, Chapter 4731. of the Revised Code, or the rules adopted by the board," as that clause is used in division (B)(3) of section 4730.25 of the Revised Code.

4731-11-04.1            **Controlled substances: utilization for chronic weight management.**

TO BE RESCINDED

(A) A physician shall determine whether to utilize a controlled substance anorexiant for purposes of chronic weight management as an adjunct to a reduced calorie diet and increased physical activity. The determination shall be made in compliance with the provisions of this rule.

(1) Before initiating treatment utilizing any controlled substance anorexiant, the physician shall complete all of the following requirements:

(a) Obtain a thorough history;

(b) Perform a physical examination of the patient;

(c) Determine the patient's BMI;

(d) Review the patient's attempts to lose weight in the past for indications that the patient has made a substantial good faith effort to lose weight in a regimen for weight reduction based on caloric restriction, nutritional counseling, intensive behavioral therapy, and exercise without the utilization of controlled substance anorexiant. The review shall include available records from the physician's own prior treatment of the patient, prior treatment provided by another physician, prior participation in a weight-loss program, or prior treatment by a dietitian;

(e) Rule out the existence of any recognized contraindications to the use of the controlled substance anorexiant to be utilized;

(f) Assess and document the patient's freedom from signs of drug or alcohol abuse;

(g) Access OARRS and document in the patient's record the receipt and assessment of the information received; and

(h) Develop and record in the patient record a treatment plan that includes, at a minimum, a diet and exercise program for weight loss.

(2) The physician shall not initiate treatment utilizing a controlled substance anorexiant upon ascertaining or having reason to believe any one or more of the following:



- (a) The patient has a history of, or shows a propensity for, alcohol or drug abuse, or has made any false or misleading statement to the physician or physician assistant relating to the patient's use of drugs or alcohol;
    - (b) The patient has consumed or disposed of any controlled substance other than in strict compliance with the treating physician's directions; or
    - (c) The physician knows or should know the patient is pregnant.
  - (3) The physician shall not initiate treatment utilizing a controlled substance anorexiant if any of the following conditions exist:
    - (a) The patient has an initial BMI of less than thirty, unless the patient has an initial BMI of at least twenty seven with comorbid factors.
    - (b) The review of the patient's attempts to lose weight in the past indicates that the patient has not made a substantial good faith effort to lose weight in a regimen for weight reduction based on caloric restriction, nutritional counseling, intensive behavioral therapy, and exercise without the utilization of controlled substance anorexiant. The review shall include available records from the physician's own prior treatment of the patient, prior treatment provided by another physician, prior participation in a weight-loss program, or prior treatment by a dietitian.
  - (4) The physician shall prescribe the controlled substance anorexiant strictly in accordance with the F.D.A. approved labeling;
  - (5) Throughout the course of treatment with any controlled substance anorexiant the physician shall comply with rule 4731-11-11 of the Administrative Code and the physician assistant shall comply with rule 4730-2-10 of the Administrative Code.
- (B) A physician shall provide treatment utilizing a controlled substance anorexiant for weight management in compliance with paragraph (A) of this rule and the following:
- (1) The physician shall meet face-to-face with the patient for the initial visit and at least every thirty days during the first three months of treatment. If the F.D.A. approved labeling for the controlled substance anorexiant requires induction of treatment at one dose and an increase to a higher dose after a stated period of less than thirty days, the physician may give the patient a prescription for

the higher dose at the initial visit and the first thirty day period then starts from the date the prescription for the higher dose may be filled.

(2) Following the initial visit and two follow-up visits, the treatment may be continued under one of the following means:

(a) The physician may authorize refills for the controlled substance anorexiant up to five times within six months after the initial prescription date;

(b) The treatment may be provided by a physician assistant in compliance with this rule, the supervisory plan or policies of the healthcare facility, and the physician assistant formulary adopted by the board.

(3) When treatment for chronic weight management is provided by a physician assistant, the following requirements apply:

(a) The supervising physician shall personally review the medical records of each patient to whom the physician assistant has prescribed a controlled substance anorexiant following each visit; and

(b) A physician assistant shall not initiate utilization of a different controlled substance anorexiant, but may recommend such change for the supervising physician's initiation.

(4) A physician shall discontinue utilizing any controlled substance anorexiant immediately upon ascertaining or having reason to believe:

(a) That the patient has repeatedly failed to comply with the physician's treatment recommendations; or

(b) That the patient is pregnant.

(C) A violation of any provision of this rule, as determined by the board, shall constitute the following as applicable:

(1) For a physician:

(a) "Failure to maintain minimal standards applicable to the selection or administration of drugs," as that clause is used in division (B)(2) of

section 4731.22 of the Revised Code;

- (b) "Selling, giving away, personally furnishing, prescribing, or administering drugs for other than legal and legitimate therapeutic purposes," as that clause is used in division (B)(3) of section 4731.22 of the Revised Code; and
- (c) "A departure from, or the failure to conform to, minimal standards of care of similar practitioners under the same or similar circumstances, whether or not actual injury to a patient is established," as that clause is used in division (B)(6) of section 4731.22 of the Revised Code.

(2) For a physician assistant:

- (a) "A departure from, or failure to conform to, minimal standards of care of similar physician assistants under the same or similar circumstances, regardless of whether actual injury to a patient is established," as that clause is used in division (B)(19) of section 4730.25 of the Revised Code;
- (b) "Failure to comply with the requirements of this chapter, Chapter 4731. of the Revised Code, or any rules adopted by the board," as that clause is used in division (B)(2) of section 4730.25 of the Revised Code; and
- (c) "Violating or attempting to violate, directly or indirectly, or assisting in or abetting the violation of, or conspiring to violate, any provision of this chapter, Chapter 4731. of the Revised Code, or the rules adopted by the board," as that clause is used in division (B)(3) of section 4730.25 of the Revised Code.

[Journal](#)[News & Insights](#)[Disorders](#)[Treatments](#)[In Practice](#)[Non-Opioids](#)

Volume 15, Issue 6

# Status Report on Role of Stimulants in Chronic Pain Management

Stimulant administration in chronic pain patients may increase analgesia, improve mental and physical functions, and treat the comorbidities of fatigue, depression, daytime sedation, obesity, and attention deficit hyperactivity disorder (ADHD).

## CITE THIS ARTICLE

Tennant F. Status Report on Role of Stimulants in Chronic Pain Management. *Pract Pain Manag.* ;15(6).

**Aug 11, 2015****Forest Tennant, MD, DrPH**, Head, Arachnoiditis Research and Education Project

Stimulants are a class of compounds that have a sympathomimetic or uplifting action on the central nervous system (CNS). Internal or endogenous stimulants are known as catecholamines because a portion of the molecule is catechol. The best known examples are dopamine, norepinephrine, and epinephrine. The latter terms also are called adrenaline and noradrenaline, so their stimulant action on the body is often called “adrenergic.”<sup>1</sup>

Regardless of terminology, stimulant or catecholaminergic compounds have an expanding role in pain management for a number of reasons. They have been shown to have innate analgesic properties, in addition to potentiating opioids, enhancing some mental and physiologic functions, and treating some common comorbidities of chronic pain, including fatigue, depression, daytime sedation, obesity, and attention deficit hyperactivity disorder (ADHD).<sup>2-7</sup>



Some recent basic science research will accelerate this expanded role.<sup>8-10</sup> Consequently, *Practical Pain Management* brings to you this status report on stimulants.

## Recent Compelling Studies

Recent studies provide a compelling scientific basis for the increased use of stimulant compounds in chronic pain management. Collectively, these studies quite convincingly show that stimulants may be necessary for chronic pain control. In one study, Taylor et al found that inflamed microglia in chronic pain states do not adequately release and activate dopamine in the CNS, which is necessary for pain control.<sup>8</sup> They wrote: “Our findings demonstrate that a peripheral nerve injury activated microglia within reward circuitry that result in disruption of dopaminergic signaling and reward behavior. These results have broad implications that are not restricted to the problem of pain, but are also relevant to affective disorders associated with disruption of reward circuitry. Because chronic pain causes glial activation in areas of the CNS important for mood and affect, our findings may translate to other disorders, including anxiety and depression, that demonstrate high comorbidity with chronic pain.”<sup>8</sup>

In another study, Parent et al found low plasma norepinephrine and metanephrine concentrations in patients with chronic pain.<sup>9</sup> “Our results clearly show a deficit in pain inhibition, along with lower plasma norepinephrine and metanephrine concentrations in chronic pain

along with lower plasma norepinephrine and metanephrine concentrations in chronic pain subjects, compared to pain-free subjects. No differences were found in cerebrospinal fluid neurotransmitter concentrations,"they noted.<sup>9</sup> This complements a prior study that found low plasma norepinephrine in patients with diabetes with polyneuropathy.<sup>11</sup>

Other relevant research shows that descending neural pathways from the brain to the periphery generate a great deal of chronic pain.<sup>1,10,12</sup> Catecholamines play a critical role in the inhibition of descending pain signals.<sup>1,10,12</sup> Now, we have studies that document that patients with chronic pain have plasma catecholamine levels that are low and may be inadequate to inhibit descending pain signals. Taken together, these recent studies tell us we likely will need externally administered stimulants to substitute for lack of central catecholaminergic activity and to make up for a peripheral, plasma catecholamine deficiency to control descending pain signals.

## Reluctance to Use Stimulants

Given the historical effective use of stimulants in severe pain and the recent scientific evidence that catecholamine compounds are necessary for pain control, it is clear that the use of stimulants should be expanded. Physicians have been reluctant, however, to prescribe stimulants to pain patients for fear of abuse or addiction and concerns that high blood pressure and tachycardia may result.

At this time, there are no reports documenting abuse, diversion, or addiction with stimulants in patients with legitimate chronic pain. However, there are numerous reports of misuse and abuse of stimulants in patients with other conditions, especially among those being treated for ADHD. In a review on abuse of medication in patients with ADHD, Clemow and Walker wrote: "Regionally-specific, stimulant-induced elevations in brain dopamine appear to be integral to both efficacy in ADHD and potential for abuse. Overall, the data suggest that ADHD medication misuse and diversion are .... with the prevalence believed to be approximately 5% to 10% of high school students and 5% to 35% of college students, depending on the study."<sup>13</sup>

To minimize risk, certain measures are recommended. One is to use an off-label consent form when prescribing stimulants, which lays out the risks of dependence, hypertension, and tachycardia. As when prescribing opioids, regular clinic visits and monitoring for aberrant behavior involving stimulants should be done. Periodic urine and/or blood testing can be requested because stimulants now are a component of test profiles.

## Cardiovascular Risks

The risk for hypertension and tachycardia is widely overstated. Although stimulants may cause hypertension and tachycardia in patients without pain conditions, these adverse effects (AEs) rarely occur in chronic pain patients. In fact, there may be a counterintuitive physiologic effect



rarely occur in chronic pain patients. In fact, there may be a counterintuitive, physiologic effect of stimulants in chronic pain patients.<sup>14</sup> In my experience, stimulants usually lower blood pressure and pulse rates in chronic pain patients. Also, pain patients rarely, if ever, report euphoria with stimulants.

The reason for this counterintuitive effect in chronic pain patients is somewhat unclear, but it is likely related to the oversensitization of the nervous system in chronic pain states and the deficiencies of central and peripheral catecholamines. Practitioners obviously should monitor chronic pain patients for elevated blood pressure and pulse rates, but a reduction, not an elevation, in these physiologic measures is the usual finding in this population. Although there are obvious risks to stimulant treatment of chronic pain patients, the long positive history of their use, the absence of reported AEs and abuse in pain patients, and the need to treat certain comorbidities, make it clear that the benefits of stimulant treatment outweigh its risks.

## History of Stimulant Discovery

Given the emerging and expanding use of stimulants in pain management, it is most desirable that pain practitioners have some familiarity with the history of stimulant use in pain treatment, so that all concerned parties know that this is not some new, radical development.

More than a century ago, in 1904, Weber showed that catecholamines would relieve pain when he applied epinephrine (adrenaline) to exposed spinal cords of cats.<sup>15</sup> Even prior to this date, in 1896, the renowned British physician Herbert Snow recommended a mixture of morphine and cocaine for patients suffering from advanced disease.<sup>16</sup> The original and infamous “Brompton Cocktail” was invented in the 1920s at the Royal Brompton Hospital, in London. The cocktail consisted of morphine or diacetylmorphine (heroin), cocaine, ethyl alcohol, and chlorpromazine for nausea. This cocktail usually was reserved for terminally ill patients with cancer or tuberculosis.

Dextroamphetamine and morphine were found to be an excellent combination for pain relief during World War II.<sup>17</sup> Also, during the wartime period, it was found that stimulants would counteract the respiratory depression and sedation of opioids.<sup>18, 19</sup> Although the use of this combination was known, it was seldom used clinically and was essentially unreported in the medical literature for several years after the war.

Instead, researchers, commercial producers, and practitioners turned their attention to combining stimulants, including caffeine, into single commercial products because stimulants clearly potentiated opioids and aspirin.<sup>20, 21</sup> This led to the development of popular combination drugs consisting of weak stimulants with opioids and/or anti-inflammatory agents. The combination products of codeine with aspirin or acetaminophen and caffeine are widely known and have been highly prescribed for over 2 generations.<sup>21</sup>

Although not yet widely adopted, a number of excellent studies on stimulants and opioids in combination were done between 1950 and the end of the last century.<sup>22-29</sup> All of these studies, whether done in animals or humans, showed remarkable enhancement of pain relief when stimulants were combined with opioids. One of the surprising and positive findings in these studies was that stimulants not only gave better pain relief, but subjects (animals and humans) routinely performed mentally and physically better and had less respiratory depression and sedation than with opioids alone.<sup>3-5, 29</sup>

In 1977, I conducted a randomized, controlled trial of dextroamphetamine with morphine in post-operative patients and clearly documented the superior pain-relieving effects of the simultaneous use of both agents.<sup>30</sup> As noted above, studies in recent years have shown that catecholamines are necessary to control the descending pain pathways from the brain to the periphery. All told, the history and research of stimulant use in chronic pain states is compelling.

## **Analgesia and Opioid Sparing**

It is clear that stimulants possess, in themselves, analgesic properties. The historical belief that they simply potentiate opioids may be too simplistic. They increase the analgesic properties of non-opioids and provide pain relief independent of the endogenous opioid system and externally administered opioids.<sup>6, 31</sup> Norepinephrine appears to be the major catecholamine that controls pain.<sup>1, 7</sup> This explains why pure dopaminergic compounds, such as L-Dopa and amantadine, have not found a place in pain treatment. In the author's experience, stimulants may spare opioids in many chronic pain patients.<sup>14</sup> Some patients even claim that stimulants may provide equal pain relief to opioids.

## **Treatment of Comorbidities**

As noted, in addition to analgesia, stimulants treat or control some of the comorbidities commonly found in chronic pain patients: fatigue, depression, obesity, daytime sedation, and ADHD (Table 1). At least one of these comorbidities likely will be found in most severe, chronic pain patients. Fortunately, most commercially available stimulants are FDA-approved for treatment of one or more of the common chronic pain comorbidities (Table 2).



Table 1. Rationale and Indications for Stimulant Use in Patients With Chronic Pain	
<ul style="list-style-type: none"> <li>✓ Improve analgesia                             <ul style="list-style-type: none"> <li>• Activate central adrenergic centers</li> <li>• Inhibit descending pain pathways</li> </ul> </li> <li>✓ Improve physiologic and mental functions</li> <li>✓ Minimize opioid use</li> <li>✓ Treat comorbidities                             <ul style="list-style-type: none"> <li>• Fatigue</li> <li>• Depression</li> <li>• Obesity</li> <li>• Attention deficit hyperactivity disorder</li> <li>• Daytime sedation</li> </ul> </li> </ul>	

Table 2. Commercially Available Stimulants	
Drug (Brandname)	Labeled Indication
Dextroamphetamine (Dexedrine, others)	ADHD
Amphetamine / dextroamphetamine combinations (Adderall, others)	ADHD
Methylphenidate (Ritalin, Concerta, others)	ADHD
Phentermine (Adipex-P, others)	Obesity
Phendimetrazine (Bontril, others)	Obesity
Modafinil (Provigil, others)	Narcolepsy

ADHD, attention deficit hyperactivity disorder

Obesity is rampant among chronic pain patients due to multiple factors including immobility, diet, hormone abnormalities, and drugs such as opioids and benzodiazepines that slow metabolism. The weight-control stimulants, phentermine (Adipex-P, others) and phendimetrazine (Bontril, others), are well tolerated by pain patients. Phentermine was marketed with fenfluramine as a combination weight loss product under the name Fen-Phen. In 1997, fenfluramine and dexfenfluramine were voluntarily taken off the market at the request of the FDA after 24 cases of heart valve disease in Fen-Phen users were reported. Phentermine has remained on the market as a Schedule IV controlled substance. Phendimetrazine, a Schedule III controlled substance, functions as a prodrug to phenmetrazine, which was withdrawn from the market due to abuse and misuse. The author has not observed great dependence or addiction with these current agents.<sup>32</sup>

Daytime sedation in chronic pain patients may have multiple causative factors, including night-time insomnia, hormonal abnormalities, and sedating analgesics, such as long-acting opioids.

The stimulant *lisdexamfetamine dimesylate* (Dexmefinil) can be effective in some of these patients.

The stimulant for narcolepsy, modafinil (PROVIGIL), can be effective in some of these patients.

A common but little addressed problem in chronic pain patients is ADHD. Almost universally, severe, centralized, chronic pain disrupts normal neuronal function in the CNS. Patients and their families often are distraught over the pain patient's inability to concentrate, focus, read, and remember. The stimulants methylphenidate (Ritalin, Concerta, others), dextroamphetamine (Dexedrine, others), and combinations of amphetamine and dextroamphetamine (Adderall, others) are well tolerated by pain patients. Table 3 provides a checklist to aid in identifying pain patients with ADHD. Although this patient checklist has been neither validated nor quantified, it includes various behaviors that typify ADHD in adult pain patients. I consider 3 or more positive answers to likely represent the presence of some attention deficit.

**Table 3. Dr. Tennant's Patient Checklist for Attention Deficit Hyperactivity Disorder**

	Question	TRUE	FALSE
1	I can't concentrate well enough to read for more than a few minutes		
2	It is hard for me to think about one subject for more than a few minutes		
3	I'm frequently told I don't pay attention		
4	I can't sit still for very long		
5	I don't like to do detailed tasks		
6	People often tell me I'm hyper		
7	I don't finish a lot of things I start		
8	I'm easily distracted		
9	I am more irritable than other people		
10	I have difficulty following instructions		
11	I can't concentrate to write much		
12	I have too many nervous habits		
13	I do too many things on impulse		
14	My coordination is not very good		
15	I tend to be accident prone		
16	I have a short temper		

The patient who has 3 or more positive answers can be suspected to have some attention deficit hyperactivity disorder (ADHD).  
 Note: This is not a clinically proven diagnostic test and should only be used as a suggested guide for diagnosis.  
 Further testing by a pain psychologist or psychiatrist may be warranted to make a diagnosis of ADHD.

## Selection of Stimulant

There are many factors that go into selecting a stimulant. These include cost, health plan coverage, prior exposure to a stimulant, and abuse history. As a general measure, it is recommended that the stimulant selected be for a comorbidity for which the stimulant has a labeled indication. For example, phentermine for obesity and methylphenidate or dextroamphetamine for ADHD.

The initial dosage should be low. A therapeutic principle in pain management pharmacotherapy is to “start low and go slow.” Chronic, centralized pain patients have a sensitized nervous system and many autoimmune characteristics. Consequently, AEs often occur. The dosage of a stimulant should be titrated upward over time to control a comorbidity, enhance pain relief, and potentiate opioids and minimize their use.

## Summary

A long history of stimulant use for analgesia and recent clinical studies provide a sound rationale for their expanded use in chronic pain management. Catecholaminergic enhancement may be required for CNS activity and inhibition of the descending pain pathways that traverse from the brain down the spinal cord and autonomic nervous system into the periphery. To date, stimulants with catecholamine properties have not been widely used in chronic pain management for fear of abuse and complications such as hypertension and tachycardia. Accumulating evidence clearly indicates, however, that stimulants may be used in chronic pain states to achieve effective analgesia and to treat the common comorbidities of fatigue, depression, daytime sedation, obesity, and ADHD. With regular clinic monitoring, the benefits of stimulants outweigh the risks, and these agents should be more widely used in chronic pain management. The benefits of stimulant administration include enhanced analgesia, improved physical and mental function, reduced opioid use, and treatment of comorbidities.

**SEE OUR REFERENCE**

**Notes:** This article was originally published August 5, 2015 and most recently updated August 11, 2015.



**From:** [Mabe, Aaron](#)  
**To:** [Anderson, Kimberly](#)  
**Subject:** FW: OAC 4731-11-03 Concerns  
**Date:** Wednesday, October 19, 2022 4:11:38 PM

---

**From:** Kinsey Jolliff <kjolliff@metrohealth.org>  
**Sent:** Tuesday, October 11, 2022 1:30 PM  
**To:** Mabe, Aaron <Aaron.Mabe@med.ohio.gov>  
**Cc:** Allison Poulos <apoulos@metrohealth.org>  
**Subject:** OAC 4731-11-03 Concerns

Hi Aaron,

The MetroHealth System clinical staff remains concerned with changes to 4731-11-03(B)(2)(e). We submitted comments last Spring but the Board declined to make changes. I realize the rule packet is now with CSI but our clinical leaders would like to better understand from your team the reasons for the change. The crux of their clinical concern is that it's not appropriate to justify stimulants prescribing to improve functional status of patients with pain and that the new language is too vague.

Please let me know if your team can meet with our clinical leaders – Drs. Papp and Gupta. Please also let me know what times your team is available so I can coordinate scheduled on my end.

Thanks,  
Kinsey

Kinsey Jolliff  
The MetroHealth System  
Principal, Government Relations  
P: 614-348-7608  
[kjolliff@metrohealth.org](mailto:kjolliff@metrohealth.org)

**MetroHealth's Mission: Leading the way to a healthier you and a healthier community through service, teaching, discovery, and teamwork.** This email and all attachments that may have been included are intended only for the use of the party to whom/which the email is addressed and may contain information that is privileged, confidential, or exempt from disclosure under applicable law. If you are not the addressee or the employee or agent of the intended recipient, you are hereby notified that you are strictly prohibited from printing, storing, disseminating, distributing, or copying this communication. If you have received this notification in error, please contact the Privacy Officer at [HIPAAprivacy@metrohealth.org](mailto:HIPAAprivacy@metrohealth.org).

**CAUTION:** This is an external email and may not be safe. If the email looks suspicious, please do not click links or open attachments and forward the email to [csc@ohio.gov](mailto:csc@ohio.gov) or click the Phish Alert

Button if available.

**From:** [Kinsey Jolliff](#)  
**To:** [Mabe, Aaron](#); [Anderson, Kimberly](#)  
**Cc:** [Allison Poulos](#)  
**Subject:** Follow-Up - 4731-11-03  
**Date:** Wednesday, November 2, 2022 4:08:17 PM  
**Attachments:** [Associations between prescription and illicit stimulant and opioid use in the United States.pdf](#)

---

Aaron/Kim,

Per our conversation last week, here are comments from Drs. Papp and Gupta. Please let me know if you have any questions.

*We recommend removal of section(B) (2) (e) based on lack of current scientific evidence that stimulants are an effective treatment modality for chronic pain and that neither the primary nor adjunctive use of stimulants in the treatment of chronic pain are recognized by FDA as approved indications. Conversely, the risks of stimulant addiction are well described in the current literature; according to an analysis of the most recent NSDUH report (attached) 30 % of patients report misusing their prescribed stimulants while only 12 % of patients prescribed opioids reported misuse. In light of current trends of increasing stimulant deaths in the U.S, unnecessary exposure to this addictive, non – proven therapy should be avoided at all costs. The opioid epidemic began similarly, in large part due to recommendations to prescribe opioids for chronic pain without supporting scientific evidence. If stimulants are allowed to be prescribed in the same manner, it is very likely that the current stimulant crisis will worsen and unnecessarily claim thousands of lives.*

Kinsey Jolliff  
The MetroHealth System  
Principal, Government Relations  
P: 614-348-7608  
[kjolliff@metrohealth.org](mailto:kjolliff@metrohealth.org)

**MetroHealth’s Mission: Leading the way to a healthier you and a healthier community through service, teaching, discovery, and teamwork.** This email and all attachments that may have been included are intended only for the use of the party to whom/which the email is addressed and may contain information that is privileged, confidential, or exempt from disclosure under applicable law. If you are not the addressee or the employee or agent of the intended recipient, you are hereby notified that you are strictly prohibited from printing, storing, disseminating, distributing, or copying this communication. If you have received this notification in error, please contact the Privacy Officer at [HIPAAprivacy@metrohealth.org](mailto:HIPAAprivacy@metrohealth.org).

**CAUTION:** This is an external email and may not be safe. If the email looks suspicious, please do not click links or open attachments and forward the email to [csc@ohio.gov](mailto:csc@ohio.gov) or click the Phish Alert Button if available.



Contents lists available at ScienceDirect

## Journal of Substance Abuse Treatment

journal homepage: [www.elsevier.com/locate/jSAT](http://www.elsevier.com/locate/jSAT)

## Associations between prescription and illicit stimulant and opioid use in the United States, 2015–2020

Riley D. Shearer<sup>a,b,\*</sup>, Abenaa Jones<sup>c</sup>, Benjamin A. Howell<sup>d,e</sup>, Joel E. Segel<sup>f,g</sup>, Tyler N. A. Winkelman<sup>b,h</sup><sup>a</sup> University of Minnesota School of Public Health, 420 Delaware St SE, Mayo Building B681, Minneapolis, MN 55455, USA<sup>b</sup> Health, Homelessness, and Criminal Justice Lab, Hennepin Healthcare Research Institute, 701 Park Ave., Suite PP7.700, Minneapolis, MN 55415, USA<sup>c</sup> Department of Human Development and Family Studies, The Pennsylvania State University, University Park, PA, USA<sup>d</sup> SEICHE Center for Health & Justice, Yale School of Medicine, 333 Cedar St, New Haven 06510, USA<sup>e</sup> Section of General Internal Medicine, Yale School of Medicine, PO Box 208025, New Haven, CT 06520, USA<sup>f</sup> Department of Health Policy and Administration, Penn State University, University Park, PA, USA<sup>g</sup> Penn State Cancer Institute, Penn State College of Medicine, Hershey, PA, USA<sup>h</sup> Division of General Internal Medicine, Department of Medicine, Hennepin Healthcare, 716 S 7th St, Minneapolis, MN 55415, USA

## ARTICLE INFO

## Keywords:

Stimulants

Prescription misuse

Cocaine

Methamphetamine

## ABSTRACT

**Introduction:** Overdose deaths involving opioids and stimulants continue to reach unprecedented levels in the United States. Although significant attention has been paid to the relationship between prescription and illicit opioid use, little work has focused on the association between prescription and illicit stimulant use. Thus, this study explores characteristics of those who use or misuse prescription stimulants and/or opioids and associations with use of cocaine, methamphetamine, and heroin.

**Methods:** We used 2015–2020 data from the National Survey on Drug Use and Health. Using adjusted multi-variable logistic regression, we estimated the associations between past year prescription stimulant or prescription opioid prescribed use and misuse; various demographic characteristics; and past-year cocaine, methamphetamine, or heroin use.

**Results:** From 2015 to 2020, 4.9 and 9.8 million US adults annually reported misusing prescription stimulants and opioids, respectively. Individuals who misused prescription stimulants were more likely to be ages 18–25 (45.8 %; 95 % CI: 44.0–47.5) than individuals who misused prescription opioids (21.7 %; 95 % CI: 20.7–22.7). We observed higher rates of cocaine use among individuals reporting prescription stimulant misuse (12.0 %; 95 % CI: 11.0–12.9) compared to those reporting prescription opioid misuse (5.7 %; 95 % CI: 5.1–6.3,  $p < 0.001$ ). Heroin use was more common among individuals with prescription opioid misuse (2.1 %; 95 % CI: 1.7–2.2) than prescription stimulant misuse (0.6 %; 95 % CI: 0.4–0.7,  $p < 0.001$ ). However, rates of methamphetamine use among individuals with prescription stimulant misuse (2.4 %; 95 % CI: 1.9–3.0) did not differ from individuals with prescription opioid misuse (2.1 %; 95 % CI: 1.7–2.5,  $p = 0.67$ ).

**Conclusions:** Prescription stimulant misuse, compared to prescription opioid misuse, was associated with higher levels of cocaine use but not methamphetamine use. Treatment providers should consider screening for other substance use disorders among people who report prescription stimulant use or misuse. Additional research should seek to understand the mechanism underlying the different associations between prescription stimulant misuse and cocaine or methamphetamine use.

## 1. Introduction

Between 2010 and 2021, a 5-fold increase has occurred in cocaine involved overdose deaths and a 18-fold increase in psychostimulant

(methamphetamine) involved overdose deaths (Hedegaard et al., 2020). In 2021 alone, an estimated 107,622 drug overdose deaths occurred. Synthetic opioids (fentanyl), methamphetamine, and cocaine were involved in approximately 71,000, 33,000, and 25,000 overdose deaths,

\* Corresponding author at: University of Minnesota Medical School, 420 Delaware St., Minneapolis, MN, USA.

E-mail address: [shear162@umn.edu](mailto:shear162@umn.edu) (R.D. Shearer).

<https://doi.org/10.1016/j.jSAT.2022.108894>

Received 27 April 2022; Received in revised form 9 August 2022; Accepted 23 September 2022

Available online 30 September 2022

0740-5472/© 2022 Elsevier Inc. All rights reserved.



respectively (National Center for Health Statistics, 2022). The increase in stimulant overdose deaths likely reflects increasing stimulant use and concurrent use with synthetic opioids (Ciccarone, 2021). Fatal overdoses are not the only adverse outcome of stimulant use. Cocaine and methamphetamine use are also associated with increased morbidity, including high rates of infectious diseases and disability (Butler et al., 2017; Shearer et al., 2020). Although new and promising pharmacologic treatments are in development for stimulant use disorder, particularly for methamphetamine use disorder (Trivedi et al., 2021), prevention of methamphetamine and cocaine use initiation remains a critical component of reducing stimulant-related morbidity and mortality (Ballester et al., 2017; Kampman, 2019). Despite the known adverse health consequences, the underlying factors associated with cocaine and methamphetamine use remain unclear.

Consistent evidence has found that heroin use is often preceded by prescription opioid misuse (Cicero et al., 2014; Lankenau, Teti, et al., 2012; Peavy et al., 2012; Pollini et al., 2011). Furthermore, prescription opioid misuse is associated with higher rates of heroin use than prescription opioid use or no use (Jones, 2013). Research has investigated comparatively less so the associations between prescription stimulant misuse and cocaine or methamphetamine use. Although parallel increases in both self-reported misuse and emergency department visits involving prescription stimulants and methamphetamine have occurred, to what extent, if any, the trends are related is unclear (Chen et al., 2016; Vivolo-Kantor et al., 2020). A retrospective study of adolescents found that illicit substance use was often preceded by misuse of prescription substances with similar psychotropic effects (Lankenau, Schrage, et al., 2012). Furthermore, a recent study of HIV-vulnerable sexual and gender minorities who have sex with men found that individuals who misused prescription stimulants had a 2.5-fold increased risk of using methamphetamine 12 months later (Westmoreland et al., 2021). However, these past studies are small, geographically limited, and focused on specific populations. The associations between prescription stimulant use and cocaine or methamphetamine use, among the broader US population, have not been well characterized in the literature.

Studies from the extant literature have broadly grouped illicit substances, with different psychotropic effects, into one category and demonstrated high rates of substance use among individuals who report prescription stimulant misuse (Chen et al., 2015; Compton et al., 2018; Wang et al., 2015). Mustaquim and colleagues documented high rates of prescription stimulant misuse among individuals who use cocaine (Mustaquim et al., 2021). However, we know little about possible differences in cocaine, methamphetamine, and heroin use among individuals who use or misuse prescription stimulants or prescription opioids. Research describing these complex relationships is needed for researchers, clinicians, and public health officials to develop prevention programs, target screening, identify treatment needs, and expand harm reduction programs.

In this study, we assessed sociodemographic and health factors among individuals with varying prescription stimulant and opioid use patterns (including no use, use, and misuse). We compared characteristics of misuse (e.g., frequency and duration) between individuals with prescription stimulant and opioid misuse. We then compared associations between prescription stimulant or opioid use/misuse and use of three substances: cocaine, methamphetamine, and heroin. We hypothesized that: 1) rates of past year cocaine, methamphetamine, and heroin use would be highest among individuals with prescription misuse compared to prescribed use or no use; and 2) prescription misuse would be associated with higher rates of substance use with similar psychotropic effects, specifically misuse of prescription stimulants would be associated with higher rates of cocaine and methamphetamine use than prescription opioid misuse, while prescription opioid misuse would be associated with higher rates of heroin use than prescription stimulant misuse.

## 2. Materials and methods

### 2.1. Data source

We used data from the National Survey on Drug Use and Health (NSDUH), a nationally representative survey of the US civilian population aged 12 and older (Substance Abuse and Mental Health Services Administration, 2020). NSDUH provides information on the use of prescription and other substances in addition to demographic information and measures of mental and physical health. To better capture rates of prescription drug misuse, the questionnaire underwent a partial redesign in 2015. For this analysis, we pooled data from 2015 through 2020 for all adult respondents aged 18 and older.

### 2.2. Prescription opioid and stimulant measures

To compare characteristics of people who report prescription stimulant versus opioid use, we generated a unique categorical variable for each prescription substance indicating varying levels of reported use. For both prescription stimulants and opioids, we categorized respondents separately into three mutually exclusive groups based on past year use including: 1) no use, 2) use without misuse (referred to as prescribed use), and 3) misuse. Misuse, often referred to as nonmedical use, is defined by NSDUH as any use in a way not directed by a doctor.

### 2.3. Substance use outcomes

The outcomes of interest were cocaine, methamphetamine, and heroin use. For each substance, we generated a unique binary variable (past-year use vs. no past-year use) based on whether an individual reported use in the past 12 months.

### 2.4. Sociodemographic, health, and prescription misuse characteristics

We examined several characteristics among people who reported prescription stimulant and opioid use and misuse. We described self-reported sociodemographic variables including gender, race/ethnicity (non-Hispanic White, non-Hispanic Black, Hispanic, and other), age, income (defined as <100 %, 100–200 %, and >200 % of the Federal Poverty Line), health insurance status, educational attainment, rural residence, housing instability, and recent criminal legal involvement (CLI). We categorized individuals as having private, Medicaid, other health insurance (e.g. Medicare or military health care), or as uninsured. Rural residence was defined as a nonmetro county using 2013 rural/urban continuum codes 4–9. Although NSDUH does not contain an explicit question on housing stability, we defined a binary variable as moving three or more times in the past year, consistent with previous literature (Frederick et al., 2014). We generated a binary variable for recent CLI, which included reports of any arrests, probation, or parole in the past year.

Given high rates of co-occurring substance misuse and physical and/or behavioral health disorders, we included indicators of severe mental illness (SMI) and self-reported health. For the NSDUH, the Substance Abuse and Mental Health Services Administration uses a validated predictive model for SMI that accounts for measures from the Kessler Psychological Distress Scale (K6) and World Health Organization Disability Assessment Scale (Kessler et al., 2003; Substance Abuse and Mental Health Services Administration, 2019). Respondents also rated their overall health as excellent, very good, good, fair, or poor. We generated a binary variable indicating individuals who reported fair or poor health.

Among those who reported prescription stimulant or opioid misuse, we further characterized the patterns of prescription misuse. To contextualize our findings with previous research describing high rates of prescription stimulant and opioid diversion as well as co-use with other substances, we examined binary variables for whether a



respondent did not have a prescription or if they co-ingested alcohol (Compton et al., 2018; McCabe et al., 2015). We also examined whether an individual misused a substance by consuming more of it than prescribed. We created three separate binary indicators for whether an individual reported taking the prescription in greater amounts, more frequently, or for longer than prescribed. Characteristics of misuse were not mutually exclusive.

### 2.5. Statistical analysis

First, we estimated the weighted prevalence of prescribed use and misuse of prescription stimulants and opioids using the sample weights provided by NSDUH. We cross tabulated these two groups to observe the overlap. We then compared the sociodemographic characteristics between each category of prescription stimulant and opioid use. Among those who reported either past-year prescription stimulant or opioid misuse, we characterized the misuse. We calculated the proportion of individuals who did not have their own prescription, used prescription stimulants or opioids with alcohol, in greater amounts, more frequently, or for longer than prescribed.

We then estimated the associations between prescribed use or misuse and past year cocaine, methamphetamine, and heroin use with separate multivariable logistic regressions. Each regression included categorical variables for no-use, prescribed use, and misuse of prescription stimulants and opioids as well as controls for sociodemographic and health characteristics. We generated predictive margins to estimate the proportion of individuals within each category of prescription use who also used cocaine, methamphetamine, or heroin. We used an adjusted Wald test to assess whether rates of cocaine, methamphetamine, or heroin use were different between people who reported prescription stimulant prescribed use or misuse compared to prescription opioid prescribed use or misuse. Because the 2020 NSDUH data collection was affected by the COVID-19 pandemic, we also include a sensitivity analysis limited to 2015–2019 data (Appendix Tables 1–4).

All analyses included primary sampling unit, strata, and weight variables to account for NSDUH's survey design. We used Stata 17 (StataCorp, College Station, TX) for all data management and analysis. Per the Hennepin Healthcare Research Institute's Policy on using publicly available, deidentified data, this study is not human subjects research.

## 3. Results

### 3.1. Prevalence of prescription opioid and stimulant use and misuse

Our unweighted sample included 241,675 adult respondents surveyed between 2015 and 2020. More individuals reported prescribed use and misuse of prescription opioids (29.4 % and 4.0 %) than prescription stimulants (4.7 % and 2.0 %) (Table 1). Among individuals who reported any use of prescription stimulants a higher percentage (30 %) reported stimulant misuse compared to the percent of individuals reporting opioid misuse (12 %) among those who reported any use of prescription opioids. An annualized weighted total of 1.4 million (95 %

CI: 1.3–1.5) people reported misusing both prescription stimulants and opioids, which represents 29 % of all individuals who reported prescription stimulant misuse.

### 3.2. Sociodemographic, health, and prescription misuse characteristics

Compared to people who misused prescription opioids, individuals who misused prescription stimulants were more likely to be white (77.2 % [95 % CI: 75.9–78.5] vs. 61.6 % [95 % CI: 61.0–62.3]) and 18 to 25 years old (45.8 % [95 % CI: 44.0–47.5] vs. 21.7 % [95 % CI: 20.7–22.7]) (Table 2). A higher proportion of individuals who misused prescription opioids identified as Hispanic (16.0 % [95 % CI: 14.9–17.3]) or Black (10.9 % [95 % CI: 10.1–12.1]) compared to individuals who misused prescription stimulants (11.6 % [95 % CI: 10.5–12.8] and 4.7 % [95 % CI: 4.0–5.4], respectively). Individuals who misused prescription stimulants were more likely to have private insurance (68.4 % [95 % CI: 66.9–69.8]) and incomes above 200 % of the federal poverty line (64.0 % [95 % CI: 62.4–65.6]), compared to individuals who misused prescription opioids (54.3 % [95 % CI: 52.8–55.7] and 57.9 % [95 % CI: 56.2–59.5], respectively). Rates of unstable housing and CLI did not differ among individuals who misused prescription stimulants (6.6 % [95 % CI: 5.8–7.5] and 11.1 % [95 % CI: 10.0–12.3]) or misused prescription opioids (6.1 % [95 % CI: 5.5–6.8] and 11.7 % [95 % CI: 10.8–12.7]). Individuals who misused prescription opioids were more likely to report fair or poor health (19.9 % [95 % CI: 18.5–21.4]) compared to individuals who misused prescription stimulants (9.9 % [95 % CI: 8.8–11.0]).

We compared characteristics of misuse between individuals who reported prescription opioid or stimulant misuse. Individuals were more likely to misuse prescription stimulants without their own prescription (80.2 % [95 % CI: 78.8–81.6]) than prescription opioids (58.2 % [95 % CI: 56.7–59.7]) (Table 3). Conversely, compared to prescription stimulants, prescription opioids were more likely to be misused by taking greater amounts than prescribed (20.1 %; [95 % CI: 19.0–21.3] vs. 11.3 % [95 % CI: 10.2–12.5]), more frequently than prescribed (15.4 % [95 % CI: 14.4–16.4] vs. 7.1 % [95 % CI: 6.1–8.2]), and for longer than prescribed (13.4 % [95 % CI: 12.3–14.4] vs. 3.5 % [95 % CI: 2.9–4.1]). Alcohol was more commonly used with prescription stimulants (13.1 % [95 % CI: 12.0–14.2]) than prescription opioids (8.9 % [95 % CI: 8.1–9.7]). The sociodemographic, health, and misuse characteristics were largely unaffected when restricting the sample to 2015–2019 data (Appendix Tables 2 and 3).

### 3.3. Cocaine, methamphetamine, and heroin use among people with no prescription use, prescription use, and prescription misuse

Individuals with neither prescription opioid nor stimulant use had the lowest rates of cocaine, methamphetamine, and heroin use: 1.1 % (95 % CI: 1.0–1.2), 0.4 % (95 % CI: 0.4–0.5), and 0.1 % (95 % CI: 0.1–0.1), respectively (Table 4). Compared to prescribed use of opioids, prescribed use of stimulants was associated with higher rates of cocaine (3.4 % [95 % CI: 3.1–3.8] vs 2.1 % [95 % CI: 1.9–2.2],  $p < 0.001$ ), methamphetamine (1.2 % [95 % CI: 1.0–1.4] vs 0.5 % [95 % CI:

**Table 1**

Annualized weighted adults reporting prescription stimulant and opioid no use, prescribed use, and misuse (millions of individuals) – United States, 2015–2020.

		Prescription stimulant use			Total
		No use	Prescribed use	Misuse	
Prescription opioid use	No use	157.2 (63.5 %) (155.6–158.8)	5.3 (2.1 %) (5.1–5.5)	2.3 (0.9 %) (2.2–2.5)	164.9 (66.6 %) (163.2–166.6)
	Use	66.6 (26.9 %) (65.8–67.5)	5.2 (2.1 %) (4.9–5.4)	1.1 (0.4 %) (1.0–1.2)	72.9 (29.4 %) (72.0–73.8)
	Misuse	7.3 (2.9 %) (7.0–7.6)	1.1 (0.5 %) (1.0–1.2)	1.4 (0.6 %) (1.3–1.5)	9.8 (4.0 %) (9.5–10.2)
	Total	231.1 (93.4 %) (229.2–233.1)	11.6 (4.7 %) (11.2–12.0)	4.9 (2.0 %) (4.7–5.1)	

**Table 2**  
Individual sociodemographic and health characteristics by prescription substance use categories – United States, 2015–2020.

Characteristic	Weighted % (95 % CI)					
	Past year prescription stimulants			Past year prescription opioids		
	No use	Prescribed use	Misuse	No use	Prescribed use	Misuse
Weighted percentage	93.4 % (93.2–93.5)	4.7 % (4.5–4.8)	2.0 % (1.9–2.0)	66.6 % (66.3–66.9)	29.4 % (29.1–29.7)	4.0 % (3.8–4.1)
Male	48.4 (48.0–48.8)	42.0 (40.6–43.4)	56.3 (54.8–57.7)	49.9 (49.5–50.3)	43.9 % (43.3–44.6)	53.3 % (51.8–54.8)
Race/ethnicity						
White	62.9 (62.3–63.4)	74.0 (72.6–75.3)	77.2 (75.9–78.5)	61.6 (61.0–62.3)	67.8 (67.0–68.5)	67.2 (65.8–68.6)
Black	12.3 (11.9–12.7)	7.9 (7.2–8.6)	4.7 (4.0–5.4)	11.6 (11.2–12.0)	12.8 (12.2–13.3)	10.9 (10.1–12.1)
Hispanic	16.4 (16.0–16.9)	12.4 (11.3–13.6)	11.6 (10.5–12.8)	17.5 (17.1–17.9)	13.1 (12.6–13.7)	16.0 (14.9–17.3)
Other	8.4 (8.2–8.7)	5.7 (5.1–6.4)	6.5 (5.9–7.3)	9.3 (9.0–9.6)	6.3 (6.1–6.6)	5.8 (5.2–6.5)
Age (years)						
18–25	12.8 (12.6–13.0)	20.4 (19.4–21.4)	45.8 (44.0–47.5)	15.0 (14.8–15.2)	10.0 (9.8–10.3)	21.7 (20.7–22.7)
26–34	15.5 (15.2–15.7)	20.7 (20.0–21.5)	30.4 (28.6–32.3)	16.5 (16.2–16.8)	13.8 (13.5–14.2)	23.8 (22.7–24.9)
35–49	24.7 (24.4–25.0)	26.1 (25.0–27.1)	17.2 (15.6–19.0)	24.7 (24.4–25.0)	24.2 (23.7–24.8)	27.2 (26.1–28.3)
50+	47.0 (46.6–47.5)	32.8 (31.4–34.3)	6.6 (5.2–8.5)	43.8 (43.4–44.3)	51.9 (51.1–52.7)	27.3 (25.6–29.0)
Income						
<100 % FPL	14.1 (13.8–14.4)	14.9 (13.9–15.8)	18.4 (17.1–19.9)	13.6 (13.3–14.0)	14.7 (14.2–15.2)	20.1 (19.0–21.3)
100–200 % FPL	19.6 (19.3–19.9)	18.8 (17.5–20.1)	17.6 (16.2–19.0)	19.1 (18.8–19.4)	20.1 (19.6–20.5)	22.0 (20.7–23.4)
>200 % FPL	66.4 (65.9–66.8)	66.4 (64.9–67.8)	64.0 (62.4–65.6)	67.3 (66.8–67.8)	65.2 (64.5–65.9)	57.9 (56.2–59.5)
Insurance status						
Private	65.8 (65.3–66.2)	67.3 (65.6–68.9)	68.4 (66.9–69.8)	67.2 (66.8–67.7)	64.5 (63.8–65.1)	54.3 (52.8–55.7)
Medicaid	13.2 (12.9–13.4)	14.9 (13.8–16.1)	13.8 (12.5–15.2)	11.8 (11.5–12.0)	15.5 (15.1–16.0)	21.8 (20.6–23.1)
Other	11.0 (10.7–11.2)	9.4 (8.4–10.5)	4.8 (4.2–5.5)	10.1 (9.9–10.4)	12.6 (12.2–13.0)	7.9 (7.0–8.9)
Uninsured	10.1 (9.9–10.3)	8.4 (7.6–9.3)	13.0 (12.2–13.9)	10.9 (10.6–11.2)	7.5 (7.2–7.7)	16.1 (15.1–17.0)
Education						
Less than HS	12.7 (12.4–13.0)	10.3 (9.1–11.6)	6.9 (6.0–8.0)	12.7 (12.4–13.0)	11.7 (11.4–12.2)	14.1 (13.0–15.2)
HS	25.7 (25.4–26.0)	20.2 (19.2–21.3)	19.4 (18.1–20.7)	25.0 (24.6–25.3)	26.1 (25.5–26.7)	25.8 (24.4–27.3)
Some college	30.2 (29.9–30.5)	38.3 (37.0–39.7)	40.9 (39.3–42.5)	28.9 (28.5–29.3)	34.2 (33.6–34.8)	37.2 (35.6–38.8)
College grad	31.4 (30.9–31.9)	31.2 (30.0–32.4)	32.8 (31.2–34.4)	33.4 (32.9–34.0)	28.0 (27.4–28.6)	23.0 (21.5–24.5)
Rural residence	14.7 (14.3–15.1)	13.7 (12.6–14.9)	10.2 (9.4–11.1)	14.0 (13.6–14.5)	15.8 (15.3–16.4)	14.1 (13.1–15.2)
Unstably housed	2.1 (2.1–2.2)	3.9 (3.4–4.4)	6.6 (5.8–7.5)	2.0 (1.9–2.1)	2.5 (2.3–2.7)	6.1 (5.5–6.8)
Criminal legal involvement	2.6 (2.5–2.7)	4.8 (4.5–5.2)	11.1 (10.0–12.3)	2.2 (2.1–2.3)	3.3 (3.0–3.5)	11.7 (10.8–12.7)
Severe mental illness	4.1 (3.9–4.2)	13.0 (12.2–13.8)	15.7 (14.4–17.1)	3.2 (3.1–3.4)	6.5 (6.2–6.8)	16.4 (15.4–17.5)
Fair or poor health	14.0 (13.7–14.3)	17.2 (16.1–18.4)	9.9 (8.8–11.0)	10.5 (10.2–10.9)	21.2 (20.6–21.9)	19.9 (18.5–21.4)

**Table 3**  
Characteristics of prescription stimulant and opioid misuse – United States, 2015–2020.

	Weighted % (95 % CI)	
	Prescription stimulant misuse (N = 7685)	Prescription opioid misuse (N = 11,941)
Without prescription	80.2 (78.8–81.6)	58.2 (56.7–59.7)
With alcohol	13.1 (12.0–14.2)	8.9 (8.1–9.7)
Greater amounts	11.3 (10.2–12.5)	20.1 (19.0–21.3)
More often	7.1 (6.1–8.2)	15.4 (14.4–16.4)
Longer than prescribed	3.5 (2.9–4.1)	13.4 (12.3–14.4)

The proportion of individuals who reported each type of misuse among those who reported prescription stimulant or opioid misuse.

**Table 4**  
Rates of past year cocaine, methamphetamine and heroin use by prescription substance use categories – United States, 2015–2020.

Characteristic	Weighted % (95 % CI)				
	No use	Past year prescription stimulants		Past year prescription opioids	
		Prescribed use	Misuse	Prescribed use	Misuse
Cocaine use	1.1 (1.0–1.2)	3.4 (3.1–3.8) <sup>a,c</sup>	12.0 (11.0–12.9) <sup>a,d</sup>	2.1 (1.9–2.2) <sup>a</sup>	5.7 (5.1–6.3) <sup>a</sup>
Methamphetamine use	0.4 (0.4–0.5)	1.2 (1.0–1.4) <sup>a,c</sup>	2.4 (1.9–3.0) <sup>a</sup>	0.5 (0.4–0.6)	2.1 (1.8–2.5) <sup>a</sup>
Heroin use	0.1 (0.1–0.1)	0.4 (0.3–0.5) <sup>b,c</sup>	0.6 (0.4–0.7) <sup>a,d</sup>	0.2 (0.2–0.3) <sup>a</sup>	2.1 (1.7–2.5) <sup>a</sup>

Each row represents a unique multivariable logistic regression model estimating a rates of use for the given substance (left column), controlling for past year stimulant use or misuse and past year prescription opioid use or misuse. Adjusted proportions were calculated using post-estimation predictive margins.

<sup>a</sup> Different than no use  $p < 0.001$ .

<sup>b</sup> Different than no use  $p < 0.01$ .

<sup>c</sup> Different than prescription opioid use  $p < 0.001$ .

<sup>d</sup> Different than prescription opioid misuse  $p < 0.001$ .

0.4–0.6],  $p < 0.001$ ), and heroin use (0.3 % [95 % CI: 0.2–0.4] vs 0.2 % [95 % CI: 0.2–0.3],  $p < 0.001$ ). Among individuals who reported prescription stimulant misuse, cocaine use was twice as common than among individuals who reported prescription opioid misuse (12.0 % [95 % CI: 11.0–12.9] vs. 5.7 % [95 % CI: 5.1–6.3],  $p < 0.001$ ). Among individuals who reported prescription opioid misuse, heroin use was more prevalent (2.1 % [95 % CI: 1.7–2.5]) compared to individuals with prescription stimulant misuse (0.6 % [95 % CI: 0.4–0.7],  $p < 0.001$ ). Methamphetamine use did not differ between individuals reporting prescription stimulant misuse (2.4 % [95 % CI: 1.9–3.0]) and prescription opioid misuse (2.1 % [95 % CI: 1.7–2.5],  $p = 0.67$ ). In a sensitivity analysis restricted to 2015–2019 data, the magnitude and statistical significance of these associations did not substantially change (Appendix Table 4).

#### 4. Discussion

In a nationally representative sample from 2015 to 2020, we found higher rates of cocaine, methamphetamine, and heroin use among individuals who reported either prescription stimulant prescribed use or misuse compared to no use. These findings are consistent with previous results demonstrating high rates of prescription stimulant misuse among individuals with methamphetamine or cocaine use (Jones, 2020; Mustaquim et al., 2021). Additionally, we show that a larger percentage of people who misuse prescription stimulants will use cocaine compared to people who misuse prescription opioids. We build upon results from several smaller surveys that identified a similar increasing risk of cocaine use among individuals with prescription stimulant use (3–4 times as likely) and misuse (13 times as likely) compared to no use (Kelly et al., 2014; Looby et al., 2014; Sepúlveda et al., 2011). This gradient of risk for cocaine and methamphetamine use mirrors heroin-specific findings (Jones, 2013). We show an increased risk of cocaine, methamphetamine, and heroin use for individuals with prescription misuse compared to prescribed use and for prescribed use compared to no use. Our findings emphasize the importance of screening for cocaine and methamphetamine use among patients who are prescribed, or suspected to misuse, stimulants.

We found associations between cocaine and heroin, but not methamphetamine use, and misuse of prescription substances with similar psychotropic effects. Cocaine use was twice as common among individuals with prescription stimulant misuse compared to prescription opioid misuse and heroin use was almost four-times as common among individuals with prescription opioid misuse compared to prescription stimulant misuse. These findings build on extensive opioid-related research, which has suggested prescription opioid misuse may contribute to heroin use (Cicero et al., 2014; Clayton et al., 2019; Jones, 2013; Lankenau, Teti, et al., 2012; Peavy et al., 2012; Pollini et al., 2011), by showing a similar relationship between prescription stimulant and cocaine use. Interestingly, the risk of methamphetamine use did not vary between people who reported prescription stimulant or opioid misuse. Although we cannot determine causal relationships with these data, this finding maybe due to differences in the social environment, such as experiencing unstable housing, or high rates of methamphetamine and opioid polysubstance use rather than methamphetamine's specific psychotropic effect (Doran et al., 2018; Shearer et al., 2020). As overdose deaths involving cocaine and methamphetamine continue to rise, future research should further explore the divergent patterns of cocaine and methamphetamine use among individuals who also misuse prescription stimulants. Our findings suggest that different prevention policies tailored to cocaine and methamphetamine may be warranted.

We observed a high prevalence of prescription stimulant and opioid co-use. More than half of the individuals who reported prescription stimulant prescribed use or misuse also reported prescription opioid prescribed use or misuse. It may be important to discuss the risks and screen for opioid use, in addition to cocaine and methamphetamine use, among individuals who use prescription stimulants. This overlap between prescription substances is similar to recent findings of a rise in concurrent methamphetamine and heroin use (Ellis et al., 2018; Gladden et al., 2019; Jones et al., 2020). The prevalence of concurrent stimulant and opioid misuse warrants public health efforts that address the harms of substance use to account for possible co-use. This could include improving addiction treatment programs, which often address only a single substance use disorder, and expanding harm reduction programs to individuals who are prescribed stimulants.

Clinicians who provide care to patients who misuse prescription stimulants should be aware of the possibility of the use of multiple other substances and consider screening for additional substance use. The findings from this study inform populations who maybe at greater risk for prescription stimulant misuse. Misuse was more common among males, white individuals, young adults aged 18–25, and individuals experiencing unstable housing or recent CLI. Consistent with previous

research, we also found that the majority of individuals who misused prescription stimulants did not have their own prescription (Compton et al., 2018; Lasopa et al., 2015; Schepis et al., 2019). This finding underscores the importance of discussing the risks of prescription diversion among patients prescribed stimulants and screening at-risk individuals regardless of whether they are prescribed stimulant medications. Brief clinical practice strategies may be effective at reducing the likelihood of stimulant diversion (Molina et al., 2020). Additionally, given the dramatic rise in counterfeit pills containing fentanyl, seized by law enforcement, individuals who misuse stimulants without their own prescription should be counseled on the risks of accidental exposure and overdose (Palamar et al., 2022).

This study has important limitations. As NSDUH relies on self-reported measures for substance use our results could be biased if individuals did not remember or were unwilling to share accurate substance use history. To reduce this bias, the NSDUH survey uses an Audio Computer Assisted Self-Interview Software to gather responses to sensitive questions. Due to the cross-sectional nature of NSDUH and because the study did not record the age at which a respondent began misusing prescription substances, we are unable to assess whether prescription stimulant or opioid misuse initially preceded, co-occurred, or followed cocaine, methamphetamine, or heroin use. Without this chronological information we cannot analyze whether prescription misuse led to other substance use, but we are able to estimate associations between current use. Additionally, NSDUH does not contain information regarding the medical diagnosis for which stimulants or opioids are prescribed. We, therefore, cannot control for these confounding health conditions. However, we did analyze measures of health such as severe mental illness and self-reported physical health. Finally, because of the COVID-19 pandemic, the 2020 NSDUH data collection underwent significant changes. Specifically, no data were collected between mid-March through September. Beginning in October, the NSDUH used web rather than in-person data collection. This may bias our results if the 2020 sample of respondents differed or if reported past-year substance use differently compared to respondents in previous years. However, including the most recent data is important to inform the public health response to a rapidly changing overdose crisis. Additionally, we include a sensitivity analysis limited to 2015–2019 data, which would not be affected by these methodological changes.

#### 5. Conclusion

In a nationally representative sample, we found high rates of cocaine and methamphetamine use among individuals who used or misused prescription stimulants. Cocaine use was substantially higher among individuals who misused prescription stimulants compared to prescription opioids. As cocaine and methamphetamine involved overdose deaths continue to increase in the United States, individuals who use or misuse prescription stimulants may be at an increased risk. These findings further our understanding of the relationship between prescription use and other substances. These associations are important for the development of targeted screening, prevention, and harm reduction programs to reduce the morbidity and mortality that stimulant use causes. As the substance use crisis in the United States evolves and stimulants are increasingly involved, researchers and treatment providers need to understand the relationships between prescription stimulant misuse and the use of cocaine and methamphetamine.

#### Funding

This work was supported by NIH MSTP grant T32 GM008244 (R.D. S).

#### CRedit authorship contribution statement

Riley D. Shearer: Conceptualization, Methodology, Formal analysis,

Writing – original draft. **Abenaa Jones:** Conceptualization, Writing – review & editing. **Benjamin A. Howell:** Conceptualization, Writing – review & editing. **Joel E. Segel:** Conceptualization, Writing – review & editing. **Tyler N.A. Winkelman:** Conceptualization, Data curation, Writing – review & editing, Supervision.

## Declaration of competing interest

None.

## Appendix A. Supplementary data

Supplementary data to this article can be found online at <https://doi.org/10.1016/j.jsat.2022.108894>.

## References

- Ballester, J., Valentine, G., & Sofuoglu, M. (2017). Pharmacological treatments for methamphetamine addiction: Current status and future directions. *Expert Review of Clinical Pharmacology*, 10(3), 305–314. <https://doi.org/10.1080/17512433.2017.1268916>
- Butler, A. J., Rehm, J., & Fischer, B. (2017). Health outcomes associated with crack-cocaine use: Systematic review and meta-analysis. *Drug and Alcohol Dependence*, 180, 401–416. <https://doi.org/10.1016/j.drugalcdep.2017.08.036>
- Chen, L.-Y., Crum, R. M., Strain, E. C., CalebAlexander, G., Kaufmann, C., & Mojtabei, R. (2016). Prescriptions, nonmedical use, and emergency department visits involving prescription stimulants. *The Journal of Clinical Psychiatry*, 77(3), e297–e304. <https://doi.org/10.4088/JCP.14m09291>
- Chen, L.-Y., Crum, R. M., Strain, E. C., Martins, S. S., & Mojtabei, R. (2015). Patterns of concurrent substance use among adolescent nonmedical ADHD stimulant users. *Addictive Behaviors*, 49, 1–6. <https://doi.org/10.1016/j.addbeh.2015.05.007>
- Ciccarone, D. (2021). The rise of illicit fentanyl, stimulants and the fourth wave of the opioid overdose crisis. *Current Opinion in Psychiatry*, 34(4), 344–350. <https://doi.org/10.1097/YCO.0000000000000717>
- Cicero, T. J., Ellis, M. S., Surratt, H. L., & Kurtz, S. P. (2014). The changing face of heroin use in the United States: A retrospective analysis of the past 50 years. *JAMA Psychiatry*, 71(7), 821–826. <https://doi.org/10.1001/jamapsychiatry.2014.366>
- Clayton, H. B., Bohm, M. K., Lowry, R., Ashley, C., & Ethier, K. A. (2019). Prescription opioid misuse associated with risk behaviors among adolescents. *American Journal of Preventive Medicine*, 57(4), 533–539. <https://doi.org/10.1016/j.amepre.2019.05.017>
- Substance Abuse and Mental Health Services Administration, R. N. (2019). *Key substance use and mental health indicators in the United States: Results from the 2018 National Survey on Drug Use and Health. HHS publication no. PEP19-5068, NSDUH Series H-54. 82.*
- Compton, W. M., Han, B., Blanco, C., Johnson, K., & Jones, C. M. (2018). Prevalence and correlates of prescription stimulant use, misuse, use disorders, and motivations for misuse among adults in the U.S. *The American Journal of Psychiatry*, 175(8), 741–755. <https://doi.org/10.1176/appi.ajp.2018.17091048>
- Doran, K. M., Rahai, N., McCormack, R. P., Milian, J., Shelley, D., Rotrosen, J., & Gelberg, L. (2018). Substance use and homelessness among emergency department patients. *Drug and Alcohol Dependence*, 188, 328–333. <https://doi.org/10.1016/j.drugalcdep.2018.04.021>
- Ellis, M. S., Kasper, Z. A., & Cicero, T. J. (2018). Twin epidemics: The surging rise of methamphetamine use in chronic opioid users. *Drug and Alcohol Dependence*, 193, 14–20. <https://doi.org/10.1016/j.drugalcdep.2018.08.029>
- Frederick, T. J., Chwalek, M., Hughes, J., Karabanow, J., & Kidd, S. (2014). How stable is stable? Defining and measuring housing stability. *Journal of Community Psychology*, 42(8), 964–979. <https://doi.org/10.1002/jcop.21665>
- Gladden, R. M., O'Donnell, J., Mattson, C. L., & Seth, P. (2019). Changes in opioid-involved overdose deaths by opioid type and presence of benzodiazepines, cocaine, and methamphetamine—25 states, July–December 2017 to January–June 2018. *MMWR. Morbidity and Mortality Weekly Report*, 68(34), 737–744. <https://doi.org/10.15585/mmwr.mm6834a2>
- Hedegaard, H., Miniño, A. M., & Warner, M. (2020). *Drug overdose deaths in the United States, 1999–2019. NCHS Data Brief, 394, 1–8.*
- Jones, C. M. (2013). Heroin use and heroin use risk behaviors among nonmedical users of prescription opioid pain relievers – United States, 2002–2004 and 2008–2010. *Drug and Alcohol Dependence*, 132(1–2), 95–100. <https://doi.org/10.1016/j.drugalcdep.2013.01.007>
- Jones, C. M. (2020). Patterns and characteristics of methamphetamine use among adults—United States, 2015–2018. *MMWR. Morbidity and Mortality Weekly Report*, 69. <https://doi.org/10.15585/mmwr.mm6912a1>
- Jones, C. M., Underwood, N., & Compton, W. M. (2020). Increases in methamphetamine use among heroin treatment admissions in the United States, 2008–17. *Addiction*, 115(2), 347–353. <https://doi.org/10.1111/add.14812>
- Kampman, K. M. (2019). The treatment of cocaine use disorder. *Science Advances*, 5(10). <https://doi.org/10.1126/sciadv.aax1532>
- Kelly, B. C., Wells, B. E., Pawson, M., LeClair, A., & Parsons, J. T. (2014). Combinations of prescription drug misuse and illicit drugs among young adults. *Addictive Behaviors*, 39(5), 941–944. <https://doi.org/10.1016/j.addbeh.2013.12.003>
- Kessler, R. C., Barker, P. R., Colpe, L. J., Epstein, J. F., Gfroerer, J. C., Hiripi, E., Howes, M. J., Normand, S.-L. T., Manderscheid, R. W., Walters, E. E., & Zaslavsky, A. M. (2003). Screening for serious mental illness in the general population. *Archives of General Psychiatry*, 60(2), 184–189. <https://doi.org/10.1001/archpsyc.60.2.184>
- Lankenau, S. E., Schrage, S. M., Silva, K., Kecojevic, A., Jackson Bloom, J., Wong, C., & Iverson, E. (2012). Misuse of prescription and illicit drugs among high-risk young adults in Los Angeles and New York. *Journal of Public Health Research*, 1(1), 6. <https://doi.org/10.4081/jphr.2012.e6>
- Lankenau, S. E., Teti, M., Silva, K., Bloom, J. J., Harocopos, A., & Treese, M. (2012). Initiation into prescription opioid misuse amongst young injection drug users. *International Journal of Drug Policy*, 23(1), 37–44. <https://doi.org/10.1016/j.drugpo.2011.05.014>
- Lasopa, S. O., Striley, C. W., & Cottler, L. B. (2015). Diversion of prescription stimulant drugs among 10–18-year-olds. *Current Opinion in Psychiatry*, 28(4), 292–298. <https://doi.org/10.1097/YCO.0000000000000172>
- Looby, A., Kassman, K. T., & Earleywine, M. (2014). Do negative stimulant-related attitudes vary for prescription stimulants and cocaine among college students? *Addictive Behaviors*, 39(6), 1100–1105. <https://doi.org/10.1016/j.addbeh.2014.03.012>
- McCabe, S. E., West, B. T., Schepis, T. S., & Teter, C. J. (2015). Simultaneous co-ingestion of prescription stimulants, alcohol and other drugs: A multi-cohort national study of US adolescents. *Human Psychopharmacology*, 30(1), 42–51. <https://doi.org/10.1002/hup.2449>
- Molina, B. S. G., Kipp, H. L., Joseph, H. M., Engster, S. A., Harty, S. C., Dawkins, M., Lindstrom, R. A., Bauer, D. J., & Bangalore, S. S. (2020). Stimulant diversion risk among college students treated for ADHD: Primary care provider prevention training. *Academic Pediatrics*, 20(1), 119–127. <https://doi.org/10.1016/j.acap.2019.06.002>
- Mustaquim, D., Jones, C. M., & Compton, W. M. (2021). Trends and correlates of cocaine use among adults in the United States, 2006–2019. *Addictive Behaviors*, 120, Article 106950. <https://doi.org/10.1016/j.addbeh.2021.106950>
- National Center for Health Statistics. (2022). U.S. overdose deaths in 2021 increased half as much as in 2020—But are still up 15%. Centers for Disease Control and Prevention. [https://www.cdc.gov/nchs/pressroom/nchs\\_press\\_releases/2022/2022\\_05.htm](https://www.cdc.gov/nchs/pressroom/nchs_press_releases/2022/2022_05.htm)
- Palamar, J. J., Ciccarone, D., Rutherford, C., Keyes, K. M., Carr, T. H., & Cottler, L. B. (2022). Trends in seizures of powders and pills containing illicit fentanyl in the United States, 2018 through 2021. *Drug and Alcohol Dependence*, 234, Article 109398. <https://doi.org/10.1016/j.drugalcdep.2022.109398>
- Peavy, K. M., Banta-Green, C. J., Kingston, S., Hanrahan, M., Merrill, J. O., & Coffin, P. O. (2012). “Hooked on” prescription-type opiates prior to using heroin: Results from a survey of syringe exchange clients. *Journal of Psychoactive Drugs*, 44(3), 259–265. <https://doi.org/10.1080/02791072.2012.704591>
- Pollini, R. A., Banta-Green, C. J., Cuevas-Mota, J., Metzner, M., Teshale, E., & Garfein, R. S. (2011). Problematic use of prescription-type opioids prior to heroin use among young heroin injectors. *Substance Abuse and Rehabilitation*, 2, 173–180. <https://doi.org/10.2147/SAR.S24800>
- Schepis, T. S., Wilens, T. E., & McCabe, S. E. (2019). Prescription drug misuse sources of controlled medications in adolescents RH = adolescent prescription misuse sources. *Journal of the American Academy of Child and Adolescent Psychiatry*, 58(7), 670–680. <https://doi.org/10.1016/j.jaac.2018.09.438>
- Sepúlveda, D. R., Thomas, L. M., McCabe, S. E., Cranford, J. A., Boyd, C. J., & Teter, C. J. (2011). Misuse of prescribed stimulant medication for ADHD and associated patterns of substance use: Preliminary analysis among college students. *Journal of Pharmacy Practice*, 24(6), 551–560. <https://doi.org/10.1177/0897190011426558>
- Shearer, R. D., Howell, B. A., Bart, G., & Winkelman, T. N. A. (2020). Substance use patterns and health profiles among US adults who use opioids, methamphetamine, or both, 2015–2018. *Drug and Alcohol Dependence*, 214, Article 108162. <https://doi.org/10.1016/j.drugalcdep.2020.108162>
- Substance Abuse and Mental Health Services Administration. (2020). *2019 national survey on drug use and health public use file codebook.*
- Trivedi, M. H., Walker, R., Ling, W., dela Cruz, A., Sharma, G., Carmody, T., Ghitza, U. E., Wahle, A., Kim, M., Shores-Wilson, K., Sparenborg, S., Coffin, P., Schmitz, J., Wiest, K., Bart, G., Sonne, S. C., Wakhlu, S., Rush, A. J., Nunes, E. V., & Shoptaw, S. (2021). Bupropion and naltrexone in methamphetamine use disorder. *New England Journal of Medicine*, 384(2), 140–153. <https://doi.org/10.1056/NEJMoa2020214>
- Vivolo-Kantor, A. M., Hoots, B. E., Seth, P., & Jones, C. M. (2020). Recent trends and associated factors of amphetamine-type stimulant overdoses in emergency departments. *Drug and Alcohol Dependence*, 216, Article 108323. <https://doi.org/10.1016/j.drugalcdep.2020.108323>
- Wang, Y., Cottler, L. B., & Striley, C. W. (2015). Differentiating patterns of prescription stimulant medical and nonmedical use among youth 10–18 years of age. *Drug and Alcohol Dependence*, 157, 83–89. <https://doi.org/10.1016/j.drugalcdep.2015.10.006>
- Westmoreland, D. A., Goldshear, J. L., Carrico, A. W., & Grov, C. (2021). Associations of prescription stimulant misuse with subsequent methamphetamine use among a U.S. cohort of HIV-vulnerable sexual and gender minorities who have sex with men. *Drug and Alcohol Dependence*, 226, Article 108841. <https://doi.org/10.1016/j.drugalcdep.2021.108841>





October 13, 2022

Ms. Kimberly Anderson, Esq.  
State Medical Board of Ohio  
30 East Broad Street  
3<sup>rd</sup> Floor  
Columbus, OH 43215

**RE: Rule: 4731-11-04**

*Submitted electronically via: Kimberly.Anderson@med.ohio.gov*

Dear Ms. Anderson:

Cleveland Clinic is a not-for-profit, integrated healthcare system dedicated to patient-centered care, teaching and research. Cleveland Clinic has been caring for patients struggling with obesity for many years. To support these patients, Cleveland Clinic employs more than 40 physicians who are specifically licensed in obesity medicine and who are certified by the American Board of Obesity Medicine. Cleveland Clinic also employs more than 10 advanced practice providers (APPs) whose practice is dedicated to seeing patients with obesity and who are licensed by the Ohio State Medical Board to prescribe anti-obesity medications.

We are pleased with the Board's amendments and redrafting of Rule 4731-11-04. We believe that the revisions are in accordance with the suggestions made to the Board by several organizations and physicians who care and advocate for patients with obesity in Ohio. We agree that phentermine and other sympathomimetics used in the management of obesity are not for short-term weight loss, rather they are for the long-term treatment of the chronic disease of obesity.

**4731-11-04(C) – Proposed Language**

A physician may utilize a schedule III or IV controlled substance short term anorexiant, that bears appropriate F.D.A. approved labeling for weight loss, in the treatment of obesity as an adjunct, in a regimen of weight reduction based on caloric restriction, provided that:

**Cleveland Clinic Comments**

We urge the Board to modify the language to reflect the fact that weight reduction based on caloric restrictions is not always the chosen intervention, and that comprehensive lifestyle interventions include making healthy changes in diet, physical activity, sleep and circadian rhythm and stress are often the chosen course of treatment. Each of these lifestyle factors alone may help with health and weight loss, but it varies in individuals with obesity.

Consistent with these comments, we suggest the agency instead adopt the following language:  
A prescriber may utilize a schedule III or IV controlled substance that bears appropriate F.D.A. approved labeling for weight loss, in the treatment of obesity as an adjunct, ~~in a regimen of weight reduction based on caloric restriction~~ to a lifestyle intervention, provided that:

Proposed Language

**4731-11-04(C)(2)**

The prescriber shall personally furnish controlled substances for weight reduction or chronic weight management. For any controlled substance that is personally furnished, the prescriber shall not exceed a total of two thousand five hundred dosage units in any thirty-day period and shall not in any seventy-two hour period, personally furnish an amount that exceeds the amount necessary for the patient's use in a seventy-two hour period. Dosage unit means any of the following:

- (a) A single pill, capsule, ampule, or tablet;
- (b) In the case of a liquid solution, one milliliter;
- (c) In the case of a cream, lotion or gel, one gram; or
- (d) Any other form of administration available as a single unit.

Cleveland Clinic Comments: We suggest that phentermine follow the prescribing pattern that is currently used for Vyvanse, where three prescriptions can be issued at one time. We don't think obesity should be treated differently than other diseases.

Proposed Language

**4731-11-04 (C)(4)(a)**

The prescriber shall assess the patient at least once every three months and shall obtain the patient's weight, blood pressure, pulse, heart and lungs. The findings shall be entered in the patient's record.

Cleveland Clinic Comments:

Patients have become accustomed to telehealth and are adept at using heart rate and blood pressure monitors at home to assess the presence of uncommon side effect with this medication.

Consistent with these comments, we suggest the agency instead adopt the following language:

The prescriber shall assess the patient at least once every three months and shall obtain the patient's weight, blood pressure, and heart rate, ~~heart and lungs~~. The findings shall be entered in the patient's record.

Again, we appreciate the ongoing discussions and amendments the Board has made to Rule 4731-11-04. We believe these changes are a significant improvement and will provide patients with obesity in Ohio with appropriate care. Please do not hesitate to contact us if you need additional information.

Sincerely,



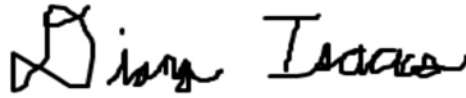
Barto Burguera, M.D. Ph.D  
Chairman Endocrinology & Metabolism Institute  
Professor of Medicine, Cleveland Clinic Lerner College of Medicine



W. Scott Butsch, M.D. MSc. FTOS  
Director of Obesity Medicine, Bariatric and Metabolic Institute



Marcio L. Griebeler, M.D.  
Director, Obesity EMI Programs



Diana Isaacs, PharmD, BCPS, BCACP, BC-ADM, CDE  
Clinical Pharmacy Specialist

**From:** [Anderson, Kimberly](#)  
**To:** ["dhoffman@gmx.com"](mailto:dhoffman@gmx.com); [CSIPublicComments](#)  
**Subject:** RE: Timeline question re : OAC 4731-11-04 : Repeal of 12 week limit on phentermine  
**Date:** Friday, October 7, 2022 9:56:00 AM

---

Ms. Hoffman-

Thank you for your comments. They will be shared with the Medical Board.

After the rules are completed with the Common Sense Initiative, they must next be filed with the Joint Committee on Agency Rule Review. The JCARR review process is a minimum of 65 days.

Kimberly Anderson  
Chief Legal Counsel  
State Medical Board of Ohio  
30 East Broad Street, 3rd Floor  
Columbus, Ohio 43215  
o: 614-466-7207  
c: 614-230-9077  
[Kimberly.Anderson@med.ohio.gov](mailto:Kimberly.Anderson@med.ohio.gov)

Confidentiality Notice: This message is intended for use only by the individual or entity to whom or which it is addressed and may contain information that is privileged, confidential and/or otherwise exempt from disclosure under applicable law. If the reader of this message is not the intended recipient, or the employee or agent responsible for delivering the message to the intended recipient, you are hereby notified that any dissemination, distribution or copying of this communication is strictly prohibited. If you have received this communication in error, please notify me immediately by telephone.

-----Original Message-----

From: [dhoffman@gmx.com](mailto:dhoffman@gmx.com) <[dhoffman@gmx.com](mailto:dhoffman@gmx.com)>  
Sent: Wednesday, October 5, 2022 9:14 PM  
To: Anderson, Kimberly <[Kimberly.Anderson@med.ohio.gov](mailto:Kimberly.Anderson@med.ohio.gov)>; [CSIPublicComments](#) <[CSIPublicComments@governor.ohio.gov](mailto:CSIPublicComments@governor.ohio.gov)>  
Subject: Timeline question re : OAC 4731-11-04 : Repeal of 12 week limit on phentermine

I know the public comment period goes until October 14...how long after that would a new or revised regulation typically be effective?

Thanks in advance,

Sent using the mobile mail app

On 10/5/22 at 9:12 PM, [dhoffman@gmx.com](mailto:dhoffman@gmx.com) wrote:

> From: [dhoffman@gmx.com](mailto:dhoffman@gmx.com)  
> Date: October 5, 2022  
> To: [Kimberly.Anderson@med.ohio.gov](mailto:Kimberly.Anderson@med.ohio.gov)  
> Cc: [CSIPublicComments@governor.ohio.gov](mailto:CSIPublicComments@governor.ohio.gov)  
> Subject: OAC 4731-11-04 : Repeal of 12 week limit on phentermine  
>



- >
- > I'm relieved to hear that the 12 week limitation is being removed on the phentermine and returning to the medical judgment of your doctor. I'm currently taking an expensive brand name medication, Qsymia, which is a combination of phentermine and topamax, only because of the time limitation on plain phentermine.
- >
- > The side effects from adding the topamax have been horrible including extreme fatigue which makes it nearly impossible to work and cook let alone go to the gym! Along with hair loss and irritability - again from an add on medication I have no other reason to take, except the patented combination medicine is allowed in Ohio indefinitely, while the generic half that actually works with minimal side effects is not.
- >
- > Even taking half the regular phentermine dose helped me significantly, with no side effects, lose weight as I enter my 50s. Until this dumb law shut it down. I have zero need for this topamax other than it comes bundled with the phentermine.
- >
- > Yes, please get rid of it. The Qsymia manufacturer will lose some money, but I'm sure they'll figure that out. Some people drive to Pennsylvania, with gas costs and losing time from work, because they got rid of this requirement and let their doctors practice medicine in their judgment a long time ago.
- >
- >
- >
- >

CAUTION: This is an external email and may not be safe. If the email looks suspicious, please do not click links or open attachments and forward the email to [csc@ohio.gov](mailto:csc@ohio.gov) <<mailto:csc@ohio.gov>> or click the Phish Alert Button if available.

**From:** [McNamee, Cameron](#)  
**To:** [Anderson, Kimberly](#)  
**Subject:** FW: Rules Filed with CSI  
**Date:** Tuesday, September 27, 2022 9:47:47 AM  
**Attachments:** [image001.png](#)  
[image003.png](#)  
[image004.png](#)  
[BIA and Attachments-Controlled Substance Rules.pdf](#)

Kim,

Our compliance folks reviewed the CS rules and had one comment:

4731-11-04 (C)(2)

(C) (2) The prescriber **shall** **may** personally furnish controlled substances for weight reduction or chronic weight management.....

Change SHALL to MAY. The way it's currently written takes out any pharmacist involvement. Makes the patient go back every 3 days for another supply of medication.

Best,  
Cameron



**STATE OF OHIO**  
BOARD OF PHARMACY

**Cameron J. McNamee (he/him/his)**

Director of Policy and Communications  
77 South High Street, 17<sup>th</sup> Floor, Columbus, Ohio 43215  
T: (614) 466.7322 | C: (614) 581.5203 | F: (614) 752.4836  
[Cameron.McNamee@pharmacy.ohio.gov](mailto:Cameron.McNamee@pharmacy.ohio.gov)  
[www.pharmacy.ohio.gov](http://www.pharmacy.ohio.gov)

*This e-mail may contain sensitive law enforcement and/or privileged information. If you are not the intended recipient (or have received this e-mail in error) please notify the sender and destroy this e-mail. Any unauthorized copying, disclosure or distribution of the material in this e-mail is strictly forbidden. This message and any response to it may constitute a public record and thus may be publicly available to anyone who requests it.*



**From:** Rodriguez, Judith <Judith.Rodriguez@med.ohio.gov>

**Sent:** Friday, September 23, 2022 8:54 AM

**To:** Dipasquale, Anita <ADiPasquale@nursing.ohio.gov>; Abby Benjamin <benjamin@sppgrp.com>; Alvin Zachariah <alzach@aol.com>; Aneta Homer MD <ahomer@southwoodshealth.com>; Barry T. Doyle (todoye@aol.com) <todoye@aol.com>; Bruce B. Whitman (bbwhitmanlaw@aol.com) <bbwhitmanlaw@aol.com>; McNamee, Cameron <Cameron.McNamee@pharmacy.ohio.gov>; Damion Clifford <dclifford@arnlaw.com>; Daniel Zinsmaster (daniel.zinsmaster@dinsmore.com) <daniel.zinsmaster@dinsmore.com>; David Paragas <david.paragas@btlaw.com>; Deborah R. Lydon (lydon@dinslaw.com) <lydon@dinslaw.com>; Elaine M. Hiatt PhD <Ehiatt@AIAM.edu>; Eric Vinyard <eric.vinyard@hickspartners.com>; Greg Warren <g.warren@columbusstrategygroup.com>; James Leo <jjleoincolumbus@yahoo.com>; James McGovern (jmcgovern@grafflaw.com) <jmcgovern@grafflaw.com>; Jeffrey Jurca (jjurca@jurcalashuk.com) <jjurca@jurcalashuk.com>; Jennifer Armstrong <jenkarmstrong@hotmail.com>; Jessica Bechtel <jbechtel@taftlaw.com>; Joe Feltes <JFeltes@BDBLAW.com>; John R. Irwin <John@johnrirwin.com>; Judi Hatcher <jhatcher@copcp.com>; Kay Mavko <kmavko@columbus.rr.com>; Lana Mullet <lmullet@emp.com>; Levi Tkach <levi@grafflaw.com>; Lori Herf <LHerf@bakerlaw.com>; M. D. Roland Benton <rbrmd\_99@yahoo.com>; Mike Mathy OFAMA <mmathy@ohfama.org>; Patricia Weisbach <Patricia\_Weisbach@trihealth.com>; patrick@americanmedspa.org; Shannon Urena <shannonurena1@gmail.com>; Tuch, Socrates <Socrates.Tuch@odh.ohio.gov>; Stefanie Frank <sf@stateside.com>; Steven Greer <sgreer6@kent.edu>; Thomas W. Hess (thess@dinslaw.com) <thess@dinslaw.com>; Jenkins, Vicki <Vicki.Jenkins@dodd.ohio.gov>; (roseman@sssnet.com) <roseman@sssnet.com>; Allison Poulos <apoulos@metrohealth.org>; amandasines@sbcglobal.net; Ann Spicer <ASpicer@OhioAFP.org>; Ann Warner <woostereye@aol.com>; Belinda Jones (bjones@capitol-consulting.net) <bjones@capitol-consulting.net>; Blair Barnhart-Kinkle (barnhab@ccf.org) <barnhab@ccf.org>; Bryn Hunt <Bryn.Hunt@ohiohospitals.org>; Carolyn Townner <carolyntowner@sbcglobal.net>; Catherine Olohan Zwissler <OlohanZwiss@aol.com>; Doug Graff <doug@grafflaw.com>; Elizabeth Collis (E-mail) <bethel1234@aol.com>; Eric Plinke (eric.plinke@dinslaw.com) <eric.plinke@dinslaw.com>; George Dunigan <gfdunigan@aol.com>; Greg Fouche <GFouche@jcarr.state.oh.us>; Gregory W. Bee <bee@taftlaw.com>; Holly Dorr <hdorr@ohacep.org>; Inez 617 (inez617@msn.com) <inez617@msn.com>; J Richard Ludgin (E-mail) <rludgin@ix.netcom.com>; James Lindon <JLindon@LindonLaw.com>; Jeffrey Fisher <OEHN@aol.com>; Joel Selmeier (E-mail) <'joelselm@joel.com'>; John Booher <JWBooher@aol.com>; Kevin Devaney <kdevaney@eastmansmith.com>; Roe, Sonja <sonja.roe@cos.ohio.gov>; Larry Wolpert <LWolpert@jcarr.state.oh.us>; Emrich, Lisa <lemrich@nursing.ohio.gov>; Lloyd DePew <ldepew@baileycav.com>; M. D. Eliot Mostow (emostow@akronderm.com) <emostow@akronderm.com>; Matt Donnelly <dannelm1@ccf.org>; McGovern Jim (jamesmcmcgovern@yahoo.com) <jamesmcmcgovern@yahoo.com>; Melissa Guzman <mdgzman95@gmail.com>; Michael Oros <michaeloros1@gmail.com>; Michael R. Moran <mrmoran@mrmoran.com>; OHA - Mary Gallagher <Maryg@OHANET.org>; Paul Bryson <pbryson@adena.org>; Paul Hilderbrant <philderbrant@yahoo.com>; rainykgal <rainykgal@gmail.com>; Ricardo del Castillo <UAGSAT@uag.edu>; Richard Greely <rgreely@cscc.edu>; Richard Kasmer (ohiolawce@yahoo.com) <ohiolawce@yahoo.com>; Rogers Carol (cjrogers65@msn.com) <cjrogers65@msn.com>; Scott P. Sandrock <spsandrock@bmdllc.com>; Sean McGlone <seanm@ohanet.org>; Sharon Barnes Ph. D. <sbarnes112@aol.com>; Ross, Ronald <Ronald.Ross@psy.ohio.gov>; Steve Lanier (stevelanier@yahoo.com) <stevelanier@yahoo.com>; ADA Teresa Lampl <lampl@theohiocouncil.org>; Terry Guzek <tguzek@ehove-jvs.k12.oh.us>; Tim Cosgrove (E-mail) <tcosgrove@ssd.com>; Dilling, Thomas <Tdilling@nursing.ohio.gov>; Victor Goodman

<vgoodman@bfca.com>; wfitzgibbon@cwslaw.com; Willa Ebersole <willa@tompappas.com>; ACADEMY OF MED. OF CINCINNATI (E-mail) <academy@academyofmedicine.org>; lwealton@aol.com; Dayton Academy of Osteopathic Medicine (daytonacademy@sbcglobal.net) <daytonacademy@sbcglobal.net>; jjohns@amcno.org; Lorain Co. Medical Society <lcmed@centurytel.net>; MAHONING COUNTY MEDICAL SOCIETY (E-mail) <mahoningcountymed@zoominternet.net>; Nancy Gillette, OSMA <Gillette@osma.org>; Pam Fairbanks <pfairbanks@academyofmedicine.org>; PICKAWAY COUNTY MEDICAL SOCIETY (E-mail) <JWMILKS@AOL.COM>; Sandusky County Medical Society <lamarfarm@yahoo.com>; Stark Medical Society <starkmedical@ameritech.net>

**Subject:** Rules Filed with CSI

#### Comments due October 14, 2022

**The State Medical Board of Ohio has filed proposed actions concerning rules with the Common Sense Initiative Office. The proposals are attached.**

A state rule-making agency may propose to adopt a new rule, amend or rescind an existing rule, or propose to continue a rule without any changes. Executive Order 2011-01K and Sections 107.62 and 121.82, Ohio Revised Code, require state agencies to draft rules in collaboration with stakeholders, assess and justify any adverse impact on the business community, and provide an opportunity for the affected public to provide input on the proposed rules. The Business Impact Analysis for the proposed rules discusses the purpose of the rule and identifies the nature of the adverse impact on licensees. The Common Sense Initiative review must be completed before the rules can begin the formal rule-making process through the Joint Committee on Agency Rule Review.

Comments on the proposed rules must be received no later than **October 14, 2022**. Please provide comments to both of the following:

Medical Board at: [Kimberly.Anderson@med.ohio.gov](mailto:Kimberly.Anderson@med.ohio.gov)

AND

Common Sense Initiative Office at: [CSIPublicComments@governor.ohio.gov](mailto:CSIPublicComments@governor.ohio.gov).

Judy Rodriguez  
Subpoena Coordinator

State Medical Board of Ohio  
30 East Broad Street, 3rd Floor  
Columbus, Ohio 43215  
o: 614-466-7260  
Email: [judith.rodriguez@med.ohio.gov](mailto:judith.rodriguez@med.ohio.gov)  
w: [med.ohio.gov](http://med.ohio.gov)



Confidentiality Notice: This message is intended for use only by the individual or entity to whom or which it is addressed and may contain information that is privileged, confidential and/or otherwise exempt from disclosure under applicable law. If the reader of this message is not the intended recipient, or the employee or agent responsible for delivering the message to the intended recipient, you are hereby notified that any dissemination, distribution or copying of this communication is strictly prohibited. If you have received this communication in error, please notify me immediately by telephone.

**From:** [Anderson, Kimberly](#)  
**To:** [Steven Carp](#)  
**Subject:** RE: Rule Number(s): 4731-11-03, 4731-11-04, 4731-11-04.1  
**Date:** Wednesday, October 5, 2022 8:48:00 AM  
**Attachments:** [image002.png](#)  
[image004.png](#)  
[image005.png](#)

---

Thank you for your comment. It will be shared with the Board.

Kimberly Anderson  
Chief Legal Counsel  
State Medical Board of Ohio  
30 East Broad Street, 3rd Floor  
Columbus, Ohio 43215  
o: 614-466-7207  
c: 614-230-9077  
[Kimberly.Anderson@med.ohio.gov](mailto:Kimberly.Anderson@med.ohio.gov)



Confidentiality Notice: This message is intended for use only by the individual or entity to whom or which it is addressed and may contain information that is privileged, confidential and/or otherwise exempt from disclosure under applicable law. If the reader of this message is not the intended recipient, or the employee or agent responsible for delivering the message to the intended recipient, you are hereby notified that any dissemination, distribution or copying of this communication is strictly prohibited. If you have received this communication in error, please notify me immediately by telephone.

---

**From:** Steven Carp <[drcarp@carpcosmetic.com](mailto:drcarp@carpcosmetic.com)>  
**Sent:** Wednesday, October 5, 2022 6:48 AM  
**To:** Anderson, Kimberly <[Kimberly.Anderson@med.ohio.gov](mailto:Kimberly.Anderson@med.ohio.gov)>  
**Subject:** Rule Number(s): 4731-11-03, 4731-11-04, 4731-11-04.1

Members of the Board

I would like to express my thoughts on Rule Number(s): 4731-11-03, 4731-11-04, 4731-11-04.1. I believe that the use of medications like phentermine, has shown to be extremely safe when administered and monitored by trained providers. Ohio is possibly the only state that places a limitation on prescribing periods. The medication is effective as an additional tool to help combat obesity.

I strongly urge the Board to work with all agencies/boards, including the Board of Pharmacy to remove these restrictions. This will place Ohio inline with nearly, if not all other, States.

Sincerely,

Steven Carp, MD  
American Board of Plastic Surgery  
[www.carpcosmetic.com](http://www.carpcosmetic.com)



**CAUTION:** This is an external email and may not be safe. If the email looks suspicious, please do not click links or open attachments and forward the email to [csc@ohio.gov](mailto:csc@ohio.gov) or click the Phish Alert Button if available.



**MEMORANDUM**

TO: Betty Montgomery, President  
Members, State Medical Board of Ohio

FROM: Kimberly C. Anderson, Chief Legal Counsel

RE: Rule 4731-11-14, Chronic Pain

DATE: November 4, 2022

---

HB 193, which became effective September 23, 2022, created a category of drugs called overdose reversal drugs. Overdose reversal drugs include naloxone and any other drug that is approved by the FDA for reversal of a known or suspected opioid-related overdose.

The Medical Board has some rules, including Rule 4731-11-14, OAC, which require the prescriber to offer a prescription for naloxone. The proposed amended rule updates the language by replacing “naloxone” with “overdose reversal drug”.

**Requested Action:** Approve the proposed amended rule for initial circulation to interested parties.

---

**\*\*\* DRAFT - NOT YET FILED \*\*\***

4731-11-14

**Prescribing for subacute and chronic pain.**

- (A) Prior to treating, or continuing to treat subacute or chronic pain with an opioid analgesic, the physician shall first consider and document non-medication and non-opioid treatment options.
- (1) If opioid analgesic medications are required as determined by a history and physical examination, the physician shall prescribe for the minimum quantity and potency needed to treat the expected duration of pain and improve the patient's ability to function.
  - (2) The physician shall comply with the requirements of rule 4731-11-02 of the Administrative Code.
- (B) Before prescribing an opioid analgesic for subacute or chronic pain, the physician shall complete or update and document in the patient record assessment activities to assure the appropriateness and safety of the medication including:
- (1) History and physical examination including review of previous treatment and response to treatment, patient's adherence to medication and non-medication treatment, and screening for substance misuse or substance use disorder;
  - (2) Laboratory or diagnostic testing or documented review of any available relevant laboratory or diagnostic test results. If evidence of substance misuse or substance use disorder exists, diagnostic testing shall include urine drug screening;
  - (3) Review the results of an OARRS check in compliance with rule 4731-11-11 of the Administrative Code;
  - (4) A functional pain assessment which includes the patient's ability to engage in work or other purposeful activities, the pain intensity and its interference with activities of daily living, quality of family life and social activities, and the physical activity of the patient;
  - (5) A treatment plan based upon the clinical information obtained, to include all of the following components:
    - (a) Diagnosis;
    - (b) Objective goals for treatment;

\*\*\* DRAFT - NOT YET FILED \*\*\*

4731-11-14

2

- (c) Rationale for the medication choice and dosage; and
  - (d) Planned duration of treatment and steps for further assessment and follow-up.
- (6) Discussion with the patient or guardian regarding:
- (a) Benefits and risks of the medication, including potential for addiction and risk of overdose; and
  - (b) The patient's responsibility to safely store and appropriately dispose of the medication.
- (7) The physician shall offer a prescription for an overdose reversal drug ~~naloxone~~ to the patient receiving an opioid analgesic prescription under any of the following circumstances:
- (a) The patient has a history of prior opioid overdose;
  - (b) The dosage prescribed exceeds a daily average of eighty MED or at lower doses if the patient is co-prescribed a benzodiazepine, sedative hypnotic drug, carisprodol, tramadol, or gabapentin; or
  - (c) The patient has a concurrent substance use disorder.
- (C) Prior to increasing the opioid dosage to a daily average of fifty MED or greater the physician shall complete and document the following in the patient's medical record:
- (1) The physician shall review and update the assessment completed in paragraph (B) of this rule, if needed. The physician may rely on an appropriate assessment completed within a reasonable time if the physician is satisfied that he or she may rely on that information for purposes of meeting the further requirements of this chapter of the Administrative Code;
  - (2) The physician shall update or formulate a new treatment plan, if needed;
  - (3) The physician shall obtain from the patient or the patient's guardian written informed consent which includes discussion of all of the following:
    - (a) Benefits and risks of the medication, including potential for addiction and



\*\*\* DRAFT - NOT YET FILED \*\*\*

4731-11-14

3

risk of overdose.

- (b) The patient's responsibility to safely store and appropriately dispose of the medication.
- (4) Except when the patient was prescribed an average daily dosage that exceeded fifty MED before the effective date of this rule, the physician who is neither a specialist in the area of the body affected by the pain nor a pain management specialist shall document consideration of the following:
- (a) Consultation with a specialist in the area of the body affected by the pain;
  - (b) Consultation with a pain management specialist;
  - (c) Obtaining a medication therapy management review by a pharmacist; and
  - (d) Consultation with a specialist in addiction medicine or addiction psychiatry, if aberrant behaviors indicating medication misuse or substance use disorder are noted.
- (5) The physician shall consider offering a prescription for ~~naloxone~~ an overdose reversal drug to mitigate risk of overdose.
- (D) Prior to increasing the opioid dosage to a daily average of eighty MED or greater, the physician shall complete all of the following:
- (1) Enter into a written pain treatment agreement with the patient that outlines the physician's and patient's responsibilities during treatment and requires the patient or patient guardian's agreement to all of the following provisions:
    - (a) Permission for drug screening and release to speak with other practitioners concerning the patient's condition or treatment;
    - (b) Cooperation with pill counts or other checks designed to assure compliance with the treatment plan and to minimize the risk of misuse or diversion;
    - (c) The understanding that the patient shall only receive opioid medications from the physician treating the chronic pain unless there is written agreement among all of the prescribers of opioids outlining the

\*\*\* DRAFT - NOT YET FILED \*\*\*

4731-11-14

4

responsibilities and boundaries of prescribing for the patient; and

- (d) The understanding that the dosage may be tapered if not effective or if the patient does not abide by the treatment agreement.
- (2) Offer a prescription for ~~naloxone~~ overdose reversal drug to the patient as described in paragraph (B) of this rule.
- (3) Except when the patient was prescribed an average daily dosage that exceeded eighty MED before the effective date of this rule, the physician who is neither a specialist in the area of the body affected by the pain nor a pain management specialist shall obtain at least one of the following based upon the patient's clinical presentation:
- (a) Consultation with a specialist in the area of the body affected by the pain;
  - (b) Consultation with a pain management specialist;
  - (c) Obtain a medication therapy management review; or
  - (d) Consultation with a specialist in addiction medicine or addiction psychiatry if aberrant behavior indicating medication misuse or substance use disorder may be present.
- (E) The physician shall not prescribe a dosage that exceeds an average of one hundred twenty MED per day. This prohibition shall not apply in the following circumstances:
- (1) The physician holds board certification in pain medicine, board certification in hospice and palliative care, board certification in hematology, or board certification in oncology;
  - (2) The physician has received a written recommendation for a dosage exceeding an average of one hundred twenty MED per day from a board certified pain medicine physician or board certified hospice and palliative care physician who based the recommendation on a face-to-face visit and examination of the patient. The prescribing physician shall maintain the written recommendation in the patient's record; or
  - (3) The patient was receiving an average daily dose of one hundred twenty MED or

**\*\*\* DRAFT - NOT YET FILED \*\*\***

4731-11-14

5

more prior to the effective date of this rule. The physician shall follow the steps in paragraph (E)(2) of this rule prior to escalating the patient's dose.

- (F) During the course of treatment with an opioid analgesic at doses below the average of fifty MED per day, the physician shall provide periodic follow-up assessment and documentation of the patient's functional status, the patient's progress toward treatment objectives, indicators of possible addiction, drug abuse or drug diversion and the notation of any adverse drug effects.
- (G) During the course of treatment with an opioid analgesic at doses at or above the average of fifty MED per day, the physician shall complete and document in the patient record the following no less than every three months:
- (1) Review of the course of treatment and the patient's response and adherence to treatment.
  - (2) The assessment shall include a review of any complications or exacerbation of the underlying condition causing the pain through appropriate interval history, physical examination, any appropriate diagnostic tests, and specific treatments to address the findings.
  - (3) The assessment of the patient's adherence to treatment including any prescribed non-pharmacological and non-opioid treatment modalities;
  - (4) Rationale for continuing opioid treatment and nature of continued benefit, if present.
  - (5) The results of an OARRS check in compliance with rule 4731-11-11 of the Administrative Code.
  - (6) Screening for medication misuse or substance use disorder. Urine drug screen should be obtained based on clinical assessment of the physician with frequency based upon presence or absence of aberrant behaviors or other indications of addiction or drug abuse.
  - (7) Evaluation of other forms of treatment and the tapering of opioid medication if continued benefit cannot be established.
- (H) This rule does not apply to the physician who prescribes an opioid in any of the following situations:

**\*\*\* DRAFT - NOT YET FILED \*\*\***

4731-11-14

6

- (1) The medication is for a patient in hospice care.
  - (2) The patient has terminal cancer or another terminal condition, as that term is defined in rule 4731-11-01 of the Administrative Code.
- (I) This rule does not apply to inpatient prescriptions as defined in rule 4729-17-01 of the Administrative Code.



**SMBO Legislative Update:  
November 2022**

**Recent activity:**

**SB 364 – Mental Health Assistants (Sen. Gavarone) (Companion HB 730)**

To license certified mental health assistants (CMHA)

**Of Note:**

- Defines “Certified Mental Health Assistant” as an individual who, under physician supervision, provides mental health care by engaging in any of the activities authorized in the bill
- Only practice under a supervision agreement with a supervising physician. Diagnose and provide treatment based on patient’s diagnosis. Order, prescribe, personally furnish drugs. Refer patient for voluntary or involuntary admission for substance abuse disorder treatment or inpatient psychiatric care.
- CMHA may only prescribe the following controlled substances: Buprenorphine only for a patient actively engaged in opioid use disorder treatment. Benzodiazepine in the following circumstances – a patient diagnosed as having a chronic anxiety disorder or a patient with acute anxiety or agitation but only in an amount for 7 days. Stimulant approved by the FDA for treatment of ADHD
- SMBO rule making authority for: Standards and procedures for issuing and renewing licenses to practice, Application fees for initial license and renewed license, Application process, fees, requirements for approval, reapproval, and curriculum standards for education programs

**Status:** Introduced in Senate 10/17/2022

**HB 730 – Mental Health Assistants (Rep. Pavliga) (Companion SB 364)**

To license certified mental health assistants (CMHA)

**Of Note:**

- Defines “Certified Mental Health Assistant” an individual who, under physician supervision, provides mental health care by engaging in any of the activities authorized in the bill
- Only practice under a supervision agreement with a supervising physician, Diagnose and provide treatment based on patient’s diagnosis, Order, prescribe, personally furnish drugs, Refer patient for voluntary or involuntary admission for substance abuse disorder treatment or inpatient psychiatric care.
- CMHA may only prescribe the following controlled substances: Buprenorphine only for a patient actively engaged in opioid use disorder treatment, Benzodiazepine in the following circumstances – a patient diagnosed as having a chronic anxiety disorder or a patient with acute anxiety or agitation but only in an amount for 7 days, Stimulant approved by the FDA for treatment of ADHD
- SMBO rule making authority for: Standards and procedures for issuing and renewing licenses to practice, Application fees for initial license and renewed license, Application

process, fees, requirements for approval, reapproval, and curriculum standards for education programs

**Status:** Introduced in House 10/17/2022

### **HB 714 – Respiratory Therapists (Rep. T. Young and Rep. John)**

To license advanced practice respiratory therapists (APRT)

**Of Note:**

- Allows for an APRT licensed under 4761.31 to exercise physician-delegated prescriptive authority. Prohibits a prescription for a controlled substance to be used outside of the healthcare facility the APRT is practicing
- Defines “Health Care Facility” as a hospital, A site where a medical practice is operated and provides direct patient care, an entity owned or controlled, in whole or in part, by a hospital or by an entity that owns or controls, in whole or in part, one or more hospitals, and any other facility designated in rule by the state medical board
- Requires supervising physician to be physically present at the location where the APRT is practicing or be readily available to the APRT through telecommunication in a location reasonably close to where the APRT is practicing

**Status:** Introduced in the House 8/31/2022.

### **HB 203 – Occupational Licenses (Rep. Powell) (companion SB 131)**

To require an occupational licensing authority to issue a license or government certification to an applicant who holds a license, government certification, or private certification or has satisfactory work experience in another state under certain circumstances.

**Of Note:**

- Requires automatic licensure of out of state applicants that meet certain criteria.

**Status:** Introduced in the House 3/10/2021. 1<sup>st</sup> House State & Local Government hearing 4/21/2021. 2<sup>nd</sup> House State & Local Government hearing 5/5/2021. 3<sup>rd</sup> House State & Local Government Hearing 6/10/2021. 4<sup>th</sup> House State and Local Government hearing 10/27/2021. 5<sup>th</sup> hearing House State and Local Government 1/26/2022. Reported out of House State & Local 4/6/2022. Passed the House 6/1/2022

### **SB 131 – Occupational Licensing (Reciprocity) (Sen. Roegner and Sen. McColley) (companion HB 203)**

To require an occupational licensing authority to issue a license or government certification to an applicant who holds a license, government certification, or private certification or has satisfactory work experience in another state under certain circumstances.

**Of note:**

- Requires automatic licensure of out of state applicants that meet certain criteria.
- Allows for the licensing authority to take disciplinary action against an applicant, deny an application and determine fitness to practice of an applicant.
- Amended – A person who holds a license issued through an interstate licensure compact to which Ohio is a party is not required to obtain a license through reciprocity

- Amended – Delays the bill's effective date to 270 days after the bill's effective date

**Status:** Introduced in the Senate 3/16/2021. 1<sup>st</sup> Senate Workforce & Higher Education hearing 5/19/2021. 2<sup>nd</sup> Senate Workforce & Higher Education hearing 5/26/2021. 3<sup>rd</sup> Senate Workforce & Higher Education hearing 3/22/2022. 4<sup>th</sup> Senate Workforce & Higher Education hearing 5/18/2022. 5<sup>th</sup> Senate Workforce & Higher Education hearing 5/25/2022. Reported out of Senate Workforce & Higher Education 5/25/2022. Passed the Senate 6/1/2022.

**HB 196 – Surgical Assistants (Rep. Kelly and Rep. Carruthers)** To Regulate the practice of surgical assistants.

**Of Note:**

- Creates a new license type for surgical assistants to be overseen by the Medical Board.
- Amended – Revises the bill's provision allowing an applicant who is not credentialed by a national organization as a surgical assistant to be eligible for licensure if the applicant has instead practiced as a surgical assistant at an Ohio hospital or facility during any part of the 6 month period that precedes the bill's effective date by increasing that period to 18 months

**Status:** Introduced in the House 3/9/2021. 1<sup>st</sup> House Health hearing 4/20/2021. 2<sup>nd</sup> House Health hearing 5/11/2021. 3<sup>rd</sup> House Health hearing 12/7/21. 4<sup>th</sup> House Health hearing 2/15/2022. 5<sup>th</sup> House Health hearing 3/1/2022 \*Approved sub bill. 6<sup>th</sup> House Health hearing 5/17/2022. 7<sup>th</sup> House Health hearing 5/24/2022. Reported out of House Health 5/24/2022

**HB 81 – Massage Therapy (Rep. Plummer and Rep. Manchester) (companion bill SB 55)** To make changes to the laws governing massage establishments and massage therapy.

**Of note:**

- Change current law to no longer limit “massage therapy” to the treatment of disorders of the human body
- Standardizes, for purposes of regulation by the State Medical Board, townships, and municipal corporations, terminology regarding massage therapy and individuals authorized to perform massage therapy
- Eliminates township authority to issue licenses to individuals who perform massage therapy
- Requires that if a township opts to regulate massage establishments, the regulations must require all massage therapy to be performed only by specified state-licensed professionals or massage therapy students

**Status:** Introduced in the House 2/9/2021. Passed out of the House 6/24/2021. Referred to Senate Health 9/8/2021. 1<sup>st</sup> Senate Health hearing 5/18/2022. 2<sup>nd</sup> Senate Health hearing 6/1/2022.

## Actively Monitoring

### SB 322 – Sex Offenses (Sen. Hackett)

Regarding sex offenses and individuals regulated by the State Medical Board

**Of Note:**

- Modifies the law governing sex offenses and medical professionals
- Increasing reporting requirements of suspected sexual activity by medical professionals; Allowing the board to suspend a license upon an indictment, as well as permitting an automatic 90 day suspension of a license of an individual whose license was suspended, revoked or surrendered in another jurisdiction; Requiring licensees to provide notification of their probationary status to their patients; Allowing the board to share the confidential investigation status of a licensee with the complainant; Adding a public member of the board to the internal investigatory process, to allow additional board insight into the handling of sexual misconduct

**Status:** Introduced in the Senate 4/12/2022. Referred to Senate Health committee 5/18/2022

### SB 261- Changes to Medical Marijuana law (Sen. S. Huffman)

**Of Note:**

- Transfers portions of the Medical Marijuana Program from the Board of Pharmacy to the Department of Commerce; Expands the types of qualifying medical conditions; Adds a telehealth provision; Modifies the requirement that a CTR applicant demonstrate they don't have ownership or investment interest with an entity licensed as a dispensary; Allows the medical director of a dispensary who is a licensed CTR to recommend medical marijuana.

**Status:** Passed Senate 12/15/2022. 1<sup>st</sup> House Government Oversight hearing 2/17/22. 2<sup>nd</sup> Government Oversight hearing 3/16/2022. 3<sup>rd</sup> House Government Oversight hearing 3/24/2022. 4<sup>th</sup> Government Oversight hearing 4/27/2022

### HB 60 – Authorize medical marijuana for autism spectrum disorder (Rep. Brent and Rep. Seitz)

**Of Note:**

- Allows Autism Spectrum Disorder to be included in qualifying conditions.

**Status:** Passed House 3/2/2022. 1<sup>st</sup> Senate Health Hearing 3/30/2022

### HB 286 – Court of Common Pleas (Rep. Bill Seitz) (companion SB 189)

To generally change the venue in which appeal from an agency order is proper to the local court of common pleas.

**Of note:**



- Modifies the current Administrative Procedure Act by generally providing that a party adversely affected by an order of an agency may appeal from the order to the court of common pleas of the county in which the place of business of the party is located or the county in which the party is a resident.
- Removes the current provision that any party adversely affected by an order of an agency issued pursuant to any other adjudication may appeal, with certain exceptions, to the Franklin County Court of Common Pleas.
- Amended - Requires appeals from an administrative order by any party who is not a resident of Ohio must be to the Franklin County Court of Common Pleas.

**Status:** Passed out of the House 3/30/2022. Referred to Senate Judiciary Committee 4/6/2022. 1<sup>st</sup> Senate Judiciary hearing 5/17/2022. 2<sup>nd</sup> Senate Judiciary hearing 5/24/2022

### **SB 189 – Change venue for appeal from an agency order (Sen. Lang and Sen. McColley) (companion SB 286)**

**Of Note:**

- To generally change the venue in which appeal from an agency order is proper to the local court of common pleas.
- Modifies the current Administrative Procedure Act by generally providing that a party adversely affected by an order of an agency may appeal from the order to the court of common pleas of the county in which the place of business of the party is located or the county in which the party is a resident.
- Removes the current provision that any party adversely affected by an order of an agency issued pursuant to any other adjudication may appeal, with certain exceptions, to the Franklin County Court of Common Pleas.

**Status:** Introduced in the Senate 5/26/2021. 1<sup>st</sup> Senate Judiciary hearing 6/16/2021. 2<sup>nd</sup> Senate Judiciary Hearing 9/28/2021. 3<sup>rd</sup> Senate Judiciary hearing 10/5/2021. 4<sup>th</sup> Senate Judiciary hearing 10/26/2021. 5<sup>th</sup> Senate Judiciary hearing 3/29/2022.

### **HB 318 – Anesthesiologist Assistants (Rep. Swearingen and Rep. Plummer)**

To revise the law governing the practice of anesthesiologist assistants.

**Of Note:**

- Adds anesthesiologist assistants to the list of individuals authorized to prescribe drugs or dangerous drugs or drug therapy related devices during professional practice.
- Adds anesthesiologist assistant list of practitioners from which a respiratory care therapist may receive orders or prescriptions.

**Status:** First House Health Hearing 10/12/2021. Second House Health Hearing 2/8/2022. Third House Health Hearing 3/1/2022 \*Approved sub bill. 4<sup>th</sup> House Health hearing 5/31/2022 \*Approved sub bill. Passed out of House Health Committee 5/31/2022

### **HB 509 – Revise and streamline occupational regulations (Rep. John and Rep. Fowler Arthur)**

**Of Note:**

- Requires each occupational licensing board to prepare a report including fee structure for each license issued by the board, whether the fee structure can competitively align with neighboring states, whether the fee structure is a financial barrier for license holders.
- Requires the report be submitted to the Senate President, Speaker of the House and chairpersons of committees responsible for reviewing occupational licensing boards

**Status:** Passed out of the House 3/23/2022. Referred to Senate Workforce & Higher Education 3/29/2022. 1<sup>st</sup> Senate Workforce & Higher Education hearing 5/25/2022

### **SB 55 – Massage Therapy (Sen. Brenner) (companion bill HB 81)**

To make changes to the laws governing massage establishments and massage therapy.

#### **Of Note:**

- Requires any individual practicing massage within the state to obtain the current massage therapy license issued by the State Medical Board.

**Status:** Introduced in Senate 2/9/2021. 1<sup>st</sup> Senate Health hearing 2/24/2021. 2<sup>nd</sup> Senate Health hearing 3/3/2021. 3<sup>rd</sup> Senate Health hearing 3/10/2021. 4<sup>th</sup> Senate Health hearing 3/17/2021. 5<sup>th</sup> Senate Health hearing 5/19/2021. Passed out of Senate Health Committee 5/19/2021.

### **HB 356 – Drugs (Rep. Loychik and Rep. Bird)**

Regarding drug offenses and treatment.

#### **Of Note:**

- Proposes to reduce the abuse of prescription opioids, establish addiction treatment facilities, increase penalties for drug trafficking violations, modify penalties for drug possession, require an offender convicted of a drug possession or drug trafficking offense involving certain drugs to be subject to ten years of post-release control, allow a criminal defendant who has a severe substance use disorder involving certain drugs to be confined by a state detoxification provider while awaiting trial, create restitution work programs, and make an appropriation.
- Limits opioid prescriptions for acute pain to three days. Then, re-examination of the patient is required, and the prescriber may issue a new prescription for more than 3 days.
- Allows health related licensing board to adopt rules specifying circumstances under which a prescriber may issue an initial prescription for an opioid to treat acute pain in an amount that exceeds three days.

**Status:** Introduced in the House 6/21/2021. 1<sup>st</sup> House Criminal Justice hearing 11/10/2021. 2<sup>nd</sup> House Criminal Justice hearing 3/24/2022. 3<sup>rd</sup> House Criminal Justice hearing 4/6/2022

### **HB 476 – Create Parkinson’s disease registry; change awareness month (Rep. Bird and Rep. Lightbody)**

Establish a Parkinson’s disease registry and to change the observance of “Parkinson’s Disease Awareness Month” from September to April

#### **Of Note:**

- Requires that each individual case of Parkinson’s disease be reported to the registry by the physician, physician assistant, group practice, hospital or health care facility that employs the professional who diagnosed or treated the patients Parkinson’s disease
- A health care provider may be disciplined by the provider’s licensing board for failure to comply with the bill’s reporting requirements

**Status:** Passed out of the House 4/6/2022. Referred to Senate Health committee 5/18/2022

### **HB 631 – Promote Alternative Treatments for COVID (Rep. Jordan)**

To protect the health care professional-patient relationship, to promote alternative drugs and therapies for the treatment of SARS-CoV-2, including its variants, and COVID-19.

#### **Of Note:**

- Allows for off label drug use for patients diagnosed with COVID-19 or its variants
- Requires each health board and department to promote and increase distribution of these drugs
- Denies the department of health, state medical board or board of nursing from suppressing the promotion or access to these drugs
- Denies reprimand of health care professionals for prescribing or promoting these drugs

**Status:** Introduced in House 4/21/2022. Referred to House Civil Justice committee 5/17/2022

### **SB 296 – Narcotics (Sen. Manning and Sen. S. Huffman)**

Regards access to naloxone and certain narcotics testing products

#### **Of Note:**

- Adds physician assistants and advanced practice registered nurses to those who may authorize a pharmacist or pharmacy intern to dispense naloxone without a prescription.

**Status:** Introduced in the Senate 2/15/2022. 1<sup>st</sup> Senate Health hearing 3/16/2022. 2<sup>nd</sup> Senate Health hearing 3/23/22. 3<sup>rd</sup> Senate Health hearing 3/30/2022. 4<sup>th</sup> Senate Health hearing 4/6/2022

### **SB 311 – Coroners and Death Certificates (Sen. S. Huffman and Sen. Johnson)**

Revise the law governing coroners and death certificates

#### **Of Note:**

- Requires that collaboration agreements between APRN’s and collaborating physicians, and supervision agreements between physician assistants and supervising physicians, contain an agreement that the physician must complete and sign the medical certificate of death, regardless or coroner jurisdiction

**Status:** Introduced in the Senate 3/10/2022. 1<sup>st</sup> Senate Health hearing 3/30/2022. 2<sup>nd</sup> Senate Health hearing 4/6/2022

### HB 64 – Regards fraudulent assisted reproduction (Rep. Powell)

To create the crime of fraudulent assisted reproduction and civil actions for an assisted reproduction procedure without consent.

#### Of Note:

- Prohibits a health care professional from purposely or knowingly using human reproductive material from a donor while performing an assisted reproduction procedure if the person receiving the procedure has not expressly consented to the use of that donor's material.
- Creates the crime of fraudulent assisted reproduction, making it a third-degree felony and allows for civil action against a fertility doctor within ten years of the offense.

**Status:** Introduced in the House 2/4/2021. 1<sup>st</sup> House Criminal Justice hearing 2/25/2021. 2<sup>nd</sup> House Criminal Justice hearing 3/17/2021. 3<sup>rd</sup> House Criminal Justice hearing 3/3/2022. 4<sup>th</sup> House Criminal Justice hearing 4/6/2022. Reported out of House Criminal Justice 4/6/2022

### HB 451- Physician administered drugs (Rep. Manning, Rep. Oelslager)

To amend the law related to physician-administered drugs

#### Of Note:

- Prohibits a health benefit plan from requiring that physician-administered drugs be dispensed by a pharmacy, limiting coverage when such drugs are not dispensed by a pharmacy or affiliated pharmacy, or covering such drugs with higher cost-sharing if dispensed in a setting other than a pharmacy

**Status:** 1<sup>st</sup> House Insurance hearing 1/26/22. 2<sup>nd</sup> House Insurance hearing 2/9/2022. 3<sup>rd</sup> House Insurance hearing 3/23/2022. 4<sup>th</sup> House Insurance hearing 5/18/2022. 5<sup>th</sup> House Insurance hearing 5/25/2022

### HB 50 – Medical Devices (Rep. Miranda)

Enact Paige's Law re: medical identifying devices

#### Of Note:

- Modifies the law governing the use of medical identifying devices, including by recognizing devices containing bar or quick response codes that may be scanned to obtain medical information in an emergency

**Status:** Introduced in the House 2/4/2021. 1<sup>st</sup> House Health hearing 1/25/2022. 2<sup>nd</sup> House Health hearing 2/15/2022. 3<sup>rd</sup> House Health hearing 5/17/2022

### HB 378 – Abortion Reversal (Rep. Koehler and Rep. Fowler Arthur)

Regarding pretreatment notice about the possibility of reversing a mifepristone abortion.

#### Of Note:

- Prohibits a physician from performing a mifepristone abortion without both informing the patient of the possibility to reverse the mifepristone abortion if she changes her mind and providing information from the Department of Health website on assistance with reversing the effects of the of the mifepristone abortion

- Criminalizes violations of the previous requirements as a misdemeanor of the first degree.
- Allows a patient who a mifepristone abortion is performed on to file a wrongful death suit against an individual who fails to inform the patient of the possibility of reversal.

**Status:** Introduced in the House 7/15/2021. Referred to House Health 9/16/2021. 1<sup>st</sup> House Health hearing 2/15/2022. 2<sup>nd</sup> House Health hearing 3/8/2022. 3<sup>rd</sup> House Health hearing 3/22/2022

### **Closely monitoring**

#### **HB 41– Exempt mental health care providers' info from Public Records Law (Rep. Lanese and Rep. Liston)**

To exempt certain mental health care providers' residential and familial information from disclosure under the Public Records Law.

**Of Note:**

- Adds forensic mental health providers, mental health evaluation providers, and regional psychiatric hospital employees to the list of professions, consolidated in continuing law into the term “designated public service worker,” whose residential and familial information is exempted from disclosure under the Public Records Law.

**Status:** Passed out the House 2/4/2021. 1<sup>st</sup> Senate Health hearing 3/24/2021. 2<sup>nd</sup> Senate Health hearing 10/6/2021

#### **HB 435 – Vaccinations (Rep. Carfagna and Rep. Seitz)**

To extend certain timelines for qualified civil immunity and expand immunity to include hearing aid dealers and hearing aid fitters; to authorize emergency medical technicians to administer COVID-19 tests; to expressly cover COVID-19 vaccine injuries under the workers' compensation system.

**Of Note:**

- Sunsets June 30, 2023
- Provides vaccine mandate exemption for vaccines that have not received an FDA biologics license.
- Most public and private sector would be able to receive exemptions:
  - a) Medical contraindications; - shall provide a written statement from primary care provider
  - b) Natural immunity: - responsible for any costs or fees associated with demonstrating natural immunity to the employer.
  - c) Reasons of conscience, including religious convictions. -shall provide a written statement

**Status:** Introduced in the House 9/28/2021. Reported 9/29/2021. Re-referred to House Rules and Reference 9/29/2021.

**SB 150 – Physician Contracts (Sen. Johnson and Sen. Williams)**

To prohibit the use of noncompete provisions in physician employment contracts.

**Of Note:**

- Would prohibit the use of noncompete provisions in physician employment contracts.

**Status:** Introduced in the Senate 3/31/2021. 1<sup>st</sup> Senate Small Business & Economic Opportunity hearing 5/5/2021. 2<sup>nd</sup> Senate Small Business & Economic Opportunity hearing 5/12/2021. 3<sup>rd</sup> Senate Small Business & Economic Opportunity hearing 10/27/21.

**SB 151 – Infant Medical Treatment (Sen. Johnson)**

To establish standards for the medical treatment of certain infants and to name the act Emery and Elliot's Law.

**Of Note:**

- Outlines medical treatment for mothers and infants in emergency situations or infants with a disability.

**Status:** Introduced in the Senate 3/31/2021. 1<sup>st</sup> Senate Health hearing 6/2/2021. 2<sup>nd</sup> Senate Health hearing 9/15/2021

**SB 48 – Cultural Competency (Sen. Maharath and Sen. Antonio)**

To require certain health care professionals to complete instruction in cultural competency.

**Of Note:**

- Requires certain health care professionals to complete instruction in cultural competency and provide proof of completion at initial application for licensure and at renewal.
- Includes: dentists, nurses, pharmacists, physicians, psychologists, and social workers.

**Status:** Introduced in the Senate 2/3/2021. 1<sup>st</sup> Senate Health hearing 6/16/2021.

**HB 160 – Health Estimates (Health care price transparency) (Rep. Holmes)**

Regarding the provision of health care cost estimates.

**Of Note:**

- Authorizes the relevant regulatory boards to impose administrative remedies on a health plan issuer or health care provider who fails to comply with the bill's health care price transparency provisions.

**Status:** Introduced in the House 2/18/2021. 1<sup>st</sup> House Insurance Hearing 3/10/2021.

**HB 43– Authorize public bodies to meet via video- and teleconference (Rep. Sobecki and Rep. Hoops)**

To authorize public bodies to meet via teleconference and video conference.

**Of Note:**

- Allows public bodies to meet and hold hearings via teleconference or video conference.
- Requires public bodies to provide the public with access to meetings and hearings commensurate with the method in which the meeting is being conducted.

**Status:** Introduced in the House 2/4/2021. Referred to House Government Oversight committee 2/4/2022. 1<sup>st</sup> House Government Oversight hearing 2/11/2021.

**SB 123 – Abortion (Sen. Roegner and Sen. O’Brien) (companion HB 598)**

To enact the Human Life Protection Act to prohibit abortions based upon a condition precedent.

**Of Note:**

- Prohibits, as the crime of criminal abortion, a person from purposely causing or inducing an abortion by using a drug or substance or an instrument or other means.
- Provides that criminal abortion is a felony of the fourth degree.
- Provides an affirmative defense to a criminal abortion charge if the physician performed or induced the abortion, or attempted to do so, under the determination that it was necessary to prevent the woman’s death or a serious risk of the substantial and irreversible impairment of a major bodily function.
- Requires the State Medical Board to revoke a physician’s license to practice if the physician is guilty of abortion manslaughter, criminal abortion, or promoting abortion.

**Status:** Introduced in the Senate 3/9/2021. 1<sup>st</sup> Senate Health hearing 9/29/2021. 2<sup>nd</sup> Senate Health Hearing 10/27/2021.

**HB 598 – Abortion (Rep. Schmidt) (companion SB 123)**

To enact the Human Life Protection Act to prohibit abortions based upon a condition precedent

**Of Note:**

- Prohibits, as the crime of criminal abortion, a person from purposely causing or inducing an abortion by using a drug or substance or an instrument or other means.
- Provides that criminal abortion is a felony of the fourth degree.
- Provides an affirmative defense to a criminal abortion charge if the physician performed or induced the abortion, or attempted to do so, under the determination that it was necessary to prevent the woman’s death or a serious risk of the substantial and irreversible impairment of a major bodily function.
- Requires the State Medical Board to revoke a physician’s license to practice if the physician is guilty of abortion manslaughter, criminal abortion, or promoting abortion.

**Status:** Introduced in the House 3/15/2022. Referred to House Government Oversight 3/22/2022. 1<sup>st</sup> House Government Oversight hearing 4/27/2022. 2<sup>nd</sup> House Government Oversight hearing 5/19/2022. 3<sup>rd</sup> House Government Oversight hearing 5/26/2022.

**SB 161 – Surgical Smoke (Sen. Brenner)**

Regards surgical smoke.

**Of Note:**

- Requires that not later than one year after the effective date of enactment, each ambulatory surgical facility shall adopt and implement a policy designed to prevent



human exposure to surgical smoke during any planned surgical procedure that is likely to generate surgical smoke.

- The policy shall include the use of a surgical smoke evacuation system.

**Status:** Introduced in the Senate 4/15/2021. 1<sup>st</sup> Senate Health hearing 9/22/2021. 2<sup>nd</sup> Senate Health hearing 11/10/2021. 3<sup>rd</sup> Senate Health hearing 3/16/2022.

### **SB 206 – Art & Music Therapists (Sen. Yuko and Sen. Brenner) (companion HB 359)**

To license and regulate art therapists and music therapists.

#### **Of Note:**

- Creates a new license type for music therapists to be regulated under the Medical Board

**Status:** Introduced in the Senate 7/1/2021. Assigned to Senate Health 9/8/2021. 1<sup>st</sup> Senate Health hearing 5/18/2022

### **HB 359 – Art & Music Therapists (Rep. Russo and Rep. Callender) (companion SB 206)**

To license and regulate art therapists and music therapists.

#### **Of Note:**

- Creates a new license type for music therapists to be regulated under the Medical Board

**Status:** Introduced in the House 6/24/2021. Referred to House State and Local Government 9/21/2021. Referred to House Primary & Secondary Education 6/25/2021

### **HB 221 – Advanced Practice Registered Nurses (Rep. Brinkman and Rep. Gross)**

To modify the laws governing the practice of advanced practice registered nurses and to designate these provisions as the Better Access, Better Care Act.

#### **Of Note:**

- Would allow an APRN who has completed 2,000 clinical practice hours under a standard care arrangement the option to practice without a collaboration agreement.
- Allows an APRN who has not completed the required hours to enter into a standard care arrangement with an APRN who has completed 2,000 clinical practice hours.

**Status:** Introduced in the House 3/17/2021. Referred to House Health 3/23/2021.

### **HB 355 – Pregnancy (Rep. Boggs and Rep. Hicks-Hudson)**

To authorize a pregnant minor to consent to receive health care to maintain or improve her life or the life of the unborn child she is carrying.

#### **Of Note:**

- Allows a pregnant minor to consent to receive health care, such as prenatal health care, health care during delivery, post-delivery health care, and family planning services, to maintain or improve her life or the life of the unborn child she is carrying.



- States that the bill does not remove or limit any person's responsibility under Ohio law to report child abuse or neglect.

**Status:** Introduced in the House 5/19/2021. Referred to House Families, Aging and Human Services 6/24/2021.

### **HB 388 – Vaccine Refusal (Rep. Jordan)**

To prohibit taking certain actions against an individual because the individual refuses to be vaccinated against a disease.

**Of Note:**

- Prohibits certain discriminatory actions against unvaccinated people

**Status:** Introduced in the House 8/12/2021.

### **HB 402 – Ohio Midwife Practice Act (Rep. Boyd and Rep. Hicks-Hudson)**

To regulate the practice of certified professional midwives and to name this act the Ohio Midwife Practice Act.

**Of Note:**

- Regulates the practice of certified professional midwives

**Status:** Introduced in the House 8/12/2021. Referred to House Families, Aging and Human Services 9/21/2021.

### **HB 495- Create Patient Protection Act (Representative Gross)**

**Of Note:**

- Requires specified health care professionals (including physicians, PA's, anesthesiology assistants, limited branch licensees, acupuncturists and genetic counselors) to offer patients medical chaperones and to establish certain mandatory reporting requirements for health care professionals.
- The health care professional may refuse to conduct an exam if the patient or patient's representative declines to have a medical chaperone present during the exam

**Status:** Introduced in the House 11/23/2021. Referred to the House Families Aging and Human Services 12/7/2021

### **HB 496 – Regulate the Practice of Certified Midwives (Rep. Koehler)**

To regulate the practice of certified nurse-midwives, certified midwives, and certified professional midwives

**Of Note:**

- Regulates the practice of certified professional midwives

**Status:** Introduced in the House 11/29/2021. Referred to House Families Aging and Human Services 12/7/21. 1<sup>st</sup> House Families, Aging & Human Services hearing 2/7/2022. 2<sup>nd</sup> House Families, Aging & Human Services hearing 5/19/2022

**HB 645 – Dispensing Pharmacies (Rep. Fraizer and Rep. Holmes)**

To authorize the operation of remote dispensing pharmacies

**Of Note:**

- Authorized the operation of remote dispensing pharmacies and charges the State Board of Pharmacy with their regulations
- Requires a remote dispensing pharmacy to be staffed by two or more pharmacy interns or certified pharmacy technicians and overseen and operated by both a supervising pharmacy and pharmacist through the use of a telepharmacy system.

**Status:** Introduced in the House 5/11/2022. Referred to House Health 5/17/2022. 1<sup>st</sup> House Health hearing 5/24/2022.

**HB 652 – Automated Rx Reporting System (Rep. Plummer and Rep. T. Young)**

To revise the law governing the review of patient information in the Ohio Automated Rx Reporting System, to establish requirements on the dispensing of opioid analgesics, to provide for a cash transfer.

**Of Note:**

- Requires health related licensing boards to adopt guidelines regarding patient counseling and education to be provided by a health care professional when prescribing an opioid analgesic for five or more days
- Revises the law requiring prescribers to review patient information in OARRS, by eliminating an exception for an opioid analgesic prescribed or personally furnished for seven days

**Status:** Introduced in the House 5/12/2022. Referred to House Health committee 5/17/2022. 1<sup>st</sup> House Health hearing 5/24/2022

**HB 680 – Preventative Care Act (Rep. T. Young and Rep. Stein)**

Regards certain off-label use of drugs, products, and devices approved or authorized by the USFDA

**Of Note:**

- Allows for off-label drug treatment for patients at risk of having another qualifying condition
- Other qualifying condition means a preventable, acute or chronic health condition caused by a contagion that has resulted in the death of at least one person in this state

**Status:** Introduced in the House 5/16/2022. Referred to House Health committee 5/18/2022

**HB 454 – Sex Alteration (Rep. Glick and Rep. Grendell)**

Enact the Save Adolescents from Experimentation (SAFE) Act

**Of Note:**

- Bans physicians, mental health providers, or other medical health care professionals from performing gender transition procedures or referring to a medical health care professional for gender transition procedures if the individual is under 18 years old
- Any violation will be considered unprofessional conduct and subject to disciplinary action from the licensing body

**Status:** Introduced in the House 10/19/2021. Referred to House Families, Aging and Human Services 10/26/2021. 1<sup>st</sup> House Families, Aging and Human Services hearing 2/17/2022. 2<sup>nd</sup> House Families, Aging and Human Services hearing 5/19/2022. 3<sup>rd</sup> House Families, Aging and Human Services hearing 5/26/2022. 4<sup>th</sup> House Families, Aging and Human Services hearing 6/1/2022.

## Operationalizing

### SB 6 – Join Interstate Medical Licensure Compact (Sen. Roegner and Sen. Steve Huffman)

#### Of Note:

- Actively working through implementation

**Status:** Passed out of the legislature 6/24/2021. Signed by Governor DeWine 7/1/2021. Required to be operational by 9/28/2022.

**HB 110 – State Operating Budget (Rep. Oelslager)**

Creates appropriations for FY 2022-2023.

**Of Note:**

- The Medical Board budget request was granted in the first version of the bill and remained in the final version.

**Status:** Passed out of the legislature 6/28/2021. Signed by Governor DeWine 6/30/2021. Provisions with appropriations are effective 6/30/2021. All other provisions are effective 9/30/2021.

**Sub HB 51- Valuation determinations for property damage from natural events with language to reauthorize remote hearing authority for Ohio public entities. Contains emergency clause.****Of Note:**

- Public bodies could choose to meet remotely through June 30.

**Status:** House concurred in Senate Amendments 2/9/2022. Signed by Governor DeWine (2/17/2022). Effective date 2/17/2022

**SB 9 – Regulations (Sen. McColley and Sen. Roegner)**

To reduce regulatory restrictions in administrative rules.

**Of Note:**

- Requires certain agencies to reduce the number of regulatory restrictions in their administrative rules.
- Changes the criteria that all agencies must use when conducting a five-year review of an existing rule to match the act's criteria for elimination of regulatory restrictions

**Status:** Passed out of the Senate 3/10/2021. Third hearing in House Government Oversight held 10/28/2021. Passed House 3/2/2022. Senate concurred in House Amendments 3/2/2022. Signed by Governor DeWine 3/10/2022. Effective Date: 6/7/2022

**HB 193 – Electronic Prescriptions (Rep. Cutrona and Rep. Pavliga)**

Regarding electronic prescriptions and schedule II-controlled substances.

**Of Note:**

- Requires that all schedule II drugs be prescribed electronically.
- Exceptions a prescriber may issue a written rather than electronic prescriptions for a schedule II controlled substance: temporary technical, electrical, or broadband failure; prescription is issued for a nursing home resident or hospice care patient; the prescriber is employed by or under contract with the same entity that operates the pharmacy; the prescriber determines that an electronic prescription cannot be issued in a timely manner and the patient's medical condition is at risk; the prescriber issues per year not more than 50 prescriptions for schedule II controlled substances; prescription

issued from a health care facility or emergency department and the prescriber determines an electronic prescription would be impractical

- Amended – Modifies a provision of existing law, which allows a physician licensed in another state or territory, but unlicensed in Ohio, to provide consultation to physician licensed in Ohio, by requiring that the Ohio-licensed physician who receives the consultation from the out-of-state physician must have an established physician-patient relationship with the patient who is the subject of the consultation

**Status:** Passed out of the House 6/23/2021. 1<sup>st</sup> Senate Health hearing 10/20/2021. 2<sup>nd</sup> Senate Health hearing 11/17/21. 3<sup>rd</sup> Senate Health hearing 1/26/2022. 4<sup>th</sup> Senate Health hearing 6/1/2022. Reported out of Senate Health 6/1/2022. Passed out of the Senate 6/1/2022. House concurred with Senate amendments 6/1/2022. Signed by Governor 6/24/2022. Effective 9/24/2022

### **Enacted but no operational changes needed**

#### **HB 6 – Modify laws governing certain professions due to COVID-19 (Rep. Roemer)**

To modify the laws governing certain health professionals and educator preparation programs due to COVID-19.

**Of Note:**

- Allows pharmacists to administer immunization for influenza, COVID-19, and any other disease but only pursuant to prescription for persons seven or older.
- Allows pharmacists to administer immunizations for a disease to those 13 and older.
- Allows podiatrists to administer vaccinations for individuals seven and older for influenza and COVID-1.

**Status:** Enacted 5/14/2021. Certain provisions effective 10/9/2021.

#### **HB 176 – Athletic Training (Rep. Carfagna and Rep. Hall)**

To revise the law governing the practice of athletic training.

**Of note:**

- Makes changes to the law governing the practice of athletic training, including by requiring an athletic trainer to practice under a collaboration agreement with a physician or podiatrist.
- Amendment was included in the final version to prohibit an athletic trainer from administering intratendinous and intra-articular injections.

**Status:** Passed out of the House 5/5/2021. Passed out of the Senate 9/28/2021. Signed 10/28/2021. Effective 1/25/2022.

**HB 37– Emergency Prescription Refills (Rep. Gayle Manning)**

Regards emergency prescription refills.

**Of Note:**

- Increases from one to three the number of times that a pharmacist may dispense, without a prescription, certain drugs (dangerous drugs, other than a schedule II controlled substance) to a specific patient within a 12-month period.

**Status:** Passed out the House 5/5/2021. Third Senate Health hearing 10/6/2021. 1/26/22, voted out of Senate Health Committee with one technical amendment from LSC. Passed Senate 2/9/2022. House concurred in Senate Amendments 2/16/2022. Signed by Governor DeWine 3/2/2022. Effective 6/1/2022

**HB 138 – Emergency Medical Services (Rep. Baldrige)**

Regarding the scope of emergency medical services provided by emergency medical service personnel.

**Of Note:**

- Eliminates the enumeration of specific services that may be provided by emergency medical services (EMS) personnel.
- Requires the State Board of Emergency Medical, Fire, and Transportation Services to establish the scope of practice for EMS personnel through rulemaking.
- Permits EMS personnel to comply with a do-not-resuscitate order issued by a physician assistant or advanced practice registered nurse.
- Requires the medical director or cooperating physician advisory board of each EMS organization to establish protocols for EMS personnel to follow when providing services at all times.

**Status:** Passed out of the House 6/16/2021. 1<sup>st</sup> Senate Health hearing 9/29/2021. 2<sup>nd</sup> Senate Health hearing 10/20/2021. 3<sup>rd</sup> Senate Health hearing 2/9/2022. 4<sup>th</sup> Senate Health hearing. Reported out of Senate Health 3/2/2022. Passed out of the Senate 3/16/2022. House Concurred in Senate Amendments 3/23/2022. Signed by Gov. DeWine 4/6/2022, Effective Date 7/4/2022



---

**MEMORANDUM**

**TO:** Board Members  
**FROM:** Benton Taylor, Board Parliamentarian  
**DATE:** November 2, 2022  
**RE:** Proposed Board Meeting Dates for 2024

---

The following are proposed meeting dates for the year 2024:

January 10	July 10
February 14	August 14
March 13	September 11
April 10	October 9
May 8	November 13
June 12	December 11

**Proposed motion:** I move to adopt the proposed 2024 meeting dates for the State Medical Board of Ohio, as listed in the Agenda Materials.