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Medical Error Prevention and Root Cause Analysis

This course fulfills the Florida requirement for 2 hours of education on the Prevention of Medical Errors.

Audience
This course is designed for all licensed healthcare professionals.

Course Objective
The purpose of this course is to satisfy the requirement of the Florida law and provide all licensed healthcare professionals with information regarding the root cause process, error reduction and prevention, and patient safety.

Learning Objectives
Upon completion of this course, you should be able to:

1. Describe how the Institute of Medicine defines "medical error."
2. Describe the types of sentinel events the Joint Commission has identified.
3. Discuss what factors must be included in a root cause analysis in order for the Joint Commission to consider it "thorough" and "credible."
4. Identify what types of adverse incidents must be reported to the Florida Agency for Healthcare Administration.
5. Identify the most common sentinel events reported to the Joint Commission.
6. Evaluate the most common misdiagnoses, as recognized by the Florida Board of Medicine, and outline the safety needs of special populations, including non-English-proficient patients.

Faculty
Marjorie Conner Allen, BSN, JD, received her Bachelor of Science in Nursing degree from the University of Florida, Gainesville, in 1984. She began her nursing career at Shands Teaching Hospital and Clinics at the University of Florida, Gainesville. While practicing nursing at Shands, she gave continuing education seminars regarding the nursing implications for dealing with adolescents with terminal illness. In 1988, Ms. Allen moved to Atlanta, Georgia where she worked at Egleston Children's Hospital at Emory University in the bone marrow transplant unit. In the fall of 1989, she began law school at Florida State University. After graduating from law school in 1992, Ms. Allen took a two-year job as law clerk to the Honorable William Terrell Hodges, United States District Judge for the Middle District of Florida. After completing her clerkship, Ms. Allen began her employment with the law firm of Smith, Hulsey & Busey in Jacksonville, Florida where she has worked in the litigation department defending hospitals and nurses in medical malpractice actions. Ms. Allen resides in Jacksonville and is currently in-house counsel to the Mayo Clinic Jacksonville.

Faculty Disclosure
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Special Approvals
This course fulfills the Florida requirement for 2 hours of education on the Prevention of Medical Errors.

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INTRODUCTION

The Institute of Medicine's (IOM) 1999 publication *To Err is Human: Building a Safer Health System*, illuminated the unfortunate reality of medical errors in the healthcare industry. The report reviewed the prevalence of medical errors in the United States and highlighted measures that should be taken to prevent them. Specifically, the authors of the report noted that at least 44,000 and perhaps as many as 98,000 Americans were dying in hospitals each year as a result of medical errors and many more were being seriously injured [1]. They further noted that, even when using the lower estimate of 44,000, deaths in hospitals due to medical errors exceeded the annual deaths attributable to motor vehicle accidents (43,458), breast cancer (42,297), or AIDS (16,516) [1]. A 2016 report stated that the average number of annual in-hospital deaths attributable to medical error might actually be much higher, at around 400,000 [2]. This report places medical errors as the third leading cause of death in the United States. Certainly, these numbers must be balanced against the millions of admissions to hospitals in the United States, which is in excess of 33 million annually [1; 3].

It does appear that some progress has been made in the past decade. The Agency for Healthcare Research and Quality found a 17% decline in hospital-acquired conditions between 2014 and 2017, or 910,000 fewer conditions and 20,500 fewer deaths than if the 2014 rate had remained steady [4]. Though the precise mechanism(s) responsible for this decline is not clear, it occurred following a concerted effort by federal agencies, organizations, and individual providers to curtail medical errors. However, the statistics indicate that medical errors continue to be an issue. Healthcare professionals should commit to continuing to pay greater attention to evaluating approaches for reducing errors and to building new systems to reduce the incidence of medical errors.

Spurred by a commitment to reducing medical error incidents, the Florida Legislature mandates that all healthcare professionals in Florida complete a two-hour course on the topic of prevention of medical errors [5]. This continuing education course is designed to satisfy the requirements of the Florida law and provide all licensed healthcare professionals with information regarding the root cause analysis process, error reduction and prevention, and patient safety, as well as information regarding the five most misdiagnosed conditions as determined by the Florida Board of Medicine.

DEFINING "MEDICAL ERROR"

The IOM Committee on Quality of Healthcare in America defines error as "the failure of a planned action to be completed as intended or the use of a wrong plan to achieve an aim" [1]. It is important to note that medical errors are not defined as intentional acts of wrongdoing and that not all medical errors rise to the level of medical malpractice or negligence. Errors depend on two kinds of failures: either the correct action does not proceed as intended, which is described as an "error of execution," or the original intended action is not correct, which is described as an "error of planning" [1]. A medical error can occur at any stage in the process of providing patient care, from diagnosis to treatment, and even while providing preventative care. Not all errors will result in harm to the patient. Medical errors that do result in injury are sometimes called preventable adverse events or sentinel events—sentinel because they signal the need for immediate investigation and response [6].

Preventable adverse events or sentinel events are defined as those events that cause an injury to a patient as a result of medical intervention or inaction on the part of the healthcare provider whereby the injury cannot reasonably be said to be related to the patient's underlying medical condition. Thus, for example, if a patient has a surgical procedure and dies postoperatively from pneumonia, the patient has suffered an adverse event. But was that adverse event preventable; was it caused by medical intervention or inaction? The specific facts of this case must be analyzed to determine whether the patient acquired the pneumonia as a result of poor handwashing techniques of the medical staff (i.e., an error of execution), which would indicate a preventable adverse event, or whether the patient acquired the pneumonia because of age and comorbidities, which would indicate a nonpreventable adverse event.

Healthcare professionals can learn much by closely scrutinizing and evaluating adverse events that lead to serious injury or death. The evaluation of such events would also enable healthcare professionals to improve the delivery of health care and reduce future mistakes. In addition, healthcare professionals should have a process in place to evaluate those instances in which a medical error occurred and did not cause harm to the patient. By reviewing these processes, healthcare professionals are afforded the unique opportunity to identify system improvements that have the potential to prevent future adverse events. The Joint Commission, recognizing the importance of analyzing both preventable adverse events and near-misses, has established guidelines for recognizing these events and requires healthcare facilities to conduct a root cause analysis to determine the underlying cause of the event [7].

ROOT CAUSE ANALYSIS PROCESS

The Joint Commission is a national organization with a mission to improve the quality of care provided at healthcare institutions in the United States. It accomplishes this mission by providing accredited status to healthcare facilities. Accreditors play an important role in encouraging and supporting actions within healthcare organizations by holding them accountable for ensuring a safe environment for patients. Healthcare organizations should actively engage in a cooperative relationship with the Joint Commission through this accreditation process and participate in the process to reduce risk and facilitate desired outcomes of care.

Root cause analysis, as defined by the Joint Commission, is "a process for identifying the basic or causal factors that underlie variation in performance, including the occurrence or possible occurrence of a sentinel event" [6]. In the 2022 update, the Joint Commission defines a sentinel event as a "patient safety event (not primarily related to the natural course of the illness or underlying condition) that reaches a patient and results in death, severe harm (regardless of duration of harm), or permanent harm (regardless of severity of harm)" [6; 10]. Furthermore, the Joint Commission revision clarified the terms "severe" and "permanent" harm with regard to sentinel events. "Severe harm" is an event or condition that reaches the individual, resulting in life-threatening bodily injury (including pain or disfigurement) that interferes with or results in loss of functional ability or quality of life that requires continuous physiologic monitoring or a surgery, invasive procedure, or treatment to resolve the condition [6; 10]."Permanent harm" is an event or condition that reaches the individual, resulting in any level of harm that permanently alters and/or affects an individual's baseline [6; 10].

The following subsets of sentinel events are subject to review by the Joint Commission [6; 11]:

- The event has resulted in an unanticipated death or major permanent loss of function, not related to the natural course of the patient's illness or underlying condition

or

- The event is one of the following (even if the outcome was not death or major permanent loss of function unrelated to the natural course of the patient's illness or underlying condition):

- Suicide of any patient receiving care, treatment, and services in a staffed around-the-clock care setting or within 72 hours of discharge
- Unanticipated death of a full-term infant
- Abduction of any patient receiving care, treatment, and services
- Any elopement (i.e., unauthorized departure) of a patient from a staffed around the-clock care setting (including the emergency department), leading to death, permanent harm, or severe temporary harm to the patient
- Discharge of an infant to the wrong family
- Rape, assault (leading to death or permanent loss of function), or homicide of any patient receiving care, treatment, and services
- Rape, assault (leading to death or permanent loss of function), or homicide of a staff member, licensed independent practitioner, visitor, or vendor while on site at the healthcare organization
- Hemolytic transfusion reaction involving administration of blood or blood products having major blood group incompatibilities (e.g., ABO, Rh, other blood groups)
- Invasive procedure, including surgery, on the wrong patient or wrong site
- Unintended retention of a foreign object in a patient after surgery or other invasive procedures
- Severe neonatal hyperbilirubinemia (bilirubin >30 mg/dL)
- Fluoroscopy resulting in permanent tissue injury when clinical and technical optimization were not implemented and/or recognized practice parameters were not followed
- Fire, flame, or unanticipated smoke, heat, or flashes occurring during an episode of patient care
- Any intrapartum (related to the birth process) maternal death
- Severe maternal morbidity
- Fall resulting in: any fracture; surgery, casting, or traction; required consult/management or comfort care for a neurological or internal injury; a patient with coagulopathy who receives blood products as a result of the fall; or death or permanent harm as a result of injuries sustained from the fall (not from physiologic events causing the fall)

Alternatively, the following examples are events that are NOT considered reviewable under the Joint Commission's sentinel event policy [6]:

- Any close call ("near miss")
- Full or expected return of limb or bodily function to the same level as prior to the adverse event by discharge or within two weeks of the initial loss of said function, whichever is the longer period
- Any sentinel event that has not affected a recipient of care (e.g., patient, individual, resident)
- Medication errors that do not result in death or major permanent loss of function
- Suicide other than in an around-the-clock care setting or following elopement from such a setting
- A death or loss of function following a discharge against medical advice
- Unsuccessful suicide attempts unless resulting in major permanent loss of function
- Minor degrees of hemolysis not caused by a major blood group incompatibility and with no clinical sequelae

For further definition of terms, please refer to the Joint Commission's Sentinel Event Policy and Procedures at https://www.jointcommission.org/resources/patient-safety-topics/sentinel-event/sentinel-event-policy-and-procedures.

As part of the accreditation requirement, the Joint Commission requires that healthcare organizations have a process in place to recognize these sentinel events, conduct thorough and credible root cause analyses that focus on process and system factors, and document a risk-reduction strategy and internal corrective action plan that includes measurement of the effectiveness of process and system improvements to reduce risk [6]. This process must be completed within 45 business days of the organization having become aware of the sentinel event.

The Joint Commission will consider a root cause analysis acceptable for accreditation purposes if it focuses primarily on systems and processes, not individual performance [6]. In other words, the healthcare organization should minimize the individual blame or retribution for involvement in a medical error. In addition, the root cause analysis should progress from special causes in clinical processes to common causes in organizational processes, and the analysis should repeatedly dig deeper by asking why, then, when answered, why again, and so on. The analysis should also identify changes that can be made in systems and processes, either through redesign or development of new systems or processes, which would reduce the risk of such events occurring in the future. The Joint Commission requires that the analysis be thorough and credible. To be considered thorough, the root cause analysis must include [6]:

- A determination of the human and other factors most directly associated with the sentinel event and the process(es) and systems related to its occurrence
- Analysis of the underlying systems and processes through a series of "why" questions to determine where redesign might reduce risk
- Inquiry into all areas appropriate to the specific type of event
- Identification of risk points and their potential contributions to this type of event
- A determination of potential improvement in processes or systems that would tend to decrease the likelihood of such events in the future, or a determination, after analysis, that no such improvement opportunities exist

To be considered credible, the root cause analysis must meet the following standards [6]:

- The organization's leadership and the individuals most closely involved in the process and systems under review must participate in the analysis.
- The analysis must be internally consistent; that is, it must not contradict itself or leave obvious questions unanswered.
- The analysis must provide an explanation for all findings of "not applicable" or "no problem."
- The analysis must include consideration of any relevant literature.

Finally, as previously discussed, after conducting this root cause analysis, the organization must prepare an internal corrective action plan. The Joint Commission will accept this action plan if it identifies changes that can be implemented to reduce risk or formulate a rationale for not undertaking such changes, and if, where improvement actions are planned, it identifies who is responsible for implementation, when the action will be implemented, and how the effectiveness of the actions will be evaluated [6].

FLORIDA LAW

Healthcare professionals have an obligation to report adverse events to leadership and ensure that organizations have processes in place to satisfy the Joint Commission requirement. In Florida, certain serious adverse incidents must also be reported to Florida's Agency for Health Care Administration (AHCA). Florida law requires that licensed facilities, such as hospitals, establish an internal risk management program. As part of that program, licensed facilities must develop and implement an incident reporting system, which requires the development of appropriate measures to minimize the risk of adverse incidents to patients, as well as imposes an affirmative duty on all healthcare providers and employees of the facility to report adverse incidents to the risk manager or to his or her designee. The risk manager must receive these incident reports within 3 business days of the incident, and depending on the type of incident, the risk manager may have to report the incident to AHCA within 15 days of receipt of the report.

Florida Statute 395.0197 specifically defines an adverse incident as [8]:

For purposes of reporting to the agency pursuant to this section, the term "adverse incident" means an event over which health care personnel could exercise control and which is associated in whole or in part with medical intervention, rather than the condition for which such intervention occurred, and which:

a) Results in one of the following injuries:
   1. Death;
   2. Brain or spinal damage;
   3. Permanent disfigurement;
   4. Fracture or dislocation of bones or joints;
   5. A resulting limitation of neurological, physical, or sensory function which continues after discharge from the facility;
   6. Any condition that required specialized medical attention or surgical intervention resulting from nonemergency medical intervention, other than an emergency medical condition, to which the patient has not given his or her informed consent; or
   7. Any condition that required the transfer of the patient, within or outside the facility, to a unit providing a more acute level of care due to the adverse incident, rather than the patient's condition prior to the adverse incident

b) Was the performance of a surgical procedure on the wrong patient, a wrong surgical procedure, a wrong-site surgical procedure, or a surgical procedure otherwise unrelated to the patient's diagnosis or medical condition;

c) Required the surgical repair of damage resulting to a patient from a planned surgical procedure, where the damage was not a recognized specific risk, as disclosed to the patient and documented through informed-consent process; or

d) Was a procedure to remove unplanned foreign objects remaining from a surgical procedure.

In 2021, the Florida AHCA reported that a total of 184 deaths occurred as a result of hospital error, 21.4% of 859 adverse incidents reported for the year. The next most common incidents during this period were transfer of the patient to a unit providing a more acute level of care due to the adverse incident (18.7%), fracture or dislocation of bones or joints (17.0%), surgical procedures unrelated to the patient's diagnosis or medical needs (10.4%), surgical procedure to remove foreign

object from a previous surgical procedure (10.2%), brain or spinal damage (5.0%), and surgical procedure performed on wrong site (4.3%) [9]. The following adverse incidents must be reported to the AHCA within 15 calendar days after their occurrence [8]:

- The death of a patient
- Brain or spinal damage to a patient
- The performance of a surgical procedure on the wrong patient
- The performance of a wrong-site surgical procedure
- The performance of a wrong surgical procedure
- The performance of a surgical procedure that is medically unnecessary or otherwise unrelated to the patient's diagnosis or medical condition
- The surgical repair of damage resulting to a patient from a planned surgical procedure, where the damage is not a recognized specific risk, as disclosed to the patient and documented through the informed-consent process
- The performance of procedures to remove unplanned foreign objects remaining from a surgical procedure

Each incident will be reviewed by the AHCA, who will then determine the penalty to be imposed upon the responsible party [8]. All Florida healthcare professionals who practice in licensed facilities should familiarize themselves with these requirements and ensure that the facility in which they practice has processes in place to ensure compliance.

Unlike Florida's mandatory reporting of serious adverse incidents, the Joint Commission recommends that healthcare organizations voluntarily report sentinel events, and it encourages the facilities to communicate the results of their root cause analyses and their corrective action plans. As a result of the sentinel events that have been reported, the Joint Commission has compiled Sentinel Event Alerts. These alerts are intended to provide healthcare organizations with important information regarding reported trends and, by doing so, highlight areas of potential concern so an organization may review its own internal processes to maximize error reduction and prevention with regard to a particular issue [7].

ERROR REDUCTION AND PREVENTION

Between 2005 and 2021, the Joint Commission reviewed 14,731 sentinel events [11]. Some events, such as fire, impacted multiple patients. Sentinel event reviews during this time period were frequently conducted for patient fall; delay in treatment; unintended retention of a foreign body; wrong-patient, wrong-site, wrong-procedure surgery; patient suicide; operative and postoperative complications; and medication error [11].

PATIENT FALLS

In 2021, the Joint Commission introduced a separate sentinel event line item for patient falls, making it the most frequently reported sentinel event that year. Patients who are at highest risk include the elderly, those who have an altered mental status due to chronic mental illness or acute intoxication, and those who have a history of prior falls. Additionally, the Joint Commission calls for an increased awareness to an under-recognized population at risk for falls. Newborns and infants are at risk for falls and/or drops, often due to maternal risk factors such as cesarean birth, use of pain medication within four hours, second or third postpartum night (specifically around midnight to early morning hours), and drowsiness associated with breastfeeding. It is obvious from these factors that a thorough and complete patient history may be the key to identifying those at risk.

The root causes of patient falls that healthcare facilities identified as sentinel events and reported to the Joint Commission included inadequate assessment; communication failures; lack of adherence to protocols and safety practices; inadequate staff orientation, supervision, staffing levels, or skill mix; deficiencies in the physical environment; and lack of leadership [19]. Risk reduction strategies to these root causes are fairly straightforward, although in practice, preventing falls is difficult. The most important are the use of a standardized assessment tool to identify fall and injury risk factors, assessing an individual patient's risks that may not have been captured through the tool, and interventions tailored to an individual patient's identified risks [19].

Because patient falls often result in morbidity, mortality, immobility, and early nursing home placement for patients, it is imperative that healthcare facilities initiate adequate fall prevention programs, which will ultimately reduce injuries. Failure to do so will result in a spiraling increase in the number of falls in healthcare facilities, particularly among the elderly who are at highest risk. As more Americans live beyond 65 years of age, the need to develop mobility protocols and programs to reduce the risk of falls and injuries for the older adult grows more urgent.

DELAYS IN TREATMENT

According to the Joint Commission, more than half of all reported delay in treatment sentinel events in 2010–2014 resulted in patient death [16]. It is important to keep in mind that delays in treatment can occur in any healthcare setting. The most common reason for a delay in treatment is misdiagnosis; however, delays can also result from delayed test results, lack of physician availability, delayed administration of ordered care, incomplete treatment, and even inability to get an initial appointment or follow-up appointment in a timely manner [16]. The main root causes contributing to delays in treatment are inadequate assessments, poor planning, communication failures, and human factors. Additionally, 48% of patients self-reported a delay in accessing healthcare during the COVID-19 pandemic. One study suggests that delays in

treatment are likely due to widespread public health messages to avoid unnecessary visits, triage uncertainty, lack of providers, and lack of resources [36]. Recommendations from the Joint Commission include avoiding cognitive shortcuts, improving health information technology, incorporating diagnostic checklists into the electronic record, promoting provider-to-provider communication, engaging leadership in developing solutions, focusing organization attention on the scheduling process and on ordering tests and reporting test results, improving access to care, implementing a standardized communications method, maintaining adequate staffing levels, and increasing patient and family engagement/activation [16].

UNINTENDED RETENTION OF A FOREIGN BODY

In 2021, unintended retained foreign objects were the third most frequently reported sentinel event reported to the Joint Commission [11]. The prevalence of these events has remained relatively stable since 2009, indicating that preventing these errors remains difficult for practitioners and facilities. The most commonly retained items are sponges, followed by catheter guidewires and other (a broad category encompassing a wide variety of items) [11].

In addition to harming patients and contributing to distrust in the medical system, the unintended retention of foreign objects significantly contributes to patient care costs [13]. The average total cost of care related to unintended retained foreign objects is $166,000 to $200,000 [13].

According to the sentinel event data, the most common root causes of unintended retained foreign objects reported to the Joint Commission are [13]:

- The absence of policies and procedures
- Failure to comply with existing policies and procedures
- Problems with hierarchy and intimidation
- Failure in communication with physicians
- Failure of staff to communicate relevant patient information
- Inadequate or incomplete education of staff

WRONG-SITE SURGERY

Operating on the wrong part of a patient's body is an obvious sign that there is a problem in the operating room system. Interestingly, wrong-site surgery occurred more commonly in orthopedic procedures than in all other surgical specialties combined. The American Academy of Orthopaedic Surgeons takes this issue seriously, and it has taken special steps to eliminate the problem. For example, it recommends that a surgeon sign their initials at the correct site of surgery with an indelible pen. Unless the initials are visible, the surgeon should not make an incision [12]. Writing "NO" in large black letters on the side not to be operated on was suggested in the past, but this is discouraged due to possible confusion with the surgeon's initials. In spinal surgery, the Academy recommends that an intraoperative radiograph and radiopaque marker be used to determine the exact vertebral level of spinal surgery [12]. Whatever the mechanism used to prevent and reduce the incidence of this error, it is clear that this is not just the surgeon's problem. All operating room personnel, including physicians, nurses, technicians, anesthesiologists, and other preoperative allied health personnel, should monitor procedures to ensure verification procedures are followed, especially for high-risk procedures.

Due to the prevalence of wrong-site, wrong-procedure, and wrong-person surgeries, the Joint Commission, along with more than 50 professional healthcare organizations, convened two summits to help reduce the occurrence of these errors. The first summit, convened in 2003, developed a Universal Protocol that consisted of the following: a preprocedure verification process; marking the operative/procedure site with an indelible marker; taking a "time-out" with all team members immediately before starting the procedure; and adaptation of the requirements to all procedure settings, including bedside procedures. However, the incidence of wrong-site surgeries continued to increase, and in 2007 and 2010, additional summits were organized to pinpoint barriers in compliance and discover new strategies to eliminate these errors [14]. As of 2019, the Universal Protocol has been incorporated into the National Patient Safety Goal chapter of the Joint Commission accreditation manual [15].

PATIENT SUICIDE

It is estimated that between 48 and 65 hospital inpatient suicides occur per year in the United States. Most of these cases (31 to 52) occur in psychiatric units or involve psychiatric inpatients. The most common method is hanging [50]. Times of care transition are particularly risky, with a 200% increase in risk in the week after discharge from a psychiatric facility; the elevated risk continues for four years [18]. Other risk factors include previous suicide attempt or self-injury, mental or emotional disorders, history of trauma or loss, serious illness or chronic pain, substance use disorder, social isolation, and access to lethal means.

The most common root cause documented for patient suicide reported between 2010 and 2014 was shortcomings in assessment, most commonly psychiatric assessment [18]. In addition, nearly 25% of behavioral health facilities accredited by the Joint Commission were found noncompliant with the requirement to conduct an adequate suicide risk assessment in 2014.

The Joint Commission has recommended a number of suicide risk reduction strategies, including [18]:

- Review each patient's personal and family medical history for suicide risk factors.
- Screen all patients for suicide ideation, using a brief, standardized, evidence-based screening tool.
- Review screening questionnaires before the patient leaves the appointment or is discharged.

- Establish a collaborative, ongoing, and systematic assessment and treatment process with the patient involving the patient's other providers, family, and friends, as appropriate.
- To improve outcomes for at-risk patients, develop treatment and discharge plans that directly target suicidality.
- Educate all staff in patient care settings about how to identify and respond to patients with suicide ideation.
- Document decisions regarding the care and referral of patients with suicide risk.

A simple review of these measures demonstrates that healthcare providers can avoid the devastating impact of an inpatient suicide by implementing routine preventative strategies, such as removing harmful items and careful screening through the admission and discharge processes.

OPERATIVE AND POSTOPERATIVE COMPLICATIONS

Many of the sentinel events reported to the Joint Commission regarding operative and postoperative complications occurred in relation to nonemergent procedures, such as interventional imaging and/or endoscopy, tube or catheter insertion, open abdominal surgery, head and neck surgery, orthopedic surgery, and thoracic surgery [17]. The majority of the reporting healthcare facilities cited miscommunication as the primary root cause. Other identified causes include failure to follow established procedures, incomplete preoperative assessment, inconsistent postoperative monitoring procedures, and failure to question inappropriate orders. In order to reduce the risk, reporting facilities have identified a number of strategies, including improving staff orientation and training, increasing educational opportunities for physicians, clearly defining expected channels of communication, and monitoring consistency of compliance with procedures. Healthcare facilities should review postoperative patient monitoring procedures to ensure an adequate level appropriate to the needs of the patient, regardless of the setting (e.g., operating room, endoscopy suite, radiology department) [17]. Based upon these findings, it is clear that direct communication among healthcare providers is key to preventing operative and postoperative complications. Healthcare facilities should provide more staff education regarding preventative measures, and healthcare providers can do their part by engaging in a healthy and mutual respect for all of the members of the healthcare team [17].

MEDICATION ERRORS

Unquestionably, medication errors are one of the most common causes of avoidable harm to patients. These errors may occur at any of these critical points: when ordered or prescribed by a physician; during documentation; while transcribing; when dispensed by a pharmacist; when administered by a nurse; or during monitoring.

The National Coordinating Council for Medication Error Reporting and Prevention defines a medication error as [20]:

> Any preventable event that may cause or lead to inappropriate medication use or patient harm while the medication is in the control of the healthcare professional, patient or consumer. Such events may be related to professional practice, healthcare products, procedures, and systems, including prescribing: order communication; product labeling; packaging, and nomenclature; compounding; dispensing; distribution; administration; education; monitoring; and use.

It has been estimated that up to 50% of medication errors are caused by a provider writing the wrong medication, the wrong route or dose, or the wrong frequency, and nearly 75% of medication errors have been attributed to distraction of the care provider [24]. In addition, a number of medication errors can be linked to the prescriber who continually uses potentially dangerous abbreviations and dose expressions. Despite repeated warnings by the Institute for Safe Medication Practices about the dangers associated with using certain abbreviations when prescribing medications, this practice continues. To eliminate this factor, there are fairly simple steps that can eliminate much confusion. Prescribers should [21]:

- Avoid the use of the symbol "U" or "u" but rather spell "units" when ordering drugs, such as insulin.
- Spell out medication names completely rather than using abbreviations and acronyms.
- Avoid using abbreviations for "daily" (QD), "every other day" (QOD), or "four times daily" (QID), which are easily confused.
- Use leading zeros before a decimal point (e.g., 0.2 mg instead of .2 mg), and do not use trailing zeros (e.g., 2 mg instead of 2.0 mg).
- Write out "morphine sulfate" and "magnesium sulfate" instead of using the abbreviations (MS, MSO_4, $MgSO_4$).

The Institute for Safe Medication Practices publishes a list of error-prone abbreviations, symbols, and dose designations online at https://www.ismp.org/recommendations/error-prone-abbreviations-list.

Other factors contributing to prescriber errors are illegible or confusing handwriting and, a frequently cited cause of many adverse and sentinel events, the failure of healthcare providers to assess risk and prevent errors. Addressing illegibility may include developing appropriate policies and procedures, tracking and trending patterns, and evaluating results through peer review committees. Improving communication might include developing protocols for the use of verbal orders to assure that those from an onsite practitioner would be limited to an

emergency situation only. No verbal orders should be taken for certain medications, such as for chemotherapy, and all verbal orders should be repeated for clarification and, whenever possible, reiterated to a third person. Another method of improving communication might involve reviewing the hospital formulary in collaboration with the Pharmacy and Therapeutics Committee of the medical staff to limit, where appropriate, the number of therapeutically and generically equivalent products [22].

It has been estimated that between 0.2% and 10% of prescriptions are dispensed incorrectly [23]. The three most common dispensing errors are: dispensing an incorrect medication, dosage strength, or dosage form; miscalculating a dose; and failing to identify drug interactions or contraindications [24]. Safe medication dispensing practices may include a number of risk reduction strategies to reduce the incidence of errors that may cause harm to patients [22; 25; 54; 61]:

- Ensure that appropriate and current drug reference texts and/or online resources are immediately available to pharmacy personnel.
- Ensure that essential patient information, such as allergies, age, weight, current diagnoses, pertinent lab values, and current medication regimen, is available to the pharmacist prior to the dispensing of a new medication order.
- Require clarification of any order that is incomplete, illegible, or otherwise questionable using an established process for resolving questions.
- Whenever possible, dispense dosage units in a ready-to-administer form.
- Dispense single-dose vials and ampoules rather than multidose vials.
- Select oral rather than injectable routes, when possible.
- Require that a pharmacist double-check all mathematical calculations for neonatal and pediatric dilutions, parenteral nutrition solutions, and other compounded pharmaceutical products.
- Create an environment for the dispensing area that minimizes distractions and interruptions, provides appropriate lighting, air conditioning, and air flow, safe noise levels, and includes ergonomic consideration of equipment, fixtures, and technology.
- Require that a second pharmacist double-check the accuracy of order entry and dose calculations for all orders involving antineoplastic agents and other high-risk drugs dispensed by the pharmacy.
- Enhance the awareness of look-alike and sound-alike medications, and use warning signs to help differentiate medications from one another, especially when confusion exists between or among strengths, similar looking labels, or similar sounding names.
- Separate look-alike and sound-alike medications in pharmacy dispensing areas or consider repackaging or using different vendors.
- Follow-up and periodically evaluate the need for continued drug therapy for individual patients.

Once again, communication is likely the key to avoiding dispensing errors. Pharmacists should work closely with their staff to ensure that proper protocols are followed, and most importantly, when questions arise regarding a prescription, the pharmacist should take the time to contact the prescriber directly to obtain clarification.

The healthcare provider who has the responsibility to administer a medication has the final opportunity to avoid a mistake. In most cases, particularly in inpatient settings, this responsibility falls to the nurse. Nurses are often taught in nursing school to review the five "rights" prior to administering any medication: the right patient is given the right drug in the right dose by the right route at the right time [26]. Medication errors generally fall into four categories, which mimic these five "rights." The first is the failure to follow procedural safeguards, such as ensuring that essential patient information, including allergies, age, weight, and current medication regimen, is available. The second is unfamiliarity with a drug. In one case, a jury determined that a nurse was negligent for giving a drug without having reviewed the literature, which stated that the necessary precautions for the administration of the drug required the specialized skill of an anesthesiologist. The third category of drug administration is failure to use the correct mode of administration. A nurse in Delaware was held liable for administering a medication by injection after an order had been written to change the route to oral. The final category involves failure to obtain clarification if an order is incomplete, illegible, or otherwise questionable. In a case tried in Louisiana, a nurse was held liable for administering a medication that a physician ordered, notwithstanding that the dose was excessive. The nurse's administration of the drug led to the patient's death [27].

In addition, healthcare facilities should implement appropriate guidelines, policies, and procedures to ensure safe medication administration practice. These policies should require that staff members who administer medications [24; 25; 54; 61]:

- Are knowledgeable about the drug's uses, precautions, contraindications, potential adverse reactions, interactions, and proper method of administration
- Resolve questions prior to medication administration
- Only administer medications that have been properly labeled with medication name, dose to be administered, dosage form, route, and expiration date
- Utilize a standard medication administration time schedule and receive education on how and when to incorporate newly started medication orders safely into the standardized schedule

- Have a second person verify a dosage calculation if a mathematical calculation of a dose is necessary
- Receive adequate education on the operation and use of devices and equipment used for medication administration (for example, patient-controlled anesthesia pumps and other types of infusion pumps)
- Have another person double-check infusion pump settings when critical, high-risk drugs are infused
- Document all medications immediately after administration

Finally, healthcare facilities should have proper quality assurance measures in place to monitor medication administration practices. Included among these would be protocols and guidelines for use with critical and problem-prone medications to help optimize therapies and minimize the possibility of adverse events and to integrate "triggers" to indicate the need for additional clinical monitoring [25].

It is important to note that the pediatric population is especially vulnerable to medication errors. When children are prescribed adult medications, care must be taken to adjust dosage according to weight, requiring the physician to use pediatric-specific calculations. Also, many healthcare settings are not trained to care for the pediatric patient. Intolerance due to physiologic immaturity is also a factor in adverse response to medications, and in many cases, this population cannot communicate their discomfort due to adverse reactions. Risk reduction strategies include standardizing and effectively identifying medications and processes for drug administration, ensuring pharmacy oversight, and using technology, such as medication dispensing programs, infusion pumps, and bar-coding, judiciously [28].

COMMON MISDIAGNOSES

As Florida healthcare professionals, it is important to be aware that in addition to wrong-site/wrong-procedure surgery, several medical conditions also continue to be misdiagnosed. As of 2022, the Florida Board of Medicine has determined the five most misdiagnosed conditions to be [29]:

- Cancer-related conditions
- Gastroenterology-related issues
- Cardiology-related issues
- Neurologic conditions
- Missed spinal cord compression

It is important to be aware of the possibility of misdiagnosis and incorporate this knowledge into practice.

Cancer

The early detection and diagnosis of cancers is crucial for selecting the appropriate treatment approach and to ensure an optimum outcome. However, an estimated 12% of cancer patients are initially misdiagnosed, and the missed or delayed diagnosis of cancers remains a significant cause of medical malpractice claims [30; 31]. The causes of missed diagnoses vary widely among cancers in different parts of the body. In many cases, patients who do not fit the typical profile for a specific cancer (e.g., young age) may be underdiagnosed, and it is important that cancer is considered as part of the differential diagnosis in ambiguous cases [31; 32; 33]. In order to prevent missed or delayed cancer diagnosis, practitioners may take steps to ensure adherence to clinical guidelines for screening and diagnosis, use tools to facilitate communication, and engage strategies to ensure appropriate follow-up [55].

Gastroenterology-Related Conditions

Gasteroenterologic conditions may present with nonspecific complaints (e.g., abdominal pain, nausea) common to a variety of illnesses, complicating and delaying diagnosis. In one study of patients with pancreatic cancer, more than 30% were initially misdiagnosed, most commonly with gall bladder disease [58]. Diagnosis and screening for gastrointestinal disorders may be complicated by a lack of definitive test (e.g., irritable bowel syndrome) or by limits on screening recommendations (e.g., colorectal cancer). However, delayed diagnosis can lead to worsening conditions and poorer prognosis.

In general, gastrointestinal syndromes/symptoms may be classified into three general diagnostic categories: organic, motility, or functional disorders [59; 60]. Functional GI disorders are idiopathic disorders of gut-brain interaction and, unlike organic and motility disorders, diagnosis involves identification of symptom clusters. As such, misdiagnosis is more common.

Another important consideration is GI symptom-specific anxiety, an important perpetuating factor that describes threatening interpretation and out-of-proportion behavioral response to GI sensations. This anxiety to real GI symptoms and the frequency of psychiatric comorbidity can lead to functional GI syndromes being dismissed as psychological or psychosomatic in nature.

Cardiology-Related Issues

The clinical presentation of chest pain has many possible etiologies, ranging from benign (e.g., panic/anxiety, pneumonia, peptic ulcer, gastroesophageal reflux disease, and pericarditis) to life-threatening (e.g., pulmonary embolism, acute coronary syndrome [ACS], aortic dissection, and pneumothorax). In many cases, it is best to rule out the more urgently threatening possibilities before testing for other causes.

Of the potentially life-threatening causes of chest pain, ACS is the most prevalent. Although a large percentage of individuals with suspected ACS will be seen initially in emergency departments, patients in any healthcare setting, regardless of other diagnoses, may abruptly develop chest pain suspicious for ACS. When a patient presents with clinical signs suspicious for myocardial infarction, immediate medical intervention is directed at confirming a diagnosis and stratifying the person's risk for adverse events such as cardiac arrest and severe/significant damage to the myocardium [41]. It is important to note that while some patients will present with classic ACS-related chest pain (tightness, sensation of pressure, heaviness,

crushing, vise-like, aching pain in the substernal or upper left chest), many patients, particularly women and older patients, will present with "atypical" ACS-related chest pain [45; 46]. Words commonly used to describe "atypical" chest pain associated with ACS include numbness, tingling, burning, stabbing, or pricking. Atypical chest pain location includes any area other than substernal or left sided, such as the back, area between shoulder blades, upper abdomen, shoulders, elbows, axillae, and ears [43; 44; 45; 46]. Aside from atypical clinical presentation, other possible causes of missed ACS diagnosis include failure of interpretation of the history, failure to correctly interpret the electrocardiogram, failure to perform an electrocardiogram when necessary, and lack of proper use of cardiac enzyme test [47].

Neurologic/Spinal Cord-Related Conditions

Delayed or missed diagnoses of neurologic conditions may result in serious morbidity and mortality. Headaches are a common presenting condition in acute and primary care, and an estimated 5% of all patients admitted to emergency departments have neurologic symptoms [34]. Acute headache with neurologic symptoms may be misdiagnosed as stroke [35; 64]. In addition, missed spinal fracture diagnoses are one of the leading causes of malpractice claims against radiologists [48].

One of the most common neurologic conditions is headache; however, it has been estimated that 50% of migraine patients remain undiagnosed or misdiagnosed, and only a small number (8% to 10%) of individuals with migraine take migraine-specific medications such as triptans or ergotamines [65; 66]. Patients suffering from daily migraines may be misdiagnosed with chronic sinusitis or rhinitis and repeatedly and unsuccessfully treated with broad-spectrum antibiotics [62; 63]. The diagnosis of migraine is based solely on a constellation of signs and symptoms, and a comprehensive medical and neurological examination is required to exclude secondary headache [56]. Useful evidence-based clinical guidelines for migraine screening have been developed and are summarized in the mnemonic POUND: pulsatile headache; one-day duration (4 to 72 hours); unilateral location; nausea or vomiting; and disabling intensity [57]. Competence of the clinician and effective communication with the patient play a crucial role in the diagnosis of migraine.

Missed Spinal Cord Compression

Epidural compression syndrome is an umbrella term that encompasses spinal cord compression, cauda equina syndrome, and conus medullaris syndrome. While these conditions differ in the level of neurologic deficit at presentation, they are otherwise similar in symptoms, evaluation, and management. Massive herniation of a midline disk, typically at the L4 to L5 disk level, is the most common cause of epidural compression syndrome. Tumor, epidural abscess, spinal canal hematoma, or lumbar spine spondylosis represent other causes [37].

Spinal cord compression is often secondary to herniated disk, vertebral fracture, or space-occupying lesion. Missing this diagnosis, typically by attributing the associated pain to muscle or nerve causes, will miss potentially catastrophic conditions [38; 39; 40; 41]. In a study of 3,786 individuals, the estimated prevalence of asymptomatic spinal cord compression in a healthy population was 24.2%, with a significantly higher prevalence in older populations compared with younger populations and American/European populations compared with Asian populations [42].

In patients with spinal cord compression, neurologic status at diagnosis is the greatest predictor of ultimate neurologic outcome and underscores the importance of early accurate diagnosis. The dominant symptom is back pain with accelerating pain severity. Pain from epidural spinal cord compression is made worse with recumbent positioning, and unilateral or bilateral radiculopathy may develop over time. For many patients, leg pain or neurologic symptoms are more dominant than back pain. Also common at diagnosis is symmetrical lower extremity weakness that may have progressed to gait disturbance or paralysis. Decreased lower extremity reflexes are associated with cauda equina syndrome [37].

OTHER CONSIDERATIONS FOR PATIENT SAFETY

The most important issue to improving patient safety is being aware of the particular safety hazards that may exist for various patient populations and on particular specialty units. In addition, education of the patient and the family should be a priority.

Infants and young children are not developmentally or cognitively able to participate in care and decision making, thus putting them at higher risk, especially for medication errors. In addition, when a medication error occurs in this population, infants and young children are at higher risk because of their physical immaturity and increased sensitivity to the effects of drugs. The family or guardian of a pediatric patient should be encouraged to ask questions, especially if something seems wrong. In addition, a meta-analysis found that computerized provider order entry with clinical decision support reduced pediatric medication errors by 36% to 87% [51]. As such, the adoption of electronic support systems may help to reduce or eliminate these errors.

An estimated 30% of individuals 65 years of age or older who are living in the community fall each year [52]. Older patients may have poor vision, as a result of cataracts, glaucoma, and/or macular degeneration, and cardiovascular problems, which might result in syncope or postural hypotension. These conditions may affect patients' balance and stability. Bladder dysfunction, such as nocturia, may cause an elderly patient to have to ambulate more during the night in an unfamiliar environment, thereby increasing the risk of a fall. Lower extremity

dysfunctions, such as arthritis, muscle weakness, or peripheral neuropathy, may make it more difficult to ambulate at any time. In addition to being at greater risk for falls, the elderly are also more prone to medication errors as their ability to understand instructions or to recognize an unfamiliar medication may be affected by dementia or other cognitive disorders. Interventions that can help prevent falls in the elderly include exercise programs, tai chi, vision improvement (e.g., first cataract surgery), and multifactorial assessment and intervention [52].

There are also unique factors that increase the risk of medical errors on specialty units. For instance, in critical care units, patients may be suffering from environmental psychosis, which could inhibit participation in their care. This is also true of lethargic and comatose patients. These patients are at particular risk because they cannot participate in the identification process. On psychiatric wards, patients may be suicidal or depressed, which may cause them to act out or attempt to harm themselves or others. Patients may also experience orthostatic side effects due to certain psychiatric medications, which may increase the incidence of falls. Obstetric patients are at higher risk for falls because they may have decreased sensation and mobility due to administration of epidural anesthesia, and they may also suffer from excessive blood loss, which could lead to postural hypotension [49]. Again, the key is identifying the unique needs of the particular population.

With regard to education, a number of organizations have developed guidelines to facilitate the role of patients as their own safety advocates. These guidelines are not intended to shift the burden of monitoring medical error to patients. Rather, they encourage patients to share responsibility for their own safety. As healthcare professionals, we should ensure that all of our patients are familiar with these guidelines. The Agency for Healthcare Research and Quality has developed a "Patient Fact Sheet" that outlines 20 tips for patients to help prevent medical errors [53]. Although some of these suggestions may seem extreme, many patients now desire to have a more active role in their care. Some of these items have become routine or are currently required, such as consultations by pharmacists when a patient picks up a prescribed medication.

USE OF AN INTERPRETER

As a result of the evolving racial and immigration demographics in the United States, interaction with patients for whom English is not a native language is inevitable. Because patient education is such a vital aspect of preventing medical errors, it is each practitioner's responsibility to ensure that information and instructions are explained in such a way that allows for patient understanding. When there is an obvious disconnect in the communication process between the practitioner and patient due to the patient's lack of proficiency in the English language, an interpreter is required.

Interpreters are more than passive agents who translate and transmit information back and forth from party to party. They should be professionally trained in ethics, accuracy, completeness, and impartiality. Furthermore, it is the interpreter's role to negotiate cultural differences and promote culturally responsive communication and practice. When they are enlisted and treated as part of the interdisciplinary clinical team, they serve as cultural brokers, who ultimately enhance the clinical encounter. In any case in which information regarding diagnostic procedures, treatment options, or medication/treatment measures is being provided, the use of an interpreter should be considered.

CONCLUSION

Although the United States has one of the top healthcare systems in the world, it is apparent that the numbers of medical errors are at unacceptably high levels. The consequences of medical errors are often more severe than the consequences of mistakes in other industries. They may lead to death or to serious and long-term disability, which underscores the need for aggressive action in this area. As a starting point, we should become an active part of the solution. This will only happen if all healthcare professionals voice their concerns when they identify problems in a system or process. In addition, we should actively participate in the root cause analysis process, understanding that the goal is not to assign blame, but rather to identify how we can improve the process to provide the best quality care to our patients. Medical errors are costly, not only because patients may lose their lives or livelihoods, but also because patients lose trust in the system and colleagues lose faith in each other. To preserve the integrity of our system, we must correct this problem, and the solution begins with each of us.

Customer Information/Answer Sheet insert located between pages 60–61.

COURSE TEST - #91334 MEDICAL ERROR PREVENTION AND ROOT CAUSE ANALYSIS

This is an open book test. Please record your responses on the Answer Sheet.
A passing grade of at least 70% must be achieved in order to receive credit for this course.

This 2 contact hour activity must be completed by August 31, 2025.

1. **The Institute of Medicine's (IOM) Committee on Quality of Healthcare in America defines error as the failure of a planned action to be completed as intended or the use of a wrong plan to achieve an aim.**
   A) *True*
   B) *False*

2. **Patient rape is an example of a sentinel event subject to review by the Joint Commission.**
   A) *True*
   B) *False*

3. **A "thorough" root cause analysis is one in which the participants identify risk points and their potential contributions to this type of event.**
   A) *True*
   B) *False*

4. **A credible root cause analysis must be based upon a survey of everyone employed at the healthcare institution.**
   A) *True*
   B) *False*

5. **A wrong-site surgical procedure that did not result in the death of the patient must be reported to the risk manager within three business days according to Florida law.**
   A) *True*
   B) *False*

6. **The Joint Commission prepares and distributes Sentinel Event Alerts in order to recommend ways in which the healthcare facility can terminate employees whose actions result in a sentinel event.**
   A) *True*
   B) *False*

7. **Infant abduction is among the most common sentinel events reported to the Joint Commission.**
   A) *True*
   B) *False*

8. **The most common root cause documented for patient suicide was shortcomings in assessment, most commonly psychiatric assessment.**
   A) *True*
   B) *False*

9. **A medication error may occur when ordered by a physician, administered by a nurse, or dispensed by a pharmacist.**
   A) *True*
   B) *False*

10. **Approximately 32% of patients with cancer are initially misdiagnosed.**
    A) *True*
    B) *False*

Be sure to transfer your answers to the Answer Sheet insert located between pages 60–61.
PLEASE NOTE: Your postmark or facsimile date will be used as your test completion date.

Domestic Violence: The Florida Requirement

This course fulfills the Florida requirement for 2 hours of Domestic Violence education every third renewal period.

Have you already completed your Domestic Violence requirement? You can skip this course and still receive 26 hours of continuing education.

Audience

This course is designed for all Florida healthcare professionals required to complete domestic violence education.

Course Objective

The purpose of this course is to enable healthcare professionals in all practice settings to define domestic violence and identify those who are affected by domestic violence in the United States. This course describes how a victim can be accurately diagnosed and identifies the community resources available in the state of Florida for domestic violence victims.

Learning Objectives

Upon completion of this course, you should be able to:

1. Define domestic violence and its impact on health care.
2. Cite the general prevalence of domestic violence on a national and state level and identify state laws pertaining to the issue.
3. Describe how to screen and assess individuals who may be victims or perpetrators of domestic violence, including the importance of conducting a culturally sensitive assessment.
4. Identify community resources presently available for domestic violence victims and their perpetrators throughout Florida concerning legal aid, shelter, victim and batterer counseling, and child protection services.

Faculty

Marjorie Conner Allen, BSN, JD, received her Bachelor of Science in Nursing degree from the University of Florida, Gainesville, in 1984. She began her nursing career at Shands Teaching Hospital and Clinics at the University of Florida, Gainesville. While practicing nursing at Shands, she gave continuing education seminars regarding the nursing implications for dealing with adolescents with terminal illness. In 1988, Ms. Allen moved to Atlanta, Georgia where she worked at Egleston Children's Hospital at Emory University in the bone marrow transplant unit. (A complete biography appears at the end of this course.)

Alice Yick Flanagan, PhD, MSW, received her Master's in Social Work from Columbia University, School of Social Work. She has clinical experience in mental health in correctional settings, psychiatric hospitals, and community health centers. In 1997, she received her PhD from UCLA, School of Public Policy and Social Research. Dr. Yick Flanagan completed a year-long post-doctoral fellowship at Hunter College, School of Social Work in 1999. In that year she taught the course Research Methods and Violence Against Women to Masters degree students, as well as conducting qualitative research studies on death and dying in Chinese American families. (A complete biography appears at the end of this course.)

Faculty Disclosure

Contributing faculty, Marjorie Conner Allen, BSN, JD, has disclosed no relevant financial relationship with any product manufacturer or service provider mentioned.

Contributing faculty, Alice Yick Flanagan, PhD, MSW, has disclosed no relevant financial relationship with any product manufacturer or service provider mentioned.

Division Planner

Jane C. Norman, RN, MSN, CNE, PhD

Director of Development and Academic Affairs

Sarah Campbell

Division Planner/Director Disclosure

The division planner and director have disclosed no relevant financial relationship with any product manufacturer or service provider mentioned.

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INTRODUCTION

Domestic violence continues to be a prevalent problem in the United States today. Because of the number of individuals affected, it is likely that most healthcare professionals will encounter patients in their practice who are victims. Accordingly, it is essential that healthcare professionals are taught to recognize and accurately interpret behaviors associated with domestic violence. It is incumbent upon the healthcare professional to establish and implement protocols for early identification of domestic violence victims and their abusers. In order to prevent domestic violence and promote the well-being of their patients, healthcare professionals in all settings should take the initiative to properly assess all women for abuse during each visit and, for those women who are or may be victims, to offer education, counseling, and referral information.

Victims of domestic violence suffer emotional, psychologic, and physical abuse, all of which can result in both acute and chronic signs and symptoms of physical and mental disease, illness, and injury. Frequently, the injuries sustained require abused victims to seek care from healthcare professionals immediately after their victimization. Subsequently, physicians and nurses are often the first healthcare providers that victims encounter and are in a critical position to identify domestic violence victims in a variety of clinical practice settings where victims receive care. Accordingly, each healthcare professional should educate himself or herself to enhance awareness of the presence of abuse victims in his or her particular practice or clinical setting.

Specifically, healthcare professionals should be aware of the signs and symptoms associated with domestic violence. In addition, when family violence cases are identified, there should be a plan of action that includes providing information on, and referral to, local community resources related to legal aid, sheltering, victim counseling, batterer counseling, advocacy groups, and child protection.

DEFINING DOMESTIC VIOLENCE

Domestic violence, which is sometimes also referred to as spousal abuse, battering, or intimate partner violence (IPV), refers to the victimization of an individual with whom the abuser has or has had an intimate or romantic relationship. Researchers in the field of domestic violence have not agreed on a uniform definition of what constitutes violence or an abusive relationship. The Centers for Disease Control and Prevention (CDC) defines IPV as, "violence or aggression that occurs in a romantic relationship" [1]. According to the Florida Department of Children and Families, domestic violence is "a pattern of abusive behaviors that adults use to maintain power and control over their intimate partners or former partners. People who abuse their partners use a variety of tactics to coerce, intimidate, threaten, and frighten their

victims" [2]. Domestic violence may include physical violence, sexual violence, emotional abuse, economic abuse, isolation, pet abuse, threats relating to children, and a variety of other behaviors meant to increase fear, intimidation, and power over the victim [2]. Florida law defines domestic violence as "any assault, aggravated assault, battery, aggravated battery, sexual assault, sexual battery, stalking, aggravated stalking, kidnapping, false imprisonment, or any criminal offense resulting in physical injury or death of one family or household member by another family or household member" [3]. Family or household members, according to Florida definition, must "be currently residing or have in the past resided together in the same single dwelling unit" [3]. Domestic violence knows no boundaries. It occurs in intimate relationships regardless of race, religion, culture, or socioeconomic status [2].

Whatever the definition, it is important for healthcare professionals to understand that domestic violence, in the form of emotional and psychologic abuse, sexual abuse, and physical violence, is prevalent in our society. Because of the similar nature of the definitions, this course will use the terms "domestic violence" and "IPV" interchangeably.

NATIONAL AND STATE STATISTICS AND LEGISLATION

Domestic violence is one of the most serious public health problems in the United States [4]. More than 36.4% of women and 33.6% of men have a lifetime history of IPV [4]. In Florida, the weighted lifetime prevalence of IPV (including rape, physical violence, and/or stalking) is 37.4% among women and 29.3% among men [5]. Although many of these incidents are relatively minor and consist of pushing, grabbing, shoving, slapping, and hitting, IPV resulted in approximately 1,500 deaths in the United States in 2019, with 214 of those deaths occurring in Florida in the same year. Statistics indicate a slightly higher rate in 2020, with 217 deaths in Florida in 2020 [7; 8]. One of the difficulties in addressing the problem is that abuse is prevalent in all demographics, regardless of age, ethnicity, race, religious denomination, education, or socioeconomic status [2].

Victims of abuse often suffer severe physical injuries and will likely seek care at a hospital or clinic. The health and economic consequences of domestic violence are significant. Statistics vary from report to report, and due to the lack of studies on the national cost of domestic violence, the U.S. Congress funded the CDC to conduct a study to determine the cost of domestic violence on the healthcare system [9]. The 2003 CDC report, which relied on data from the National Violence Against Women Survey conducted in 1995, estimated the costs of IPV by measuring how many female victims were nonfatally injured; how many women used medical and mental healthcare services; and how many women lost time from paid work and household chores. The estimated total annual cost of IPV against women in the 1995 survey was more than $5.8 billion [9]. When updated to 2017 dollars, the amount was more than $9.3 billion annually. The costs associated with IPV at this time would be considerably more, but no further studies have been conducted [10]. It should be noted that the costs of any one victimization may continue for years; therefore, these statistics most likely underestimate the actual cost of IPV [9].

The national rate of nonfatal domestic violence against women declined 72% between 1993 and 2011 [11]. The rate of overall violent crime fell by nearly 60% in this same time period [11]. Studies reveal that several factors may have contributed to the reduction in violence, including a decline in the marriage rate and decrease of domesticity, better access to federally funded domestic violence shelters, improvements in women's economic status, and demographic trends, such as the aging of the population [13; 14]. Of note, declines in the economy and stress associated with financial hardship and unemployment are significant contributors to IPV in the United States. Following the economic downturn in late 2008, there was a significant increase in the use of the National Domestic Violence Hotline in 2009, with more than half of victims reporting a change in household financial situation in the last year [15]. This trend continued with the COVID-19 pandemic, with stressors from lockdown orders, unemployment, financial insecurity, childcare and homeschool responsibilities, and poor coping strategies (e.g., substance abuse) increasing the rate of domestic violence. Reports showed a 9.7% increase in domestic violence calls for service in the first two months state-mandated lockdowns were imposed; furthermore, the National Commission on COVID-19 and Criminal Justice reported an increase of 8.1% in domestic violence incidents within the first months of mandated stay-at-home orders [6].

FLORIDA

In response to troubling domestic violence statistics, Governor Lawton Chiles appointed a Task Force on Domestic Violence on September 28, 1993, to investigate the problems associated with domestic violence in Florida and to compile recommendations as to how the problems should be approached and ultimately resolved. On January 31, 1994, the Task Force issued its first report on domestic violence. This report recommended standards to accurately measure the extent of domestic violence and strategies for increasing public awareness and education. It identified programs and resources that are available to victims in Florida, made legislative and budgetary suggestions for needed changes, provided a methodology for implementing these changes, and identified areas of domestic violence that require further study.

As a result of this report, Florida enacted legislation during the 1995 session implementing various suggestions of the Task Force. Specifically, the Legislature amended Section 455.222 of the Florida Statutes to require that all physicians, osteopaths, nurses, dentists, dental hygienists, midwives, psychologists, and psychotherapists obtain, as part of their biennial continuing education requirements, a one-hour continuing education course on domestic violence [17]. In June of 2006, Governor Jeb Bush signed into law House Bill 699. The bill, which went

into effect July 1, 2006, changed the domestic violence continuing education requirement from one hour every renewal period to two hours every third renewal period.

In 1997, at the request of the Governor's Task Force, a workgroup was established by the Florida Department of Law Enforcement (FDLE) to evaluate the feasibility of tracking incidents of domestic violence in the state [18]. This resulted in the creation of the Domestic Violence Data Resource Center (DVDRC). The original mission of the DVDRC was to collect information related to domestic violence and to report and maintain the information in a statewide tracking system [19]. Domestic Violence Fatality Review Teams were established to examine those cases of domestic violence that resulted in a fatality and identify potential changes in policy or procedure that might prevent future deaths. The teams were comprised of representatives from law enforcement, the courts, social services, state attorneys, domestic violence centers, and others who may come into contact with domestic violence victims and perpetrators [20]. In 2000, the creation of Florida Statute 741.316 required the FDLE to annually publish a report based on the data gathered by the Fatality Review Teams [19]. Due to budgetary constraints, responsibility of compiling this data transferred to the Department of Children and Families in 2008 [21].

As part of Governor Jeb Bush's initiative, the "Family Protection Act" was signed into law in 2001. The act requires a 5-day mandatory jail term for any crime of domestic battery in which the perpetrator deliberately injures the victim. The law also makes a second battery crime a felony offense, treating offenders as serious criminals. Additional legislation, signed into law in 2002, includes Senate Bills 716 and 1974. Senate Bill 716 protects domestic violence victims by including dating relationships of six months in the definition of domestic violence laws. Senate Bill 1974 requires judges to inform victims of their rights, including the right to appear, be notified, seek restitution, and make a victim-impact statement. Governor Bush also created the Violence Free Florida campaign to increase public awareness of domestic violence issues [22].

In 2003, Governor Bush signed House Bill 1099, which transferred funding authority of the Florida Domestic Violence Trust Fund from the Department of Children and Families to the Florida Coalition Against Domestic Violence. According to the Domestic Violence in Florida 2010–2011 Annual Report to the Legislature, this has strengthened domestic violence services provided by streamlining the process of allocating funds [23].

In 2007, the Domestic Violence Leave Act was signed into law by Governor Charlie Crist [21]. This law requires employers with 50 or more employees to provide guaranteed leave for domestic violence issues.

In 2020, the FDLE reported 106,736 domestic violence offenses [8]. In general, domestic violence rates have been declining since 1998. An estimated 19.5% of domestic violence incidents involved spouses and 27.8% involved cohabitants; 11.6% of the victims were parents of the offenders. Domestic violence offenses resulted in the death of 217 victims in Florida in 2020, a number that has been decreasing since 2014 [8]. Domestic violence accounted for 16.9% of the state's murders in 2020 [8].

In their 2019 Annual Report, Fatality Review Teams summarized 31 cases of domestic violence fatalities and near fatalities [49]. The most significant findings included the following observations [49]:

- The perpetrators were predominantly male (94%) with female victims (90%) and had prior criminal histories, non-domestic-violence-related (67%) and for domestic violence specifically (69%).
- In 31% of fatalities, the perpetrators had a known "do not contact" order filed against them, and 13% of perpetrators had a known permanent injunction for protection against them filed by someone other than the victim.
- Substance abuse histories by the perpetrator was identified in 77% of the cases and diagnosed mental health disorders in 45%.
- In most cases, neither the decedent nor perpetrator sought help from the various intervention programs available to them.

To obtain a copy of the most current Florida Statewide Domestic Violence Fatality Review report, please visit https://www.myflfamilies.com/service-programs/domestic-violence/publications.shtml.

IDENTIFYING GROUPS AT RISK FOR DOMESTIC VIOLENCE

Healthcare professionals are in a critical position to identify domestic violence victims in a variety of clinical practice settings. Nurses are often the first healthcare provider a victim of domestic violence will encounter in a healthcare setting and should therefore be prepared to provide care and support for these victims. Although women are most often the victims, domestic violence extends to others in the household as well. For example, domestic violence includes abused men, children abused by their parents or parents abused by their children, elder abuse, and abuse among siblings [3].

Many victims of abuse sustain injuries that lead them to present to hospital emergency departments. Research has found that 49.6% of women seen in emergency departments reported a history of abuse and 44% of women who were ultimately killed by their abuser had sought help in an emergency department in the two years prior to their death [25; 50]. Another study of 993 police-identified female victims of IPV found that only 28% of the women were identified in the emergency department as being victims of IPV [26]. These alarming statistics demonstrate that healthcare professionals who work in acute care, such as hospital emergency rooms, should maintain a

high index of suspicion for battering of the patients that they see. Healthcare professionals who work in these settings should work with hospital administrators to establish and institute assessment mechanisms to accurately detect these victims.

For every victim of abuse, there is also a perpetrator. Like their victims, perpetrators of domestic violence come from all socioeconomic backgrounds, races, religions, and walks of life [1; 4]. Accordingly, healthcare professionals should likewise be aware that seemingly supportive family members may, in fact, be abusers.

PREGNANT WOMEN

Because a gynecologist or obstetrician is frequently a woman's primary care physician, the American College of Obstetricians and Gynecologists (ACOG) recommends that all women be routinely assessed for signs of IPV (i.e., physical and psychologic abuse, reproductive coercion, and progressive isolation), including during prenatal visits, and providers should offer support and referral information for those being abused [25]. According to the ACOG, IPV affects as many as 324,000 pregnant women each year [25]. A meta-analysis of 92 independent studies found that the average reported prevalence of emotional abuse during pregnancy was 28.4%, physical abuse was 13.8%, and sexual abuse was 8% [51]. As with all domestic violence statistics, these estimates are presumed to be lower than the actual incidence as a result of under-reporting and lack of data on women whose pregnancies ended in fetal or maternal death. This makes IPV more prevalent among pregnant women than some of the health conditions included in prenatal screenings, including pre-eclampsia and gestational diabetes [25]. Because 96% of pregnant women receive prenatal care, this is an optimal time to assess for domestic violence and develop trusting relationships with the women. Possible factors that may predispose pregnant women to IPV include being unmarried, lower socioeconomic status, young maternal age, unintended pregnancy, delayed prenatal care, lack of social support, and use of tobacco, alcohol, or illegal drugs [25; 51].

The overarching problem of violence against pregnant women cannot be ignored, especially as both mother and fetus are at risk. At this particularly vulnerable time in a woman's life, an organized clinical construct leading to immediate diagnosis and medical intervention will ensure that therapeutic opportunities are available to the pregnant woman and will reduce the potential negative outcomes [29]. Healthcare professionals should also be aware of the possible psychologic consequences of abuse during pregnancy. There is a higher risk of stress, depression, and addiction to alcohol and drugs in abused women. These conditions may result in damage to the fetus from tobacco, drugs, and alcohol and a loss of interest on the part of the mother in her or her baby's health [16; 30]. Possible direct injuries to the fetus may result from maternal trauma [25].

Control of reproductive or sexual health is also a recognized trend in IPV. This type of abuse includes trying to impregnate or become pregnant against a partner's wishes, refusal to use birth control (e.g., condoms, oral contraceptives), or stopping a partner from using birth control [4].

CHILDREN

Children exposed to family violence are at high risk for abuse and for emotional damage that may affect them as they grow older. The Department of Justice estimates that of the 76 million children in the United States, 46 million will be exposed to some type of violence during their childhood [52]. Results of the National Survey of Children's Exposure to Violence indicated that 11% of children were exposed to IPV at home within the last year, and as many as 26% of children were exposed to at least one form of family violence during their lifetimes [31]. Of those children exposed to IPV, 90% were direct eyewitnesses of the violence; the remaining children were exposed by either hearing the violence or seeing or being told about injuries [31]. Of note, according to Florida criminal law, witnessing domestic violence is defined as "violence in the presence of a child if an offender is convicted of a primary offense of domestic violence, and that offense was committed in the presence of a child under age 16 who is a family or household member with the victim or perpetrator" [32].

A number of studies indicate that child witnesses are at increased risk for post-traumatic stress disorder, impaired development, aggressive behavior, anxiety, difficulties with peers, substance abuse, and academic problems than the average child [33; 54; 55]. Children exposed to violence may also be more prone to dating violence (as a perpetrator or a victim), and the ability to effectively cope with partnerships and parenting later in life may be affected, continuing the cycle of violence into the next generation [34; 56].

In addition to witnessing violence, various studies have shown that these children may also become direct victims of violence, and children who both witness and experience violence are at the greatest risk for adverse psychosocial outcomes [53]. Research indicates that between 30% and 65% of husbands who batter their wives also batter their children [27; 35]. Moreover, victims of abuse will often turn on their children; statistics demonstrate that 85% of domestic violence victims abuse or neglect their children. The 2020 Crime in Florida report found that more than 13% of domestic homicide victims were children killed by a parent [8]. Teenage children are also victimized. According to the U.S. Department of Justice, between 1980 and 2008, 17.5% of all homicides against female adolescents 12 to 17 years of age were committed by an intimate partner [36]. Among young women (18 to 24 years of age), the rate is estimated to be 43% in the United States and 8% to 57% globally. Abused teens often do not report the abuse. Individuals 12 to 19 years of age report only 35.7% of crimes against them, compared with 54% in older age groups [28; 37]. Accordingly, healthcare professionals who see young children and adolescents in their practice (e.g., pediatricians, family physicians, school nurses, pediatric nurse practitioners, community health nurses) should have the tools necessary to detect these "silent victims" of domestic violence and to

intervene quickly to protect young children and adolescents from further abuse. Without such critical intervention, the cycle of violence will never end.

ELDERLY

Abused and neglected elders, who may be mistreated by their spouses, partners, children, or other relatives, are among the most isolated of all victims of family violence. In a national study conducted by the National Institute of Justice in 2010, 4.6% of participants (community dwelling adults 60 years of age or older) were victims of emotional abuse in the past year, 1.6% physical abuse, 0.6% sexual abuse, 5.1% potential neglect, and 5.2% current financial abuse by a family member [38]. A 2017 study found a self-reported incidence of 11.6% psychological abuse, 2.6% physical abuse, 6.8% financial abuse, 4.2% neglect, and 0.9% sexual abuse [59]. The estimated annual incidence of all elder abuse types is 2% to 10%, but it is believed to be severely under-measured. According to one study, only 1 in 24 cases of elder abuse are reported to the authorities [39].

The prevalence rate of elder abuse in institutional settings is not clear. However, in a 2019 review of nine studies, 64% of elder care facility staff disclosed to having perpetrated abuse against an elderly resident in the past year [40]. In a random sample survey, 24.3% of respondents reported at least one incident of elder physical abuse perpetrated by a nursing home staff member [57].

As healthcare professionals in Florida, which leads the nation in percentage of older residents, it is important to understand that the needs of older Floridians will increase as will the numbers of elder victims of domestic violence. Because elder abuse can occur in family homes, nursing homes, board and care facilities, and even medical facilities, healthcare professionals should remain keenly aware of the potential for abuse. When abuse occurs between elder partners, it is primarily manifested in one of two ways: either as a long-standing pattern of marital violence or as abuse originating in old age. In the latter case, abuse may be precipitated by issues related to advanced age, including the stress that accompanies disability and changing family relationships [39].

It is important to understand that the domestic violence dynamic involves not only a victim but a perpetrator as well. For example, an adult son or daughter who lives in the parents' home and depends on the parents for financial support may be in a position to inflict abuse. This abuse may not always manifest itself as violence but can lead to an environment in which the elder parent is controlled and isolated. The elder may be hesitant to seek help because the abuser's absence from the home may leave the elder without a caregiver [39]. Because these elderly victims are often isolated, dependent, infirm, or mentally impaired, it is easy for the abuse to remain undetected. Healthcare professionals in all settings should remain aware of the potential for abuse and keep a watchful eye on this particularly vulnerable group.

MEN

Statistics confirm that domestic violence is predominantly perpetrated by men against women; however, there is evidence that women also exhibit violent behavior against their male partners [4]. Studies demonstrate approximately 5% of homicides against men are perpetrated by intimate partners [36]. It is persuasively argued that the impact on the health of female victims of domestic violence is generally much more severe than the impact on the health of male victims [42]. Approximately 512,770 women were raped and/or physically assaulted by an intimate partner in 2008, compared to 101,050 men [58]. In addition, 1 in 4 women has been physically assaulted, raped, and/or stalked by an intimate partner, compared with 1 out of every 10 men [1]. Rape, non-contact unwanted sexual experiences, and stalking against men are primarily perpetrated by other men, while other forms of violence against men were perpetrated mostly by women [5]. Male victims of IPV experienced 3 victimizations per 1,000 boys and men 12 years of age or older in 1994, and this rate decreased by 64%, to 1.1 per 1,000, in 2010 [11]. Of all homicides committed against men between 1980 and 2008, 7.1% were committed by an intimate partner [36]. Although women are more often victims of IPV, healthcare professionals should always keep in mind that men can also be victimized and assess accordingly.

LESBIAN, GAY, BISEXUAL, TRANSGENDER, AND QUEER/QUESTIONIONG VICTIMS

Domestic violence exists in lesbian, gay, bisexual, transgender, and queer/questioning (LGBTQ+) communities, and the rates are thought to mirror those of heterosexual women—approximately 25% [43]. However, women living with female intimate partners experience less IPV than women living with men [8]. Conversely, men living with male intimate partners experience more IPV than do men who live with female intimate partners [8]. In addition, 78% of IPV homicide victims reported in 2017 were transgender women or cisgender men [24]. This supports other statistics indicating that IPV is perpetrated primarily by men. A form of abuse specific to the gay community is for an abuser to threaten or to proceed with "outing" a partner to others [41; 43].

Transgender individuals appear to be at particular risk for violence. According to a large national report, transgender victims of IPV were 1.9 times more likely to experience physical violence and 3.9 times more likely to experience discrimination than other members of the LGBTQ+ community [24].

In 2017, an annual national report recorded 52 incidences of hate violence-related homicides of LGBTQ+ people, the highest incident number recorded in its 20-year history [24]. This increasing prevalence of anti-LGBTQ+ violence can exacerbate IPV in LGBTQ+ communities. For example, a person who loses their job because of anti-trans bias may be more financially reliant on an unhealthy relationship. An abusive partner may also use the violence that an LGBTQ+ person experiences from their family as a way of isolating that person further [24].

Because of the stigma of being LGBTQ+, victims may be reticent to report abuse and afraid that their sexual orientation or biologic sex will be revealed. In one study, the three major barriers to seeking help were a limited understanding of the problem of LGBTQ+ IPV, stigma, and systemic inequities [41]. Many in this community feel that support services (e.g., shelters, support groups, crisis hotlines) are not available to them due to homophobia of the service providers. Unfortunately, this results in the victim feeling isolated and unsupported. Healthcare professionals should strive to be sensitive and supportive when working with homosexual patients.

CHARACTERISTICS OF PERPETRATORS OF DOMESTIC VIOLENCE

Abuser characteristics have been studied far less frequently than victim characteristics. Some studies suggest a correlation between the occurrence of abuse and the consumption of alcohol. A man who abuses alcohol is also likely to abuse his mate, although the abuser may not necessarily be inebriated at the time the abuse is inflicted [44]. Domestic violence assessment questionnaires should include questions that explore social drinking habits of both victims and their mates.

Other studies demonstrate that abusive mates are generally possessive and jealous. Another characteristic related to the abuser's dependency and jealousy is extreme suspiciousness. This characteristic may be so extreme as to border on paranoia [12]. Domestic violence victims frequently report that abusers are extremely controlling of the everyday activities of the family. This domination is generally all encompassing and often includes maintaining complete control of finances and activities of the victim (e.g., work, school, social interactions) [12].

In addition, abusers often suffer from low self-esteem and their sense of self and identity is directly connected to their partner [12]. Extreme dependence is common in both abusers and those being abused. Due to low self-esteem and self-worth, emotional dependence often occurs in both partners, but even more so in the abuser. Emotional dependence in the victim stems from both physical and psychologic abuse, which results in a negative self-image and lack of self-worth. Financial dependence is also very common, as the abuser often withholds or controls financial resources to maintain power over the victim [1; 4].

SCREENING FOR DOMESTIC VIOLENCE AND ABUSE

There is no universal guideline for identifying and responding to domestic violence, but it is universally accepted that a plan for screening, assessing, and referring patients of suspected abuse should be in place at every healthcare facility. Guidelines should review appropriate interview techniques for a given setting and should also include the utilization of assessment tools. Furthermore, protocols within each facility or healthcare setting should include referral, documentation, and follow-up. This section relies heavily on the guidelines outlined in the Family Violence Prevention Fund's *National Consensus Guidelines on Identifying and Responding to Domestic Violence Victimization in Health Care Settings*; however, protocols should be customized based on individual practice settings and resources available [35]. The CDC has provided a compilation of assessment tools for healthcare workers to assist in recognizing and accurately interpreting behaviors associated with domestic violence and abuse, which may be accessed at https://www.cdc.gov/violenceprevention/pdf/ipv/ipvandsvscreening.pdf [45].

Several barriers to screening for domestic violence have been noted, including a lack of knowledge and training, time constraints, lack of privacy for asking appropriate questions, and the sensitive nature of the subject [35]. Although awareness and assessment for IPV has increased among healthcare providers, many are still hesitant to inquire about abuse [46]. At a minimum, those exhibiting signs of domestic violence should be screened. Although victims of IPV may not display typical signs and symptoms when they present to healthcare providers, there are certain cues that may be attributed to abuse. The obvious cues are physical. Injuries range from bruises, cuts, black eyes, concussions, broken bones, and miscarriages to permanent injuries such as damage to joints, partial loss of hearing or vision, and scars from burns, bites, or knife wounds. Typical injury patterns include contusions or minor lacerations to the head, face, neck, breast, or abdomen and musculoskeletal injuries. These are often distinguishable from accidental injuries, which are more likely to involve the extremities of the body. Abuse victims are also more likely to have multiple injuries than accident victims. When this pattern of injuries is seen, particularly in combination with evidence of old injury, physical abuse should be suspected [44].

In addition to physical signs and symptoms, domestic violence victims also exhibit psychologic cues that resemble an agitated depression. As a result of prolonged stress, various psychosomatic symptoms that generally lack an organic basis often manifest. For example, complaints of backaches, headaches, and digestive problems are common. Often, there are reports of fatigue, restlessness, insomnia, or loss of appetite. Great amounts of anxiety, guilt, and depression or dysphoria are also typical. Women who experienced IPV are also more likely to report asthma, irritable bowel syndrome, and diabetes [4]. Healthcare professionals should look beyond the typical symptoms of a domestic violence victim and work within their respective practice settings to develop appropriate assessment mechanisms to detect victims who exhibit less obvious symptoms.

The unique relationship dynamics of the abuser and abused are not easily detected under the best of circumstances. They may be especially difficult to uncover in circumstances in which the parties are suspicious and frightened, as might be expected when a victim presents to the emergency department. The key to detection, however, is to establish a proper assessment tool

ASSESSMENT OF IMMEDIATE SAFETY FOR DOMESTIC VIOLENCE VICTIMS
Are you in immediate danger?
Is your partner at the health facility now?
Do you want to (or have to) go home with your partner?
Do you have somewhere safe to go?
Have there been threats or direct abuse of the child(ren) (if applicable)?
Are you afraid your life may be in danger?
Has the violence gotten worse or is it getting scarier? Is it happening more often?
Has your partner used weapons, alcohol, or drugs?
Has your partner ever held you or your child(ren) against your will?
Does your partner ever watch you closely, follow you or stalk you?
Has your partner ever threatened to kill you, him/herself or your child(ren)?
Source: [35] *Table 1*

that can be utilized in the particular setting and to maintain a keen awareness for the cues described in this course. Screening for IPV should be carried out at the entry points of contact between victims and medical care (e.g., primary care, emergency services, obstetric and gynecologic services, psychiatric services, and pediatric care) [35].

The key to an initial assessment is to obtain an adequate history. Establishing that a patient's injuries are secondary to abuse is the first task. Clearly, there will be times when a victim is injured so severely that treatment of these injuries becomes the first priority. After such treatment is rendered, however, it is important that healthcare professionals not ignore the reasons that brought the victim to the emergency department [35].

ASSESSING DOMESTIC VIOLENCE AND ABUSE

Healthcare providers have reported that even if routine screening and inquiry results in a positive identification of IPV, the next steps of assessing and referring are often difficult, and many feel that they are not adequately prepared [46]. According to the Family Violence Prevention Fund, the goals of the assessment are to create a supportive environment, gather information about health problems associated with the abuse, and assess the immediate and long-term health and safety needs for the patient to develop an intervention [35].

Assessment of domestic violence victims should occur immediately after disclosure of abuse and at any follow-up appointments. Assessing immediate safety is priority. Having a list of questions readily available and well-practiced can help alleviate the uncertainty of how to begin the assessment (***Table 1***). If the patient is in immediate danger, referral to an advocate, support system, hotline, or shelter is indicated [35].

If the patient is not in immediate danger, the assessment may continue with a focus on the impact of IPV on the patient's mental and physical health and the pattern of history and current abuse [35]. These responses will help formulate an appropriate intervention.

CULTURALLY SENSITIVE ASSESSMENT

During the assessment process, a practitioner should be open and sensitive to the patient's worldview, cultural belief systems and how he/she views the illness [47]. This may reduce the tendency to over-pathologize or minimize health concerns of ethnic minority patients.

Pachter proposed a dynamic model that involves several tiers and transactions [48]. The first component of Pachter's model calls for the practitioner to take responsibility for cultural awareness and knowledge. The professional should be willing to acknowledge that he/she does not possess enough or adequate knowledge in health beliefs and practices among the different ethnic and cultural groups he/she comes in contact with. Reading and becoming familiar with medical anthropology is a good first step.

The second component emphasizes the need for specifically tailored assessment [48]. Pachter advocates the notion that there is tremendous diversity within groups. For example, one cannot automatically assume that a Cuban immigrant adheres to traditional beliefs. Often, there are many variables, such as level of acculturation, age at immigration, educational level, and socioeconomic status, that influence health ideologies. Finally, the third component involves a negotiation process between the patient and the professional [48]. The negotiation consists of a dialogue that involves a genuine respect of beliefs. It is important to remember that these beliefs may affect symptoms or appropriate interventions in the case of domestic violence.

Culturally sensitive assessment involves a dynamic framework whereby the practitioner engages in a continual process of questioning. By incorporating cultural sensitivity into the assessment of individuals with a history of being victims or perpetrators of domestic violence, it may be possible to intervene and offer treatment more effectively.

INTERVENTIONS FOR DOMESTIC VIOLENCE AND ABUSE

After the assessment is complete, the patient may or may not want immediate assistance or referral. It is important for healthcare providers to assure patients in a nonjudgmental manner that the decision of what they would like in terms of assistance is their choice and that the provider will help regardless of the decisions they are currently ready to make [35].

If the patient would like to immediately implement a plan of action, information for referral to a local domestic violence shelter to assist the victim and the victim's family should be readily available. The acute situation should be referred immediately to local law enforcement officials. Other resources in an acute situation include crisis hotlines and rape relief centers. After a victim is introduced into the system, counseling and follow-up are generally available by individual counselors who specialize in the care of battered women and their spouses and children. These may include social workers, psychologists, psychiatrists, other mental health workers, and community mental health services. The goals are to make the resources accessible and safe and to enhance support for those who are unsure of their options [35].

In Florida, a 24-hour domestic violence hotline is available for toll-free counseling and information. The number is 800-500-1119. The counselors answering the toll-free line may refer the victim to her or his local domestic violence center. A list of Florida certified domestic violence centers organized by county may also be found on the Florida Department of Children and Families website at https://www.myflfamilies.com/service-programs/domestic-violence. Florida's domestic violence centers provide information and referral services, counseling and case management services, a 24-hour hotline, temporary emergency shelter for more than 24 hours, educational services for community awareness relative to domestic violence, assessment and appropriate referral of resident children, and training for law enforcement personnel.

DOCUMENTATION AND FOLLOW-UP

It is imperative that healthcare professionals document all findings and recommendations regarding domestic violence in the victim's medical record, including a patient's denial of abuse, if applicable. If domestic violence is disclosed, documentation should include relevant history, results of the physical examination, findings of laboratory and other diagnostic procedures, and results of the assessment, intervention, and referral. The medical record can be an invaluable document in establishing the credibility of the victim's story when seeking legal aid [35].

Healthcare professionals should offer a follow-up appointment if disclosure of past or current abuse is present. Reassurance that assistance is available to the patient at any time is critical in helping to break the cycle of abuse [35].

FACULTY BIOGRAPHIES

Marjorie Conner Allen, BSN, JD, received her Bachelor of Science in Nursing degree from the University of Florida, Gainesville, in 1984. She began her nursing career at Shands Teaching Hospital and Clinics at the University of Florida, Gainesville. While practicing nursing at Shands, she gave continuing education seminars regarding the nursing implications for dealing with adolescents with terminal illness. In 1988, Ms. Allen moved to Atlanta, Georgia where she worked at Egleston Children's Hospital at Emory University in the bone marrow transplant unit. In the fall of 1989, she began law school at Florida State University. After graduating from law school in 1992, Ms. Allen took a two-year job as law clerk to the Honorable William Terrell Hodges, United States District Judge for the Middle District of Florida. After completing her clerkship, Ms. Allen began her employment with the law firm of Smith, Hulsey & Busey in Jacksonville, Florida where she has worked in the litigation department defending hospitals and nurses in medical malpractice actions. Ms. Allen resides in Jacksonville and is currently in-house counsel to the Mayo Clinic Jacksonville.

Alice Yick Flanagan, PhD, MSW, received her Master's in Social Work from Columbia University, School of Social Work. She has clinical experience in mental health in correctional settings, psychiatric hospitals, and community health centers. In 1997, she received her PhD from UCLA, School of Public Policy and Social Research. Dr. Yick Flanagan completed a year-long post-doctoral fellowship at Hunter College, School of Social Work in 1999. In that year she taught the course Research Methods and Violence Against Women to Masters degree students, as well as conducting qualitative research studies on death and dying in Chinese American families.

Previously acting as a faculty member at Capella University and Northcentral University, Dr. Yick Flanagan is currently a contributing faculty member at Walden University, School of Social Work, and a dissertation chair at Grand Canyon University, College of Doctoral Studies, working with Industrial Organizational Psychology doctoral students. She also serves as a consultant/subject matter expert for the New York City Board of Education and publishing companies for online curriculum development, developing practice MCAT questions in the area of psychology and sociology. Her research focus is on the area of culture and mental health in ethnic minority communities.

Customer Information/Answer Sheet insert located between pages 60–61.

COURSE TEST - #97923 DOMESTIC VIOLENCE: THE FLORIDA REQUIREMENT

This is an open book test. Please record your responses on the Answer Sheet.
A passing grade of at least 70% must be achieved in order to receive credit for this course.

This 2 contact hour activity must be completed by July 31, 2025.

1. **Most healthcare professionals will encounter patients in their practice who are victims of domestic violence.**
   A) *True*
   B) *False*

2. **The Florida Department of Children and Families' definition of domestic violence may include pet abuse, physical abuse, and/or emotional abuse.**
   A) *True*
   B) *False*

3. **Florida law defines domestic violence exclusively as spouse abuse or battering.**
   A) *True*
   B) *False*

4. **House Bill 1099 strengthened domestic violence services by streamlining the process of allocating funds.**
   A) *True*
   B) *False*

5. **Domestic violence resulted in 217 deaths in Florida in 2020.**
   A) *True*
   B) *False*

6. **The majority of children exposed to intimate partner violence are direct eyewitnesses.**
   A) *True*
   B) *False*

7. **Domestic violence injury patterns are more likely than accidental injuries to involve the extremities of the body.**
   A) *True*
   B) *False*

8. **In addition to physical signs and symptoms, domestic violence victims may also exhibit psychologic cues that resemble an agitated depression.**
   A) *True*
   B) *False*

9. **Assessment of domestic violence victims should occur immediately after disclosure of abuse and at any follow-up appointments.**
   A) *True*
   B) *False*

10. **Florida does not presently have a toll-free domestic violence hotline, although this was a recommendation of the Governor's Task Force on Domestic Violence.**
    A) *True*
    B) *False*

Be sure to transfer your answers to the Answer Sheet insert located between pages 60–61.
PLEASE NOTE: Your postmark or facsimile date will be used as your test completion date.

Laws and Rules for Florida Nurses

This course fulfills the Florida requirement for 2 hours of education on Laws and Rules.

Audience
This course is designed for all nurses licensed in Florida.

Course Objective
The purpose of this course is to provide basic knowledge of the laws and rules governing the practice of nursing in Florida in order to increase compliance and improve patient care. Florida nurses are legally obligated to be aware of standards that govern professional accountability. Information contained in this course is not intended to be used in lieu of lawful guidelines, but as a learning tool that increases the understanding of some regulations as they apply to nurses who are licensed within the state of Florida.

Learning Objectives
Upon completion of this course, you should be able to:

1. Describe the legislative purpose for the Nurse Practice Act.
2. Identify specific laws and rules related to the practice of nursing and nursing assisting.
3. Outline the pertinent levels of nursing practice in the State and the general scope of practice of each.
4. Discuss the general requirements for continuing licensure in the State.
5. Differentiate between ethical and legal practice.
6. Discuss the process for discipline related to nursing practice.
7. Create a professional plan for career maintenance and development within the limits of the law.

Faculty
Jane C. Norman, RN, MSN, CNE, PhD, received her undergraduate education at the University of Tennessee, Knoxville campus. There she completed a double major in Sociology and English. She completed an Associate of Science in Nursing at the University of Tennessee, Nashville campus and began her nursing career at Vanderbilt University Medical Center. Jane received her Masters in Medical-Surgical Nursing from Vanderbilt University. In 1978, she took her first faculty position and served as program director for an associate degree program. In 1982, she received her PhD in Higher Education Administration from Peabody College of Vanderbilt University. In 1988, Dr. Norman took a position at Tennessee State University. There she has achieved tenure and full professor status. She is a member of Sigma Theta Tau National Nursing Honors Society. In 2005, she began her current position as Director of the Masters of Science in Nursing Program.

Faculty Disclosure
Contributing faculty, Jane C. Norman, RN, MSN, CNE, PhD, has disclosed no relevant financial relationship with any product manufacturer or service provider mentioned.

Division Planner
Sharon Cannon, RN, EdD, ANEF

Senior Director of Development and Academic Affairs
Sarah Campbell

Division Planner/Director Disclosure
The division planner and director have disclosed no relevant financial relationship with any product manufacturer or service provider mentioned.

Accreditations & Approvals
In support of improving patient care, NetCE is jointly accredited by the Accreditation Council for Continuing Medical Education (ACCME), the Accreditation Council for Pharmacy Education (ACPE), and the American Nurses Credentialing Center (ANCC), to provide continuing education for the healthcare team.

Designations of Credit
NetCE designates this continuing education activity for 2 ANCC contact hours.

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Special Approvals
This course fulfills the Florida requirement for 2 hours of education on Laws and Rules.

About the Sponsor
The purpose of NetCE is to provide challenging curricula to assist healthcare professionals to raise their levels of expertise while fulfilling their continuing education requirements, thereby improving the quality of healthcare.

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Disclosure Statement
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INTRODUCTION

Nursing practice acts have a long history in the United States, with the first standards being enacted in the early 1900s. In Florida, a period of major growth and expansion during this period resulted in an increase in the number of hospitals and training schools, which spurred the formation of professional nurses' associations and an interest in establishing standards for the delivery of nursing care [1]. The first practice act passed the Florida Legislature and was signed into law on June 7, 1913 [1].

The Florida Nurse Practice Act was legislated to safeguard the public, and the purpose of the Act is to ensure that minimum safety requirements are met by every nurse practicing in the state. The Nurse Practice Act, Chapter 464 of the Florida Statutes, includes laws governing scope of practice, licensure and certification, and violations and penalties [3]. Chapter 464 established the Florida Board of Nursing as an authority to adopt rules, develop standards for nursing programs, and discipline nurses who violate regulations [2]. Nurses who fall below Florida's required minimum competency or who present a danger to patients, coworkers, or others are prohibited from working in the state.

In addition to Chapter 464, nurses in Florida are regulated by Chapter 456, which includes general provisions for all health professions, and Title 64B9 of the Florida Administrative Code. Together, these laws and rules form the basis for the legal practice of nursing and the regulation of nursing by the state of Florida.

This course fulfills the education requirement on the laws and rules that govern the practice of nursing in Florida for all levels of nursing, including registered nurses (RNs), licensed practical nurses (LPNs), and advanced practice registered nurses (APRNs) [3]. While this course will provide an overview of the pertinent sections of the laws and rules, all nurses are encouraged to review them in their entirety in order to ensure compliance.

STANDARDS OF PRACTICE

The basic standards of competent practice directly impact how all nurses in Florida provide care. Not only must a nurse possess the knowledge of lawful and current care standards, but the knowledge must be demonstrated through consistent practice and intervention to prevent unauthorized, inappropriate, erroneous, illegal, contraindicated, or intentional nonperformance of care.

The Nurse Practice Act governs the practice of RNs, LPNs, and APRNs. LPNs are those persons licensed to practice practical nursing, while RNs and APRNs are licensed to practice professional nursing, with various levels of specialization [3]. Both professional and practical nurses are responsible and accountable for making decisions that are based upon their educational preparation and experience in nursing.

According to the Nurse Practice Act, the practice of practical nursing means [3]:

> The performance of selected acts, including the administration of treatments and medications, in the care of the ill, injured, or infirm; the promotion of wellness, maintenance of health, and prevention of illness of others under the direction of a registered nurse, a licensed physician, a licensed osteopathic physician, a licensed podiatric physician, or a licensed dentist; and the teaching of general principles of health and wellness to the public and to students other than nursing students. A practical nurse is responsible and accountable for making decisions that are based upon the individual's educational preparation and experience in nursing.

The practice of professional nursing is defined by the Act as "the performance of those acts requiring substantial specialized knowledge, judgment, and nursing skill based upon applied principles of psychological, biological, physical, and social sciences" [3]. The Florida Statutes further define the scope of practice of professional nursing as [3]:

- The observation, assessment, nursing diagnosis, planning, intervention, and evaluation of care; health teaching and counseling of the ill, injured, or infirm; and the promotion of wellness, maintenance of health, and prevention of illness of others
- The administration of medications and treatments as prescribed or authorized by a duly licensed practitioner authorized by the laws of this state to prescribe such medications and treatments
- The supervision and teaching of other personnel in the theory and performance of any of the above acts

ADVANCED PRACTICE REGISTERED NURSES

In addition to the practice of professional nursing, APRNs are certified in advanced or specialized nursing practice. This umbrella term includes certified nurse midwives, certified nurse practitioners, certified registered nurse anesthetists, clinical nurse specialists, and psychiatric nurses [3]. In accordance with the Act, APRNs may perform acts of nursing diagnosis and treatment of alterations of the health status as well as medical diagnosis and treatment, prescription, and operation as authorized within the framework of an established supervisory protocol [3]. Specifically, within the established framework, an APRN may [3]:

- Prescribe, dispense, administer, or order any drug; however, an APRN may prescribe or dispense a controlled substance only if she or he has graduated from a program leading to a Master's or doctoral degree in a clinical nursing specialty area with training in specialized practitioner skills
- Initiate appropriate therapies for certain conditions
- Perform additional functions as may be determined by rule
- Order diagnostic tests and physical and occupational therapy
- Order any medication for administration to a patient in a facility as defined by rule

All APRNs are required to obtain and maintain malpractice insurance or demonstrate proof of financial responsibility prior to licensure, with some exceptions [10]. Proof of compliance with this rule or exemption must be provided to the Board office within 60 days of certification and at each biennial renewal.

Rule 64B9-4.011 states, "APRNs whose protocols permit them to dispense medications…must register with the Board of Nursing by submitting a completed Dispensing Application for Advanced Practice Registered Nurse (APRN), form number DH-MQA 1185" [10]. The APRN dispensing practitioner must comply with all applicable state and federal laws and regulations.

CONTINUING LICENSURE IN FLORIDA

The Florida Board of Nursing is responsible for adopting rules establishing the procedure for the biennial renewal of nursing licenses. All Florida nurses are required to renew their licenses and complete mandated continuing education every two years. The Act stipulates that up to 30 hours of continuing education may be required each biennium [3]. Initial licenses that were issued for less than 24 months are required to complete one hour for each month for which the license was valid. As part of this requirement, all licensees must complete an approved two-hour course on the prevention of medical errors and a two-hour course on the laws and rules that govern the practice of nursing in Florida. Starting in 2019, licensees must also complete a two-hour course on human trafficking every renewal period. Beginning with 2018 renewals, a two-hour course on recognition of impairment in the workplace must be completed every other biennium. Every third renewal (or every six years), licensees must successfully complete two hours of continuing education on domestic violence in addition to the 24-hour requirement. A one-hour course on HIV/AIDS must be completed prior to a licensee's first renewal. In addition to these requirements, beginning in 2017, all APRNs must complete at least three hours of continuing education on the safe and effective prescription of controlled substances for each

biennial renewal. Beginning with 2021 renewals, each biennial, APRNs who engage in autonomous practice must complete at least 10 hours of continuing education (in addition to other mandated continuing education) appropriate to this level of care as approved by the Board [3].

Completion of all mandated continuing education must be reported to the Board. Failure to document compliance with the continuing education requirements or furnishing false or misleading information regarding compliance is grounds for disciplinary action.

A nurse may maintain his or her license in inactive status if there is no intent to practice nursing in the upcoming biennium. However, this requires that the licensee apply for inactive status and renew the license as inactive every two years; completion of continuing education is not required for these renewals. A license to practice nursing that is not renewed at the end of the biennium shall automatically revert to delinquent status [10].

In accordance with Rule 64B9-1.013 of the Florida Administrative Code, all licensed nurses must maintain on file with the Board of Nursing the current address at which any notice required by law may be served [10]. If a nurse moves, even out of state, he or she must notify the Board in writing of the new address within 60 days. In addition, all licensed nurses must alert the Board to their current place of practice. Place of practice is defined as one of the following [10]:

- Acute care facility
- Long-term care facility
- Rehabilitation facility
- Clinic
- Physician's office
- Home health care agency
- Educational institution
- Office of independent nursing practice
- Correctional facility
- Mental health facility
- Occupational health facility
- Managed health care organization or insurance company
- Community health facility
- Other

If a nurse wishes to activate an inactive license, he or she may do so by applying to the Department and paying a reactivation fee. As part of the application process, the licensee must disclose convictions or findings of guilt and/or disciplinary action(s) in or out of state [10]. In addition, the nurse must provide proof of completion of all continuing education for all biennial licensure periods for which the individual was inactive.

Completion of a Board-approved nursing refresher course is required to activate a license that has been inactive for five years or more if the licensee does not hold an active license in good standing in another state [10]. The refresher course must include at least 80 hours of classroom instruction and 96 hours of clinical experience in medical/surgical nursing and any specialty area of practice of the licensee.

ETHICAL AND LEGAL ISSUES IN NURSING PRACTICE

In addition to their legal obligations, nurses have ethical obligations to their patients. The practice of nursing is primarily one of caring, and the ethical theories for nursing are often referred to as "the ethics of caring." Nurses are expected to address both ethical and legal issues in their practice, which can be complex. As medical advancements and new technology progress, these must be incorporated into established ethical standards. The American Nurses Association has established the Code of Ethics for Nurses, which is intended to act as "a guide for nurses to use in ethical analysis and decision-making" [5]. The full text of this Code is available at https://www.nursingworld.org/practice-policy/nursing-excellence/ethics/code-of-ethics-for-nurses. Major ethical issues that may arise in the practice of nursing are related to the provision of patient-centered care, confidentiality, advocacy, delegation, self-care, and supporting colleagues and the profession.

There are also a variety of legal issues that affect the provision of nursing care and maintenance of a nursing license. It is important to note that, although possibly related, the laws governing nursing practice are different from the ethical framework(s) that nurses use to guide decision making. Laws pertaining to documentation, licensure, and standards of care have been established to ensure that nurses practice within a defined scope of practice and are aware of the boundaries of independent nursing action and responsibilities. These laws also act to hold nurses accountable for maintaining an acceptable standard of patient care. However, perhaps the greatest concern for nurses is the threat of negligence or malpractice claims.

According to tort law, four elements must be established for a ruling of malpractice [6]:

- Duty: The nurse owed a duty to meet a particular standard of care.
- Breach of duty: The nurse failed to perform the owed duty.
- Causation: There is a causal connection between the nurse's failure and the patient's injury.
- Damages: An injury occurred for which monetary compensation is adequate relief.

These elements must be shown by a "preponderance of the evidence," defined as more than 50% probability, a lower standard than the "beyond a reasonable doubt" used in criminal law [7; 8]. Malpractice cases are decided on the basis of what a "jury is likely to think is fact" rather than actual fact [9].

DISCIPLINARY ACTIONS

The Board of Nursing was created to assure protection of the public from nurses who do not meet minimum requirements for safe practice or who pose a danger to the public [3]. Violations of the laws established by the Board to ensure safe nursing practice are punishable by disciplinary action. These penalties are in addition to the results of any legal or civil proceedings that may be brought by the State or by patients or affected parties.

Acts requiring disciplinary or legal action are outlined in sections 464.016, 464.017, and 464.018 of the Nurse Practice Act [3]. According to section 464.016, the following acts are considered felonies in the third degree [3]:

- Practicing advanced or specialized, professional, or practical nursing unless holding an active license or certificate to do so
- Using or attempting to use a license or certificate that has been suspended or revoked
- Knowingly employing unlicensed persons in the practice of nursing
- Obtaining or attempting to obtain a license or certificate by misleading statements or knowing misrepresentation

In addition, the following acts constitute misdemeanors in the first degree [3]:

- Using the name or title "Nurse," "Registered Nurse," "Licensed Practical Nurse," "Clinical Nurse Specialist," "Certified Registered Nurse Anesthetist," "Certified Nurse Practitioner," "Certified Nurse Midwife," "Advanced Practice Registered Nurse," or any other name or title that implies that a person was licensed or certified as same, unless such person is duly licensed or certified
- Knowingly concealing information relating to violations of this part

These actions are punishable by law according to sections 775.082, 775.083, and 775.084 of the Statutes, Constitution, and Laws of Florida [3].

Several actions are also considered grounds for denial of a license or disciplinary action. According to section 464.018, this includes [3]:

- Procuring, attempting to procure, or renewing a license to practice nursing by bribery, by knowing misrepresentations, or through an error of the Department or the Board
- Having a license to practice nursing revoked, suspended, or otherwise acted against, including the denial of licensure, by the licensing authority of another state, territory, or country
- Being convicted or found guilty of, or entering a plea of *nolo contendere* to, regardless of adjudication, a crime in any jurisdiction that directly relates to the practice of nursing or to the ability to practice nursing
- Being convicted of or found guilty of, or entering a plea of guilty or *nolo contendere* (no contest) to, regardless of adjudication, any of the following offenses:
  - A forcible felony
  - Theft, robbery, and related crimes
  - Fraudulent practices
  - Lewdness and indecent exposure
  - Assault, battery, and culpable negligence
  - Child abuse, abandonment, and neglect
  - Abuse, neglect, and exploitation
  - For an applicant for a multistate license or for a multistate license-holder, a felony offense under Florida law or federal criminal law
- Having been found guilty of, regardless of adjudication, or entered a plea of no contest or guilty to, any offense prohibited under Section 435.04 or similar statute of another jurisdiction; or having committed an act which constitutes domestic violence
- Making or filing a false report or record, intentionally or negligently failing to file a report or record required by state or federal law, or willfully impeding or obstructing such filing or inducing another person to do so (limited to reports or records signed in the nurse's capacity as a licensed nurse)
- False, misleading, or deceptive advertising
- Unprofessional conduct
- Engaging or attempting to engage in the possession, sale, or distribution of controlled substances for any other than legitimate purposes
- Being unable to practice nursing with reasonable skill and safety to patients by reason of illness or use of alcohol, drugs, narcotics, or chemicals or any other type of material or as a result of any mental or physical condition

- Failing to report any person who the licensee knows is in violation of this part or of the rules of the Department or the Board to the Department or a consultant operating an impaired practitioner program, if appropriate
- Knowingly violating any provision of this part, a rule of the Board or the Department, or a lawful order of the Board or Department previously entered in a disciplinary proceeding or failing to comply with a lawfully issued subpoena of the Department
- Failing to meet minimal standards of acceptable and prevailing nursing practice, including engaging in acts for which the licensee is not qualified by training or experience
- Delegating professional responsibilities to a person when the nurse delegating such responsibilities knows or has reason to know that such person is not qualified by training, experience, certification, or licensure to perform them

For a full list of punishable acts, please refer to Chapter 464.018 of the Florida statutes.

Sexual misconduct is considered a breach of mutual trust and can irreparably damage the nurse-patient relationship. According to section 464.017, "Sexual misconduct in the practice of nursing means violation of the nurse-patient relationship through which the nurse uses said relationship to induce or attempt to induce the patient to engage, or to engage or attempt to engage the patient, in sexual activity outside the scope of the practice or the scope of generally accepted examination or treatment of the patient" [3]. Sexual misconduct in the practice of nursing is prohibited and is grounds for disciplinary action.

Disciplinary actions encompass a wide range of possible punishments, and the action chosen will depend on the individual circumstances (e.g., the severity of the violation, the number of past offenses). The Board may take the following actions in response to violations listed above [4]:

- Refusal to certify, or to certify with restrictions, an application for a license
- Suspension or permanent revocation of a license
- Restriction of practice or license
- Imposition of an administrative fine not to exceed $10,000 for each count or separate offense
- Issuance of a reprimand or letter of concern
- Placement of the licensee on probation for a period of time and subject to such conditions as the Board may specify
- Corrective action
- Imposition of an administrative fine for violations regarding patient rights
- Refund of fees billed and collected from the patient or a third party on behalf of the patient
- Requirement that the practitioner undergo remedial education

Nurses who have been found guilty on three separate occasions of violations relating to the use of drugs or narcotics or involving the diversion of drugs or narcotics from patients to personal use or sale are not eligible for reinstatement of licensure [3].

In the annual report of fiscal year 2020–2022, more than 800 nurses licensed in Florida had received disciplinary actions. The most common orders are suspension of the nursing license (36%), limitations/obligations of a nursing license (12%), revocation of the nursing license (10%), and voluntary surrender of a nursing license (8%) [11]. In most cases, nurses are also responsible for paying any costs associated with their order (e.g., investigation, court costs).

Certain offences may be resolved by mediation. Rule 64B9-8.012 states that mediation is an acceptable resolution for the first instance of the following violations [10]:

- Issuance of a worthless bank check to the Department or the Board for initial licensure or renewal of license, provided the licensee does not practice on a delinquent license
- Failure to report address changes, provided the failure does not constitute failure to comply with an order of the Board
- Failure to pay fines and investigative costs by the time ordered
- Failure to timely submit documentation of completion of continuing education imposed by Board order
- Failure to update a practitioner profile within 15 days

EXCEPTIONS

In addition to the limitations listed in this course, it is important to note that there are exceptions to the Nurse Practice Act. The law expressly states that the Act does not prohibit [3]:

- The care of the sick by friends or members of the family without compensation, the incidental care of the sick by domestic servants, or the incidental care of non-institutionalized persons by a surrogate family
- Assistance by anyone in the case of an emergency
- The practice of nursing by students enrolled in approved schools of nursing
- The practice of nursing by graduates of prelicensure nursing education programs, pending the result of the first licensing examination for which they are eligible following graduation, provided they practice under direct supervision of a registered professional nurse

- The rendering of services by nursing assistants acting under the direct supervision of a registered professional nurse
- Any nurse practicing in accordance with the practices and principles of the body known as the Church of Christ Scientist
- The practice of any legally qualified nurse or licensed attendant of another state who is employed by the U.S. Government, or any bureau, division, or agency thereof, while in the discharge of official duties
- Any nurse currently licensed in another state or territory of the United States from performing nursing services in this state for a period of 60 days after furnishing to the employer satisfactory evidence of current licensure in another state or territory and having submitted proper application and fees to the Board for licensure prior to employment. If the nurse licensed in another state or territory is relocating to this state pursuant to his or her military-connected spouse's official military orders, this period shall be 120 days after furnishing to the employer satisfactory evidence of current licensure in another state or territory and having submitted proper application and fees to the Board for licensure prior to employment. The Board may extend this time for administrative purposes when necessary.
- The rendering of nursing services on a fee-for-service basis or the reimbursement for nursing services directly to a nurse rendering such services by any government program, commercial insurance company, hospital or medical services plan, or any other third-party payor
- The establishment of an independent practice by one or more nurses for the purpose of rendering to patients nursing services within the scope of the nursing license
- The furnishing of hemodialysis treatments in a patient's home, using an assistant chosen by the patient, provided that the assistant is properly trained (as defined by the Board by rule) and has immediate telephonic access to a registered nurse who is licensed pursuant to this part and who has dialysis training and experience
- The practice of nursing by any legally qualified nurse of another state whose employment requires the nurse to accompany and care for a patient temporarily residing in this state for not more than 30 consecutive days, provided the patient is not in an inpatient setting, the Board is notified prior to arrival of the patient and nurse, the nurse has the standing physician orders and current medical status of the patient available, and prearrangements with the appropriate licensed healthcare providers in this state have been made in case the patient needs placement in an inpatient setting
- The practice of nursing by individuals enrolled in board-approved remedial courses

CONCLUSION

It is the responsibility of the Florida Board of Nursing to enforce the laws and rules regulating the practice of nursing as the law is currently stated—not how individuals may wish the law to be. However, as nurses are affected by these rules and regulations, they have the responsibility to keep informed of regulatory changes and provide public comment regarding regulations. Board meetings are held every two months, generally during the first week of every even month, and are open to the public. The full board meetings include disciplinary cases, application review, committee reports, rule discussions, and other necessary Board actions. For more information, please contact the Board at 850-488-0595 or https://floridasnursing.gov.

Customer Information/Answer Sheet insert located between pages 60–61.

COURSE TEST - #31253 LAWS AND RULES FOR FLORIDA NURSES

This is an open book test. Please record your responses on the Answer Sheet.
A passing grade of at least 70% must be achieved in order to receive credit for this course.

This 2 contact hour activity must be completed by October 31, 2025.

1. **The purpose of the Nurse Practice Act is to encourage the growth and expansion of hospitals and training schools.**
   A) *True*
   B) *False*

2. **The Nurse Practice Act is Chapter 464 of the Florida Statutes.**
   A) *True*
   B) *False*

3. **The Nurse Practice Act governs the practice of registered nurses, licensed practical nurses, and advanced practice registered nurses.**
   A) *True*
   B) *False*

4. **According to the Nurse Practice Act, the practice of practical nursing may be conducted under the direction of a registered nurse, licensed dentist, or licensed physician.**
   A) *True*
   B) *False*

5. **Ordering diagnostic tests and physical and occupational therapy is a part of the scope of practice for licensed practical nurses.**
   A) *True*
   B) *False*

6. **At least 40 hours of continuing education must be completed every biennium in order to maintain a nursing license in Florida.**
   A) *True*
   B) *False*

7. **Apology is one of the elements that must be established for a ruling of malpractice.**
   A) *True*
   B) *False*

8. **Using the name or title "Registered Nurse" without being duly licensed or certified is considered a misdemeanor in the first degree under the Nurse Practice Act.**
   A) *True*
   B) *False*

9. **Nurses who have been found guilty on three separate occasions of violations relating to the use of drugs or narcotics involving the diversion of drugs or narcotics from patients to personal use or sale are not eligible for reinstatement of licensure.**
   A) *True*
   B) *False*

10. **Board meetings are held annually.**
    A) *True*
    B) *False*

Be sure to transfer your answers to the Answer Sheet insert located between pages 60–61.
PLEASE NOTE: Your postmark or facsimile date will be used as your test completion date.

Recognizing Impairment in the Workplace: The Florida Requirement

This course fulfills the Florida requirement for 2 hours of education on Recognizing Impairment in the Workplace.

Have you already completed your Impairment in the Workplace requirement? You can skip this course and still receive 26 hours of continuing education.

Audience
This course is designed for nurses in Florida who may intervene to prevent or identify impairment in the workplace.

Course Objective
The purpose of this course is to provide nurses with an appreciation of the impact of impairment on the provision of nursing care and on patient health as well as the skills to identify and report instances of workplace impairment.

Learning Objectives
Upon completion of this course, you should be able to:

1. Outline the epidemiology and scope of impairment in the healthcare workplace.
2. Discuss unique risk factors for substance abuse in nurses.
3. Identify the signs of impairment in the nursing workplace.
4. Analyze the process and legal obligations involved in reporting an instance of impairment in the workplace.
5. Describe the treatment programs available for nurses who have been impaired in the workplace.

Faculty
Nancy Campbell, RN, BSN, PHN, received her Bachelor of Science in Nursing degree from California State University, Bakersfield in 1987. She has nursing experience in a variety of clinical settings, including medical/surgical, community health, and preschool health. She was a nurse case manager for a community program supporting teen parents and a public health nurse focusing on communicable disease management. Her primary focus and passion is on direct patient care and patient education. She is presently employed as a registered nurse for the Head Start program in Tulare County, California.

Faculty Disclosure
Contributing faculty, Nancy Campbell, RN, BSN, PHN, has disclosed no relevant financial relationship with any product manufacturer or service provider mentioned.

Division Planner
Jane C. Norman, RN, MSN, CNE, PhD

Senior Director of Development and Academic Affairs
Sarah Campbell

Division Planner/Director Disclosure
The division planner and director have disclosed no relevant financial relationship with any product manufacturer or service provider mentioned.

Accreditations & Approvals
In support of improving patient care, NetCE is jointly accredited by the Accreditation Council for Continuing Medical Education (ACCME), the Accreditation Council for Pharmacy Education (ACPE), and the American Nurses Credentialing Center (ANCC), to provide continuing education for the healthcare team.

Designations of Credit
NetCE designates this continuing education activity for 2 ANCC contact hours.

AACN Synergy CERP Category B.

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Special Approvals
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INTRODUCTION

Impairment of a healthcare professional can place everyone in a workplace at risk for injury. First and foremost is the risk to patients, who trust healthcare professionals to provide safe, reliable, and effective care. The ethical duty to not harm patients is a cornerstone of nursing, yet impaired healthcare workers injure patients daily. Another concern is the potential for impaired nurses to harm other professionals in the workplace, either directly or indirectly. Direct harm falls on a spectrum ranging from serious, injury-causing accidents to excessive absenteeism, which puts additional strain on staff. Presenteeism (i.e., reporting for work while impaired) places colleagues in the difficult position of having to work harder as a result of another's impairment, working in a potentially dangerous environment, and facing the dilemma of reporting a coworker, colleague, or friend.

Reporting impairment can be a difficult ethical situation for healthcare professionals, who often cover for impaired colleagues out of friendship or loyalty and who fear that reporting may ruin the nurse's career or their own. The truth is that the circumstances causing impairment have already eroded a nurse's professional abilities to some degree, and in most states, including Florida, good-faith reporters (i.e., those with sincere and honest intentions) are protected from retaliation by whistleblower laws. Conversely, not reporting a known impaired nurse is a violation of the Nurse Practice Act that can lead to disciplinary action by the Florida Board of Nursing.

Injury to patients and coworkers is increasingly likely when a worker is impaired, but impairment also gravely affects the individual nurse, whose health, safety, career, and social and financial standing are at risk if interventions are not undertaken. The American Nurses Association (ANA) definition of impairment describes a broad array of conditions that can interfere with workplace functioning, including mental or physical illness, fatigue, substance abuse, and other personal circumstances that adversely affect job performance [2]. Though fatigue and certain personal circumstances may be more easily resolved, these types of impairment still pose a danger. Fatigue, acute physical illness, and personal issues (e.g., stress, relationship problems) are generally dealt with in a different manner than impairment related to chemical dependence, other psychologic disorders, and chronic physical conditions. It should be remembered that alcohol and/or substance abuse is a type of medical and psychologic disorder, and helping the nurse obtain treatment so she or he can get healthy and return to work is the ultimate goal of reporting and intervention. Nearly all states, including Florida, now offer nurses found to be impaired at work an alternative to criminal prosecution, the chance to retain their license, and a return to nursing if they agree to enter and participate in an intervention program.

This course presents information on recognizing the signs and symptoms of emotional-, mental health-, and substance-related workplace impairment. Strategies for intervention and reporting (e.g., how and to whom impairment should be reported) are also outlined, particularly within the context of the Florida Nurse Practice Act. Treatment of impairment, including intervention programs, employer initiatives for impaired nurses, and returning to work, will be discussed. In the state of Florida, the Intervention Project for Nurses (IPN) is the Department of Health's contracted program to address nurse impairment; this program will be discussed in detail.

SCOPE OF THE PROBLEM

Historically, the rate of substance use disorder among healthcare professionals was thought to be much higher than in the general public, due to job stress and easy access to pharmaceutical drugs. However, the rate among nurses and physicians is now estimated to be only slightly higher than or equal to the rate found in the general public (10% to 15%) [3; 5; 6; 9]. The ANA has reported that approximately 15% of all nurses abuse substances to the point at which interference with vocational practice can be expected [13; 17]. Based on these data, up to 525,000 of the more than 3.5 million nurses in the United States have substance use disorders that may affect job performance [12]. Furthermore, one survey indicated that alcohol abuse continues to rise among nurses, particularly since the start of the COVID-19 pandemic [4]. Nurses make up the greatest proportion of healthcare workers in the country; therefore, substance-related impairment among nurses is a major healthcare problem, despite similar rates of abuse and dependency among other healthcare professionals [9].

According to the Nurse Worklife and Wellness Study, past-year illicit drug use among nurses was 5.7% and prescription drug misuse was 9.9% [6]. Another study found that while the rate of drug dependence was similar among female nurses and women in the general population, the rate of prescription drug abuse was much higher (more than double) among nurses; use of street-type drugs (e.g., cocaine, cannabis) was found to be lower in nurses than in the general population [5]. Reasons cited for the higher rates of prescription drug abuse included easier access, familiarity with dosages and effects, and comfort experimenting with drugs commonly prescribed to patients [6]. This phenomenon, referred to as "pharmacologic optimism," is based on the ingrained belief that pharmaceutical drugs cause profound healing with few to no negative effects, an idea that is established early in some nurses [9]. Aside from alcohol, which is the most commonly abused substance among nurses, one study identified the classes of drugs most often abused, in order of frequency, as amphetamines, opioids, sedatives, tranquilizers, and inhalants. In this study, abuse was defined as prescription drug use without a script, using greater than the prescribed dosage, or using a drug for indications other than those prescribed [6; 9]. In many instances of abuse, drugs were obtained through diversion. Drugs are diverted in several different ways [6; 11]:

- A physician writes a prescription for the nurse in the absence of a true indication.
- The nurse steals scripts and falsifies prescriptions for him- or herself.
- A whole dose of an injectable drug ordered for a patient is used by the nurse and replaced with saline, or the nurse retains the correct (drug-filled) syringe and replaces it with another filled with saline.
- Partial doses of medications are administered to patients while the nurse saves or uses the remainder.
- A nurse applies a skin patch to him- or herself before transferring it to the patient.
- A nurse removes syringes or ampules from a sharps waste container to scavenge any remaining drugs.
- The nurse has a colleague who, without actually witnessing the disposal, cosigns a record indicating waste while the nurse actually retains or takes the drug dose.
- The nurse obtains medications for patients who have not asked for them or who refused them.
- The nurse signs out medications for a patient who has been transferred.

All of these examples of diversion techniques have been documented, including cases in which patients have been infected with hepatitis C when a nurse used a syringe of opioid narcotic intended for them before replacing the missing contents with saline and injecting the patient [11]. One study found that 65% of nurses addicted to a pharmaceutical drug were diverting medication from their workplace [19]. Most addicted nurses in this study admitted to treating patients while impaired.

UNIQUE RISK FACTORS

In addition to the common risk factors for substance abuse in all individuals, several unique risk factors have been identified for nurses, including [9; 15]:

- Positive attitudes toward drugs and drug use (i.e., "pharmacologic optimism")
- Relaxed physician prescribing practices in the facility
- Lack of pharmaceutical controls in a facility
- Little or no education regarding substance use disorders
- Enabling by peers and managers
- Role strain

The prevalence of substance misuse varies by nurse specialty. Critical care, psychiatric, emergency room, and oncology nurses have been found to have the highest rates of substance misuse , but alcohol misuse, particularly binge drinking (four or more drinks for women or five or more drinks per occasion for men), is a significant problem among oncology nurses

[9; 19]. Another study found that binge drinking was more common among all nurses than in the general population 35 years of age or older [10]. The Nurse Worklife and Wellness Study showed the highest rates of drug misuse among nurses occurred in those working in home health/hospice care (19%) followed by those working nursing homes (15.8%) [6]. In addition, staff nurses, charge nurses/coordinators/managers, and other administrators had 9- to 12-times the odds of substance use disorder compared with educators/researchers [6].

Gender is another factor for substance abuse in nursing professions. Male nurses are more likely to abuse substances and are over-represented in treatment programs [9]. However, the majority of RNs (90.9%) and LPNs (92.4%) in the United States are women; therefore, the vast majority of nurses with substance use disorders are women [9; 12]. Studies have shown that men's addiction runs a more acute course, with less pronounced physical and mental effects; men also tend to seek help sooner for the actual addiction. In contrast, women's addiction tends to be prolonged, with a greater mental and physical toll. Women typically seek help for the manifestations of addiction, such as depression, anxiety, and insomnia, which can delay treatment for the root cause [9].

IDENTIFYING IMPAIRMENT IN THE WORKPLACE

It is important that nurses have the ability to recognize signs and symptoms of impaired practice and be able to differentiate a pattern of impairment from isolated incidents that may be caused by job stress. Studies have shown that most nurses are not able to accurately identify impairment in the workplace because they have little education on signs and symptoms of impairment in a professional setting and among other professionals [3; 18]. This is compounded by the fact that some individuals, particularly experienced healthcare providers, may be able to function at a high level while under chemical influence. Failure to identify impairment or a belief that reporting is unnecessary because an individual is able to function normally despite alcohol/drug abuse may result in a failure to document and report suspected impairment, inadvertently enabling the substance abuse [3]. On the other hand, nurses who have the knowledge and confidence to identify impairment are empowered to confront colleagues and report their peers according to employer protocol.

DEFINITION OF IMPAIRMENT

The Florida Legislature defines impairment among health professionals as "a potentially impairing health condition that is the result of the misuse or abuse of alcohol, drugs, or both, or a mental or physical condition that could affect a practitioner's ability to practice with skill and safety." [21].As defined, Impaired practice is not strictly related to substance abuse disorders; common mental health disorders, such as depression and anxiety, have the potential to interfere with nurses' ability to provide adequate patient care as well [24].

In a meta-analysis of research related to the impact of mental disorders on the work performance of nurses and other healthcare professionals, strong evidence was found to support a relationship between mental disorders and general errors, medication errors, near errors, impaired patient safety, and decreased patient satisfaction [26]. This is a particular concern given the fact that nurses are at greater risk for certain mental health issues (e.g., depression) than the general public [24].

Physical disability may also impede nurses' performance, and steps should be taken to create disability inclusive workplaces [27]. Some nurses may be hesitant to disclose disabilities or known limitations for fear of losing their jobs [28]. Physical limitations are not grounds for dismissal, and failure to disclose poses a greater safety risk than working with healthcare professionals with known disabilities.

SIGNS OF IMPAIRMENT

Signs of impairment related to substance abuse among healthcare professionals fall into three general categories: job performance issues, emotional and mental status, and workplace drug diversion [7]. Impairment specifically related to substance abuse may present differently in nurses than in the general public. Signs of impairment related to job performance include [7; 8; 22]:

- An excessive number of mistakes at work (e.g., frequent medication errors, errors of judgment in patient care)
- "Job shrinkage" (i.e., the nurse progressively performs the minimal amount of work necessary)
- Increased difficulty meeting deadlines or adhering to schedules
- Frequent or unexplained disappearances
- Implausible and/or elaborate excuses for unusual behavior
- Dishonesty over trivial matters
- Illegible or sloppy charting
- Tremors or shaking
- Extended breaks or lunch hours
- Excessive absence due to alleged illness, particularly following scheduled days off
- Last-minute requests for time off
- Absence without notice
- Smell of alcohol or cannabis
- Excessive use of breath mints, chewing gum, mouthwash, or perfume

Signs of changes in emotional and mental status include [7; 8; 22]:

- Inappropriate or uncharacteristic responses to criticism (e.g., crying, uncontrolled anger, snapping at or arguing with colleagues)

- Emotional lability (e.g., becoming uncommonly gregarious or quiet, withdrawn, or irritable; has recurrent mood swings and is unpredictable)
- Reduced alertness (e.g., forgetfulness, preoccupation, appearing dazed and confused, slow reaction time)
- Increasing isolation from coworkers (e.g., avoiding informal staff gatherings, eating or taking breaks alone, requesting transfer to another shift)
- Increased and uncharacteristic problem with authority
- Change in dress and/or appearance

Signs that a healthcare professional is diverting drugs for personal use include [7; 8; 22]:

- Volunteering to work with patients who receive regular or large amounts of pain medication
- Consistently volunteering to be the medication administrator
- Often signing out more controlled drugs than coworkers
- Failing to obtain co-signatures
- Frequently reporting medication spills or other waste
- Reports reflecting excessive use of pain medications on patients
- Discrepancies in end-of-shift medication counts
- Evidence of tampering with vials, other drug containers, or medication counts
- Waiting until alone to open the narcotics box or cabinet, or disappearing after opening it
- An increase in patients' complaints of unrelieved pain
- Defensiveness when questioned about medication errors
- Consistently coming to work early and staying late

Nurse supervisors and managers should maintain an active role in identifying impairment in the workplace by refusing to allow personal manipulation by another nurse or to fear confronting a nurse if patient safety is in jeopardy. It is important to reduce or change a nurse's role or patient assignment and not accept excuses for or ignore poor performance [16]. Several tools have been developed to assess nurses' job performance and fitness for work, such as the Common Risky Behaviors Checklist, which assesses five dimensions: absence/tardiness, cognitive impairment, unprofessional communication/boundaries, physical impairment, and drug diversion [24; 25]. These measures may be completed by supervisors or individual nurses (i.e., self-report).

REPORTING COLLEAGUES AND MANDATORY REPORTING LAW

Florida law requires that a Board-licensed nurse make a good faith report of another individual's known workplace impairment, whether the situation is acute or there is growing suspicion. But, reporting a colleague is a decision with which many nurses struggle [3]. Experienced, older nurses are more likely to report impairment because they have likely witnessed the negative effects in coworkers at some point; younger and less experienced nurses are less likely to report. Many professionals choose to ignore the problem because they think someone else will or is already handling the situation [1; 3]. One study identified several factors that contribute to failure to report by coworkers, including feeling like a "tattle-tale," fear of revenge or retaliation, fear the colleague might react in a violent manner, not wanting to be responsible for jeopardizing a colleague's job, not being confident enough in one's own observations or instincts to confront a colleague, not being an expert in chemical dependence, and believing the intervention would be better dealt with by an expert [3]. Although these concerns may be valid, nursing is a profession that holds patient safety and healing as the highest duty—and not one of these concerns seems related to protecting patients. Furthermore, few of the reasons for non-reporting show any regard for helping a coworker to heal. Nursing is about action, and there is no excuse for failing to act.

FLORIDA LAW

The Florida Statutes Chapter 464.018 Disciplinary Actions defines nursing impairment and describes the conditions and actions an impaired nurse will face. The section states that the following constitutes grounds for disciplinary action or denial of a license [14]:

> Being unable to practice nursing with reasonable skill and safety to patients by reason of illness or use of alcohol, drugs, narcotics, or chemicals or any other type of material or as a result of any mental or physical condition. In enforcing this paragraph, the department shall have, upon a finding of the State Surgeon General or the State Surgeon General's designee that probable cause exists to believe that the licensee is unable to practice nursing because of the reasons stated in this paragraph, the authority to issue an order to compel a licensee to submit to a mental or physical examination by physicians designated by the department. If the nurse refuses to comply with such order, the department's order directing such examination may be enforced by filing a petition for enforcement in the circuit court where the nurse resides or does business. The nurse against whom the petition is filed shall not be named or identified by initials in any public court records or documents, and the proceedings shall be closed to the public...A nurse affected by this paragraph shall at reasonable intervals be afforded an opportunity to demonstrate that she or he can resume the competent practice of nursing with reasonable skill and safety to patients.

The Florida Statutes Chapter 464.018 Disciplinary Actions also contains the mandatory reporting law. Reporting known impairment in Florida is mandatory, not optional. Failure to

report an impaired individual who is providing health care can lead to disciplinary action by the Board of Nursing. The following act constitutes grounds for denial of a license or disciplinary action [14]:

> Failing to report to the department any person who the nurse knows is in violation of this part or of the rules of the department or the board. However, a person who the licensee knows is unable to practice nursing with reasonable skill and safety to patients by reason of illness or use of alcohol, drugs, narcotics, chemicals, or any other type of material, or as a result of a mental or physical condition, may be reported to a consultant operating an impaired practitioner program...rather than to the department.

HOW TO REPORT AN IMPAIRED NURSE

Nurses should be familiar with their organization's policies and procedures for reporting employee substance abuse or other impairment and those regarding assistance programs [16]. When aware of the resources available to an impaired nurse, including the process, programs, and benefits of employee assistance programs or alternative-to-discipline programs, nurses are better prepared and more likely to report impairment. In 1983, the Florida legislature established the IPN as a contact point for nursing impairment reporting, as a treatment and rehabilitation facilitator, and as a monitoring program for impaired nurses within the state [20]. Florida nurses are required to report suspected impaired practice to the IPN and/or the Florida Department of Health [21]. Reporting to either of these entities fulfills the mandatory reporting obligation. With the knowledge that recovery, nonpunitive rehabilitation, and returning to work are the goals of such programs, nurses should feel confident that their colleagues will receive the help they need to overcome their impairment [3]. In the long-term, the report will be beneficial to the impaired nurse, and in the short-term, patients are being protected from harm.

Before making a report, documenting changes in the suspected nurses' behavior and work performance is recommended [16]. The signs and symptoms listed in the previous section of this course are a good starting point. Taking note of specific actions or behaviors will help when making the report and/or confronting a colleague or supervisee.

In the past, professional organizations recommended confronting the impaired individual directly, but this strategy was found to be unrealistic and is no longer endorsed [2; 3; 16; 22]. The ANA Code of Ethics no longer recommends confronting colleagues as the initial course of action before notifying a supervisor [3]. The 2015 ANA Code of Ethics states that "the nurse's duty is to take action to protect patients and to ensure that the impaired individual receives assistance. This process begins with consulting supervisory personnel, followed by approaching the individual in a clear and supportive manner and by helping the individual access appropriate resources" [2]. The Code further states that "nurses must follow policies of the employing organization, guidelines outlined by the profession, and relevant laws to assist colleagues whose job performance may be adversely affected by mental or physical illness, fatigue, substance abuse, or personal circumstances" [2]. The Florida Nurse Practice Act clearly states that the IPN or the Department of Health must be notified, but does not specify how an intervention must proceed [21].

Some sources suggest that the best outcomes are achieved when a professional or other personnel trained in intervention confronts the individual [22]. Many facilities have employee assistance or human resources personnel who are trained to intervene. The IPN offers intervention training [23].

The ANA Code of Ethics also provides the following additional advice regarding intervening in cases of suspected workplace impairment [2]:

- The nurse should extend compassion and caring to colleagues throughout the processes of identification, remediation, and recovery.
- Care must also be taken in identifying impairment in one's own practice and in seeking immediate assistance.
- In instances of impaired practice, nurses within all professional relationships should advocate for appropriate assistance, treatment, and access to fair institutional and legal processes. Advocacy includes supporting the return to practice of individuals who have sought assistance and, after recovery, are ready to resume professional duties.
- If impaired practice poses a threat or danger to patients, self, or others, regardless of whether the individual has sought help, a nurse must report the practice to persons authorized to address the problem.
- Nurses who report those whose job performance creates risk should be protected from retaliation or other negative consequences.
- If workplace policies for the protection of impaired nurses do not exist or are inappropriate—that is, they deny the nurse who is reported access to due legal process or they demand resignation—nurses may obtain guidance from professional associations, state peer assistance programs, employee assistance programs, or similar resources.

TREATMENT PROGRAMS

When a nurse is reported to either the IPN or the Department of Health, the referral triggers a consultation with the reporter and/or the employer of the impaired nurse [1]. This is followed by an intervention and evaluation. The intervention typically occurs one to three days after a report (whereas a standard disciplinary process typically takes 9 to 12 months to remove a nurse from practice) [1]. If a nurse self-reports to the IPN, the intake and evaluation process begins immediately. In Florida, the IPN is charged with accepting reports,

evaluating referrals, determining the proper course of action, monitoring the nurse's progress in treatment, and case managing all individuals returning to work [13]. The IPN program objectives are to [13]:

- Ensure public health and safety through a program that provides close monitoring of nurses who are unsafe to practice due to the use of drugs, including alcohol, and/or psychiatric, psychologic, or physical condition
- Require the nurse to withdraw from practice immediately, and until such time that the IPN is assured that he/she is able to safely return to the practice of nursing
- Facilitate early intervention, thereby decreasing the time between the nurse's acknowledgment of the problem and his/her entry into a recovery program
- Provide a program for affected nurses to be rehabilitated in a therapeutic, non-punitive, and confidential process
- Provide an opportunity for retention of nurses within the nursing profession
- Provide a cost-effective alternative to the traditional disciplinary process
- Develop a statewide resource network for referring nurses to appropriate services
- Provide confidential consultations for nurse managers

Although the IPN assesses referrals to the program to decide the best course of action for the individual, the program does not actually provide treatment for addiction or other diseases/disorders. Rather, the IPN directs individuals to approved treatment programs and providers [1]. Additional services provided by the IPN include advocacy for participants; tracking meeting attendance and discussing recovery progress with group facilitators; comprehensive monitoring of nurses following discharge from treatment; providing random drug screening of participants and detecting relapse; and reporting compliance issues to the proper authority [1; 13]. If at any time during the process the nurse refuses to participate in the program or fails to comply with program guidelines, including after returning to work, the individual is referred to the Department of Health for discipline, which entails investigation, hearings, and disciplinary action.

RETURNING TO WORK

Following completion of approved treatment, the IPN determines if nurses in the program are ready to return to practice based on several criteria, including the individual's stability in recovery, cognitive functioning, decision-making/problem-solving ability, use of good judgment, ability to deal with stressful situations, and development of a support system [1]. A signed advocacy contract and completed relapse prevention workbook must also be submitted. Stability in recovery is crucial and is indicated by advocacy contract compliance, consistently negative random urine drug screens, regular attendance at support and monitoring groups, and favorable monitoring reports [1]. Progress reports are generated by treatment providers, nurse support group facilitators, and by the nurses in recovery (i.e., self-reports).

The support system for nurses returning to work includes a weekly support group for ongoing self-care and relapse prevention. A coworker is also established as a workplace monitor to provide feedback to the IPN on the nurse's job performance [1]. If a nurse was referred to the IPN due to pharmaceutical use or diversion, it is recommended that the nurse be assigned a labor exchange colleague assigned to handle patient medication duties. Other restrictions for these individuals may include no overtime or floating; no multiple employers; and no agency, hospice, or home care employment [1].

The Florida Board of Nursing allows nurses two opportunities to return to work after referral for diversion of drugs or narcotics [14]. A nurse will not have their license reinstated after a third violation of drug diversion for sale or personal use.

PROMOTING SAFETY IN THE WORKPLACE AND PROVIDING ASSISTANCE

Employers should have clear policies and procedures for fostering and maintaining a drug- and alcohol-free workplace and ensuring that nurses are fit to practice. When system deficiencies are found to exist, these should be remedied. Employees benefit from a sense that policies are enforced equally and without exception; otherwise, uncertainty will exist as to whether poor behavior is overlooked or ignored if an employee is well liked or has perceived seniority. The National Council of State Boards of Nursing (NCSBN) recommends several employer policies to promote safety, including drug testing before employment, testing when there is suspicion of drug use, and conducting regular fitness-to-practice evaluations [9].

All employees should be familiar with and abide by their facility's policies, guidelines, and procedures. The NCSBN recommends that nurses be familiar with procedures (internal and external) related to how to document concerns, how and when to report impairment, return to practice after treatment, and relapse management [9]. Nurses should also be provided with information about employee assistance programs (if applicable), including a clear understanding of the confidentiality of such programs.

Customer Information/Answer Sheet insert located between pages 60–61.

COURSE TEST - #31112 RECOGNIZING IMPAIRMENT IN THE WORKPLACE: THE FLORIDA REQUIREMENT

This is an open book test. Please record your responses on the Answer Sheet.
A passing grade of at least 70% must be achieved in order to receive credit for this course.

This 2 contact hour activity must be completed by October 31, 2025.

1. **The rate of alcohol and drug dependency among nurses and physicians is estimated to be slightly higher than or equal to the rate found in the general public (10% to 15%).**
   A) *True*
   B) *False*

2. **Use of street-type drugs (e.g., cocaine, cannabis) is higher in nurses than in the general population.**
   A) *True*
   B) *False*

3. **A positive attitude toward drugs and drug use (i.e., "pharmacologic optimism") is a unique risk factor for substance use in nurses.**
   A) *True*
   B) *False*

4. **Male nurses are more likely than female nurses to abuse substances and are over-represented in treatment programs.**
   A) *True*
   B) *False*

5. **Impaired nursing practice is defined as isolated incidents that may be caused by job stress.**
   A) *True*
   B) *False*

6. **Frequently reporting medication spills or other waste may be a sign that a healthcare professional is diverting drugs for personal use.**
   A) *True*
   B) *False*

7. **Experienced, older nurses are more likely to report impairment because they have likely witnessed the negative effects in coworkers at some point.**
   A) *True*
   B) *False*

8. **Reporting suspected impaired practice to Florida's Intervention Project for Nurses does not fulfill the mandatory reporting obligation.**
   A) *True*
   B) *False*

9. **The American Nurses Association Code of Ethics recommends confronting potentially impaired colleagues as the initial course of action, before notifying a supervisor.**
   A) *True*
   B) *False*

10. **When a nurse is reported for suspected impairment at work, intervention typically occurs within one to three days.**
    A) *True*
    B) *False*

Be sure to transfer your answers to the Answer Sheet insert located between pages 60–61.
PLEASE NOTE: Your postmark or facsimile date will be used as your test completion date.

Recognizing and Reporting Human Trafficking in Florida

This course fulfills the Florida requirement for 2 hours of education on Human Trafficking.

Audience
This course is designed for all health and mental health professionals in Florida who may identify and intervene in cases of human trafficking and exploitation.

Course Objective
The purpose of this course is to provide physicians, nurses, and other healthcare professionals an in-depth, practical review of human trafficking, including the definition and scope of the problem, the means of identification and assessment of individuals who may be victims, guidance on reporting of cases, and interventions and resources available to victims.

Learning Objectives
Upon completion of this course, you should be able to:

1. Define human trafficking.
2. Identify the forms of human trafficking.
3. Identify economic, political, social, and cultural factors that contribute to human trafficking.
4. Analyze the trafficking experience, including how traffickers recruit and the financial implications of trafficking.
5. Explain the psychological, health, and social consequences of human trafficking.
6. Utilize interviewing strategies to assess and identify victims and promote the ethical treatment of trafficking victims.
7. Describe the appropriate steps for reporting suspected cases of trafficking.
8. Describe various interventions and resources for human trafficking victims.

Faculty
Alice Yick Flanagan, PhD, MSW, received her Master's in Social Work from Columbia University, School of Social Work. She has clinical experience in mental health in correctional settings, psychiatric hospitals, and community health centers. In 1997, she received her PhD from UCLA, School of Public Policy and Social Research. Dr. Yick Flanagan completed a year-long post-doctoral fellowship at Hunter College, School of Social Work in 1999. In that year she taught the course Research Methods and Violence Against Women to Masters degree students, as well as conducting qualitative research studies on death and dying in Chinese American families. (A complete biography appears at the end of this course.)

Faculty Disclosure
Contributing faculty, Alice Yick Flanagan, PhD, MSW, has disclosed no relevant financial relationship with any product manufacturer or service provider mentioned.

Division Planners
Jane C. Norman, RN, MSN, CNE, PhD

Senior Director of Development and Academic Affairs
Sarah Campbell

Division Planners/Director Disclosure
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Special Approvals
This course meets the Florida requirement for Human Trafficking education.

About the Sponsor
The purpose of NetCE is to provide challenging curricula to assist healthcare professionals to raise their levels of expertise while fulfilling their continuing education requirements, thereby improving the quality of healthcare.

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- Read the following course.
- Complete the test.
- Return your Customer Information/Answer Sheet and payment to NetCE by mail or fax, or complete online at **www.NetCE.com/FL24**.
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INTRODUCTION

Although human trafficking has always existed, it has begun to receive increased attention as a result of awareness and outreach efforts. Gaining recognition of a problem as a social issue often involves various groups making compelling claims using persuasive rhetoric and dramatic statistics [1]. Human trafficking, sometimes referred to as "modern slavery," has garnered attention as a human rights issue from a broad spectrum of organizations, including feminists, religious conservatives, labor activists, immigration specialists, mental health and healthcare professions, the media, politicians, and the public, all of whom have responded to the gravity of the condition. It is through this process of claims-making and counter claims-making that "conditions" that may not necessarily have initially attracted attention can develop into a recognized social problem [1; 2]. How the problem is described or constructed will influence public opinion, which will then ultimately facilitate action from governmental agencies, social service organizations, and international agencies [3; 4; 5].

This course will provide a basic overview of human trafficking (e.g., the scope, definitions and frameworks, contributing factors, different forms). The course will attempt to provide practitioners a glimpse of the lives of human trafficking victims, including the physical, psychological, social, and sexual abuse that human trafficking victims experience and the types of control tactics perpetrators use. Specific interventions and responses will be covered, including mental health, social services, educational, prevention, and legal efforts. Finally, for practitioners who do work with human trafficking victims, the emotional toil that it takes upon practitioners as well as the importance of self-care will be discussed. The course will end by offering an array of resources. Practitioners will be encouraged to view films and documentaries about human trafficking, as this is one way to "enter the lives" of human trafficking victims and better understand the dynamics of the complex world of human trafficking.

SCOPE OF HUMAN TRAFFICKING

As the issue of human trafficking is so complex, it is difficult to determine the scope of the problem. Many scholars and researchers believe that published estimates are just educated guesses. On a global level, the International Labour Organization has estimated that there are 40.3 million human trafficking victims at any given time [6]. The estimates for the United States are not totally clear, but there were approximately 78,000 human trafficking victims reported to the U.S. State Department in 2016; only an estimated 0.2% are rescued [7; 120]. According to Polaris, which founded and runs the National Human Trafficking Hotline, there have been a total of 73,946 cases of human trafficking reported since 2007 [7; 12; 120; 121].

Weitzer's content analysis of websites and publications about human trafficking found that human trafficking is portrayed as an epidemic, growing at alarming rates, with some government reports estimating 40,000 to 50,000 individuals trafficked in the United States each year [8; 120]. Weitzer argues that many of the reports have overestimated the scope of the problem and points out that the estimates fluctuate drastically year to year [9]. Sex trafficking tends to be portrayed more frequently due to its sensationalism. In a study of 50 human trafficking campaigns in Spain between 2004 and 2017, 40 (80%) depicted sex trafficking and exploitation involving women [10].

The U.S. Department of Justice reported 1,045 convictions for human trafficking-related crimes in 2017, including forced labor and sex trafficking of adults and minors. This was an increase of more than 78% over the number reported in 2015 [6]. In 2016, the International Labour Organization stated that there were 4.8 million victims of sex trafficking, and 15.4 million in forced marriages. The majority (62%) of those trafficked are in Asia and Pacific regions [11]. In 2017, it is estimated that there are 24.9 million people around the world who are in forced labor [11].

Florida ranks third in the United States in terms of cases of trafficked persons [12]. In 2020, the National Human Trafficking Hotline received 2,539 contacts (e.g., phone calls, texts, e-mails) and 738 human trafficking cases reported in Florida. The most common type was sex trafficking (70.1%), followed by labor trafficking (14.6%) and combined sex/labor trafficking (5.6%) [12]. The majority of victims were female (82.1%) and adult (67.3%).

DEFINITIONS OF HUMAN TRAFFICKING

The United Nations defines human trafficking as [13]:

> The recruitment, transportation, transfer, harbouring or receipt of persons, by means of threat or use of force or other forms of coercion, of abduction, of fraud, of deception, of the abuse of power or of a position of vulnerability, or of the giving or receiving of payments or benefits to achieve the consent of a person having control over another person, for the purpose of exploitation. Exploitation shall include, at a minimum, the exploitation or the prostitution or other forms of sexual exploitation, forced labour or services, slavery or practices similar to slavery, servitude, or the removal of organs.

In essence, this definition involves three elements: the transport of the person, the force or coercion of the victim, and the abuse and exploitation [14]. The United Nations Office on Drugs and Crime divides the definition of human trafficking into three sections: the act, means, and purpose [15]. The act, or what is done, generally refers to activities such as recruitment, transportation, transfer, harboring, or receipt of persons. The means of trafficking consists of threats or use of force, coercion, abduction, fraud, deception, abuse of power or vulnerability, or giving payments or benefits to a person in control of the victim. Finally, these acts are carried out for the purpose of exploitation, which includes prostitution, sexual exploitation, forced labor, slavery or forced servitude, and the removal of organs [15]. It is important to remember that human trafficking is not human smuggling. Human smuggling involves an individual being brought into a country through illegal means and is voluntary. The individual has provided some remuneration to another individual or party to accomplish this goal [16].

interactive activity

Watch the 12-minute video clip The Top 10 Facts About the "S" Word at https://www.youtube.com/watch?v=TJlDBKZmRrE.

This video provides a snapshot of modern slavery, including the economics of slavery and the various types of slavery worldwide.

The Trafficking Victims Protection Act (TVPA) defines human trafficking to include both sex trafficking and labor trafficking [17]. Sex trafficking is the recruitment, harboring, transportation, provision, obtaining, patronizing, or soliciting of a person for the purposes of a commercial sex act, in which the commercial sex act is induced by force, fraud, or coercion, or in which the person induced to perform such an act has not attained 18 years of age. Labor trafficking is the recruitment, harboring, transportation, provision, or obtaining of a person for labor or services, through the use of force, fraud, or coercion for the purposes of subjection to involuntary servitude, peonage, debt bondage, or slavery. A victim need not be physically transported from one location to another for the crime to fall within this definition.

In many cases, women and children are considered the typical victims of human trafficking. Hart posits that women are more vulnerable to trafficking due to the lack of social safety nets in many developing countries [18]. Coupled with women's subordinate social statuses in many cultures, this leads to the "feminization of poverty." Although the social conditions may make women and children more vulnerable to human trafficking, the reality is that men are also victims of human trafficking.

Overall, the definition of human trafficking is ambiguous because of the many intersections with other issues (e.g., sexual abuse, domestic violence, forced marriage, forced labor) [19]. It occurs both domestically and internationally, but is primarily a hidden problem. This makes research efforts, the prosecution of perpetrators, and policy and community efforts to protect victims even more challenging [19].

FORMS OF TRAFFICKING

SEX TRAFFICKING

The TVPA of 2000 is a U.S. federal statute passed by Congress to address the issue of human trafficking and offers protection for human trafficking victims [17]. This statute defines sex trafficking as, "the recruitment, harboring, transportation, provision, or obtaining of a person for the purpose of a commercial sex act" [17]. A commercial sex act is, "any sex act on account of which anything of value is given to or received by any person" [17]. In other words, it usually involves the illegal transport of humans into another country to be exploited in a sexual manner for financial gains [20]. However, it does not always involve the transport of victims from one region to another; such cases are referred to as "internal trafficking" [21]. Victims of sex trafficking could be forced into prostitution, stripping, pornography, escort services, and other sexual services [22]. Victims may be adult women or men or children, although there is a higher prevalence of women and girls. The term "domestic minor sex trafficking" has become a popular term used to connote the buying, selling, and/or trading of children younger than 18 years of age for sexual services within the country, not internationally [22; 23]. An element of force, fraud, or coercion is not necessary, as the victims are children and inherently vulnerable [23]. In the United States, the children most vulnerable to domestic minor sex trafficking are those who are homeless, abused, runaways, and/or in child protective services [22].

Although highly controversial, it is said that sex trafficking victims differ from sex workers in that sex trafficking victims are forced to involuntarily perform sexual services and are often not paid for their "work." Sex trafficking involves the use of force and coercion and can encompass other forms of criminal sexual activities, including forced erotic dancing, "mail-order brides," and pornography [21]. On the other hand, individuals involved in prostitution make a decision to provide sex services for a fee. The decision to enter prostitution does not eliminate the possibility of being a victim of trafficking if one is held against his/her will through physical and/or psychological abuse [24]. It is also important to remember that this does not necessarily mean prostitution is a choice these individuals would have made if other options were available or that they have a choice in selecting their sexual partners and/or sexual activities [25].

interactive activity

Visit the PBS Frontline website (https://www.pbs.org/wgbh/pages/frontline/slaves/map) and read the transcripts of interviews with a sex trafficker and five Eastern European female victims who were deceived into sexual slavery.

BONDED LABOR/FORCED LABOR

The United Nations has defined debt bondage as [26]:

> The status or condition arising from a pledge by a debtor of his personal services or of those of a person under his control as security for a debt, if the value of those services as reasonably assessed is not applied towards the liquidation of the debt or the length and nature of those services are not respectively limited and defined.

Essentially, because the individual does not have money as collateral for the debt owed, the individual pledges his/her labor or, in some cases, the labor of a child or another individual for an unspecified amount of time [27]. These individuals may be transported or trafficked into another country for the purpose of forced labor.

In many cases of bonded labor, the initial loan may be welcomed by the individual. However, the victims do not realize that with the low wages, unspoken high interest rates and other continually accruing fees, and the perpetrator's manipulation of the "accounts," laborers can never repay the loans. Some estimate that half of all persons in forced labor are bonded laborers. The majority of bonded labor cases occur in India, Bangladesh, and Pakistan [28]. Some families find themselves in a cycle of poverty as the debt cannot be paid off and is passed down from generation to generation [27]. Bonded labor can involve laborers in brick kilns, mines, stone quarries, looming factories, agricultural farms, and other manufacturing factories [27]. In the United States, individuals may be trafficked to work long hours in garment factories, restaurants, and other manufacturing sectors. Frequently, the employer/captor will take away victims' identifications, monitor their movements, socially isolate them, and/or threaten deportation if they do not comply [29]. Migrant workers are at high risk of forced labor [24].

In the United States, forced labor is predominantly found in five sectors [29]:

- Prostitution and sex industry
- Domestic servitude
- Agriculture
- Sweatshops and factories
- Restaurant and hotel work

It is speculated that most of the forced labor occurs in California, Florida, New York, and Texas, all major routes for international travel [29].

Domestic servitude refers to a category of domestic workers (usually female) who work as servants, housekeepers, maids, and/or caregivers, often in private homes. In some cases, young women are lured with the promise of a good education and work, and when they arrive in the United States, they are exploited economically, physically, and/or sexually. Their passports or identification papers are taken away, and they are told

they have to pay off the debt incurred for their travel, processing fees, and any other bogus expenses. Because they do not speak English, they find they have no other recourse but to endure exploitive working conditions [30]. Unfortunately, as in many sectors of forced labor, there are no regulations to monitor the conditions under which domestic servants operate [29].

interactive activity

Watch the 20-minute documentary A Global Alliance Against Forced Labour, produced by the International Labour Organization (ILO) at https://www.netce.com/courseoverview.php?courseid=2424.

CHILD LABOR

Child labor can be viewed as a specific form of bonded labor or forced labor. However, not all child laborers have been trafficked. Child labor is defined by International Labour Organization (ILO) as economic labor performed by a child younger than 15 years of age or hazardous labor done by a child 18 years of age or younger. Child labor is deeply rooted in poverty and the infrastructure and political stability of the country as well as market forces [31]. A joint report by UNICEF and the ILO estimates that there are 160 million child laborers in the world as of 2020, of which 63 million are girls and 97 million are boys. This report indicates an increase of 8.4 million child laborers, and the first time that rates have increased in more than two decades of declining child labor [32]. The largest numbers of child laborers are found in Asia and the Pacific region; however, there is evidence that the number of child laborers in sub-Saharan Africa is increasing due to population growth, extreme poverty, and inadequate social protection measures [32].

The definition of child labor is controversial because the definitions for "work" and "childhood" are ambiguous and often culturally defined [33]. On a conceptual level, work may be beneficial for the socialization and educational processes of children [33; 34]. So, it is important to differentiate between child work and child labor. Child work has been defined as activities that are supervised by an adult and that promote the development and growth of the child, while child labor does not benefit the child [31]. Many definitions of child labor create a dichotomy whereby child work is considered not harmful while child labor has negative emotional, intellectual, and social consequences [35]. Work that is exploitive for children has been defined as working long hours at a young age, work that is poorly compensated, and work that produces physical, social, and psychological stress that will hamper development, access to education, and self-esteem [36]. The ILO adds that child labor is work that interferes, deprives, and interrupts schooling and places children in the position of trying to balance school and long work hours [34].

It is important to remember that child labor occurs in the United States. Runaway and homeless youths are at greatest risk, often lured by promises of work and housing [37]. The Polaris Project found that the top three forms of child labor trafficking in the United States were begging, peddling, and traveling sales crews [37].

CHILD CONSCRIPTION

In some cases of trafficking, children are kidnapped and trafficked to serve as soldiers. Other times, children are coerced by a narrative indicating they will be serving a higher purpose and avenge the deaths of family and friends; this is known as comradeship [38]. Some children are actively recruited and may be promised a small salary to "voluntarily" join. In a study of 132 cases of child conscription in Columbia, 18% of the children were motivated by perceived economic rewards [39]. Many children lack educational opportunities or hope for a better future, perceiving soldiering as the only option [38]. Conscripted girls often cite educational opportunities as a motive [38]. In Nepal, former female soldiers also indicated they were driven to volunteer in the armed groups by a fear that if they stayed with their families they would be married away as children or raped [38].

It is estimated that at any one time 250,000 to 300,000 children younger than 18 years of age are currently serving as child soldiers [40; 41]. Traffickers prefer to recruit children to serve as soldiers because they are inexpensive and more easily molded and shaped to comply and obey without question [42]. They are also more likely to kill fearlessly and recklessly. Child soldiers are treated as adults, without any regard to how the physical and psychological rigors of war will affect them psychologically and developmentally. In Uganda, where children are kidnapped or recruited as child soldiers relatively often, the Lord's Resistance Army has been known to initiate new child soldiers in brutal ritualized killings of others so as to terrorize them into submission and annihilate any moral conscience they may have about killing [42]. In Afghanistan, children have been recruited by the Taliban and have served as suicide bombers [28].

It can be difficult to comprehend the atrocities that these children witness and experience. Bayer, Klasen, and Adam conducted a study involving 169 former Ugandan and Congolese child soldiers who were an average of 15.3 years of age [43]. Almost all (92.9%) reported having witnessed a shooting, 89% witnessed someone wounded, and 84% witnessed someone seriously beaten. A total of 54.4% reported having killed someone, and 27.8% reported that they were forced to engage in sexual activity [43]. In another study, the researchers found that the experience of conscription among children produced significant emotional and psychological traumas and a host of cognitive and behavioral problems [24]. In this study of 19 child soldiers, 18 had volunteered to join the army and one had been abducted. Although most of the children volunteered into the army, their participation became involuntary. Some tried to run away or disobey, which resulted in beatings and

imprisonment. If captured, they were told to commit suicide [24]. The reintegration of child soldiers is not easy. Many are stigmatized when they return to their home villages, as their families and friends fear that these former child soldiers may be violent [41; 44].

interactive activity

Listen to a National Public Radio interview with Ishmael Beah, a former child soldier, at https://www.npr.org/2007/02/21/7519542/ishmael-beahs-memoirs-of-a-boy-soldier.

FACTORS THAT CONTRIBUTE TO HUMAN TRAFFICKING

GLOBALIZATION

Human trafficking has been called one of the "darkest sides of globalization" [45]. Globalization is the term used to describe the interconnectedness of countries and nations, which facilitates easy communication, exchange of ideas, and flow of goods, capital, and services [45]. Crimes such as human trafficking are affected by globalization just as legitimate businesses are [46]. Furthermore, the ideals of Western capitalism may reinforce human trafficking as a business or industry, with its emphasis on the free market and the flow of goods and services across international borders [46].

Globalization has also created the need for cheaper labor [28; 47]. A study involving 160 countries examined the effects of globalization and human trafficking trends [48]. Researchers found a positive relationship between globalization and trafficking for forced labor, prostitution, and debt bondage.

POVERTY

Poverty and incessant economic stressors caused by civil wars, natural disasters, and collapses of government systems all contribute to human trafficking [18; 23; 49]. Families entrenched in deep poverty may feel they have no other recourse but to sell a child or may be more easily lured with promises of money and a better future [49; 50; 51]. In one study, the odds of being trafficked were nine times greater for those who felt extremely hopeless about upward mobility compared with those with lower levels of hopelessness [49].

SOCIAL AND FAMILIAL DISORGANIZATION

Community factors (such as high social disorganization characterized by violence, unemployment, substance use disorder, and high crime) contribute to higher risk of trafficking [23]. In addition, families marked by instability (e.g., domestic violence, child abuse, continual unemployment) are also at higher risk of having a member trafficked [23].

CORRUPTION

Human trafficking cannot occur without the existence of corruption within existing infrastructures. Public officials, police officers, and local leaders in many developing countries have been known to take bribes to provide protection to parties involved in various aspects of human trafficking [45; 48; 52].

DIGITAL TECHNOLOGY

The rampant use of digital technology, such as the Internet, greatly facilitates sex trafficking. The relative anonymity of online contact can empower traffickers to recruit or sell victims. Graphic images of women and children engaged in sexual acts can be easily disseminated over the Internet [53]. Traffickers may employ the Internet for advertising, marketing to those interested in making pornography [53]. In addition, social media sites such as Facebook, Craigslist, and Instagram have been used as a means of facilitating trafficking (e.g., by connecting and grooming potential victims) [54; 55; 56]. Newsgroups offer opportunities for those interested in locating women and children for sexual exploitation.

In a qualitative study, smartphones were found to be integral in the business of trafficking [54]. Researchers indicated the phones were used "to maintain contact with each other, in order to facilitate the business 'transactions' and stay in touch with transnational 'partners' and other traffickers who remained in the country of origin" [54; 55].

RACIALIZED SEXUAL STEREOTYPES

Race and ethnicity have been inextricably linked to sexual violence and victimization. Myths regarding sexuality in certain cultures or racial fetishization may affect trafficking patterns. For example, there is an over-representation of Asian women on American Internet pornography sites in part due to popular myths sexualizing, eroticizing, and exoticizing Asian women. This has translated into trafficking, as traffickers respond to the demand for young Asian women and girls in part fueled by these stereotypes of exotic, docile, submissive, and eager-to-please Asian women [30]. These stereotypes devalue and dehumanize people, which is the underlying core of human trafficking. This contributes to the acceptability of the exploitation of individuals, particularly members of marginalized groups [57].

These racial stereotypes go beyond simply framing the victims in a particular manner [58]. They raise implicit questions regarding how the powers of state are depicted. In other words, the patriarchal attitudes of certain countries lead to "bad" or "backward" cultural practices or ways of being that then cause trafficking—setting up is a dichotomy of the "West" and "others" [58].

CULTURE

Although many are careful in linking cultural factors to the etiology of human trafficking for fear of imposing judgment on a particular culture, many maintain that cultural ideologies that tolerate sexual trafficking, bonded labor, and child labor may

be a stronger factor than poverty in predicting trafficking rates [30; 36]. For example, some cultures emphasize collectivism and prioritizing the needs of the family and group first before the needs of the individual. Some children may feel they have to sacrifice themselves for their family when traffickers promise money [30]. Traffickers also know that they can threaten to hurt victims' families to keep them from escaping [30].

Furthermore, in many cultures, boys are more highly valued than girls, and as a result, girls are considered more dispensable [30]. Sons are considered the family's social security, staying with the family while daughters marry into other families. Therefore, girls may be more likely to be sold into slavery than boys.

Child labor is also inextricably tied to cultural factors. In India, for example, child labor is common because it is believed that children in the lower levels of caste system (i.e., the "untouchables") should be socialized early to understand their positions in society [36]. It has been observed that when traditional cultural and societal norms about women's roles were relaxed in some European countries and more women entered the labor force, child labor decreased [36]. Ultimately, it is difficult to unravel the effects of poverty and culture because the pressures of poverty can lead families to use tradition as a justification to sacrifice young men, women, and children [36].

Ultimately, the conversation about human trafficking is complex, and to attempt to isolate the causes is beyond challenging. Multiple factors have been suggested as possibly predicting human trafficking, including macroeconomic factors (e.g., gross domestic product per capita), unemployment rates, LGBTQ+ discrimination, cultural oppression, and lack of protection of women's rights [59; 60]. In addition, the COVID-19 pandemic has potentially exacerbated the rates of isolation, poverty, and lack of resources/funding, all of which are risk factors for human trafficking [24]. In one study, ease of land access to the destination country appeared to be a powerful predictor in terms of the number of individuals trafficked [59].

THE TRAFFICKING EXPERIENCE

Five stages of the trafficking experience have been identified [61; 62; 63]:

- Pre-departure stage: The period before the victim becomes involved in the trafficking situation. This may include recruitment and preparing for travel.
- Travel and transit stage: The time after recruitment during which the victim "agrees" or is coerced into the trafficked situation. This phase also includes the journey whereby the trafficker(s) brings the victim(s) to their work destination. It is important to remember that this stage can be very dangerous and can involve numerous transit points.
- Destination stage: This is the period during which the victim arrives at the intended destination. This stage is marked by exploitation, abuse, victimization, and coercion. One way to control the victims is to continually inflate their debt so they have to constantly work to pay it off. Another is to confine and isolate victims.
- Detention, deportation, and criminal evidence stage: If a victim is arrested by the police or immigration authorities, victims are held in legal proceedings and they often fear deportation, and/or retaliation from the trafficker(s).
- Integration and re-integration stage: During this stage, government and nongovernment agencies provide services to victims that involve a long process of attempting to reintegrate the victim back into his/her community.

TRAFFICKERS: AN OVERVIEW

Much attention has been focusing on victims of trafficking; however, it is important to also understand the perpetrators.

Methods of Recruitment

It has been suggested human traffickers employ five general strategies to recruit and traffic victims [64; 65; 66; 67]:

- Kidnapping: Traffickers may kidnap their victims. They may lure them with food or treats or take them by force. Victims with few if any social ties are highly vulnerable, as no one will miss them or report their disappearance.
- Targeting poor families: Traffickers may convince families to sell their children (often daughters). Because many families in developing countries live in abject poverty, traffickers will stress to victims' families how the money will help them to survive. Other traffickers may tell families that selling their daughter will provide her with more promising opportunities.
- Developing a false romantic relationship with victim: A tactic often used with young girls, perpetrators pose as boyfriends by romancing victims, buying gifts, and proclaiming their love. Victims have a difficult time believing that their boyfriends would hurt or deceive them, making them easy targets for trafficking.
- Fake storefronts: Some employment, modeling, or marriage agencies are fronts for illegal trafficking operations. A potential victim might be lured with the promise of employment, a lucrative modeling contract, or an arranged marriage in the United States. After victims have been lured in, traffickers come to assess their "product." Perpetrators may be family members or friends.
- Legal storefronts: Some legal businesses in the tourism, entertainment, and leisure industries integrate trafficking activities into their business structure.

- Recruiting local sex workers: Traffickers might hire sex workers working in local night clubs from brothel owners or simply lure sex workers by promising them a more affluent future. As victims get older, they may later recruit younger victims.

The Financial Profits

Unfortunately, human trafficking can be a lucrative business. According to the ILO, profits from forced labor, trafficking, and modern slavery are estimated to be $150 billion annually [68]. The majority of this total is attributable to commercial sexual exploitation ($99 billion) followed by construction/manufacturing/mining ($34 billion), agriculture ($9 billion), and domestic work ($8 billion) [68].

The receiving country and location of trafficking will affect the profits. For example, if a girl is kidnapped from a village in Nepal and taken to India, she can be sold in India for $1,000 [64]. If she is then trafficked to the United States, she could be sold for $20,000.

Interestingly, the "cost" of a slave has not risen over time. According to Bales, the cost of obtaining a slave to work in the agriculture sector in 2007 was about $100; in 1850, this same slave would cost the equivalent of $40,000 in 2007 currency [69]. In one study, it was approximated that in the United States, a trafficker can make an average of about $300,000 per victim lifetime, which would total $32 billion annually [70]. Income in larger cities (e.g., Atlanta, San Diego, Washington, DC) may be even greater.

CONSEQUENCES OF HUMAN TRAFFICKING: IMPACT ON VICTIMS

The social realities of victims of human trafficking are difficult to comprehend, and some may wonder why victims remained silent and complied with their traffickers. The Silence Compliance Model was created to explore the factors that promote victims' seeming willingness to comply to their traffickers' demands [71]. This model has three categories: coercion, collusion, and contrition. Victims are coerced, brutalized, and threatened, and basic necessities of life are withheld from them. Methods of psychological coercion include isolation, induced exhaustion, threats, degradation, and monopolizing perception [72]. This serves to silence victims and create a sense of helplessness. By isolating and controlling victims' movements and limiting their exposure to the outside world, traffickers have complete monopoly of their attention and perception of reality [72]. Victims are then forced to collude with the traffickers as a result of their relative isolation, fear, false sense of belonging, and complete dependence on the trafficker. Finally, victims feel contrite, ashamed, stigmatized, and remorseful of the things they have been made to do [71].

PSYCHOLOGICAL AND MENTAL HEALTH CONSEQUENCES

Victims of trafficking experience a host of psychological, mental health, and emotional distress. Depression, suicidal ideation, substance use, and anxiety are typically cited mental health problems [23]. Post-traumatic stress disorder (PTSD) is also common given the trauma many victims experience, including physical and/or sexual violence and abuse; victims forced into prostitution experience continual, daily sexual assault [73]. In a study of 192 European women who were trafficked but who managed to escape, the overwhelming majority (95%) disclosed that they experienced physical and sexual violence during the time of their trafficked experience [74]. More than 90% reported sexual abuse, and 76% reported physical abuse.

Trafficked victims experience fear from the start of their capture through the transit phase and after they arrive at their destination. During the transit stage, many victims experience dangerous border crossings, risky types of transports, injury, beatings, and sexual assault [61]. Upon arrival to their destination, many trafficking victims have been socially isolated, held in confinement, and deprived of food [75]. All sense of security is stripped from them—their personal possessions, identity papers, passports, visas, and other documents [61; 75]. The continual fear for their personal safety and their families' safety and the perpetual threats of deportation ultimately breed a sense of loss of control and learned helplessness. It is not surprising that depression, anxiety, and PTSD are common symptoms experienced by trafficked victims.

In a study of 164 survivors of human trafficking who returned to Nepal, the authors examined the extent to which they experienced PTSD, depression, and anxiety [76]. All of the survivors experienced some level of these disorders, but the survivors who were trafficked for sex experienced higher levels of depression and PTSD compared to those who were not trafficked for sex. In a study with Moldovan survivors of human trafficking, researchers found that six months after their return, 54% had diagnosable mental health issue. Specifically, 35.8% met the diagnostic criteria for PTSD, 12.5% met the criteria for major depression, and 5.8% were diagnosed with an anxiety disorder [77].

There is also some evidence that trafficked victims may experience complex PTSD, a type of PTSD that involves an acute change of the victims' sense of self, their relationship with others, and their relationship with God or higher being [78]. These persons direct anger inwardly (toward themselves) in addition to toward their perpetrators, which results in a loss of faith in themselves and the world [63; 75; 78]. Perhaps due to self-directed anger and shame, some will engage in risky sexual behaviors, self-harm, and substance abuse. Some victims also have difficulty managing and expressing how they are feeling, while others experience dissociation [75].

Substance abuse is also common among victims. In interviews, trafficked women discussed how traffickers forced them to use substances like drugs and/or alcohol so they could work longer hours, take on more clients, and/or perform sexual acts that they could not normally [61]. Other victims used substances as a means to cope with their situations. Trafficked individuals who are gender and/or sexual minorities report shame, confusion, and sexual identity issues if forced into heterosexual relationships [63].

Children forced into labor experience grueling hours and are frequently beaten by their captors. According to Clawson and Goldblatt, underage victims of domestic sex trafficking fluctuate through a range of emotions from despair, shame, guilt, hopelessness, anxiety, and fear [79]. Depending upon the level of trauma, some engage in self-destructive behaviors like self-mutilation or suicide attempts. For some, their ambivalence toward the perpetrators may be confusing. On the one hand, they want to escape the abuse, yet simultaneously, they may have a sort of traumatic bond with the perpetrators [79].

Children forced into conscription will also experience a host of psychological symptoms. In a study comparing former Nepalese child soldiers and children who were never conscripted, former child soldiers experienced higher levels of depression, anxiety, PTSD, psychological difficulties, and functional impairments [80]. In another study of former child soldiers from the Congo and Uganda, one-third met the criteria for PTSD [43]. The researchers found there was a relationship between greater levels of PTSD symptoms and higher levels of feelings of revenge and lower levels of openness to reconciliation [43]. In-depth narrative interviews of former child soldiers from northern Uganda found that the children spoke of the violence and atrocities they witnessed without any emotion, as if they had removed themselves from their experiences [81]. This speaks to how the victims have to numb themselves psychologically in order to cope. The researchers also found that the children who lost their mothers were more traumatized by this experience than the violence they witnessed as soldiers.

Some have argued that the diagnostic criteria of PTSD may not be easily applied to those from different cultures. As a result, it is important to assess for other psychiatric disorders, such as depression. Japan, for example, never used the PTSD diagnosis prior to 1995, despite the fact that they have a large and intricate mental health system [82]. Ultimately, PTSD cannot be universally applied to every culture and for every humanitarian crisis; therefore, if a human trafficking victim does not necessarily fall within the Diagnostic and Statistical Manual of Mental Disorders criteria for PTSD, one cannot necessarily conclude that they have not experienced trauma or are not traumatized [82].

SOCIAL CONSEQUENCES

When rescued and attempting to reintegrate into their communities, victims of human trafficking often experience stigma, ostracism, and marginalization [80; 83]. For example, in Nepal, community members perceived returning child soldiers who had performed acts such as carrying dead bodies or coed sleeping as in violation of Hindu cultural norms [80]. One documentary following former child soldiers living in a refugee camp in northern Uganda found that preconceived notions and myths about child soldiers often led to ridicule and ostracism after they were liberated from the army and returned home.

However, girls who were recruited as soldiers, who were forced to have sex, or who return with children appear to be the most marginalized group [84]. In a qualitative study of former girl soldiers in Sierra Leone, researchers found that, compared to returning boy soldiers, girls were perceived to have violated gender norms and values about sexuality. Although psychologically and developmentally they were still children, the community perceived and treated them as "damaged" or "unclean" women. Their communities were not able to integrate them back in despite the victimization they experienced. These girls lacked voice and experienced shame, marginalization, poverty, and powerlessness upon their return [84]. In a study of former child soldiers in Uganda, the children reported having difficulty finding jobs or getting married when they returned home. Girls who had been raped were stigmatized and made to feel unwelcome in their communities. Others stated that their community perceived them as murderers [44].

HEALTH CONSEQUENCES

In studies of trafficked women, headaches, fatigue, dizziness, back pain, pelvic pain, stomach pain, sexually transmitted infections (STIs), unwanted pregnancies, and gynecologic infections were common, generally the result of continual physical, psychological, and sexual abuse [23; 74]. Victims of labor trafficking also experience health issues related to the type of work, workplace conditions, malnutrition, and violence [85]. It is important to remember that some of these somatic complaints, such as headaches, fatigue, and gastrointestinal problems, may be underlying symptoms of anxiety, depression, and stress [74]. Some cultural groups might not use the terms "depression," "sad," or "anxious," but may use metaphors and somatic symptoms to describe their pain, all of which are embedded within cultural ideologies. The most common culture-based idioms of distress are somatic symptoms. Some groups tend not to psychologize emotional problems; instead, they experience psychological conflicts as bodily sensations (e.g., headaches, bodily aches, gastrointestinal problems, and dizziness).

Using an in-depth, direct interview survey designed to explore each stage of the trafficking experience, a multi-country European study identified a range of aversive health, sexual, and reproductive consequences common among women and adolescent victims of human trafficking [61]:

- Pre-departure stage: All victims reported having had limited knowledge of the health implications of having sex with strangers, and only 1 in 25 felt well-informed regarding the risks of acquiring HIV or other STIs.
- Travel and transit stage: Half of those interviewed reported having been confined, beaten, and/or raped during the journey.
- Destination stage: A large majority reported having been "intentionally hurt" (as evidenced by contusions, lacerations, loss of consciousness, and signs of head trauma); subjected to solitary confinement and deprived of human contact and adequate food and nutrition; subject to a variety of physical ailments, including headache, fever, undiagnosed pelvic pain, urinary tract infection, STIs, rash/scabies, and oral/dental health issues. All had experienced repeated sexual abuse or coercion, and 1 in 4 reported at least one unintended pregnancy (often involving negative outcomes of abortions performed in unsafe and unhealthy conditions).

In the context of forced prostitution among trafficked victims, safeguards against infection (e.g., regular condom use), early diagnosis, and adequate antimicrobial treatment are inconsistently employed or absent entirely [61]. Consequently, in addition to unwanted pregnancy, the risk for pelvic inflammatory disease and subsequent infertility is relatively high. Moreover, the relationship between forced prostitution and HIV infection is stronger when sexual violence is involved. Women who are forced into prostitution are 11 times more likely to become HIV-infected than women who entered prostitution voluntarily [86]. Sexual violence may increase the transmission risk as a result of open abrasions and injuries to the vagina. Furthermore, sexual violence can negatively impact self-esteem, which could then deter victims from advocating more strongly for condom use [86].

Among child victims of human trafficking, healthy growth and development is especially problematic. Malnourishment and poor hygiene often lead to delayed bone growth, poorly formed teeth, and early dental caries [87]. The intense nature of child labor also has severe negative physical and health consequences. Children working in unsafe conditions without protection, such as in mines or mills, can lead to respiratory problems such as asthma and bronchitis [88]. A study of adult and child laborers on tobacco farms in Kazakhstan found that the workers were unaware that exposure to tobacco and pesticides could affect their health. Protective garments were also rare, with many children not even having gloves [89].

Under normal circumstances, young children are still developing physically; however, such adverse conditions can halt their development. The lungs of adolescent boys typically experience the most rapid growth around 13 to 17 years of age; working in conditions characterized by excessive toxic dust or unclean air makes them more vulnerable to developing silicosis and fibrosis [88]. In the United States, young children participating in agricultural work are at risk of the major traumas associated with farm work, such as injuries caused by tractors or falling from heights, in addition to those injuries associated with repetitive stress and exposure to toxins. Children have thinner layers of epidermis, which make them more vulnerable to the toxicity of pesticides, and this can ultimately increase their risks for certain cancers [88]. Children working in gold mines do intensive digging, lifting, and transporting and mix mercury with the crushed ore, often with their bare hands. Mercury toxicity can lead to neurologic symptoms such as loss of vision, tremors, and memory loss [89].

IDENTIFICATION AND ASSESSMENT

Healthcare providers are often the most likely to encounter a victim of human trafficking under circumstances that provide an opportunity to intervene. Yet, many providers lack the training and confidence to identify and assist victims. In a survey of 110 emergency department physicians, nurses, and physician assistants, the majority (76%) reported having a knowledge of human trafficking, but only 13% felt equipped to identify a trafficking victim and only 22% were confident in their ability to provide satisfactory care for such patients [90]. Less than 3% had ever received any training on this topic. In a separate survey of healthcare and social service providers, only 37% had ever received training on identification of trafficking victims [91].

Because human trafficking and exploitation are, by nature, covert processes, the identification and rescue of the victim can be difficult. Traffickers move victims from one area to another to reduce the risk of identification, and one of the main problems with the assessment of such individuals is that practitioners may only have a one-time encounter with the victim [92; 119].

POTENTIAL RED FLAGS

Bruises, scars, and other signs of physical abuse may be missed on examination, as victims are often beaten in areas hidden by clothing (e.g., the lower back) so as not to affect the victim's outer appearance. Physical trauma symptoms may be present, commonly on the torso, breast, and/or genital areas [70]. Burns, broken bones, pelvic pain, and/or STIs (particularly in children) may also be red flags [93]. However, more common physical injuries are also typical with other circumstances, making physical exam of limited value. The entire clinical picture should be considered.

It may also be helpful to assess for tattoos and/or other modifications (e.g., branding, piercings). Some perpetrators use tattoos to identify victims or to signify "ownership" [56].

With regard to episodic clinical encounters, recommendations for providing safe assessments in a culturally sensitive manner are lacking. The U.S. Department of Homeland Security maintains a useful website that addresses practical issues of human trafficking for allied professional groups, known as the Blue Campaign [87]. Included are diagnostic and interviewing tips to help healthcare providers recognize, intervene, and

refer trafficking victims. Emergency and primary care providers should be cognizant of clues that a patient may be the victim of trafficking and prepared to engage in greater depth of inquiry with special attention to the following indicators [87; 93; 94; 95; 119]:

- Does someone, other than family, who behaves in a controlling manner, accompany the patient? Traffickers attempt to guard and control most every aspect of the victim's life, while maintaining isolation from family, friends, and other common forms of human interaction.
- Are there inconsistencies in answers to basic questions (e.g., name, age, address)?
- Does the patient speak English? If not, has he or she recently been brought to this country, and from where? Many victims of human trafficking have recently been trafficked from other countries. As discussed, common sending countries/regions include Eastern Europe, Asia, Latin America, Africa, India, and Russia.
- If the patient is accompanied by someone other than a family member, who does the talking, and why? Attempt to interview and examine the patient separately and alone, using an interpreter if necessary. Probe in a sensitive manner for detailed information on the situation and relationship.
- Does the patient show signs of psychosocial stress (e.g., appears withdrawn, submissive, fearful, anxious, depressed)? Can the individual account for this?
- Are there visible signs of physical abuse (e.g., bruises, lacerations, scars)? How does the individual explain these?
- Does the patient lack a passport or other immigration and identification documentation (e.g., driver's license, social security number, visa)? If so, what explanation is given? To control victims' movements, traffickers often take away passports and any legal identification documents.
- What is the patient's home and work situation? Basic questions about what they eat, where they live and sleep, who else lives with them, and what work they do can be revealing. For example, "Can you leave your work or job situation if you wish?" or "When you are not working, can you come and go as you please?"
- Is the explanation given for the clinical visit consistent with the patient's presentation and clinical findings?
- Does the victim appear fearful when asked questions about citizenship, country of origin, immigration status, or residence? This may indicate a fear of deportation.
- If the victim is a minor, is s/he in school? Living with parents or relatives? If not, what reasons are given for these circumstances?

SCREENING QUESTIONS

Examples of questions to screen for human trafficking include [96; 97; 98]:

- Can you tell me about your living situation?
- Has anyone ever threatened you with violence if you attempted to leave?
- Does anyone force/require you to have sexual intercourse for your work?
- Has anyone ever threatened your family if you attempted to leave?
- Does anyone make you feel scared at work?
- Are you free to come and go as you wish?
- Does your home have bars on windows, blocked windows/doors, or security cameras?
- How many hours do you work?
- Have you ever worked without receiving payment you thought you would get?
- Do you owe your employer money?
- Do you have to ask permission to eat, sleep, use the bathroom, or go to the doctor?

The Polaris Project has developed a flow chart for the assessment of potential trafficking victims, available at https://humantraffickinghotline.org/sites/default/files/Assessment%20Tool%20-%20Medical%20Professionals.pdf. If a person is thought to be a victim, one should follow workplace protocols and/or contact the National Human Trafficking Hotline at (888) 373-7888 for next steps.

INTERVIEWING TRAFFICKED VICTIMS: BEST PRACTICE GUIDELINES

Service providers should repeatedly weigh the risks and benefits of various actions when interviewing human trafficking victims [65; 99; 100]. The following interviewing recommendations were published by the World Health Organization to encourage service providers to continually and ethically promote human trafficking victims' safety during every phase of the interviewing process [93; 101]:

- Each victim and trafficking situation should be treated as unique; there are no standard templates of experiences. Listen carefully to the victim's story. Each story told is unique, and each patient will voice distinctive concerns. Believe each story, no matter how incredible it may seem. As rapport and trust build (perhaps very slowly), accounts may become more extensive.
- Always be safe and assume the victim is at risk of physical, psychological, social, and legal harm.
- Evaluate the risks and benefits of interviewing before starting the interviewing process. The interviewing process should not invoke more distress. In other words, the interviewing process should not end up re-traumatizing the victim.

- Provide referrals for services where necessary; however, it is necessary to be realistic and not make promises that cannot be kept. Trust is vital because it has been severed on so many levels for trafficking victims.
- Victims' readiness to change will not be based on what societal defines as "ready" or social expectations. Some victims will eagerly grasp new opportunities, while others may be fearful of potential traffickers' threat and be less receptive to help.
- Determine the need for interpreters and if other service providers should be present during the interviewing phase. Ensure that everyone involved is adequately prepared in their knowledge about human trafficking, how perpetrators control their victims, and how to ask questions in a culturally sensitive manner. Keep in mind that often times, traffickers will offer to help with the interpreting. Using interpreters from the same community of the victim should be avoided to prevent breaches in confidentiality.
- All involved should be prepared for an emergency plan. For example, is there a set plan for a victim who indicates he/she is suicidal or in danger of being hurt?
- Always be sure to obtain informed consent. Remember the informed consent process is going to be unfamiliar to many victims. In addition, self-determination and autonomy have been compromised by continual threats and being forced to commit dehumanizing acts. Avoid using legal and technical jargon.

It is important to use a trauma-informed approach when assessing and caring for potential victims, which requires that practitioners understand the impact of trauma on all areas of an individual's life [102]. Physical, emotional, and psychological safety is at the heart of trauma-informed care. Providers should assume that human trafficking victims are describing their reality to the best of their ability, given the trauma they have experienced. Responses and behaviors (e.g., being guarded, defensive, belligerent) may be coping mechanisms [102].

REPORTING

If screening and assessment findings indicate that an individual may be a victim of human trafficking, one should contact the National Human Trafficking Hotline at 1-888-373-7888. A text telephone (TTY) option for people who are deaf, hard of hearing, or speech impaired can be accessed by dialing 711. Reporting by text is available by texting the National Human Trafficking Hotline at 233733. Online chat is also accessible at https://humantraffickinghotline.org.

The National Human Trafficking Hotline collects information about the location of the trafficking case and the name of the suspected trafficker. The hotline will also request non-personally identifying information, such as the city and state of the reporter and how he or she learned of the hotline; reporting can be done anonymously. Reporters and/or victims are only asked to provide information they feel comfortable sharing, and the hotline does not share information with external agencies unless permission is given or when required by law. Hotline calls are managed by anti-trafficking hotline advocates, who are specifically trained. After receiving a report of suspected human trafficking, the National Human Trafficking Hotline will assess each case individually to determine if a case should be reported to a local, state, or federal investigative and/or service agency equipped to investigate the tip and/or respond to the needs of the potential victim.

Under the child abuse laws, practitioners who are mandated reporters and who are suspicious that a minor is being abused should immediately report the abuse. Persons in Florida who know, or have reasonable cause to suspect, that a child is abused, neglected, or abandoned must immediately report such knowledge or suspicion to the Florida Abuse Hotline of the Department of Children and Families at 1-800-96-ABUSE (1-800-962-2873).

INTERVENTIONS AND RESOURCES

EDUCATION AND PREVENTION

Education is believed to be a key ingredient in the prevention of human trafficking. Raising awareness through advertisements, campaigns, and other creative vehicles regarding recruitment threats, the various deception techniques employed, the different forms of human trafficking, and the consequences of human trafficking can decrease the incidence [64; 103]. Because the general public often believes human trafficking is a problem that only occurs in developing countries, there is a clear need for public education about trafficking and safety for young children and women in and outside the United States [22]. The U.S. Department of Homeland Security provides brochures and posters about human trafficking through its Blue Campaign, which are available to be ordered (at no cost) from https://www.dhs.gov/blue-campaign/request-materials [87]. Posting these brochures or posters increases the possibility that a trafficked victim will self-report [100].

Education about human trafficking has become a higher international priority. Innovative and creative approaches are being implemented to disseminate information about human trafficking, particularly how perpetrators recruit high-risk groups (e.g., youths with disabilities, runaways) [67]. For example, groups have used street plays to educate communities about child labor dangers in India [104].

interactive activity

Watch a video produced by the ILO exploring the use of street plays to educate communities about child labor in India at https://www.netce.com/courseoverview.php?courseid=2424.

Although the topic of human trafficking has become more common in public discourse, service providers and law enforcement authorities remain under-educated about human trafficking. They are not sure what to look for, what to ask, and what to do if they do identify individuals who are victims of human trafficking [103]. Law enforcement officials require training to identify and assess potential victims at various borders and ports of entry. If a minor is accompanied by an adult who is not the child's parent or legal guardian, this should raise a red flag [103]. Furthermore, to work effectively to identify human trafficking victims, there is a need for service providers to navigate and collaborate with a complex host of government, social service, mental health, and nongovernment legal entities [103].

MENTAL HEALTH AND SOCIAL SERVICES

Care and services provided to victims can be organized into three distinct categories: immediate and concrete services at the time of rescue; services related to recovery; and long-term services pertaining to reintegration [105]. When trafficking victims are rescued, a great deal of counseling services and practical, day-to-day assistance will be required. Housing, transportation, food, clothing, medical care, dental care, financial assistance, educational training, reunification (for those who wish to return to their homeland), and legal aid are some of the concrete services needed [71]. Practitioners should connect, coordinate, and case manage these services as much as possible. During this stage, it is also important to understand victims' needs, their strengths, and their risks and vulnerabilities [75].

Safety planning is also crucial in the immediate rescue stage. Traffickers may be continuing to try to locate some victims; placing victims in safe houses may be necessary [63]. The National Human Trafficking Hotline encourages that safety planning be based on the unique needs and circumstances of the individual.

During the recovery and reintegration stages, as discussed, human trafficking victims experience an array of mental health and psychological issues. Mental health counseling is vital, but it is important to remember that the concept of counseling or talk therapy may be foreign to victims from non-Western cultures [65]. The expression of emotions may be in opposition to cultural values of emotional restraint, which can be intensified by feelings of shame and guilt resulting from experiences with sexual and physical assault. Beyond the paramount importance of the practitioner gaining the patient's trust, practitioners may educate patients about the counseling process and explore their patients' expectations about counseling, healing, and recovery [106]. As noted, victims' symptoms may not only be a manifestation of the trauma but also coping mechanisms to cope with self-blame, shame, and trauma [56].

Given differing cultural beliefs about healing, it is crucial that practitioners be open to alternative treatment and explore with patients the use of traditional healing methods [65]. There are many indigenous healing interventions victims may be using, including cultural rituals, faith healing, therapeutic touch, herbal remedies, and spiritual practices [107]. These interventions are multi-layered, taking into account the physical, psychological, communal, and spiritual [107]. These healing methods are historically rooted in specific cultures, and therefore, practitioners should become familiar with traditional healing methods and how they can be integrated with Western counseling techniques [106]. For example, given many cultural groups' beliefs that unmarried girls are defiled if raped, a cultural cleansing ritual may be needed as a first step to help a community accept a returning victim who was sexually assaulted during her trafficking experience [30]. After this ritual is performed, it is possible that both the patient and her family may be more open to counseling and other services.

Other trauma interventions that might be beneficial include cognitive-behavioral therapies, eye movement and desensitization reprocessing therapies, mindfulness techniques, and expressive therapies [56; 63].

Physicians, social workers, nurses, therapists, and counselors must be familiar with legal, case management, educational, job and life skills training, and housing services in the community. Human trafficking victims are not only unfamiliar with navigating the social service system, but many are also not proficient in English. Therefore, practitioners will serve as coordinators and advocates, linking necessary services. In one study, the majority of agencies had to rely on collaboration in order to refer clients [108]. Social workers and practitioners relied on word-of-mouth and community meetings to learn about services in order to better meet the needs of human trafficking victims. Furthermore, because many community organizations and agencies are not familiar with human trafficking, practitioners must take a primary role in educating colleagues about the complex dynamics of human trafficking.

It is important to remember that the evidence supporting interventions and therapies for victims of human trafficking is in its infancy [105]. Most efficacy studies of therapies and interventions do not involve experimental designs, which makes it difficult to draw definitive conclusions regarding efficacy. Future work is needed to develop and evaluate interventions that address the multilayered and complex needs of human trafficking survivors.

interactive activity

For more information on how to identify and assist victims, watch the information video Labor Trafficking Awareness: Medical Clinic, produced by the Blue Campaign public awareness campaign, an initiative of the U.S. Department of Homeland Security, at https://www.dhs.gov/medialibrary/assets/video/21856.

ADVOCACY

Physicians, social workers, nurses, allied health professionals, counselors, and psychologists will find themselves in multiple roles when working with victims of human trafficking. Advocacy is one of these roles and involves the practitioner being an agent for change. This consists of engaging in activities that alter the social conditions at the individual, family, community, and institutional levels [109]. One way to advocate on behalf of human trafficking victims is by signing petitions or joining credible organizations concerned with changing the circumstances that lead to human trafficking. Many organizations have petitions established on their websites for individuals to persuade policymakers, legislators, and government officials to advocate for the protection of human trafficking victims, create greater awareness of the problem, and prosecute traffickers, including:

- https://www.freetheslaves.net
- https://polarisproject.org
- https://www.stopthetraffik.org

LAWS AND POLICIES

Justice for Victims of Trafficking Act

In 2015, the Justice for Victims of Trafficking Act (JVTA) became law, allowing survivors formal input in federal anti-trafficking policy and providing incentives for states to enact laws to prevent the prosecution of child victims for crimes committed as a direct result of being subjected to trafficking. The JVTA provides additional bases of criminal liability for those who patronize or solicit trafficking victims for commercial sex and creates a new offense prohibiting the advertising of sex trafficking activity. It also clarifies that traffickers in child sex trafficking cases who had a reasonable opportunity to observe the victim can no longer claim ignorance about a victim's age as a defense [24].

Victims of Trafficking and Violence Protection Act

A wide range of laws have been established to protect human trafficking victims and to prosecute perpetrators. A general knowledge of these laws is helpful when caring for victims and seeking appropriate social services. The TVPA was enacted in 2000 and reauthorized in 2003, 2005, 2008, 2013, and 2018 by the Trafficking Victims Protection Reauthorization Acts [24; 110]. It emphasizes the three Ps: prevention, protection, and prosecution [111]. The prevention component consists of training and awareness; the protection dimension gives trafficked victims the ability to receive services using federal funds like other refugees; and the prosecution component focuses on laws and policies for the prosecution of traffickers.

Because victims of trafficking are often viewed as criminals, this law states that victims of severe trafficking should not be penalized for any illegal behaviors or acts they engaged in as a result of being trafficked, including entering the United States with false documents or no documentation or working without appropriate paperwork [64]. This law also allows T Nonimmigrant Status (T visas) to be granted to victims of trafficking so they may remain in the United States with the purpose of collaborating with the federal authorities to prosecute the perpetrators. During this time, victims are offered a range of benefits and services, including access to the Witness Protection Program [64]. After three years, victims can apply for permanent resident status [16].

One of the criticisms of the Act is that it places the burden of demonstrating innocence and coercion on the victim [112]. The Act also fails to recognize the complex dynamics of human trafficking. For example, it focuses more on sex trafficking versus other forms [113]. Many victims have been abused and terrorized by the perpetrators, who they must now provide information and evidence against to stay in the country. Victims are continually fearful that they will be deported [112].

Victims who are of minor age are eligible for Unaccompanied Refugee Minors programs, the Children's Health Insurance program, and Temporary Assistance to Needy Families [103]. Furthermore, victims between 16 and 24 years of age are eligible for work permits and can apply for the Job Corps program [103]. However, it is important to remember that the key to this law is that the victim must have experienced a "severe form" of trafficking and the victim must be willing to assist in the apprehension and prosecution of the perpetrator to receive services [114].

Preventing Sex Trafficking and Strengthening Families Act

The Preventing Sex Trafficking and Strengthening Families Act was signed into law in 2014. In accordance with this law, child welfare agencies are required to monitor and report the number of child sex trafficking victims. Cases of suspected or known child sex trafficking must also be reported to law enforcement [37].

Trafficking Victims Protection Reauthorization Act

The Trafficking Victims Protection Reauthorization Act was introduced and signed into law in 2013. It allocated $5 million in 2009, $7 million in 2010, $7 million in 2011, $8 million annually through 2017, and $19.5 million (including $3.5 million annually for the National Human Trafficking Hotline) to provide services to victims and to prevent human trafficking [22; 110; 115; 116]. It amends the TVPA and assists foreign governments to implement programs to prevent human trafficking. Victims of human trafficking in other countries are also eligible for assistance through organizations that have grants from the U.S. government [115]. Greater monitoring of trafficking trends through databases will also be implemented. The Act also declares that it is not a defense that a defendant is not criminally liable or is subject to reduced criminal liability due to acceptance of the illicit conduct in the foreign jurisdiction.

The Prosecutorial Remedies and Other Tools to End the Exploitation of Children Today Act

The Prosecutorial Remedies and Other Tools to End the Exploitation of Children Today Act was enacted in 2003. This law maintains that all sexual activity with minors, within or outside the United States, is illegal. American citizens who engage in sex with minors in any country and who are caught will be prosecuted in the United States [64].

As of 2022, all 50 states have enacted criminal anti-trafficking laws. In addition, every state has a law on labor trafficking, and all have passed criminal statutes for sex trafficking [117].

SOAR to Health and Wellness Act

The SOAR (Stop, Observe, Ask, and Respond) to Health and Wellness Act was signed into law in 2018. It directs the Department of Health and Human Services to develop a program to train healthcare providers and practitioners to identify possible human trafficking victims, to work with law enforcement agencies, and to refer victims to services [7].

Florida House Bill 369

In 2015, The Florida Legislature passed House Bill 369, which mandates the display of a human trafficking public awareness sign in a wide range of locations, including [118]:

- Every public rest area, turnpike service plaza, weigh station, primary airport, passenger rail station, and welcome center in the state
- Emergency rooms at general acute care hospitals
- Strip clubs or other adult entertainment establishments
- A business or establishment that offers massage or bodywork services for compensation that is not owned by a healthcare professional

The sign must contain text, in both English and Spanish, regarding the steps to take if you or someone you know is the victim of trafficking, exploitation, and/or forced labor.

RESOURCES

For more information and to become involved in advocacy movements, please utilize the following resources. In some cases, the tools provided may be valuable for patient and/or peer training. In particular, the National Human Trafficking Hotline provides free, downloadable awareness materials for victims, first responders, and healthcare and mental health professionals, including a flyer available in 20 languages.

Alliance for Children in Trafficking
https://www.napnappartners.org/provider-public-resources

Coalition to Abolish Slavery & Trafficking
https://castla.org

Coalition Against Trafficking in Women
http://www.catwinternational.org

Futures Without Violence
https://www.futureswithoutviolence.org

HEAL Trafficking
https://healtrafficking.org

Human Rights Watch
https://www.hrw.org

International Justice Mission
https://www.ijm.org

International Labour Organization
https://www.ilo.org

Office of Refugee Resettlement
https://www.acf.hhs.gov/orr

National Human Trafficking Hotline
https://humantraffickinghotline.org

Polaris Project
https://polarisproject.org

Salvation Army
https://www.salvationarmyusa.org

Urban Justice Center
Sex Workers Project
https://swp.urbanjustice.org

U.S. Department of Health and Human Services
Administration for Children and Families
https://www.acf.hhs.gov

U.S. Department of Health and Human Services
Administration for Children and Families
SOAR to Health and Wellness Training
https://www.acf.hhs.gov/otip/training/soar-to-health-and-wellness-training

Services Available to Victims of Human Trafficking: A Resource Guide for Social Service Providers
https://www.acf.hhs.gov/otip/training-technical-assistance/resource/services-available-victims-human-trafficking

U.S. Department of Homeland Security
Blue Campaign
https://www.dhs.gov/blue-campaign

U.S. Department of Justice
Bureau of Justice Assistance
https://www.bja.ojp.gov

U.S. Department of Justice
Office for Victims of Crime
https://ovc.ojp.gov

U.S. Department of Labor
Bureau of International Labor Affairs
https://www.dol.gov/agencies/ilab

U.S. Department of State
Office to Monitor and Combat Trafficking in Persons
https://www.state.gov/bureaus-offices/under-secretary-for-civilian-security-democracy-and-human-rights/office-to-monitor-and-combat-trafficking-in-persons

CONCLUSION

Human trafficking is a severe human rights violation. Because the roots of human trafficking are multifaceted, no one solution exists to eliminate this problem. Unfortunately, as the problem grows, practitioners will be confronted with the issue in their patient populations. Practitioners should be committed to the collaboration amongst disciplines to address poverty, racism, discrimination, and oppression in order to reduce the vulnerable positions of human trafficking victims and their families. Because of the social justice component in the codes of ethics of professionals such as physicians, nurses, social workers, psychologists, and counselors, all practitioners can play a key role in the individual, community, and systemic levels to help address this gross abuse of power. One way to begin is to educate oneself and one's respective disciplines about the global nature of human trafficking and the complex dynamics of the problem.

interactive activity

To view an excerpt of U.S. Vice President Kamala Harris's keynote address at Examining the Roots of Human Trafficking and Exploitation, the 2014–2015 UCLA School of Law Symposium, visit http://www.netce.com/coursecontent.php?courseid=2424.

FACULTY BIOGRAPHY

Alice Yick Flanagan, PhD, MSW, received her Master's in Social Work from Columbia University, School of Social Work. She has clinical experience in mental health in correctional settings, psychiatric hospitals, and community health centers. In 1997, she received her PhD from UCLA, School of Public Policy and Social Research. Dr. Yick Flanagan completed a year-long post-doctoral fellowship at Hunter College, School of Social Work in 1999. In that year she taught the course Research Methods and Violence Against Women to Masters degree students, as well as conducting qualitative research studies on death and dying in Chinese American families.

Previously acting as a faculty member at Capella University and Northcentral University, Dr. Yick Flanagan is currently a contributing faculty member at Walden University, School of Social Work, and a dissertation chair at Grand Canyon University, College of Doctoral Studies, working with Industrial Organizational Psychology doctoral students. She also serves as a consultant/subject matter expert for the New York City Board of Education and publishing companies for online curriculum development, developing practice MCAT questions in the area of psychology and sociology. Her research focus is on the area of culture and mental health in ethnic minority communities.

Customer Information/Answer Sheet insert located between pages 60–61.

COURSE TEST - #97111 RECOGNIZING AND REPORTING HUMAN TRAFFICKING IN FLORIDA

This is an open book test. Please record your responses on the Answer Sheet.
A passing grade of at least 70% must be achieved in order to receive credit for this course.

This 2 contact hour activity must be completed by August 31, 2025.

1. **The United Nations Office on Drugs and Crime divides the definition of human trafficking into three sections: the act, means, and purpose.**
   A) *True*
   B) *False*

2. **Domestic servitude refers to a category of domestic workers (usually female) who work as servants, housekeepers, maids, and/or caregivers, often in private homes.**
   A) *True*
   B) *False*

3. **Digital technology, such as the Internet, greatly inhibits sex trafficking.**
   A) *True*
   B) *False*

4. **Myths that certain races or ethnicities are more erotic and exotic do not affect sex trafficking patterns.**
   A) *True*
   B) *False*

5. **Developing a false romantic relationship with a victim is a method of recruitment used by human traffickers.**
   A) *True*
   B) *False*

6. **Post-traumatic stress disorder is uncommon among human trafficking victims.**
   A) *True*
   B) *False*

7. **Child laborers who work in agricultural fields might be more susceptible to certain cancers due to their rapid growth.**
   A) *True*
   B) *False*

8. **When interviewing a victim of human trafficking, it is important to assess if an interpreter is needed and ensure the interpreter is knowledgeable about the dynamics of human trafficking.**
   A) *True*
   B) *False*

9. **If a practitioner suspects an individual is a victim of human trafficking, he/she should contact the National Human Trafficking Hotline.**
   A) *True*
   B) *False*

10. **One of the criticisms of the Trafficking Victims Protection Act of 2000 is that it places the burden of demonstrating innocence and coercion on the victim.**
    A) *True*
    B) *False*

Be sure to transfer your answers to the Answer Sheet insert located between pages 60–61.
PLEASE NOTE: Your postmark or facsimile date will be used as your test completion date.

Strategies for Appropriate Opioid Prescribing: The Florida APRN/PA Requirement

This course fulfills the Florida APRN requirement for 3 hours of education on the Prescribing of Controlled Substance Medications.

RNs and LPNs will receive general hours for completing this course.

Audience

This course is designed for all nurses and physician assistants who may alter prescribing practices or intervene to prevent drug diversion and inappropriate opioid use.

Course Objective

The purpose of this course is to provide clinicians who prescribe or distribute opioids with an appreciation for the complexities of opioid prescribing and the dual risks of litigation due to inadequate pain control and drug diversion or misuse in order to provide the best possible patient care and to prevent a growing social problem.

Learning Objectives

Upon completion of this course, you should be able to:

1. Define opioid prescribing and opioid misuse.
2. Apply epidemiologic trends in opioid use and misuse to current practice so at-risk patient populations can be more easily identified, assessed, and treated.
3. Create comprehensive treatment plans for patients with chronic pain that address patient needs as well as drug diversion prevention.
4. Identify state and federal laws governing the proper prescription and monitoring of controlled substances.
5. Evaluate behaviors that may indicate drug seeking or diverting as well as approaches for patients suspected of misusing opioids.

Faculty

Mark Rose, BS, MA, LP, is a licensed psychologist in the State of Minnesota with a private consulting practice and a medical research analyst with a biomedical communications firm. Earlier healthcare technology assessment work led to medical device and pharmaceutical sector experience in new product development involving cancer ablative devices and pain therapeutics. Along with substantial experience in addiction research, Mr. Rose has contributed to the authorship of numerous papers on CNS, oncology, and other medical disorders. He is the lead author of papers published in peer-reviewed addiction, psychiatry, and pain medicine journals and has written books on prescription opioids and alcoholism published by the Hazelden Foundation. He also serves as an Expert Advisor and Expert Witness to law firms that represent disability claimants or criminal defendants on cases related to chronic pain, psychiatric/substance use disorders, and acute pharmacologic/toxicologic effects. Mr. Rose is on the Board of Directors of the Minneapolis-based International Institute of Anti-Aging Medicine and is a member of several professional organizations.

Faculty Disclosure

Contributing faculty, Mark Rose, BS, MA, LP, has disclosed no relevant financial relationship with any product manufacturer or service provider mentioned.

Division Planner

Jane C. Norman, RN, MSN, CNE, PhD

Senior Director of Development and Academic Affairs

Sarah Campbell

Division Planner/Director Disclosure

The division planner and director have disclosed no relevant financial relationship with any product manufacturer or service provider mentioned.

Accreditations & Approvals

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INTRODUCTION

Pain is the leading reason for seeking medical care, and pain management is a large part of many healthcare professionals' practice. Opioid analgesics are approved by the U.S. Food and Drug Administration (FDA) for moderate and severe pain and are broadly accepted in acute pain, cancer pain, and end-of-life care, but are controversial in chronic noncancer pain. In response to the long-standing neglect of severe pain, indications for opioid analgesic prescribing were expanded in the 1990s, followed by inappropriate prescribing and increasing abuse, addiction, diversion, and overdose through the 2000s. In tandem with the continued under-treatment of pain, these practice patterns led to needless suffering from uncontrolled pain, opioid analgesic addiction, and overdose. Opioid analgesic prescribing and associated overdose peaked in 2010 with both now in multi-year decline, but information on these important trends is largely absent in the medical literature and media reporting.

Patients show substantial opioid response variations in analgesia and tolerability and may exhibit a range of psychologic, emotional, and behavioral responses that reflect inadequate pain control, an emerging opioid use problem, or both. Clinician delivery of best possible care to patients with pain requires appreciation of the complexities of opioid prescribing and the dual risks of inadequate pain control and inappropriate use, drug diversion, or overdose. A foundation for appropriate opioid prescribing is the understanding of factual data that clarify the prevalence, causality, and prevention of serious safety concerns with opioid prescribing.

DEFINITIONS

Definitions and use of terms describing opioid analgesic misuse, abuse, and addiction have changed over time, and their current correct use is inconsistent not only among healthcare providers, but also by federal agencies reporting epidemiologic data such as prevalence of opioid analgesic misuse, abuse, or addiction. Misuse and misunderstanding of these concepts and their correct definitions have resulted in misinformation and represent an impediment to proper patient care.

Inappropriate opioid analgesic prescribing for pain is defined as the non-prescribing, inadequate prescribing, excessive prescribing, or continued prescribing despite evidence of ineffectiveness of opioids [1]. Appropriate opioid prescribing is essential to achieve pain control; to minimize patient risk of abuse, addiction, and fatal toxicity; and to minimize societal harms from diversion. The foundation of appropriate opioid prescribing is thorough patient assessment, treatment planning, and follow-up and monitoring. Essential for proper patient assessment and treatment planning is comprehension of the clinical concepts of opioid abuse and addiction, their behavioral manifestations in patients with pain, and how these potentially problematic behavioral responses to opioids both resemble and differ from physical dependence and pseudoaddiction. Prescriber knowledge deficit has been identified as a key obstacle to appropriate opioid prescribing and, along with gaps in policy, treatment, attitudes, and research, contributes to widespread inadequate treatment of pain [2]. For example, a 2013 survey measuring 200 primary care physicians' understanding of opioids and addiction found that [3]:

- 35% admitted knowing little about opioid addiction.
- 66% and 57% viewed low levels of education and income, respectively, as causal or highly contributory to opioid addiction.

- 30% believed opioid addiction "is more of a psychologic problem," akin to poor lifestyle choices rather than a chronic illness or disease.
- 92% associated prescription analgesics with opioid addiction, but only 69% associated heroin with opioid addiction.
- 43% regarded opioid dependence and addiction as synonymous.

This last point is very important because confusion and conflation of the clinical concepts of dependence and addiction has led to accusations of many non-addicted patients with chronic pain of misusing or abusing their prescribed opioid and in the failure to detect treatment-emergent opioid problems [4]. Knowledge gaps concerning opioid analgesics, addiction, and pain are related to attitude gaps, and negative attitudes may interfere with appropriate prescribing of opioid analgesics. For example, when 248 primary care physicians were asked of their prescribing approach in patients with headache pain with either a past or current history of substance abuse, 16% and 42%, respectively, would not prescribe opioids under any circumstance [5]. Possibly contributing to healthcare professionals' knowledge deficit in pain treatment is the extent of educational exposure in school. A 2011 study found that U.S. medical school students received a median seven hours of pain education and Canadian medical students a median 14 hours, in contrast to the median 75 hours received by veterinarian school students in the United States [6]. Additionally, less than 3% of medical schools incorporate pain management into their curriculum, yet chronic pain is the most common reason patients see a provider, accounting for 40% of all visits in primary care [7].

The terms related to addiction are often inconsistent, inaccurate, and confusing, partially reflecting the diverse perspectives of those working in the related fields of health care, law enforcement, regulatory agencies, and reimbursement/payer organizations. Changes over time in the fundamental understanding of addiction have also contributed to the persistent misuse of obsolete terminology [8]. The *Diagnostic and Statistical Manual of Mental Disorders* (DSM), published by the American Psychiatric Association, is the standard reference for the diagnosis of addiction and all other psychiatric disorders. Prior to the 2013 release of the DSM-5, versions of the DSM eschewed the term "addiction" in favor of "substance dependence," with a separate diagnostic entity of "substance abuse" representing a less severe version of dependence [9]. Also, in earlier DSM versions, physiologic dependence, manifesting as substance tolerance and withdrawal, was considered a diagnostic criterion of substance dependence. The result was the perpetuation of patient and healthcare professional confusion between physical and substance dependence and the belief that tolerance and withdrawal meant addiction. This confusion also enhanced provider and patient fears over addiction developing from opioid analgesics and contributed to the undertreatment of pain. The DSM-5 has eliminated substance dependence and substance abuse by combining them into the single diagnostic entity of substance use disorder. The disorder is measured on a continuum from mild to severe [9].

In 2011, the American Society of Addiction Medicine (ASAM) published their latest revision in defining the disease of addiction. Owing to the increased public understanding and acceptance of addiction as a chronic brain disease, ASAM published an updated definition of addiction in 2019, with the goal of making it more accessible to patients, the media, and policy makers. The updated definition states that [10]:

> Addiction is a treatable, chronic medical disease involving complex interactions among brain circuits, genetics, the environment, and an individual's life experiences. People with addiction use substances or engage in behaviors that become compulsive and often continue despite harmful consequences.
>
> Prevention efforts and treatment approaches for addiction are generally as successful as those for other chronic diseases.

The ASAM Task Force also recommended that definitions for medication-assisted recovery (MAR) and medication-assisted treatment (MAT), which had been previously identified as transitional terms, be retired from use in ASAM documents. With the evolution of addiction treatment and its increasing integration with general medical care, the Task Force recommended that ASAM adopt general medical terminology to describe addiction treatment [10].

EPIDEMIOLOGY OF CHRONIC PAIN AND OPIOID MISUSE

Chronic pain affects about 100 million American adults—more than the total affected by heart disease, cancer, and diabetes combined [2]. It also costs the nation up to $635 billion each year in medical treatment and lost productivity and is the leading reason for receiving disability insurance [3; 11]. The lifetime prevalence of chronic pain ranges from 54% to 80%, and among adults 21 years of age and older, 14% report pain lasting 3 to 12 months and 42% report pain that persists longer than one year [2]. While 5 to 8 million Americans receive long-term opioids for the management of chronic pain, an estimated 41% of patients with chronic pain report their pain is uncontrolled, and 10% of all adults with pain suffer from severe, disabling chronic pain [11].

The increasing prevalence of chronic pain is the result of multiple factors, including the aging population; rising rates of obesity and obesity-related pain conditions, such as joint deterioration; advances in life-saving trauma interventions; poorly managed post-surgical pain; and greater public awareness of pain as a condition warranting medical attention [2]. In addition, many armed forces veterans have been returning from military action in Afghanistan and Iraq with traumatic injuries and chronic pain, and veterans' care clinicians have been reporting the perception that long-term pain management is lacking support in the veteran healthcare infrastructure [12].

There is a widespread misperception that opioid analgesic prescribing and overdose continues to grow, fueling an opioid epidemic [13; 14; 15; 16; 17]. Data from a 2019 Centers for Disease Control and Prevention (CDC) surveillance report show that between 2006 and 2018, the annual prescribing rate per 100 persons decreased from 72.4 to 51.4 for all opioids, an overall reduction of 29.0% [18]. (Opioid prescriptions, including codeine, fentanyl, hydrocodone, hydromorphone, methadone, morphine, oxycodone, oxymorphone, propoxyphene, tapentadol, tramadol, and buprenorphine, were identified using the National Drug Code. Cough and cold formulations containing opioids were not included.) The rate for all opioid prescriptions initially increased annually by 1.9% from 2006 to 2012, but then decreased annually by 5.2% from 2012 to 2016, and continued to decrease annually by 12.4% from 2016 to 2018 [18].

Although the epidemic of drug overdoses that began in the 1990s primarily involved prescription opioids prescribed for analgesia, the rapid increase in overdose deaths in 2010 was primarily attributed to heroin, and in 2013, to synthetic opioids, particularly illicitly manufactured fentanyl [18]. A total of 70,237 drug overdose deaths occurred in 2017, a rate of 21.7 per 100,000 persons. Although deaths might have involved more than one drug, prescription and/or illicit opioids were involved in 67.8% (47,600) of these drug overdose fatalities. Among opioid-involved deaths, the category synthetic opioids other than methadone (primarily illicitly manufactured fentanyl) was the most common, with 28,466 deaths. The prescription opioids category, which includes natural and semisynthetic opioids (e.g., oxycodone, hydrocodone) and methadone, was the second most common, with 17,029 deaths. Heroin was involved in 15,482 deaths. Natural and semi-synthetic opioids were involved in 14,495 deaths, and methadone was involved in 3,194 deaths. Cocaine was involved in 13,942 deaths, and 10,333 persons died from drug overdoses involving psychostimulants with abuse potential (e.g., methamphetamine) [18].

There is nearly universal agreement that opioid analgesics were injudiciously overprescribed during the 2000s. Interpretation of the broader trend of increased prescribing from 1990 might be viewed by public health professionals as entirely problematic and by pain medicine professionals as necessary in part, given the past neglect of patients in pain. This reflects the polarized nature of pain care and opioid analgesic prescribing in particular. Efforts to reduce opioid analgesic overprescribing and associated overdose have been successful but have come at a cost to patients who have faced increasing barriers to access, including stigma and abuse in a healthcare system, tapering of opioids without consideration for pain or functional improvements, and difficulty finding a physician [14; 19; 20].

Worldwide consumption of opioid analgesics increased dramatically over the past few decades, driven primarily by U.S. consumption. For example, the global consumption of oxycodone was 3 tons (2,722 kg) in 1990 and 77 tons (69,853 kg) in 2009, with 62 tons (81%) consumed in the United States [21].

Despite a decrease in global manufacture of the drug, global consumption of oxycodone increased, from 51.6 tons in 2019 to 64.9.6 tons in 2020. Consumption remained concentrated in the United States, which consumed 44.3 tons (68.2%) of the world total [22]. Global stocks of oxycodone decreased to 85.9 tons in 2020, with the United States holding 38.3 tons, or 44.7% of the world's total [22]. The United States also accounted for almost all (99.2%) of the global manufacture of hydrocodone [22]. This is partially because access to opioid analgesics is virtually or entirely non-existent for much of the world's population. An estimated 3.6 billion people (50% of the global population who reside in the poorest countries) receive less than 1% of the distributed opioids [23]. Other countries with adequate opioid access prefer dihydrocodeine or low-dose morphine over hydrocodone for use in moderate or moderately severe pain [24].

Many prescribed opioid analgesic fatalities result from the co-ingestion of central nervous system (CNS)/respiratory depressants (especially benzodiazepines) or prescribed methadone. The National Institute on Drug Abuse reported benzodiazepines contributed to 13.4% of opioid analgesic fatalities in 2020 (compared with 24% in 2017), but this may underestimate the true contribution [25]. A Canadian study evaluated 607,156 adults prescribed opioids for noncancer pain, and of those whose deaths were related to opioids, co-prescribed benzodiazepines were detected in 84.5% [26]. In another study of 2,182,374 North Carolina residents receiving one or more opioid analgesics in 2010, benzodiazepines were present in 61.4% who fatally overdosed [27]. A cross-sectional study of 386,457 ambulatory care visits in the United States from 2003 through 2015 found that the use of benzodiazepines increased substantially from 3.8% to 7.4% of visits, including co-prescribing with other sedating medications [28]. Use for back and chronic pain increased more significantly than use for anxiety and insomnia, which remained relatively unchanged. This increase likely reflects not only a growing number of individuals receiving benzodiazepines, but also an increase in those receiving them on a long-term basis, despite the lack of evidence supporting their use past 8 or 10 weeks [28].

OPIOID MISUSE IN FLORIDA

In Florida, misuse of prescription opioids became a serious problem in the 1990s and 2000s, but efforts to stem the problem appear to be working. The rate of drug overdose deaths increased 58.9% during 2003–2010, and in 2009, one in eight deaths in Florida was attributable to drug overdose [29; 30]. From 2019 to 2020, total drug-related deaths increased by 17%. Opioid-related deaths increased by 28%, and opioid-caused deaths increased by 42% [31].Of the 6,089 opioid-caused deaths reported in Florida in 2020, 1,187 of these deaths were attributed to oxycodone, a 5% increase in oxycodone-caused deaths over the previous year [31]. These trends resulted in the enactment of several measures to address prescribing that was inconsistent with best practices, and partnership with the U.S. Drug Enforcement Administration (DEA) to close and prevent "pill mills" from introducing millions of opioid dose units into illicit markets [32; 33]. In May 2017, former Florida

Governor Rick Scott signed an executive order declaring the opioid epidemic a public health emergency, providing additional funding and empowering state health professions to take steps to address this pressing issue [33]. As part of this order, the State Health Officer has issued a standing order for opioid antagonists to ensure emergency responders have access [33]. The order has been extended several times (last in 2019) [34].

Drug overdose fatalities in Florida have continued rising from increased use of heroin, synthetic cannabinoids, and novel psychoactive substances such as alpha-PVP ("flakka"). An influx of clandestine fentanyl into Florida in early 2014, and several fentanyl analogs and other novel non-pharmaceutical opioids more recently, has largely driven the increases in opioid overdose fatalities [31]. Several overdose fatalities in Florida were linked to counterfeit alprazolam, oxycodone, and hydrocodone tablets that contained fentanyl [35]. The decrease in prescription opioid fatalities, offset by increasing overdose fatalities from other opioid and non-opioid agents, reflects the intervention focus on the supply side ("pill mill laws") and neglect of treatment funding that would address the demand side of problematic drug use [36].

In Florida, fatalities with benzodiazepines present peaked in 2010 with 6,188, falling to 4,405 in 2020 (37.7% were alprazolam) [31]. Of the 44,577 deaths investigated by Florida authorities, toxicology results determined that drugs were present at the time of death in 14,708 individuals, with the vast majority revealing more than one drug occurrence [31]. Other primary contributors to opioid analgesic-related fatalities include alcohol and prescribed methadone [31; 37; 38].

In addition to the executive order issued in 2017 (and subsequently extended), several new state laws were passed in 2018 to impose additional legal requirements on controlled substance prescribers [39]. These laws will be discussed in detail later in this course.

INITIATION AND MANAGEMENT OF THE PATIENT WITH PAIN

In 2016, the CDC issued updated opioid prescribing guidelines for chronic pain that address when to initiate or continue opioids for chronic pain; opioid selection, dosage, duration, follow-up, and discontinuation; and assessing risk and addressing harms of opioid use [40]. Some of the recommendations are standard risk mitigation approaches, but others have been criticized by pain medicine physicians and patient advocates. A common criticism is the sole focus on curtailing prescribing and patient access [41; 42; 43; 44]. The 2016 guidelines communicated the intent to evaluate and reassess evidence and recommendations as new evidence became available. In 2022, the CDC posted a draft of updated guidelines for public comment, based on systematic reviews of new evidence [45; 46; 47]. Release of a final updated guideline is anticipated in late 2022 [45]. Meanwhile, the recommendations referred to in this course are taken from the CDC's 2016 opioid prescribing guideline [40].

It can be difficult to balance the benefits and harms of prescription opioids. This is exacerbated by inadequate education and by opioid prescribing guidelines based on expert opinion instead of scientific evidence. This has resulted in wide variation in clinical practice, inconsistent prescriber guidance, and clinician confusion [48]. For instance, the CDC and other opioid guidelines state that opioids should be considered only after non-opioid therapy fails. However, when pain is severe and patients require powerful analgesic control, there is little choice because no other pain medications are as effective as opioids with lower addiction risk [49].

However, many guidelines do share common recommendations. These represent the current "conventional wisdom" in opioid analgesic prescribing and can inform healthcare professionals of the best clinical practices in opioid prescribing that include approaches to the assessment of pain and function and pain management modalities. Pharmacologic and nonpharmacologic approaches should be used on the basis of current evidence or best clinical practice. Patients with moderate-to-severe chronic pain without adequate pain relief from non-opioid or nonpharmacologic therapy can be considered for a trial of opioid therapy [40; 50]. Initial treatment should always be considered individually determined and as a trial of therapy, not a definitive course of treatment [51].

ACUTE PAIN

Long-term opioid use often begins with treatment of acute pain. When opioids are used for acute pain, clinicians should prescribe the lowest effective dose of immediate-release opioids in a quantity no greater than that needed for the expected duration of severe pain. In most cases, three days or less will be sufficient; more than seven days will rarely be needed [40]. Florida law dictates that, for the treatment of acute pain, a prescription for an opioid drug may not exceed a three-day supply; an exception may be made for a seven-day supply if [52]:

- The prescriber, in his or her professional judgment, believes that more than a three-day supply of such an opioid is medically necessary to treat the patient's pain as an acute medical condition.
- The prescriber indicates "ACUTE PAIN EXCEPTION" on the prescription. (For the treatment of pain other than acute pain, a practitioner must indicate "NON-ACUTE PAIN" on a prescription.)
- The prescriber adequately documents in the patient's medical records the acute medical condition and lack of alternative treatment options that justify deviation from the three-day supply limit.

With postoperative, acute, or intermittent pain, analgesia often requires frequent titration, and the two- to four-hour analgesic duration with short-acting hydrocodone, morphine, and oxycodone is more effective than extended-release formulations. Short-acting opioids are also recommended in patients who are medically unstable or with highly variable pain intensity [53; 54; 55].

As part of House Bill 21, passed in 2018, the Florida Board of Medicine and the Board of Osteopathic Medicine are required to establish guidelines for prescribing controlled substances for acute pain [52]. In 2019, the Florida Board of Medicine approved and published *Rule No. 64B8-9.013, Standards for the Prescribing of Controlled Substances for the Treatment of Acute Pain* to satisfy this requirement [56].

PATIENT EVALUATION AND ASSESSMENT OF ADDICTION RISK

Information obtained by patient history, physical examination, and interview, from family members, a spouse, or state prescription drug monitoring program (PDMP), and from the use of screening and assessment tools can help the clinician to stratify the patient according to level of risk for developing problematic opioid behavioral responses (***Table 1***). Low-risk patients receive the standard level of monitoring, vigilance, and care. Moderate-risk patients should be considered for an additional level of monitoring and provider contact, and high-risk patients are likely to require intensive and structured monitoring and follow-up contact, additional consultation with psychiatric and addiction medicine specialists, and limited supplies of short-acting opioid formulations [40; 57].

Anxiety disorders, major depressive disorder, and intense emotional distress alter pain perception and response. Intensity and perception of reported pain is also influenced by factors such as mood, cultural background, social supports, and financial resources. A biopsychosocial model is required to inform pain assessment in order to address the biologic basis of pain and presence of social and psychologic contributors [49].

Before deciding to prescribe an opioid analgesic, clinicians should perform and document a detailed patient assessment that includes [1]:

- Pain indications for opioid therapy
- Nature and intensity of pain
- Past and current pain treatments and patient response
- Comorbid conditions
- Pain impact on physical and psychologic function
- Social support, housing, and employment
- Home environment (i.e., stressful or supportive)
- Pain impact on sleep, mood, work, relationships, leisure, and substance use
- Patient history of physical, emotional, or sexual abuse

Depression is perhaps the single most important comorbidity in patients with chronic pain and is vastly underdiagnosed and untreated. Patients with unrecognized and untreated depression are unlikely to respond to opioids and other pain therapies, but successful treatment of depression can promote analgesia [61].

If substance abuse is active, in remission, or in the patient's history, consult an addiction specialist before starting opioids [1]. In active substance abuse, do not prescribe opioids until the patient is engaged in treatment/recovery program or other arrangement made, such as addiction professional co-management and additional monitoring. When considering an opioid analgesic (particularly those that are extended-release or long-acting), one must always weigh the benefits against the risks of overdose, abuse, addiction, physical dependence and tolerance, adverse drug interactions, and accidental exposure by children [40; 62].

RISK STRATIFICATION FOR PATIENTS PRESCRIBED OPIOIDS

Low Risk
No past or current personal history of alcohol/substance use disorder (AUD/SUD)
No or minimal co-occurring psychiatric disorders
No family history of alcoholism or substance abuse
Medium Risk
Past history of AUD or SUD
Moderate concomitant psychiatric disorders
Family history of alcoholism or substance abuse/addiction
Patient history of physical, emotional or sexual abuse, especially in childhood
High Risk
Patient actively addicted to or abusing opioids, illicit drugs or alcohol
Untreated or poorly controlled major psychiatric disorder
History of diversion, prescription forgery, selling their prescription drugs

Source: [58; 59; 60] *Table 1*

Screening and assessment tools can help guide patient stratification according to risk level and inform the appropriate degree of structure and monitoring in the treatment plan. It should be noted that despite widespread endorsement of screening tool use to help determine patient risk level, most tools have not been extensively evaluated, validated, or compared to each other, and evidence of their reliability is poor [63].

Opioid Risk Tool (ORT)

The Opioid Risk Tool (ORT) is a five-item assessment to help predict aberrant drug-related behavior. The ORT is also used to establish patient risk level through categorization into low, medium, or high levels of risk for aberrant drug-related behaviors based on responses to questions of previous alcohol/drug abuse, psychologic disorders, and other risk factors [64; 65].

Screener and Opioid Assessment for Patients with Pain-Revised (SOAPP-R)

The Screener and Opioid Assessment for Patients with Pain-Revised (SOAPP-R) is a patient-administered, 24-item screen with questions addressing history of alcohol/substance use, psychologic status, mood, cravings, and stress. Like the ORT, the SOAPP-R helps assess risk level of aberrant drug-related behaviors and the appropriate extent of monitoring [66; 67].

CAGE and CAGE-AID

The original CAGE (Cut down, Annoyed, Guilty, and Eye-opener) Questionnaire consisted of four questions designed to help clinicians determine the likelihood that a patient was misusing or abusing alcohol. These same four questions were modified to create the CAGE-AID (adapted to include drugs), revised to assess the likelihood of current substance abuse [68; 69].

Diagnosis, Intractability, Risk, and Efficacy (DIRE) Tool

The Diagnosis, Intractability, Risk, and Efficacy (DIRE) risk assessment tool is a clinician-rated questionnaire that is used to predict patient compliance with long-term opioid therapy [70; 71]. Patients scoring lower on the DIRE tool are poor candidates for long-term opioid analgesia.

Mental Health Screening Tool

The Mental Health Screening Tool is a five-item screen that asks about a patient's feelings of happiness, calmness, peacefulness, nervousness, and depression in the past month [72]. A lower score on this tool is an indicator that the patient should be referred to a specialist for pain management.

CREATING A TREATMENT PLAN

Opioid therapy should be presented as a trial for a pre-defined period (e.g., ≤30 days). The goals of treatment should be established with all patients prior to the initiation of opioid therapy, including reasonable improvements in pain, function, depression, anxiety, and avoidance of unnecessary or excessive medication use [1; 40]. The treatment plan should describe therapy selection, measures of progress, and other diagnostic evaluations, consultations, referrals, and therapies. All patients prescribed an opioid for pain related to a traumatic injury (severity score ≥9) should be concurrently prescribed an antagonist (e.g., naloxone) [52].

In opioid-naïve patients, start at the lowest possible dose and titrate to effect. Dosages for opioid-tolerant patients should always be individualized and titrated by efficacy and tolerability [1]. The need for frequent progress and benefit/risk assessments during the trial should be included in patient education. Patients should also have full knowledge of the warning signs and symptoms of respiratory depression.

Prescribers should be knowledgeable of federal and state opioid prescribing regulations. Issues of equianalgesic dosing, close patient monitoring during all dose changes, and incomplete cross-tolerance with opioid conversion should be considered. If necessary, treatment may be augmented, with preference for non-opioid and immediate-release opioids over long-acting/extended-release opioids. Taper opioid dose when no longer needed [62].

Non-Opioid Pain Management Options

Nonpharmacologic Approaches

Several nonpharmacologic approaches are therapeutic complements to pain-relieving medication, lessening the need for higher doses and perhaps minimizing side effects. These interventions can help decrease pain or distress that may be contributing to the pain sensation. Approaches include palliative radiotherapy, complementary/alternative methods, manipulative and body-based methods, and cognitive/behavioral techniques. The choice of a specific nonpharmacologic intervention is based on the patient's preference, which, in turn, is usually based on a successful experience in the past.

Methods to provide distraction from pain come in a wide variety, including reciting poetry, meditating with a calm phrase, watching television or movies, playing cards, visiting with friends, or participating in crafts. Music therapy and art therapy are also becoming more widely used as nonpharmacologic options for pain management.

Non-Opioid Analgesics

Non-opioid analgesics, such as aspirin, acetaminophen (Tylenol), and nonsteroidal anti-inflammatory drugs (NSAIDs), are primarily used for mild pain and may also be helpful as coanalgesics for moderate and severe pain. Acetaminophen is among the safest of analgesic agents, but it has essentially no anti-inflammatory effect. Toxicity is a concern at high doses, and the maximum recommended dose is 3–4 g per day [73]. Acetaminophen should be avoided or given at lower doses in people with a history of alcohol abuse or renal or hepatic insufficiency [73].

NSAIDs are most effective for pain associated with inflammation. Among the commonly used NSAIDs are ibuprofen (Motrin, Advil), naproxen (Aleve, Naprosyn), and indomethacin (Indocin). There are several classes of NSAIDs, and the response differs among patients; trials of drugs for an individual patient may be necessary to determine which drug is most effective [74]. NSAIDs inhibit platelet aggregation, increasing the risk of bleeding, and also can damage the mucosal lining of the stomach, leading to gastrointestinal bleeding. There is a ceiling effect to the non-opioid analgesics; that is, there is a dose beyond which there is no further analgesic effect. In addition, many side effects of non-opioids can be severe and may limit their use or dosing.

Informed Consent and Treatment Agreements

The initial opioid prescription is preceded by a written informed consent or "treatment agreement" [1]. This agreement should address potential side effects, tolerance and/or physical dependence, drug interactions, motor skill impairment, limited evidence of long-term benefit, misuse, dependence, addiction, and overdose. Informed consent documents should include information regarding the risk/benefit profile for the drug(s) being prescribed. The prescribing policies should be clearly delineated, including the number/frequency of refills, early refills, and procedures for lost or stolen medications [1].

The treatment agreement also outlines joint physician and patient responsibilities. The patient agrees to using medications safely, refraining from "doctor shopping," and consenting to routine urine drug testing (UDT). The prescriber's responsibility is to address unforeseen problems and prescribe

scheduled refills. Reasons for opioid therapy change or discontinuation should be listed. Agreements can also include sections related to follow-up visits, monitoring, and safe storage and disposal of unused drugs.

PERIODIC REVIEW AND MONITORING

When implementing a chronic pain treatment plan that involves the use of opioids, the patient should be frequently reassessed for changes in pain origin, health, and function [1]. This can include input from family members and/or the state PDMP. During the initiation phase and during any changes to the dosage or agent used, patient contact should be increased. At every visit, chronic opioid response may be monitored according to the "5 A's" [75]:

- Analgesia
- Activities of daily living
- Adverse or side effects
- Aberrant drug-related behaviors
- Affect (i.e., patient mood)

Signs and symptoms that, if present, may suggest a problematic response to the opioid and interference with the goal of functional improvement include [76]:

- Excessive sleeping or days and nights turned around
- Diminished appetite
- Short attention span or inability to concentrate
- Mood volatility, especially irritability
- Lack of involvement with others
- Impaired functioning due to drug effects
- Use of the opioid to regress instead of re-engaging in life
- Lack of attention to hygiene and appearance

The decision to continue, change, or terminate opioid therapy is based on progress toward treatment objectives and absence of concerning adverse effects and risks of overdose or diversion [1]. Satisfactory therapy is indicated by improvements in pain, function, and quality of life. It is important to remember that for some patients with severe chronic pain, improved function may take longer than pain control. Either pain or function (not both) will improve. In some cases, preventing worsening pain/functional impairment is the best achievable outcome. Brief assessment tools to assess pain and function may be useful, as may UDTs. Treatment plans may include periodic pill counts to confirm adherence and minimize diversion.

Involvement of Family

Family members or the partner of the patient can provide the clinician with valuable information that better informs decision making regarding continuing opioid therapy [1]. Family members can observe whether a patient is losing control of his or her life or becoming less functional or more depressed during the course of opioid therapy. They can also provide input regarding positive or negative changes in patient function, attitude, and level of comfort [1]. The following questions can be asked of family members or a spouse to help clarify whether the patient's response to opioid therapy is favorable or unfavorable [76]:

- Is the person's day centered around taking the opioid medication? Response can help clarify long-term risks and benefits of the medication and identify other treatment options.
- Does the person take pain medication only on occasion, perhaps three or four times per week? If yes, the likelihood of addiction is low.
- Have there been any other substance (alcohol or drug) abuse problems in the person's life? An affirmative response should be taken into consideration when prescribing.
- Does the person in pain spend most of the day resting, avoiding activity, or feeling depressed? If so, this suggests the pain medication is failing to promote rehabilitation. Daily activity is essential, and the patient may be considered for enrollment in a graduated exercise program
- Is the person in pain able to function (e.g., work, do household chores, play) with pain medication in a way that is clearly better than without? If yes, this suggests the pain medication is contributing to wellness.

Assessment Tools

VIGIL

VIGIL is the acronym for a five-step risk management strategy designed to empower clinicians to appropriately prescribe opioids for pain by reducing regulatory concerns and to give pharmacists a framework for resolving ambiguous opioid analgesic prescriptions in a manner that preserves legitimate patient need while potentially deterring diverters. The components of VIGIL are:

- Verification: Is this a responsible opioid user?
- Identification: Is the identity of this patient verifiable?
- Generalization: Do we agree on mutual responsibilities and expectations?
- Interpretation: Do I feel comfortable allowing this person to have controlled substances?
- Legalization: Am I acting legally and responsibly?

The foundation of VIGIL is a collaborative physician/pharmacist relationship [77; 78].

Current Opioid Misuse Measure (COMM)

The Current Opioid Misuse Measure (COMM) is a 17-item patient self-report assessment designed to help clinicians identify misuse or abuse in patients with chronic pain. Unlike the ORT and the SOAPP-R, the COMM identifies aberrant behaviors associated with opioid misuse in patients already receiving long-term opioid therapy [57]. Sample questions include: In the past 30 days, how often have you had to take more of your

PATIENT RISK LEVEL AND FREQUENCY OF MONITORING			
Monitoring Tool	**Patient Risk Level**		
	Low	**Medium**	**High**
Urine drug test	Every 1 to 2 years	Every 6 to 12 months	Every 3 to 6 months
State prescription drug monitoring program	Twice per year	3 times per year	4 times per year

Source: [81] *Table 2*

medication than prescribed? In the past 30 days, how much of your time was spent thinking about opioid medications (e.g., having enough, taking them, dosing schedule)?

Pain Assessment and Documentation Tool (PADT)

Guidelines by the Federation of State Medical Boards (FSMB) and the Joint Commission stress the importance of documentation from both a healthcare quality and medicolegal perspective. Research has found widespread deficits in chart notes and progress documentation for patients with chronic pain who are receiving opioid therapy, and the Pain Assessment and Documentation Tool (PADT) was designed to address these shortcomings [79]. The PADT is a clinician-directed interview, with most sections (e.g., analgesia, activities of daily living, adverse events) consisting of questions asked of the patient [80]. However, the potential aberrant drug-related behavior section must be completed by the physician based on his or her observations of the patient.

The Brief Intervention Tool

The Brief Intervention Tool is a 26-item, "yes-no," patient-administered questionnaire used to identify early signs of opioid abuse or addiction. The items assess the extent of problems related to drug use in several areas, including drug use-related functional impairment [72].

Urine Drug Tests

UDTs may be used to monitor adherence to the prescribed treatment plan and to detect unsanctioned drug use. They should be used more often in patients receiving addiction therapy, but clinical judgment is the ultimate guide to testing frequency (***Table 2***) [81]. The CDC recommends clinicians should use UDT before starting opioid therapy and consider UDT at least annually to assess for prescribed medications as well as other controlled prescription drugs and illicit drugs [40]. However, this recommendation was based on low-quality evidence that indicates little confidence in the effect estimate.

Initially, testing involves the use of class-specific immunoassay drug panels [1]. If necessary, this may be followed with gas chromatography/mass spectrometry for specific drug or metabolite detection. It is important that testing identifies the specific drug rather than the drug class, and the prescribed opioid should be included in the screen. Any abnormalities should be confirmed with a laboratory toxicologist or clinical pathologist. Immunoassay may be used point-of-care for "on-the-spot" therapy changes, but the high error rate prevents its use in major clinical decisions except with liquid chromatography coupled to tandem mass spectrometry confirmation.

Urine test results suggesting opioid misuse should be discussed with the patient using a positive, supportive approach. The test results and the patient discussion should be documented.

CONSULTATION AND REFERRAL

It is important to seek consultation or patient referral when input or care from a pain, psychiatry, addiction, or mental health specialist is necessary. Clinicians who prescribe opioids should become familiar with opioid addiction treatment options (including licensed opioid treatment programs for methadone and office-based opioid treatment for buprenorphine) if referral is needed [1].

Ideally, providers should be able to refer patients with active substance abuse who require pain treatment to an addiction professional or specialized program. In reality, these specialized resources are scarce or non-existent in many areas [1]. Therefore, each provider will need to decide whether the risks of continuing opioid treatment while a patient is using illicit drugs outweigh the benefits to the patient in terms of pain control and improved function [82].

MEDICAL RECORDS

As noted, documentation is a necessary aspect of all patient care, but it is of particular importance when opioid prescribing is involved. All clinicians should maintain accurate, complete, and up-to-date medical records, including all written or telephoned prescription orders for opioid analgesics and other controlled substances, all written instructions to the patient for medication use, and the name, telephone number, and address of the patient's pharmacy [1]. Good medical records demonstrate that a service was provided to the patient and that the service was medically necessary. Regardless of the treatment outcome, thorough medical records protect the prescriber.

PATIENT EDUCATION ON THE USE AND DISPOSAL OF OPIOIDS

Patients and caregivers should be counseled regarding the safe use and disposal of opioids. As part of its mandatory Risk Evaluation and Mitigation Strategy (REMS) for extended-release/long-acting opioids, the FDA has developed a patient counseling document with information on the patient's specific medications, instructions for emergency situations and

incomplete pain control, and warnings not to share medications or take them unprescribed [62]. A copy of this form may be accessed online at https://www.fda.gov/media/79776/download.

When prescribing opioids, clinicians should provide patients with the following information [62]:

- Product-specific information
- Taking the opioid as prescribed
- Importance of dosing regimen adherence, managing missed doses, and prescriber contact if pain is not controlled
- Warning and rationale to never break or chew/crush tablets or cut or tear patches prior to use
- Warning and rationale to avoid other central nervous system depressants, such as sedative-hypnotics, anxiolytics, alcohol, or illicit drugs
- Warning not to abruptly halt or reduce the opioid without physician oversight of safe tapering when discontinuing
- The potential of serious side effects or death
- Risk factors, signs, and symptoms of overdose and opioid-induced respiratory depression, gastrointestinal obstruction, and allergic reactions
- The risks of falls, using heavy machinery, and driving
- Warning and rationale to never share an opioid analgesic
- Rationale for secure opioid storage
- Warning to protect opioids from theft
- Instructions for disposal of unneeded opioids, based on product-specific disposal information

There are no universal recommendations for the proper disposal of unused opioids, and patients are rarely advised of what to do with unused or expired medications [83]. According to the Office of National Drug Control Policy, most medications that are no longer necessary or have expired should be removed from their containers, mixed with undesirable substances (e.g., cat litter, used coffee grounds), and put into an impermeable, nondescript container (e.g., disposable container with a lid or a sealed bag) before throwing in the trash [84]. Any personal information should be obscured or destroyed. The FDA recommends that certain medications, including oxycodone/acetaminophen (Percocet), oxycodone (OxyContin tablets), and transdermal fentanyl (Duragesic Transdermal System), be flushed down the toilet instead of thrown in the trash [85]. Patients should be advised to flush prescription drugs down the toilet only if the label or accompanying patient information specifically instructs doing so and no other disposal method is appropriate [85].

The American College of Preventive Medicine has established best practices to avoid diversion of unused drugs and educate patients regarding drug disposal [83]:

- Consider writing prescriptions in smaller amounts.
- Educate patients about safe storing and disposal practices.
- Give drug-specific information to patients about the temperature at which they should store their medications. Generally, the bathroom is not the best storage place. It is damp and moist, potentially resulting in potency decrements, and accessible to many people, including children and teens, resulting in potential theft or safety issues.
- Ask patients not to advertise that they are taking these types of medications and to keep their medications secure.
- Refer patients to community "take back" services overseen by law enforcement that collect controlled substances, seal them in plastic bags, and store them in a secure location until they can be incinerated. Contact your state law enforcement agency or visit https://www.dea.gov to determine if a program is available in your area.

DISCONTINUING OPIOID THERAPY

The decision to continue or end opioid prescribing should be based on a physician-patient discussion of the anticipated benefits and risks. An opioid should be discontinued with resolution of the pain condition, intolerable side effects, inadequate analgesia, lack of improvement in quality of life despite dose titration, deteriorating function, or significant aberrant medication use [1; 40].

Clinicians should provide physically dependent patients with a safely structured tapering protocol. Withdrawal is managed by the prescribing physician or referral to an addiction specialist. Patients should be reassured that opioid discontinuation is not the end of treatment; continuation of pain management will be undertaken with other modalities through direct care or referral.

As a side note, cannabis use by patients with chronic pain receiving opioid therapy has traditionally been viewed as a treatment agreement violation that is grounds for termination of opioid therapy. However, some now argue against cannabis use as a rationale for termination or substantial treatment and monitoring changes, especially considering the increasing legalization of medical use at the state level [82]. Cannabis use for chronic pain in patients receiving opioid therapy continues to receive increased interest and support; however, experts caution that more evidence of improved patient outcomes is needed [86; 87; 88].

CONSIDERATIONS FOR NON-ENGLISH-PROFICIENT PATIENTS

For patients who are not proficient in English, it is important that information regarding the risks associated with the use of opioids and available resources be provided in their native language, if possible. When there is an obvious disconnect in the communication process between the practitioner and

patient due to the patient's lack of proficiency in the English language, an interpreter is required. Interpreters can be a valuable resource to help bridge the communication and cultural gap between patients and practitioners. Interpreters are more than passive agents who translate and transmit information back and forth from party to party. When they are enlisted and treated as part of the interdisciplinary clinical team, they serve as cultural brokers who ultimately enhance the clinical encounter. In any case in which information regarding treatment options and medication/treatment measures are being provided, the use of an interpreter should be considered. Print materials are also available in many languages, and these should be offered whenever necessary.

CRISIS INTERVENTION: MANAGEMENT OF OVERDOSE

Individuals who have first contact with persons suspected of experiencing an opioid-related overdose are in the position to intervene to prevent the potentially devastating consequences. In these cases, care begins with crisis intervention directed at immediate survival by reversing the potentially lethal effects of overdose with an opioid antagonist.

Opioid antagonists have obvious therapeutic value in the treatment of opioid overdose. A 2012 study found that wider distribution of naloxone and training in its administration might have prevented numerous deaths from opioid overdoses in the United States [89]. Since the first community-based opioid overdose prevention program began distributing naloxone in 1996, more than 10,000 overdoses have been reversed [89].

In Florida, licensed healthcare providers may prescribe and pharmacists may dispense opioid antagonists (even as a standing order) for at-risk individuals, these individuals' relatives or other caregivers, and emergency responders to be used in their course of duties [90]. Emergency responders include (but are not limited to) law enforcement officers, paramedics, and emergency medical technicians [90]. As noted, there is a statewide standing order for naloxone for all emergency responders in Florida [33].

OPIOID ANTAGONISTS

Relatively minor changes in the structure of an opioid can convert an agonist drug into one with antagonistic actions at one or more opioid receptor types. Opioid antagonists include naloxone, naltrexone, and nalmefene. Interestingly, naloxone also appears to block the analgesic effects of placebo medications and acupuncture. These agents have no abuse potential [91].

In response to acute overdose, the short-acting opioid antagonist naloxone is considered the gold standard, and it remains the most widely used opioid antagonist for the reversal of overdose and opioid-related respiratory depression. It acts by competing with opioids at receptor sites in the brain stem, reversing desensitization to carbon dioxide, and reversing or preventing respiratory failure and coma. There is no evidence that subcutaneous or intramuscular use is inferior to intravenous naloxone. This has prompted some states to pass laws allowing opioid antagonists to be available to the general public for administration outside the healthcare setting to treat acute opioid overdose [92].

When used for opioid overdose, a dose of 0.4–2 mg of naloxone is administered intravenously, intramuscularly, or subcutaneously [93]. If necessary, the dose may be repeated every two to three minutes for full reversal. For ease of use, naloxone is also available in a pre-filled auto-injection device. An intranasal formulation is also available in doses of 2 mg, 4 mg, or 8 mg [93]. It is important that standard Advanced Cardiac Life Support (ACLS) protocols be continued while naloxone is being administered and that medical treatment (at a healthcare facility) be given immediately.

COMPLIANCE WITH STATE AND FEDERAL LAWS

In response to the rising incidence in prescription opioid abuse, addiction, diversion, and overdose in the late 1990s and 2000s, the FDA has mandated opioid-specific REMS to reduce the potential negative patient and societal effects of prescribed opioids. Other elements of opioid risk mitigation include FDA partnering with other governmental agencies, state professional licensing boards, and societies of healthcare professionals to help improve prescriber knowledge of appropriate and safe opioid prescribing and safe home storage and disposal of unused medication [76].

Several regulations and programs at the state level have been enacted in an effort to reduce prescription opioid abuse, diversion, and overdose, including [94]:

- Physical examination required prior to prescribing
- Tamper-resistant prescription forms
- Pain clinic regulatory oversight
- Prescription limits
- Prohibition from obtaining controlled substance prescriptions from multiple providers
- Patient identification required before dispensing
- Immunity from prosecution or mitigation at sentencing for individuals seeking assistance during an overdose

CONTROLLED SUBSTANCES LAWS/RULES

The DEA is responsible for formulating federal standards for the handling of controlled substances. In 2011, the DEA began requiring every state to implement electronic databases that track prescribing habits, referred to as PDMPs. Specific policies regarding controlled substances are administered at the state level.

According to the DEA, drugs, substances, and certain chemicals used to make drugs are classified into five distinct categories or schedules depending upon the drug's acceptable medical use and the drug's abuse or dependency potential [95]. The abuse rate is a determinate factor in the scheduling of the drug; for example, Schedule I drugs are considered the most dangerous class of drugs with a high potential for abuse and potentially severe psychologic and/or physical dependence.

In Florida, the prescribing, dispensing, and consumption of certain controlled substances are governed by Chapter 893 of the Florida Statutes [96]. This law establishes the standards for controlled substance prescribing, including reporting system requirements, for prescribers and pharmacists in Florida. As of 2022, the Florida schedule of controlled substances aligns with the DEA schedule [97].

THE ELECTRONIC FLORIDA ONLINE REPORTING OF CONTROLLED SUBSTANCES EVALUATION PROGRAM

Emerging trends and patterns of prescription opioid abuse, addiction, and overdose are monitored by several industry and government agencies through data collection from a variety of sources. These include health insurance claims; the Automation of Reports and Consolidated Orders System, a DEA-run program that monitors the flow of controlled substances from manufacturing through distribution to retail sale or dispensing; the Treatment Episode Data Set, which monitors treatment admissions; the National Center for Health Statistics state mortality data; and the Researched Abuse, Diversion, and Addiction-Related Surveillance System, which monitors prescription drug abuse, misuse, and diversion [98; 99; 100; 101].

Almost all states, including Florida, have enacted PDMPs to facilitate the collection, analysis, and reporting of information on controlled substances prescribing and dispensing [1]. All prescribers must consult the Electronic Florida Online Reporting of Controlled Substances Evaluation (E-FORCSE) to review a patient's controlled substance dispensing history before prescribing or dispensing a controlled substance to a patient 16 years of age or older [39; 102]. This is mandated even for existing patients and should be done each time a controlled substance is prescribed or dispensed [39]. If the system is nonoperational or cannot be accessed due to a temporary technologic or electrical failure, the prescription may be issued (with documentation of the exception) for up to a maximum three-day supply.

All clinicians who prescribe or dispense controlled substances are required to report the action to E-FORCSE as soon as possible, but no later than the close of the next business day [39]. This should be repeated each time the substance is dispensed. This reporting requirement is waived in certain circumstances, including for [103]:

- The dispensing of a controlled substance in the healthcare system of the Department of Corrections
- The dispensing of a controlled substance to a person younger than 16 years of age

IDENTIFICATION OF DRUG DIVERSION/SEEKING BEHAVIORS

Research has more closely defined the location of prescribed opioid diversion into illicit use in the supply chain from the manufacturer to the distributor, retailer, and the end user (the patient with pain). This information carries with it substantial public policy and regulatory implications. The 2020 National Survey on Drug Use and Health asked 9.3 million non-medical users of prescription opioids how they obtained their most recently used drugs [104]. Among persons 12 years of age or older, 47.2% obtained their prescription opioids from a friend or relative. Of this, 34.4% got the prescription opioids from a friend or relative for free, 9.2% bought them from a friend or relative, and 3.7% took them from a friend or relative without asking. Another 42.0% got their opioids through a prescription from one doctor (vs. 35.4% in 2016) [104]. Less frequent sources included a drug dealer or other stranger (6.2%); multiple doctors (1.0%); theft from a doctor's office, clinic, hospital, or pharmacy (0.6%) (vs. 0.7% in 2016); and some other way (3.1%) [104].

As discussed, UDTs can give insight into patients who are misusing opioids. A random sample of UDT results from 800 patients with pain treated at a Veterans Affairs facility found that 25.2% were negative for the prescribed opioid while 19.5% were positive for an illicit drug/unreported opioid [105]. Negative UDT results for the prescribed opioid do not necessarily indicate diversion but may indicate the patient halted his/her use due to side effects, lack of efficacy, or pain remission. The concern arises over the increasingly stringent climate surrounding clinical decision-making regarding aberrant UDT results and that a negative result for the prescribed opioid or a positive UDT may serve as the pretense to terminate a patient rather than guide him/her into addiction treatment or an alternative pain management program [106].

In addition to aberrant urine screens, there are certain behaviors that are suggestive of an emerging opioid use disorder. The most suggestive behaviors are [82; 107; 108]:

- Selling medications
- Prescription forgery or alteration
- Injecting medications meant for oral use
- Obtaining medications from nonmedical sources
- Resisting medication change despite worsening function or significant negative effects
- Loss of control over alcohol use
- Using illegal drugs or non-prescribed controlled substances
- Recurrent episodes of:
  - Prescription loss or theft
  - Obtaining opioids from other providers in violation of a treatment agreement

  - Unsanctioned dose escalation
  - Running out of medication and requesting early refills

Behaviors with less association with opioid misuse include [82; 107; 108]:

- Aggressive demands for more drug
- Asking for specific medications
- Stockpiling medications during times when pain is less severe
- Using pain medications to treat other symptoms
- Reluctance to decrease opioid dosing once stable
- In the earlier stages of treatment:
  - Increasing medication dosing without provider permission
  - Obtaining prescriptions from sources other than the pain provider
  - Sharing or borrowing similar medications from friends/family

INTERVENTIONS FOR SUSPECTED OR KNOWN DRUG DIVERSION

There are a number of actions that prescribers and dispensers can take to prevent or intervene in cases of drug diversion. These actions can be generally categorized based on the various mechanisms of drug diversion.

Prevention is the best approach to addressing drug diversion. As noted, the most common source of nonmedical use of prescribed opioids is from a family member or friend, through sharing, buying, or stealing. To avoid drug sharing among patients, healthcare professionals should educate patients on the dangers of sharing opioids and stress that "doing prescription drugs" is the same as "using street drugs" [83]. In addition, patients should be aware of the many options available to treat chronic pain aside from opioids. As stated, to prevent theft, patients should be advised to keep medications in a private place and to refrain from telling others about the medications being used.

Communication among providers and pharmacies can help to avoid inappropriate attainment of prescription drugs through "doctor shopping." Prescribers should keep complete and up-to-date records for all controlled substance prescribing. When possible, electronic medical records should be integrated between pharmacies, hospitals, and managed care organizations [83]. It is also best practice to periodically request a report from the E-FORCSE to evaluate the prescribing of opioids to your patients by other providers [39; 83].

When dealing with patients suspected of drug seeking/diversion, first inquire about prescription, over-the-counter, and illicit drug use and perform a thorough examination [83; 109]. Pill counting and/or UDT may be necessary to investigate possible drug misuse. Photo identification or other form of identification and social security number may be required prior to dispensing the drug, with proof of identity documented fully. If a patient is displaying suspicious behaviors, consider prescribing for limited quantities [109].

If a patient is found to be abusing prescribed opioids, this is considered a violation of the treatment agreement and the clinician must make the decision whether or not to continue the therapeutic relationship. If the relationship is terminated, it must be done ethically and legally. The most significant issue is the risk of patient abandonment, which is defined as ending a relationship with a patient without consideration of continuity of care and without providing notice to the patient. The American Medical Association Code of Ethics states that "physicians' fiduciary responsibility to patients entails an obligation to support continuity of care for their patients" [110]. While physicians have the option of withdrawing from a case, they cannot do so without giving notice to the patient, the relatives, or responsible friends sufficiently long in advance of withdrawal to permit another medical attendant to be secured or to facilitate the transfer of care, when appropriate [110]. The notice of termination should be sent in writing, should specifically note the cause(s) for the termination, and should give a period of time prior to termination, usually 30 days [111]. Patients may also be given resources and/or recommendations to help them locate a new clinician.

Patients with chronic pain found to have an ongoing substance abuse problem or addiction should be referred to a pain specialist for continued treatment. Theft or loss of controlled substances is reported to the DEA. If drug diversion has occurred, the activity should be documented and a report to law enforcement should be made [112].

CASE STUDY

An unemployed man, 64 years of age, is brought to an emergency department by ambulance, after his wife returned from work to find him lying on the couch, difficult to arouse and incoherent. He has a past history of hypertension, diabetes (non-insulin dependent), mild chronic obstructive pulmonary disease, and chronic back and shoulder pain, for which he has been prescribed hydrocodone/acetaminophen for many years. His wife reports that while he seemed his usual self when she left for work that morning, he had, in recent weeks, been more withdrawn socially, less active, and complained of greater discomfort from the back and shoulder pain. She knows little about his actual medication usage and expresses concern that he may have been taking more than the prescribed amount of "pain medicine."

On evaluation, the patient is somnolent and arouses to stimulation but is non-communicative and unable to follow commands. His blood pressure is normal, he is afebrile, and there are no focal neurologic deficits. Oxygen saturation, serum glucose, and routine laboratory studies (blood counts and

metabolic profile) are normal except for mild elevation in blood urea nitrogen (BUN) and creatinine; the urine drug screen is negative except for opioids. Additional history from the family indicates that the patient has been admitted to other hospitals twice in the past three years with a similar presentation and recovered rapidly each time "without anything being found."

Following admission, the patient remains stable-to-improved over the next 12 to 18 hours. By the following day, he is awake and conversant and looks comfortable. On direct questioning, he reports recent symptoms of depression but no suicidal ideation. The patient describes an increased preoccupation with his pain syndrome, difficulty sleeping at night, and little physical activity during the day, in part because of physical discomfort. He is vague about his medication regimen and admits to taking "occasional" extra doses of hydrocodone for pain relief.

The family is instructed to bring in all his pill bottles from home, which they do. In addition to the hydrocodone prescribed by his primary care physician, there is a recent refill of a prescription for the medication given to the patient at the time of his last hospital discharge six months earlier.

ASSESSMENT

A full evaluation, including radiographic studies and consultation with psychiatry and physical therapy, is completed. The working diagnosis for the patient's acute illness is toxic encephalopathy caused by the sedative side effects of opioid medication on the CNS. It is explained that the combination of his advancing age and diabetes likely reduced the efficiency of his kidneys in clearing the medication and its metabolites, making him more susceptible to CNS sedation. It is noted that the patient and his wife have little understanding of the rationale, proper use and safeguards, potential side effects, and limited effectiveness of opioid use for chronic pain.

In addition, the patient is diagnosed with poorly controlled chronic pain syndrome secondary to osteoarthritis and degenerative disc disease; exacerbating factors include deconditioning and reactive depression. The use of an opioid analgesic, at least for the near term, is considered appropriate, if dosed properly, monitored closely, and integrated into a comprehensive, multidisciplinary plan that includes treatment of depression and the use of adjunctive, nonpharmacologic modalities of care. In the setting of possible early diabetic nephropathy, the option of utilizing an NSAID, except for very brief periods of break-through pain, is not considered to be a safe option.

At discharge, and in consultation with his primary care physician, a written treatment and management plan addressing all aspects of the patient's care is presented to the patient and his wife for discussion and consent. Among the key issues addressed are:

- Goals: Improvement in subjective pain experience; improved function of daily living manifested by regular walking exercise and improved social interaction with family and friends; relief of depression; and in the long-term, anticipated withdrawal of opioid medication and resumption of part-time work and/or volunteer community activity
- Outpatient physical therapy and back exercise program to increase core muscular strength, improve flexibility, reduce pain, and increase exercise tolerance
- Patient and family counseling regarding the safe use, dosage regulation, side effects, and proper disposal of opioid medication
- Joint patient-physician responsibilities as regards to regular follow-up, monitoring of goals and treatment effectiveness, avoidance of "doctor-shopping," and assent to single provider for prescription medication

FOLLOW-UP

On follow-up six weeks after discharge, the patient is noticeably improved. He reports that he feels stronger and is sleeping better. His affect is brighter, and he is getting out more. He has maintained his physical therapy and exercise routine and is compliant with his medication. Though he still has pain, it is noticeably less and he is coping better. He and his wife are encouraged by his progress, particularly in regard to his improved functional status.

CONCLUSION

For patients suffering from pain, prescribed opioid analgesics may substantially lessen pain, distress, and impairment. Inappropriate overprescribing and overdose related to opioid analgesics increased dramatically in the 2000s. These trends are in multi-year reversal, but patient safety and risk mitigation remains no less important, and clinical tools, guidelines, and recommendations are available for use when prescribing opioids to patients with pain. By implementing these tools, the clinician can effectively address issues related to the clinical management of opioid prescribing, opioid risk management, regulations surrounding the prescribing of opioids, and problematic opioid use by patients. In doing so, healthcare professionals are more likely to achieve a balance between the benefits and risks of opioid prescribing, optimize patient attainment of therapeutic goals, and avoid the risk to patient outcome, public health, and viability of their own practice imposed by deficits in knowledge.

Customer Information/Answer Sheet insert located between pages 60–61.

COURSE TEST - #91152 STRATEGIES FOR APPROPRIATE OPIOID PRESCRIBING: THE FLORIDA APRN/PA REQUIREMENT

This is an open book test. Please record your responses on the Answer Sheet.
A passing grade of at least 70% must be achieved in order to receive credit for this course.

This 3 contact hour activity must be completed by August 31, 2025.

1. **Inappropriate opioid analgesic prescribing for pain is defined as the non-prescribing, inadequate prescribing, excessive prescribing, or continued prescribing despite evidence of ineffectiveness of opioids.**
   A) True
   B) False

2. **The aging population contributes to the increasing prevalence of chronic pain in the United States.**
   A) True
   B) False

3. **In the absence of other risk factors, a patient prescribed opioids for chronic pain who has no personal or family history of alcohol or substance abuse is considered at medium risk for developing problematic opioid behavioral responses.**
   A) True
   B) False

4. **The Screener and Opioid Assessment for Patients with Pain-Revised (SOAPP-R) consists of five items.**
   A) True
   B) False

5. **When implementing a chronic pain treatment plan that involves the use of opioids, the patient should be frequently reassessed for changes in pain origin, health, and function.**
   A) True
   B) False

6. **For patients considered at medium risk for misuse of prescription opioids, urine drug testing should be completed every month.**
   A) True
   B) False

7. **There are no universal recommendations for the proper disposal of unused opioids.**
   A) True
   B) False

8. **The Office of National Drug Control Policy is responsible for formulating federal standards for the handling of controlled substances.**
   A) True
   B) False

9. **All clinicians who prescribe or dispense controlled substances are required to report the action to the Electronic Florida Online Reporting of Controlled Substances Evaluation (E-FORCSE) within one business day.**
   A) True
   B) False

10. **Injecting medications meant for oral use is suggestive of an emerging opioid use disorder.**
    A) True
    B) False

Be sure to transfer your answers to the Answer Sheet insert located between pages 60–61.
PLEASE NOTE: Your postmark or facsimile date will be used as your test completion date.

Pharmacologic and Medical Advances in Obesity Management

Audience
This course is designed for all nurses, physicians, and allied professionals involved in the care of patients who are overweight or obese.

Course Objective
The purpose of this course is to ensure that providers have current and accurate knowledge regarding the available pharmacologic and surgical options to improve outcomes among their patients, with the ultimate goal of improving patient care and outcomes.

Learning Objectives
Upon completion of this course, you should be able to:

1. Define obesity and related conditions.
2. Outline approaches to the clinical assessment of patients who are overweight or obese.
3. Review the epidemiology of obesity, including the evolving obesity epidemic.
4. Compare and contrast available energy expenditure research.
5. Describe the role of diet, physical activity, and body mass index (BMI) on the etiology of obesity.
6. Identify other etiologic factors contributing to the obesity epidemic.
7. Evaluate current knowledge of energy balance and defense of body weight in the regulation of body weight.
8. Define the four pillars of obesity management.
9. Analyze pharmacotherapeutic options for monogenic obesity syndromes.
10. Compare available pharmacotherapy for short- and long-term management of obesity.
11. Identify investigational antiobesity medications in development.
12. Review prescribing tips to improve the clinical use of antiobesity medications.
13. Outline available metabolic and bariatric surgical interventions, including indications, contraindications, and efficacy.
14. Discuss the role of endoscopic bariatric therapies in the management of obesity.
15. Describe the physiology and pathophysiology underlying obesity and driving advances in the management of obesity.

Faculty
Mark Rose, BS, MA, LP, is a licensed psychologist in the State of Minnesota with a private consulting practice and a medical research analyst with a biomedical communications firm. Earlier healthcare technology assessment work led to medical device and pharmaceutical sector experience in new product development involving cancer ablative devices and pain therapeutics. Along with substantial experience in addiction research, Mr. Rose has contributed to the authorship of numerous papers on CNS, oncology, and other medical disorders. He is the lead author of papers published in peer-reviewed addiction, psychiatry, and pain medicine journals and has written books on prescription opioids and alcoholism published by the Hazelden Foundation. He also serves as an Expert Advisor and Expert Witness to law firms that represent disability claimants or criminal defendants on cases related to chronic pain, psychiatric/substance use disorders, and acute pharmacologic/toxicologic effects. Mr. Rose is on the Board of Directors of the Minneapolis-based International Institute of Anti-Aging Medicine and is a member of several professional organizations.

Faculty Disclosure
Contributing faculty, Mark Rose, BS, MA, LP, has disclosed no relevant financial relationship with any product manufacturer or service provider mentioned.

Division Planner
Mary Franks, MSN, APRN, FNP-C

Senior Director of Development and Academic Affairs
Sarah Campbell

Division Planner/Director Disclosure
The division planner and director have disclosed no relevant financial relationship with any product manufacturer or service provider mentioned.

A full Works Cited list is available online at www.NetCE.com. ***Mention of commercial products does not indicate endorsement.***

Accreditations & Approvals

In support of improving patient care, NetCE is jointly accredited by the Accreditation Council for Continuing Medical Education (ACCME), the Accreditation Council for Pharmacy Education (ACPE), and the American Nurses Credentialing Center (ANCC), to provide continuing education for the healthcare team.

Designations of Credit

NetCE designates this continuing education activity for 15 ANCC contact hours.

This activity was planned by and for the healthcare team, and learners will receive 15 Interprofessional Continuing Education (IPCE) credits for learning and change.

NetCE designates this continuing education activity for 18 hours for Alabama nurses.

NetCE designates this continuing education activity for 12 pharmacotherapeutic/pharmacology contact hours.

AACN Synergy CERP Category A.

Individual State Nursing Approvals

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INTRODUCTION

During 2017–2018 in the United States, 42.4% of adults were obese and 9.2% were severely obese [1]. By 2030, the expected prevalence will increase for both obesity (49%) and severe obesity (24%) [2].

Obesity is a chronic, progressive, relapsing, multifactorial disease involving far more than excessive fat. Obesity leads to biomechanical complications such as obstructive sleep apnea and osteoarthritis. The pathogenic adipose tissue promotes insulin resistance, metabolic syndrome, hypertension, dyslipidemia, and type 2 diabetes, progressing to cardiometabolic endpoints of nonalcoholic steatohepatitis (NASH), cardiovascular disease, and premature mortality [3].

Weight loss maintained long-term dose dependently reduces the cardiometabolic morbidity—the more weight lost, the better the outcome. This may require 16% to 20% to reduce endpoint risks, which is seldom possible with standard lifestyle intervention [4; 5; 6].

Patients may lose 5% to 10% of initial weight over 16 to 26 weeks with caloric restriction and increased physical activity, but maintaining the lost weight is very difficult because complex biological mechanisms defend the established body-fat mass [7; 8; 9]. Weight loss triggers biological pressures to regain weight through increased hunger, enhanced neural responses to food cues, heightened drive to consume energy-dense foods, and reduced metabolic rate [10; 11; 12]. Healthy diet, exercise, and behavioral interventions are crucial components of management, but seldom achieve and maintain weight loss sufficient to reduce cardiometabolic morbidities [13; 14].

BMI DEFINITIONS OF WEIGHT			
Weight Category	**BMI Definition (kg/m^2)**		
	Adult	**Adult, East Asian**	**Pediatric[a]**
Underweight	<18.5	<18.5	<5th percentile
Normal	18.5–24.9	18.5–22.9	5th–85th percentile
Overweight	25–29.9	23–24.9	≥85th percentile
Class I obesity	30–34.9	25–29.9	Obesity: ≥95th percentile
Class II obesity	35–39.9	30–34.9	
Class III obesity (severe obesity)	≥40	≥35	Severe obesity: ≥120% of the 95th percentile
[a]Based on sex-specific BMI for age			
Source: [22; 25; 26]			*Table 1*

However, more recent and investigational antiobesity medications show average long-term weight loss previously unattainable by nonsurgical treatment, including semaglutide (15%), combination cagrilintide/semaglutide (CagriSema) (17%), tirzepatide (21%), and retatrutide (24%) [3]. Bariatric surgery can result in dramatic weight loss (≥30%) and remission of type 2 diabetes persisting years if not decades. Minimally invasive procedures show promising results while reducing the risks of surgery. A newer treat-to-target approach with antiobesity medications uses percent weight loss as a biomarker for individualized weight reduction necessary to improve clinical outcomes [3]. Obesity requires the treatment intensity and chronicity of other complex, chronic metabolic diseases, which may involve both bariatric surgery and multi-year antiobesity medications [15].

The widely accepted causes of the obesity epidemic, increasingly sedentary lifestyles and reduced physical activity with increased fatty food intake, are largely unsupported [16; 17]. Similarly, the notion of obesity as a consequence of unhealthy personal choices reversible through diet and exercise, and other erroneous beliefs, are widely held by healthcare professionals [18].

Knowledge gaps, misperceptions and bias are highly prevalent; foremost is the failure to recognize and treat obesity as a disease [19; 20]. Among patients eligible for antiobesity pharmacotherapy and bariatric surgery, only 2% and 1%, respectively, receive the respective treatment [15; 20].

The prevalence of obesity continues increasing, but obesity medicine is in its infancy, and formal education and training in obesity care is absent from most medical curricula. Primary care practitioners are among the only providers numerous enough to address the number of patients affected. The lack of any significant education in obesity biology, prevention, or treatment in most medical/nursing schools and postgraduate training programs makes the need for continuing education that much more critical [21].

DEFINITIONS OF OBESITY

The World Health Organization (WHO) codified the body mass index (BMI) as a screening index for obesity in 1995. Using weight in kilograms (kg) and height in meters (m), BMI is calculated by dividing weight (kg) by height squared (m^2), or kg/m^2 [22].

In adults, population-based actuarial studies placed the upper limit of normal BMI at 25.0, defined obesity as BMI >30.0, and designated a BMI between these values as overweight. BMI categories were created, in part, to emphasize the increased mortality risk associated with a BMI both below and above the normal range (18.5–24.9). The WHO further categorized obesity severity as Class I, II, and III (***Table 1***) [7; 23]. Pediatric overweight, obesity, and severe obesity are defined by sex-specific BMI for age using the Centers for Disease Control and Prevention (CDC) growth charts [24].

Subsequent studies in Korea and Japan found higher obesity-related morbidity and mortality at BMI levels below the WHO cutoff; thus, these national guidelines defined BMI ≥23 as overweight and ≥25 as obese [22]. In addition to these specific modifications to BMI, race and cultural issues related to obesity, eating, and physical activity should be considered.

In some cases, waist circumference is more accurate in clinical diagnosis, e.g., abdominal obesity. Abdominal or central obesity is defined as waist circumference ≥102 cm (40 in) in men and ≥88 cm (35 in) in women; and among East Asians, ≥90 cm in men and ≥85 cm in women [22; 31]. These are of value only for those with a BMI between 25.5 and 34.9. It is not useful to measure waist circumference in individuals with BMI >35, as such patients are already at increased risk.

The American Association of Clinical Endocrinology (AACE) designated obesity a chronic disease in 2012 [3; 27]. This was based on several points, including the fact that, like other chronic diseases, obesity has a complex pathophysiology

involving interactions among genes, biological factors, the environment, and behavior. It meets the three criteria that constitute a disease established by the American Medical Association (AMA) [28]:

- Outward signs or symptoms: In patients with obesity, an increase in adiposity, commonly assessed via BMI, is the primary outward sign or symptom.
- Causes morbidity or mortality: Obesity is associated with multiple complications that confer morbidity and mortality.
- Involves impaired function of ≥1 tissue: Two examples of abnormal tissue function are readily identified:
  - With expansion, adipose tissue becomes inflamed and the secretion of adipocytokines is dysregulated, resulting in alterations in metabolism and vasculature and the progression of cardiometabolic disease.
  - Interactions involving satiety hormones and central nervous system (CNS) feeding centers are abnormal, resulting in increased caloric intake and body mass.

The AMA formally recognized obesity as a chronic disease in 2013 and acknowledged it had become an alarming public health threat [28].

The Obesity Medicine Association (OMA) defines obesity as a chronic, progressive, relapsing, and treatable multifactorial, neurobehavioral disease in which increased body fat promotes adipose tissue dysfunction and abnormal fat mass physical forces, resulting in adverse metabolic, biomechanical, and psychosocial outcomes [29; 30].

CLINICAL ASSESSMENT

In 1990, the U.S. Department of Health and Human Services' Dietary Guidelines for Americans defined overweight as a BMI of at least 27 and obesity as a BMI of at least 30. Eight years later, the National Heart, Lung, and Blood Institute (NHLBI) of the National Institutes of Health (NIH) released guidelines that lowered the cutoff for overweight to a BMI of 25 but maintained the definition of obesity as a BMI of at least 30 [31]. (Note: Roughly, a BMI >25 corresponds to about 10% over one's ideal weight; a BMI >30 typically is an excess of 30 pounds for most people. These are rough estimates.) The term extreme (or morbid) obesity refers to obesity with a BMI greater than or equal to 40. These final definitions are consistent with definitions used by other national and international organizations, such as the WHO. BMI does have limitations as a measurement of overweight and obesity. Although BMI provides a more accurate measure of total body fat compared with body weight alone, it can be misinterpreted in some circumstances.

Although BMI is important, there is a growing body of evidence demonstrating the impact of central adiposity on obesity-related metabolic diseases, including diabetes [32]. A study was published that compared BMI, waist circumference, and waist-to-hip ratio in predicting the development of type 2 diabetes [33]. Researchers used information collected in the Health Professionals Follow-Up Study, a prospective cohort study of 27,270 men who were followed for 13 years. During the follow-up period, 884 men developed type 2 diabetes. Waist circumference was the best predictor. Men with waists greater than 34 inches were twice as likely to develop diabetes compared to men with smaller waist sizes (i.e., <34 inches); men with waist sizes greater than or equal to 40 inches were more than 12 times more likely to develop diabetes than men with smaller waist sizes [33]. In another study, researchers looked at waist circumference, waist-to-hip ratio, and central and subcutaneous adipose tissue measured by computed tomography (CT) as predictors of diabetes in people participating in the Diabetes Prevention Program [34]. They found that waist-to-hip ratio and waist circumference predicted diabetes; CT measurement of central adiposity also predicted diabetes but was not found to offer an important advantage over the simpler measurements. Subcutaneous adipose tissue, on the other hand, did not predict diabetes.

In 2023, the AMA adopted a policy that recognizes the issues with BMI measurement (e.g., historical harm, no consideration of gender/ethnicity) and suggests that it be used in conjunction with other valid measures of risk, including but not limited to visceral fat, body adiposity index, body composition, relative fat mass, waist circumference, and genetic or metabolic factors [35].

The AMA policy recognizes that [35]:

- BMI is significantly correlated with the amount of fat mass in the general population but loses predictability when applied on an individual level.
- Relative body shape and composition heterogeneity across race and ethnic groups, sexes, genders, and age-span are essential to consider when applying BMI as a measure of adiposity.
- BMI should not be the sole criterion used to deny appropriate insurance reimbursement.

The AMA also modified existing policy on the clinical utility of measuring BMI, body composition, adiposity, and waist circumference to support greater emphasis on education about the risk differences within and between demographic groups.

EPIDEMIOLOGY

The National Health and Nutrition Examination Survey (NHANES) is considered the authoritative source for data on obesity, diet, and related health trends [16]. NHANES is a nationally representative cross-sectional study on the health and nutritional status of noninstitutionalized U.S. civilians selected through a complex, multistage probability design. Following NHANES I (1971–1975), NHANES II (1976–1980), and NHANES III (1988–1994), biennial implementation of NHANES began in 1999 [36; 37; 38]. The U.S. Department of Agriculture (USDA) Household Food Consumption Survey

PREVALENCE OF OBESITY AND SEVERE OBESITY AMONG ADULTS AGED 20–74 YEARS						
Year	**Percent of Population Considered Obese (BMI ≥30 kg/m²)**			**Percent of Population Considered Severely Obese (BMI ≥40 kg/m²)**		
	Total	**Male**	**Female**	**Total**	**Male**	**Female**
1960–1962	13.4%	10.7%	15.8%	0.9%	0.3%	1.4%
1971–1974	14.5%	12.1%	16.6%	1.3%	0.6%	2.0%
1976–1980	15.0%	12.7%	17.0%	1.4%	0.4%	2.2%
1988–1994	23.2%	20.5%	25.9%	3.0%	1.8%	4.1%
1999–2000	30.9%	27.7%	34.0%	5.0%	3.3%	6.6%
2001	31.2%	28.3%	34.1%	5.4%	3.9%	6.8%
2003	32.9%	31.7%	34.0%	5.1%	3.0%	7.3%
2005	35.1%	33.8%	36.3%	6.2%	4.3%	7.9%
2007	34.3%	32.5%	36.2%	6.0%	4.4%	7.6%
2009	36.1%	35.9%	36.1%	6.6%	4.6%	8.5%
2011	35.3%	33.9%	36.6%	6.6%	4.5%	8.6%
2013	38.2%	35.5%	41.0%	8.1%	5.7%	10.5%
2015	40.0%	38.3%	41.6%	8.0%	5.9%	10.1%
2017–2018	42.8%	43.5%	42.1%	9.6%	7.3%	12.0%

Source: [41] *Table 2*

(1965) and the National Health Examination Survey (NHES; 1960–1962) preceded NHANES [36].

All NHANES are conducted in-person by trained interviewers using anthropometric measurements and 24-hour dietary recall questionnaires with standardized probe questions to facilitate memory. Past-month assessment of physical activity began with NHANES III [39]. A follow-up phone interview was added in 2003 [37].

The time point used as baseline for evaluating obesity prevalence trends can importantly impact the conclusions. Because prevalence estimates can fluctuate markedly between study waves, including data from several study waves before and after the period of interest can help determine whether prevalence changes at any given time point reflect a transient anomaly or a true trend [40].

In this section, all prevalence data from 1971 to the present was obtained from NHANES except where noted. In addition, all data pertain to the United States unless otherwise mentioned.

POPULATION PREVALENCE

Adults 20 Years of Age and Older

NHES 1960–1962 included adults 18 to 79 years of age. NHANES 1971–1974 and 1976–1980 excluded individuals age older than 74 years. Therefore, ***Table 2*** is limited to adults 20 to 74 years of age for consistency in long-term trends. Prevalence rates are age-adjusted to the U.S. Census 2000 estimates. As the table demonstrates, the 1980s and 1990s mark the onset of the obesity epidemic.

Following slow increases during the 1960s and 1970s, obesity rates increased sharply through the early 2000s, modestly from 2005 to 2011, then continued climbing through 2017–2018. Male obesity surpassed female rates for the first time in 2017–2018.

Female severe obesity increased 36.4% from 1960–1962 to 1976–1980, in contrast to slowly increasing obesity and male severe obesity rates, and have exceeded male rates throughout 1960 to 2018 by a wide margin. Including ages 20 years and older lowers the 2017–2018 prevalence for obesity (42.4%) and severe obesity (9.2%), which increased approximately 39% and 96%, respectively, from 1999–2000 [1].

During 2017–2018, non-Hispanic Black Americans (49.9%) had the highest age-adjusted obesity prevalence, followed by Hispanic Americans (45.6%), non-Hispanic White Americans (41.4%), and non-Hispanic Asian Americans (16.1%), who also have lower BMI thresholds for adiposopathic (adipocyte and adipose tissue dysfunction) complications [1; 29].

The association between obesity and income or educational level is complex and differs by sex and race/ethnicity. Overall, men and women with college degrees had lower obesity prevalence compared with those with less education [43].

The same obesity and education pattern occurred among non-Hispanic White, non-Hispanic Black, and Hispanic women, and non-Hispanic White men, but the differences were not all significant. Among non-Hispanic Black men, obesity prevalence increased with educational attainment. No differences

PREVALENCE OF OBESITY AND SEVERE OBESITY AMONG THOSE 2 TO 19 YEARS OF AGE						
Year	Obese			Severely Obese		
	Total	Boys	Girls	Total	Boys	Girls
1966–1970	4.6%[a]	N/A	N/A	N/A	N/A	N/A
1971–1974	5.2%	5.3%	5.1%	1.0%	1.0%	1.0%
1976–1980	5.5%	5.4%	5.6%	1.3%	1.2%	1.3%
1988–1994	10.0%	10.2%	9.8%	2.6%	2.7%	2.6%
1999–2000	13.9%	14.0%	13.8%	3.6%	3.7%	3.6%
2001	15.4%	16.4%	14.3%	5.2%	5.1%	4.2%
2003	17.1%	18.2%	16.0%	5.1%	5.4%	4.7%
2005	15.4%	15.9%	14.9%	4.7%	4.9%	4.5%
2007	16.8%	17.7%	15.9%	4.9%	5.5%	4.3%
2009	16.9%	18.6%	15.0%	5.6%	6.4%	4.7%
2011	16.9%	16.7%	17.2%	5.6%	5.7%	5.5%
2013	17.2%	17.2%	17.1%	6.0%	5.6%	6.3%
2015	18.5%	19.1%	17.8%	5.6%	6.3%	4.9%
2017–2018	19.3%	20.5%	18.0%	6.1%	6.9%	5.2%
N/A = not available. [a]Ages 12 to 17 years only						
Source: [42]						*Table 3*

in obesity prevalence by education level were noted among non-Hispanic Asian women and men or Hispanic men [43].

Among men, obesity prevalence was lower in the lowest and highest income groups compared with the middle-income group. This pattern occurred among non-Hispanic White and Hispanic men. Obesity prevalence was higher in the highest income group than in the lowest income group among non-Hispanic Black men [43].

Severe obesity patterns illustrate demographic differences, by sex (women 11.5%, men 6.9%), age (40 to 59 years 11.5%, 20 to 39 years 9.1%, and ≥60 years 5.8%), and race/ethnicity (non-Hispanic Black 13.8%, non-Hispanic White 9.3%, Hispanic 7.9%, and non-Hispanic Asian 2.0%) [1].

By 2030, it is projected that 48.9% of adults will be obese, 24.2% will have severe obesity, with severe obesity projected to become the most common BMI category among women (27.6%), non-Hispanic Black adults (31.7%), and low-income adults (31.7%) [2].

Obesity prevalence studies using higher BMI cut-offs suggest a population shift toward the upper end of the BMI distribution. For example, BMI ≥35 was greater than men than women in 1959 (1%/5%), 1988–1991 (5%/9%), and 2007–2008 (11%/19%) [40].

Defining abdominal obesity as waist circumference in men (≥102 cm) and women (≥88 cm), increasing prevalence rates were found [40]:

- Overall: 52.5% in 2006–2010, compared with 36.0% in 1986–1990
- Men: 42.0% in 2009–2010, compared with 27.5% in 1986–1990 and 29.1% in 1988–1994
- Women: 61.5% in 2009–2010, compared with 44.3% in 1986–1990 and 46.0% in 1988–1994

Military-Aged Population

Obesity and physical inactivity among the military-aged U.S. civilian population (17 to 42 years of age) are considered potential national security threats because of their impact on military recruitment. Fitness eligibility for military service is defined as BMI 19.0–27.5, and adequate physical activity as ≥300 minutes per week of moderate-intensity aerobic physical activity [44].

Among military-aged participants in the 2015–2020 NHANES, only 34.3% were BMI- and activity-eligible. The prevalence of eligible and active status was higher among men, persons who were younger and non-Hispanic White, college graduates, and those with higher family income than among their counterparts [44].

The BMI-ineligibility in this study exceeds those in previous studies. This upward trend in military ineligibility mirrors the increase in population prevalence of obesity. This study also draws attention to the military preparedness repercussions of the inequitable distribution of unhealthy weight and inadequate physical activity [44].

PREVALENCE OF OBESITY AND SEVERE OBESITY AMONG THOSE 2 TO 19 YEARS OF AGE					
Group	**Incidence per 1,000 Person-Years**				
	2001–2005	**2005–2009**	**2009–2013**	**2013–2017**	**Total (2001–2017)**
Overall	34.1	36.4	34.5	40.7	28.1
Female	30.9	35.6	33.7	38.1	26.5
Male	37.6	37.1	35.6	44.0	30.2
White	31.6	33.8	32.0	39.1	26.2
Black	60.3	62.0	61.4	57.9	47.9
Less than high school	44.8	55.8	46.1	50.3	39.4
High school diploma	38.1	45.1	45.8	50.1	34.5
More than high school	30.6	30.9	28.7	36.8	24.7

Source: [45] *Table 4*

Pediatric Population

Although adult obesity is the focus of this course, long-term population trends in pediatric obesity (age 2 to 19 years) provide an informative companion to adult trends. In ***Table 3***, note that pediatric obesity increased >300% from 1976–1980 to 2003, but only 11.4% from 2003 to 2017–2018. Compared with adult obesity, pediatric obesity shows a smaller relative increase over the past 20 years, and pediatric severe obesity has consistently greater prevalence in boys.

INCIDENCE

Using the nationally representative Panel Study of Income Dynamics (PSID), the incidence of new obesity cases (i.e., the first time a person has a BMI ≥30) was examined from 2001 to 2017 among 13,888 adults ≥20 years of age [45]. Obesity incidence, stable over 2001–2005 to 2009–2013, increased 18% in 2013–2017 to 40.7 per 1,000 person-years. This means that, on average, 4% of the adult population entered obese BMI each year during 2013–2017 (***Table 4***). This is similar to obesity prevalence, which began rising notably after 2011 following modest increase from 2005 to 2011.

During 2001–2017, Black individuals had higher obesity incidence than White individuals, which was particularly high in Black women (57.9 per 1,000 person-years) and Black young adults 20 to 29 years of age (65.5 per 1,000 person-years). Over the study period, the relative difference in obesity risk between Black and White persons decreased from 92% to 43%, but large race disparities remained in 2013–2017, consistent with obesity prevalence data.

By educational level, the incidence of obesity increased most for those who had a high school diploma (32% increase) followed by those with an education beyond high school (20%), whereas it remained roughly the same for those with less than a high school diploma. Those with less than high-school education had higher obesity incidence than those with education beyond high-school (39.4 per 1,000 person-years vs 24.7 per 1,000 person-years) [45].

By age, obesity incidence was highest in young adults (34.1 per 1,000 person-years) and declined with age (70+ years: 18.9 per 1,000 person-years). As obesity prevalence climbs, the pool of never-obese adults who may develop first-time obesity becomes smaller, which partly explains the higher incidence at younger ages [45].

With the obesity risk of overweight persons seven times higher than normal-weight persons (62.1 per 1,000 person-years vs 8.8 per 1,000 person-years), the authors state overweight should not be considered a "new normal," but a transition phase that often cascades into obesity. The obesity incidence of young adults with overweight (97.0 per 1,000 person-years) was the highest of any subgroup examined [45].

PERSONAL AND SOCIETAL BURDEN OF OBESITY

As noted, obesity is a progressive, chronic disease associated with a spectrum of complications and poor outcomes, including premature death [46]. Common clinical consequences of obesity are adiposopathic or metabolic (e.g., type 2 diabetes, hypertension, dyslipidemia, cardiovascular disease, cancer) and biomechanical stress damage from the pathogenic physical forces of excessive body fat (e.g., orthopedic abnormalities leading to immobility, sleep apnea) [29; 46]. Obesity shares many pathogenic processes of aging. The greater the age or obesity, the greater the mortality. In patients with BMI 55–60, an estimated 14 years of life is lost primarily from heart disease, cancer, and type 2 diabetes [18].

Excessive body fat is a cause of 13 cancers, including esophageal, gastric, cardiac, colorectal, liver, gallbladder, pancreas, meningioma, postmenopausal breast, endometrium, ovary, kidney, thyroid, and multiple myeloma [47]. A 5-point increase in BMI is strongly associated with increased risk of thyroid and colon cancers in men, endometrial and gallbladder cancers in women, and esophageal adenocarcinoma and renal cancers in both sexes [46]. From 2004 to 2015, the prevalence of these cancers increased 7% while cancers not known to be related

ALL-CAUSE MORTALITY BY BMI		
Weight Category	**BMI**	**Hazard Ratio**
Underweight	**15.0–18.4**	**1.51**
Healthy or normal	18.5–19.9	1.13
	20.0–22.4	1.00
	22.5–24.9	1.00
Overweight	25.0–27.4	1.07
	27.5–29.9	1.20
Class I obesity	30.0–34.9	1.45
Class II obesity	35.0–39.9	1.94
Class III obesity	≥40	2.76
Source: [53]		*Table 5*

to excessive body fat decreased 13% [46]. Overweight- and obesity-related cancers account for about 40% of all cancers. With approximately 70% of adults overweight or obese, promoting the maintenance of weight loss to decrease cancer risk is critical [47].

Obesity is also associated with increased susceptibility to nosocomial infections, wound infections, and influenza pandemics. Obesity increased the risk of COVID-19-related hospitalization (113%), intensive care admission (74%), and death (48%) [48].

Previously associated with high-income Western countries, obesity has become a growing problem in developing countries and among low-income populations. For the first time in human history, the number of overweight people exceeds the number of underweight people. Globally, the estimated $2.0 trillion annual economic impact of obesity is similar to smoking ($2.1 trillion), or armed violence, war, and terrorism combined ($2.1 trillion) [49].

In the United States, medical expenditures by BMI show a J-shaped curve, with higher costs in general for women and the lowest expenditures at a BMI of 20.5 for women and 23.5 for men. Among persons with BMI greater than 30, predicted costs continued to increase linearly, with each one-unit increase in BMI associated with an additional cost of $253 per person on average [2]. In 2019, the medical cost of adult obesity was $173 billion, with most costs from severe obesity; pediatric obesity was associated with medical costs of $1.32 billion. Adults with BMI 20–24 had the lowest medical costs in all ages [50].

Obesity-related costs increase with age starting around 30 years of age. This is similar to findings of increased relative risks of obesity-related morbidity and mortality starting at 25 to 29 years of age and 35 years of age and older, respectively. The high costs at higher levels of BMI are especially concerning given that the adult prevalence of severe obesity is projected to increase further [50].

MORTALITY

In 2013, an influential meta-analysis by Flegel et al. concluded that, relative to normal weight, class 1 obesity (BMI 30.0–34.9) was not associated with excess all-cause mortality and overweight was associated with lower all-cause mortality [51]. The hypothetically protective metabolic effects of increased body fat in apparently healthy individuals was advanced to support this claim [52].

However, uncontrolled variables may have biased the results. A subsequent meta-analysis of 239 prospective studies on BMI and mortality limited bias from confounding factors and reverse causality. Of 10.6 million participants in North America, Europe, Australia and New Zealand, and Asia, analyses was restricted to 3.9 million never-smokers without specific chronic diseases at enrollment who were still followed after five years (median follow-up: 13.7 years). The six WHO-defined BMI categories were subdivided into nine BMI groups to avoid merging importantly different risks [53].

All-cause mortality (***Table 5***), lowest at BMI 20–24.9, increased significantly with greater distance below and above this range, (e.g., 51% for BMI <18.5 and 276% for BMI ≥40 compared with BMI 20–24.9). Each 5-point increase in BMI above 25.0 increased the risk of all-cause mortality by 39% in Europe and east Asia, 31% in Australia/New Zealand, and 29% in North America, and was greater in younger than older people (52% at 35 to 49 years of age; 21% at 70 to 89 years of age) and in men than women (51% vs 30%). The hazard ratio for class 1 obesity in men (1.70) and women (1.37) suggests that men have almost double the proportional excess mortality of women (70% vs 37%).

The proportion of all-cause mortality attributable to overweight or obesity was 19% in North America, 16% in Australia/New Zealand, 14% in Europe, and 5% in east Asia [53].

The results challenge assertions that overweight and class I obesity are not associated with higher mortality risk. The results section in this paper also reproduced the findings of Flegal et al., before applying restrictions that yielded the final results [53]. The results also suggest a J-shaped curve for mortality risk below and above BMI 20–25, which includes normal-range BMI 18.5–20.

ETIOLOGY OF THE OBESITY EPIDEMIC

The development of obesity is commonly understood through the energy balance model. Energy refers calories from macronutrients (carbohydrate, protein, and fat) in meals. Energy (i.e., calories) can be ingested (intake) or burned (expenditure). Energy balance is when energy intake and expenditure are equal. In positive energy balance, energy intake exceeds expenditure. Long-term positive energy balance is considered the cause of adult obesity. Obesity, both societal and individual, is abundantly blamed on increasingly sedentary lifestyles and reduced physical activity, combined with increased fatty food intake.

Utilizing the NHANES and International Atomic Energy Agency (IAEA) databases, researchers have investigated population-level trends that may be affecting energy balance, including changes in diet, activity, and energy expenditure. The results challenge conventional wisdom about the causation of the obesity epidemic. These data are limited to U.S. adults.

DIET, PHYSICAL ACTIVITY, AND BMI

Dietary recommendations represent an important but neglected backdrop of population trends in weight-gain over the past 70 years. In the 1950s, the Diet-Heart Hypothesis (DHH) connected rising rates of coronary heart disease after World War II to high saturated fat intake: Because dietary saturated fat raises serum cholesterol and high cholesterol contributes to coronary heart disease, then saturated fat intake must also cause coronary heart disease [54]. The American Heart Association (AHA) promulgated the DHH and advocated reducing total fat consumption to 25% to 35% of calories and substituting polyunsaturated for saturated fatty acids to palliate high cholesterol in 1961 [55; 56; 57].

With little data to support the AHA's recommendation, the Minnesota Coronary Experiment (MCE) (1968–1973) was expected to provide definitive evidence. Ancel Keys, the co-investigator, had invented K-rations for the U.S. Army in WWII, devised the DHH and was also President of AHA. This double-blind randomized controlled trial, the largest and perhaps the most rigorously executed trial ever conducted on dietary change and mortality, included complete postmortem assessments. Replacement of saturated fatty acids with polyunsaturated fatty acids predictably lowered serum cholesterol. Paradoxically, MCE participants with greater reductions in cholesterol had higher mortality. The results of what would have been a landmark study remained unpublished for 43 years, until 2016 [58].

During this time, Congress formalized AHA's position and the DHH with the *Dietary Guidelines for Americans*, introduced in 1980 and updated every five years. The Surgeon General, National Research Council, and American Cancer Society also recommended low-fat/saturated fatty acid diets to reduce coronary heart disease and cancer. The *Dietary Guidelines for Americans* was pivotal in linking saturated fatty acids as a major cause of heart disease, obesity, and cancer, yet was initially opposed by some experts over potential unintended consequences, lack of evidence that lower dietary fat reduced heart disease, and evidence implicated sugar and refined carbohydrates instead of fats [57; 59; 60].

The 1980s *Dietary Guidelines for Americans* recommended reducing all fats and increasing carbohydrates to 55% of total calories, which was also proposed to help prevent overweight and obesity [36]. In 1990, total fat was capped at 30% of calories, later revised to 20% to 35%, which remained until 2010 [60]. Federal agencies and medical associations strongly supported a low-fat/saturated fatty acid, high-carbohydrate diet for everyone older than 2 years of age, and through 2008, advocated sugar as healthy for persons with diabetics and the general population [61]. The belief that dietary fat drives obesity and heart disease persists [1].

Macronutrient Intake and BMI: 1965–2011

Changes in macronutrient proportion of average daily calories and BMI have been examined in the context of dietary recommendations [36]. U.S. adults have largely followed dietary guidelines. From 1965 to 1999, total calories from fat decreased (46% to 32%) while carbohydrates concurrently increased (39% to 52%) [36]. From 1965 to 2011, the increased caloric share from carbohydrate explained 85% of increased BMI in men and 91% in women. Increases in total caloric intake since 1971 were unlikely to explain the increase in BMI [36]. In other words, increased carbohydrate proportionality, not total calories, drove rising BMI.

As discussed, the onset of rising obesity occurred during the 1980s and 1990s as the DHH became an ideology propagated by federal government dietary recommendations, public health policies, and popular health media, which these authors suggest may have initiated the obesity epidemic [36; 54; 63]. While observational data cannot establish causality, these and other findings suggest the origin of the obesity epidemic may be partially iatrogenic.

Dietary Changes: 1999–2016

From 1999 to 2016, data showed increases in total fat (1.2%) as proportion of diet, including saturated (0.36%), monounsaturated (0.19%), and polyunsaturated (0.65%) fatty acids; decreases in total (-2.02%) and low-quality (mostly sugar) (-3.25%) carbohydrates; increases in high-quality (1.23%) carbohydrates; and increased intake of whole grains, poultry, and nuts [37].

Opposing trends during 1999–2016 partly reversed those of 1971–2000, when emphasis on low-fat diets was associated with decreased fat intake and increased refined grains and added

sugar intake. During the 2000s, the benefits of healthy fats and plant sources of protein and harms of excess sugar became popularized, independent of dietary guidelines. Regardless of influence, dietary macronutrient intake during 1999–2016 shows clear evidence of improvement [37].

Caloric Intake, Physical Activity, and BMI: 1971–2008

Changes in physical activity, macronutrient intake, and BMI during 1971 to 2008 were examined using NHANES dietary (1971–2008) and physical activity (1988–2006) data of participants with BMI 18.5–50.0. Physical activity was defined as the weekly frequency of leisure time activities of moderate or greater metabolic intensity [39].

Between 1971 and 2008, BMI increased 10% in men and 11% in women, most of which occurred after 1988 [39]. Total calories per day increased by approximately 10% in men and 14% in women from 1971 to 1999, peaked in 2003, and declined to 1999 levels for both sexes by 2008. Relative caloric intake (i.e., total calories converted to cal/kg of body weight) in 2008 was similar to 1971 but increased modestly between 1988 and 1994 in both sexes. Percent of daily calories (men and women) increased for carbohydrate (13% and 10%) but decreased for fat (9% and 8%) and protein (5% and 7%) [39].

Between 1988 and 2006, physical activity per week increased 47% in men and 120% in women [39]. Adjusted for physical activity and carbohydrate and fat intake, for an equivalent amount of energy intake or physical activity, BMI was up to 2.3 higher in 2006 than in 1988. Thus, BMI increased between 1988 and 2006, even after holding energy intake, macronutrient intake, and physical activity constant.

Decreased physical activity and increased caloric consumption do not fully explain this increase in BMI. The authors conclude that other unrecognized factors may be significantly modifying how energy intake and expenditure influence body weight over time [39].

Weight Loss Attempts: 1999–2016

Over the past 40 years, as obesity prevalence increased about threefold, the prevalence of weight loss attempts by adults increased from 34% in 1999–2000 to 42% in 2015–2016. During 2013–2016, past-12-month attempts to lose weight were made by 49% of adults overall and by 67% of those with obesity. Since the late 1980s, the prevalence of dieting to lose weight has been ≥40% among women and ≥25% among men [64; 65].

Repeated weight loss efforts may also contribute to weight gain, which experts have suggested has created a "weight-loss futility cycle" that characterizes the rising prevalence of both obesity and weight loss attempts since 1980. The increasing prevalence of obesity and weight loss attempts has also been paralleled by an increase in body weight stigma, which in turn is associated with many adverse health outcomes, including higher risk of all-cause mortality, and disproportionately affects individuals with obesity [65].

ENERGY EXPENDITURE RESEARCH

Understanding the relative contribution of lower energy expenditure to the obesity epidemic is a crucial task that requires accurate measurements of energy expenditure [66; 67; 68]. The terms used in discussions of this concept should be clearly defined [70; 71; 72]:

- Basal energy expenditure: Also known as resting energy expenditure or basal metabolic rate, the minimum energy required to maintain vital physiological functions
- Activity energy expenditure: Exercise and non-exercise activity
- Physical activity: Work-time (occupational) or leisure-time energy expenditure
- Total energy expenditure: Expressed in calories/day, the sum of basal energy expenditure and activity energy expenditure

Doubly labelled water (DLW) is the criterion-standard for measuring energy expenditure and the only method that can assess this during a person's normal daily living. This method uses water with the added stable isotopes deuterium and oxygen-18 to measure energy expenditure (i.e., calories burned) [67; 73].

DLW studies began in the early 1980s. The IAEA database houses four decades of DLW study data. With the size of this database and its ongoing expansion, big questions about the causes of the obesity epidemic are being addressed [74].

Additive versus Constrained Models of Metabolic Physiology

The dominant additive model assumes a dose-dependent, additive effect of physical activity on total energy expenditure; with each increment of physical activity, total calories burned correspondingly increases [75]. This calories in/calories out paradigm of obesity led to energy restriction diets and exercise as the standard obesity intervention to reverse positive energy balance for weight loss [76; 77].

Energy compensation, or metabolic adaptation, is a normal physiobehavioral response to a change in activity or diet such that the impact of the change is blunted [12]. DLW data suggest the relationship between physical activity and total energy expenditure is more complex than additive models allow [75].

An earlier DLW study involved Hadza people, traditional hunter-gatherers who live off of wild plants and animals in Tanzania expending hundreds of calories a day on activity. Hadza men ate and burned about 2,600 calories per day and Hadza women consumed and burned about 1,900 calories per day. Even after controlling for effects of body size, fat percentage, age, and sex, the Hadza burned about the same daily calories as city dwellers in the United States [78].

DLW evidence led to the constrained model, where total energy expenditure increases with low physical activity but plateaus at higher activity levels as the body adapts to maintain total energy expenditure within a narrow range. By accounting for

energy compensation, the constrained model provides a unifying framework for seemingly contradictory results from studies of physical activity and total energy expenditure [12; 75].

The compensation may take several weeks or months. Exercise will raise energy expenditure in the short-term, and lifestyle change may also affect total energy expenditure until compensation occurs, after which physical activity will have little measurable effect on total energy expenditure [12].

Energy Compensation

Increasing activity levels may bring diminishing returns due to compensatory responses in nonactivity energy expenditure [66]. In 1,754 adults with DLW measured seven years apart, only 72% of the extra calories burned during activity translated into extra calories expended that day, because the body offset the calories burned in activities by 28%. Among those with BMI ≥34, compensation of burned activity calories increased to 46% [72].

To explain the causality of this relationship, individuals with greater body fat are either predisposed to adiposity because they are stronger energy compensators or because they become stronger compensators as they gain adiposity. Prescribing increases in activity to increase total energy expenditure and thus control weight gain or promote fat loss assumes that costs of activity are additively related to basal costs, which this study suggests is untrue [72].

Resting Energy Expenditure in Healthy Underweight Adults

Contrary to popular belief that lean individuals "eat what they want" and exercise more, a cohort of 150 healthy underweight (BMI <18.5) adults exhibited significantly lower physical activity and food intake relative to 173 normal-BMI controls and much higher than expected resting energy expenditure, measured using DLW [79]. The healthy underweight subjects were metabolically healthier than normal-BMI controls, which suggests low body weight/fat is a more potent driver of metabolic health than higher physical activity. The results extend previous longitudinal findings into a much lower range of BMI and show that markers of metabolic health continue to improve as BMI falls below 18.5 [79].

Declining Metabolic Rate and Rising Obesity

The obesity epidemic is often blamed on declining energy expenditure due to reduced occupational physical activity combined with increased sedentary behavior and screentime. This was examined in 4,800 adults with DLW data obtained between 1987 and 2017. All results were adjusted for age and body composition [80].

Men and women both showed significant declines in total energy expenditure and significantly increased activity energy expenditure, while physical activity increased significantly in men and non-significantly in women. Basal energy expenditure decreased significantly in men and non-significantly in women. Men and women showed declines in total energy expenditure (7.7% and 5.6%) and basal energy expenditure (14.7% and 2%), respectively. In both sexes, the decline in basal energy expenditure was sufficient to explain the reduction in total energy expenditure. There was no evidence that reduced physical activity leading to lowered total energy expenditure contributed to the obesity epidemic [80]. This is counterintuitive, given the established decrease in occupational physical activity and the suggested progressive increase in sedentary behavior. The increased leisure physical activity between 1965 and 1995 (and 1988–2006) may have offset reduced occupational physical activity. Increased time on computers has largely come at the expense of time watching television; with comparable energy costs, this tradeoff would have little effect on overall activity energy expenditure [80; 81].

In addition, the reduction in total energy expenditure was linked to a decline in basal energy expenditure. Declining basal energy expenditure is less easily understood, but consistent with data that body temperatures also declined over the same period as decreasing basal metabolic rate. The magnitude of change in basal metabolic rate is consistent with studies showing that basal metabolic rate increases 10% to 25% with every 1°C increase in core temperature [80]. The authors conclude that a declining basal metabolic rate may be contributing to the obesity epidemic. Identifying the cause, and if it can be reversed, is an urgent priority.

OTHER POTENTIAL ETIOLOGICAL FACTORS

Urbanization

During 1985 to 2014 in most countries, the concurrent increases in BMI and the proportion of populations living in cities compared with rural areas led to a widely accepted view that urbanization, and the resultant sedentary lifestyle, is an important contributor to the global rise in obesity [82]. However, an analysis of 2,009 population studies with direct anthropometric measurements in 112 million adults from 1985 to 2017 demonstrated that 55% of the global rise in adiposity (and >80% in some low- and middle-income regions) is explained by increased adiposity in rural areas [83].

Social Contagion

There is substantial clustering of obesity within social and geographic networks. Whether this results from causal pathways (e.g., social contagion, shared environments) or self-selection is unclear and was studied in 1,519 military families from 38 military installations around the United States who relocated to counties with obesity rates of 21% to 38% [84]. Exposure to communities with higher obesity prevalence was associated with higher BMI and overweight/obesity in parents and children. Specifically, a 1% higher county obesity rate was associated with 5% higher odds of obesity in parents and 4% higher odds of overweight/obesity in children [84].

All associations were strengthened by duration (i.e., >24 months at their current installation) and proximity (living off-base) of exposure and were unchanged after controlling for the

shared built environment in the county and neighborhood of residence. There was no evidence to support self-selection or shared environment as explanations, which may suggest the presence of social contagion in obesity [84]. Although data on the previous county obesity rate was unavailable, exposure to communities with higher obesity rates may increase individuals' BMI via the presence of social contagion, possibly by common social norms associated with obesity [85].

Medication-Induced Weight Gain

In 2017–2018, 20.3% of U.S. adults used an obesogenic medication (compared with 13.2% in 1999–2000) [86]. Many widely used drugs cause weight gain that may lead to obesity in susceptible individuals. Weight gain is consistently associated with many older antidiabetic agents, atypical antipsychotics, antidepressants, and antiepileptic drugs [87].

Dietary Sugar and Sugar-Sweetened Beverages

A study that pooled three population-based prospective cohorts of Finnish adults to examine diet and weight gain over seven years found no associations between total carbohydrate, dietary fiber, sugar, or sucrose intake and ≥5% increase in weight or waist circumference. However, the authors state that low sugar-sweetened beverage consumption in Finland compared with the United States may partially explain the lack of association between carbohydrate intake and weight gain [88].

In the United States from 1965 to 2002, daily sugar-sweetened beverage caloric consumption increased 306% per capita and 86% among consumers of sugar-sweetened beverages only. However, from 1999 to 2010, total daily caloric intake from sugar-sweetened beverages among youth (2 to 19 years of age) and adults (≥20 years of age) decreased 31% and 21%, respectively [57].

Evidence for the mainstream view that high sugar consumption leads to obesity and related metabolic diseases is inconsistent, and high sugar intake from sugar-sweetened beverages may differ from sugar-containing foods (i.e., solid sugars) in BMI/metabolic impact [89].

In a review of prospective evidence, most studies linking high sugar intake to adverse health outcomes examined sugar-sweetened beverages, while studies of solid sugar intake mostly reported null findings. High sugar-sweetened beverage consumption was dose dependently associated with increased risks of cardiovascular disease morbidity and mortality through weight gain; solid sugar sources (e.g., ice cream) were not [89; 90].

Sugar-sweetened beverages may be more likely to induce metabolic syndrome. The faster gastric emptying time of sugar-sweetened beverages and higher absorption of its fructose component may lead to fatty accumulation in the liver. Compared with solid sugars, sugar-sweetened beverages induce less satiety and may subsequent cause overeating. The gut can convert low-concentration fructose to glucose, but transports high-concentration fructose (e.g., in sugar-sweetened beverages) to the liver [89].

Increased lipogenesis and circulating triglycerides, very-low-density cholesterol, and uric acid associated with high sugar-sweetened beverage intake may induce hyperglycemia, glucose intolerance and dyslipidemia to increase risks of type 2 diabetes and cardiovascular disease. High intake of fructose-sweetened beverages may disrupt the production of appetite control hormones (decreasing leptin and insulin, increasing ghrelin), suggesting different effects on metabolic and endocrine health of liquid versus solid sugars [89].

Individuals who ingest high dietary sugar often have other unhealthy behaviors that may contribute to the pathogenesis of obesity and related disorders, complicating causal inferences. Although definitive evidence is needed, and reducing sugar remains a general recommendation, there is evidence of greater health risks with sugar-sweetened beverages that might not be comparable to those with sugar in food [89; 91].

SUMMARY

That the obesity epidemic lacks a clear explanation is a striking and poorly appreciated fact. The widely accepted causes of ever-increasing caloric intake and progressively declining physical activity are largely unsupported [16; 17]. Genetic, developmental, and environmental factors are thought to interact to cause cumulative positive energy balances resulting in weight gain and obesity [92]. Numerous factors have been associated with increased risk of obesity—but a risk factor is not necessarily a cause, and risk factors are not direct causes of disease. Associations in the obesity literature often reflect information bias, reverse causality, erroneous causal inferences, or confounding from other social and behavioral factors [54]. Although spurious, some persist to mislead science, practice, and the public [59].

Provocative evidence demonstrates that the obesity epidemic has expanded beyond humans. Mammals inhabiting human-influenced environments have also exhibited pronounced increases in weight and obesity over the past several decades, including mammals in research labs, feral rats, and domestic dogs and cats [93]. The laboratory animals include four different species of primates in National Primate Research Centers, as well as rats and mice, all living in environments where their diets are strictly controlled [17; 93]. In 2015, canine and feline obesity rates had reached pandemic proportions similar to humans [94]. An international multidisciplinary congress, Animal Obesity, was launched in 2016 [95].

A reasonable inference is that something has changed in the shared environment that is inducing weight gain, and exposure to unidentified obesity-promoting factors may be affecting all these populations in concert. There is some evidence pointing to endocrine-disrupting chemicals [17; 48; 77; 93; 96].

Endocrine-disrupting chemicals interfere with hormone action to dysregulate endocrine function, insulin signaling, and/or adipocyte function. Adipose tissue is a true endocrine organ and is therefore highly susceptible to disturbance by endocrine-disrupting chemicals. Obesogenic endocrine-disrupting chemicals promote adiposity by altering programming of fat

cell development, increasing energy storage in fat tissue, and interfering with neuroendocrine control of appetite and satiety [17; 18; 48; 77; 96; 97].

Endocrine-disrupting chemicals have become ubiquitous in our environment. Exposure occurs throughout life, but development is the most sensitive period for endocrine-disrupting chemicals to impact future weight gain across the lifespan and generations, and endocrine-disrupting chemicals can act via epigenetic mechanisms. There is an urgent need to understand how exposures to certain endocrine-disrupting chemicals may predispose the population to obesity [48; 77; 96; 98; 99].

Note that researchers in some studies have concluded that some unknown factor may be altering normal energy metabolism, as increased caloric intake and/or decreased activity could not adequately explain rising BMI and obesity. A 2023 review suggests that exposure to some yet-to-be-identified factor(s) is promoting obesity by generating false and misleading information about energy status [100].

Most importantly, uncertainty over the obesity epidemic's cause has little bearing on the effectiveness of medical interventions [16]. In fact, pharmacotherapy of obesity with novel approved and investigational agents shows weight loss efficacy and remission of comorbid disorders previously unattainable without bariatric surgery. Bariatric surgery itself can result in dramatic weight loss (≥30%) and remission of obesity-related metabolic disorders persisting for years if not decades. Newer and emerging minimally invasive bariatric procedures are showing promising results while reducing the risks of surgery.

THE REGULATION OF BODY WEIGHT

ENERGY BALANCE

When body-fat levels become established, complex biological mechanisms defend the established body mass against persistent pressures that would induce weight loss. This can be understood from an evolutionary perspective. With food scarcity during most of human evolution, evolutionary pressures on the human genetic blueprint selected for genetic variants that favored the storage and conservation of energy to ensure survival and reproduction. The underlying process that defends energy storage and conservation is called energy balance [101; 102].

The purpose of energy balance is to maintain adenosine triphosphate (ATP) availability for cells. ATP is required by all cells to sustain and maintain life. Eating acquires the oxidizable fuels that cells use to maintain ATP availability [101; 102; 103].

Energy balance is regulated by homeostatic processes. Homeostasis maintains interdependent bodily constituents within a controlled stable range. Regulation is the ability to maintain a variable within a narrow range. Control mechanisms are those that maintain the narrow range of the regulated variable. The regulated variable in energy homeostasis is ATP availability [103; 104]. Control processes that maintain ATP availability (i.e., energy homeostasis) include energy intake, energy storage, and energy expenditure. Thus, ATP availability is the apex regulated variable and pivot point for energy balance; the dynamic relationships between energy intake, storage, and expenditure are all directed toward this end [103].

Energy Intake and Storage

Glucose and free fatty acids are monomers, the oxidizable fuels for ATP production that cells require. Monomers are the breakdown products of macronutrients, released by digestion and distributed into oxidizable fuels or storage by energy partitioning, depending on current energy balance status [70; 102; 103].

Excess energy is stored as fat in adipose depots, carbohydrate (as glycogen) in liver, or protein in muscle. The energy density of adipose tissue is nearly 10-fold greater than liver (glycogen) or muscle (protein). The small storage capacity for carbohydrate can cover overnight energy needs during sleep. The larger energy stores of fat are mobilized to cover longer-term energy shortages [70; 102; 103].

However, as a substrate for energy metabolism, fat is last in the hierarchy that determines fuel selection; it is mostly stored before oxidation and is less likely to be oxidized than carbohydrate or protein. Body-fat mass and oxidation of dietary fat are inversely related—higher fat mass lowers the oxidation rate of dietary fat [70; 102; 103]. Energy expenditure is the sum of ATP generated by oxidizing monomers to drive physiological processes.

Three States of Energy Balance

Oxidizable fuels from food can fail to meet (negative), equal (balanced), or exceed (positive) requirements to maintain ATP availability within its narrow range. These are the three states of energy balance [70; 102; 103]:

- Negative: When oxidizable fuel supplies are challenged by prolonged calorie deficit, control mechanisms increase catabolism (breakdown) of fuel stores and reduce energy expenditure to maintain ATP production. During starvation, these mechanisms maintain cell function to an extent that compromises organ and systemic function. The collective outcome of processes that control blood glucose, adiposity, heat production, and eating behaviors, are directed toward maintaining ATP availability within a narrow range.
- Balanced: The rate of anabolic and catabolic processes is equal (a state of energy balance).
- Positive: Energy balance favors anabolism, which increases fuel stores.

Unlike fuels, ATP cannot be stored. An animal can survive for days or weeks without food, but its survival time is measured in seconds if a toxin shuts down oxidative phosphorylation and ATP production. Lacking ATP storage capacity, daily ATP turnover in humans is dramatic [103].

DEFENSE OF BODY WEIGHT

Positive energy balance from increased energy intake, decreased energy expenditure, or both, is considered the proximate cause of weight gain and excess fat storage leading to obesity [66; 102; 105; 106; 107].

Obesity is usually the result of small, cumulative positive energy imbalances over an extended period. The homeostatic system continually retunes itself during the upward drift in weight. At some point, for most people, these biological adaptations re-establish a balance at a higher, steady-state weight [108].

Persons with obesity may lose 7% to 10% of initial weight with a 16- to 26-week comprehensive caloric restriction, physical activity, and behavioral intervention [9]. However, it is the maintenance of weight loss that makes long-term control of obesity so difficult [7; 8].

In contrast to its subtle, permissive role in the development of obesity, biology plays a prominent, causal role in weight regain [108]. Energy-restricted weight loss mobilizes powerful biological forces that lead to increased hunger, enhanced neural responses to food cues, and heightened drive to consume energy-dense foods [11].

Because both sides of the energy balance equation are affected after weight loss, the biological pressure to gain weight is a consequence of both increased appetite and suppressed energy expenditure as the body attempts to restore energy homeostasis [15; 108]. Termed metabolic adaptation, this defense of established adiposity against weight loss recapitulates a physiological response that signals potential starvation [69; 104].

Metabolic adaptation has been understood for more than five decades but is missing in public health statements that healthier lifestyle choices are the solution to obesity [6; 109; 110; 111; 112; 113; 114]. As a consequence, patients are often blamed for obesity treatment failure [3; 6].

OVERVIEW OF CLINICAL MANAGEMENT

Obesity involves dysfunction of the tightly regulated energy homeostasis system and its underlying central, peripheral, and reward mechanisms (***Appendix***) [115; 116]. Powerful compensatory mechanisms drive weight regain following weight loss in obesity by altering appetite, food reward, and energy intake and expenditure. Peripheral changes, including reduced anorectic hormones and increased orexigenic hormones, stimulate food intake. Pressure to overeat combines with central mechanisms that drive food pleasure and reward. Metabolic adaptation reduces resting energy expenditure [117]. These dysregulated mechanisms are the targets of FDA-approved and investigational antiobesity medications and of bariatric surgery.

Knowledge of obesity pathophysiology, and clinical management based on the understanding of obesity as a chronic, progressive cardiometabolic disease, has rapidly evolved over the past decade. Consequently, some clinical practice guidelines on obesity from authoritative bodies have become outdated. For example, the most recent guideline by the AHA, American College of Cardiology, and The Obesity Society (AHA/ACC/TOS) was published in 2014 [118]. The paradigm of long-term management in this guideline is largely obsolete. A 2015 clinical practice guideline from the Endocrine Society and a 2016 guideline from the American Association of Clinical Endocrinologists and American College of Endocrinology (AACE/ACE) advanced the paradigm to the current standard of care, but available antiobesity medication options addressed in the guideline are non-recent [119; 120; 121]. Scientific statements by the Endocrine Society and clinical practice guidelines by the OMA, the American Gastroenterological Association (AGA), and the American Society for Metabolic and Bariatric Surgery (ASMBS) reflect current advances in obesity science, antiobesity medication options and their rational clinical use and bariatric surgical and noninvasive options [4; 7; 30; 122; 123; 124; 125; 126].

THE FOUR PILLARS OF OBESITY MANAGEMENT

The OMA states that obesity is a serious and multifactorial disease that requires patient access to comprehensive care, including the four pillars of healthful nutrition, physical activity, behavior modification, and medical management with antiobesity medications and surgical interventions. Comprehensive care of obesity is not only about reducing weight but also about improving the health of patients [122].

Initial comprehensive care includes medical history, review of systems, personal history (e.g., family, socioeconomic, culture, nutrition, physical activity, behavioral, and eating disorder history), evaluation for primary and secondary causes of obesity, routine preventive care, physical exam, and laboratory testing [122]. Common metabolic complications of obesity include type 2 diabetes, hypertension, dyslipidemia, nonalcoholic fatty liver disease (NAFLD), and the fat mass complication of sleep apnea. "Treat obesity first" represents a standard of care for patients with obesity-related complications that can slow the progression of metabolic complications and reduce premature mortality [122].

Healthful Nutrition

The OMA recommends that patients with obesity have access to safe, effective, personalized, and evidence-based healthful nutritional intervention. Patients should optimally have access to nutrition therapy via a registered dietitian or via nutritional counseling from obesity medicine clinicians trained in nutritional counseling. Approaches to overcome barriers to nutritional intervention engagement include individual or group videoconferencing, personalized artificial intelligence (AI)-mediated interventions applicable to precision medicine, incorporation of cultural norms, and awareness of the impact of social determinants of health [122].

Physical Activity

The OMA recommends patients with obesity be treated with a safe and effective personalized physical activity plan (i.e.,

physical activity prescription) based on the patient's underlying health and mobility. To achieve physically active objectives, the OMA recommends that patients with obesity learn the benefits of non-exercise activity thermogenesis, target dynamic goals (e.g., steps per day), and safely incorporate resistance training. The intent is to improve body composition, support weight loss maintenance, improve balance and flexibility, and reduce the risk of injury from falls or joint stress. Improving or maintaining mobility can be achieved via training to promote activities of daily living (e.g., self-dressing, -meal preparation, -bathing, -laundry). Physical activity and exercise training may occur individually or in groups, via live classes/instruction, video format, or AI educational interactions, and may be especially important in patients with sarcopenic obesity [122].

Behavior Modification

The OMA recommends patients with obesity be treated with evidence-based behavior modification. Important aspects include personalized tracking and regular clinician encounters. Optimizing social support at home and in the community may be helpful. Patients often benefit from behavior modification provided by a knowledgeable physician, nurse practitioner, physician assistant, nurse, or dietitian, or via a psychologist/psychiatrist, health coach, or another appropriate counselor. For patients for which record keeping and accountability metrics may improve health outcomes, other potential interventions include fitness trackers, smartwatches, and use of social media. Behavior modification may also be delivered through AI chatbots [122].

Medical Management

Antiobesity Medications

Medical treatment with antiobesity medication and/or bariatric procedures is the fourth pillar of obesity management. Evidence-based treatment of obesity, including pharmacotherapy, represents a standard of care for patients with obesity [122].

Obesity is associated with $174 billion in excess healthcare costs annually. To mitigate such expenditures, obesity should be treated early and effectively before its complications arise. In patients without acute complications of obesity, a "treat obesity first" approach through antiobesity medications may reduce or eliminate the need (and cost) for antidiabetic medications, antihypertension medications, lipid medications, pain medications, and possibly other medications (e.g., antidepressants) or other treatments (e.g., continuous positive airway pressure devices) [122].

When appropriate for the patient, use of lower-cost antiobesity medications may improve the cost effectiveness of medication. The forthcoming generic status of some current agents and market entry of new antiobesity medications may drive competition and lower costs [122]. However, the OMA stresses the importance of a patient-centered, personalized approach to pharmacotherapy for obesity and that such an approach may depart from the recommended prescribing information [122].

Bariatric Procedures

The OMA recommends that patients with obesity should have access to evidence-based bariatric procedures, when appropriate, as an adjunct to healthful nutrition, physical activity, behavior modification, and pharmacotherapy. Currently, less than 1% of eligible patients receive bariatric surgery, despite extensive evidence of its cost-effectiveness. Importantly, bariatric surgery is associated with reductions in overall mortality, cardiovascular events, risk of cancer, cardiovascular risk factors (e.g., type 2 diabetes, hypertension, dyslipidemia), and improvements in osteoarthritis, skin disorders, and possibly depression [116; 122; 127; 128; 129; 130].

OBESOGENIC MEDICATIONS

Obesity may result from an identifiable primary cause. Some endocrine disorders, including hypothalamic disorders, insulinoma, hypothyroidism, and hypercortisolism, are strongly associated with obesity or its onset [24]. A common culprit are drugs that promote weight gain, and a central task for clinicians caring for patients with obesity involves reviewing their use of obesogenic medications (***Table 6***) [131].

In chronic disease management, the weight-gain potential is often overlooked when choosing pharmacotherapy options. However, many commonly used medications associated with weight gain have alternatives with weight-neutral or weight-losing effects. Shifting medication choices from weight-positive to weight-neutral or -negative choices can be an effective means of facilitating weight loss [122].

Common medication classes associated with weight gain include steroids, antipsychotics, antiepileptics, glucocorticoids, and gabapentinoids. When these or other prescribed medication classes induce significant weight gain, especially to an extent that may exceed the positive treatment effects, switching patients to alternative medications that are weight-neutral or weight-loss-promoting should be considered within a shared decision-making process including the patient and prescribing provider (e.g., psychiatry, neurology, other specialists) [131].

For patients with type 2 diabetes and obesity requiring insulin therapy, adding metformin or GLP-1R agonists can reduce or nullify (with GLP-1R agonists) insulin-associated weight gain. Clinicians should add one of these agents when starting a patient with type 2 diabetes on insulin therapy. Among insulin therapies, basal insulin is associated with less weight gain than biphasic or prandial short-acting insulin and should be the first-line option [131].

Obesity and inflammatory rheumatic diseases commonly co-occur, with a hypothesized causal role due to the proinflammatory nature of adipose tissue. Patients with obesity have higher disease scores and poorer treatment response to disease-modifying antirheumatic drugs (DMARDs). Minimize or avoid corticosteroids, which tend to promote weight gain, in favor of nonsteroidal anti-inflammatory drugs (NSAIDs) and DMARDs [131].

OBESOGENIC MEDICATIONS AND WEIGHT-NEUTRAL OR -REDUCING ALTERNATIVES			
Clinical Condition or Drug Class	**Weight-Promoting**	**Weight Neutral**	**Weight-Reducing**
Type 2 diabetes with obesity	Pioglitazone Sulfonylureas Insulin	DPP-4 inhibitors	Metformin SGLT2 inhibitors GLP-1R agonists
Antidepressants	Paroxetine Amitriptyline Mirtazapine	–	Bupropion Fluoxetine
Atypical antipsychotics	Olanzapine Quetiapine Risperidone	Ziprasidone	–
Anticonvulsants and mood stabilizers	Divalproex Carbamazepine Gabapentin	Lithium Lamotrigine	Zonisamide Topiramate
Inflammatory rheumatic diseases	Corticosteroids	DMARDs NSAIDs	–
DMARDs = disease-modifying antirheumatic drugs, DPP-4 = dipeptidyl peptidase-4, NSAIDs = nonsteroidal anti-inflammatory drugs, SGLT2 = sodium-glucose cotransporter-2.			
Source: [131]			*Table 6*

PRIORITIZATION FOR PATIENTS WITH OBESITY AND CARDIOMETABOLIC DISEASE

Patients with acute metabolic abnormalities (e.g., marked hyperglycemia, uncontrolled hypertension, severe hypertriglyceridemia, cardiovascular disease, cancer) should have these illnesses urgently assessed and treated, preferably with concomitant interventions that may also improve obesity [128]. For most patients without acute illness, treatment of obesity is the priority, especially if the therapies chosen for treatment of the obesity are also expected to improve the complications of obesity [128]. In weight-loss pharmacotherapy, the initial priority should be to safely achieve maximal weight reduction, followed by sustained antiobesity medication and lifestyle therapy that may require less supervision to maintain the reduced body weight [132].

TREATING TO TARGET WITH ANTIOBESITY MEDICATIONS

Obesity is a chronic disease that involves more than excessive body fat. The fat mass leads to biomechanical complications, such as obstructive sleep apnea and osteoarthritis. The pathogenic adipose tissue promotes cardiometabolic disease, which begins with subclinical insulin resistance that eventually produces metabolic syndrome, prediabetes, hypertension, dyslipidemia, and hepatic steatosis. These conditions indicate risk for progression to the end-stage manifestations of cardiometabolic disease, namely type 2 diabetes, NASH, and cardiovascular disease. The development of obesity exacerbates insulin resistance and impels progression of cardiometabolic disease toward these ultimate outcomes. As with other chronic diseases, the complications of obesity impair health and confer morbidity and mortality [3].

In treating obesity as a chronic disease, the essential goal of weight-loss therapy is not the quantity of weight loss per se, but rather the prevention and treatment of complications to enhance health and mitigate morbidity and mortality. This paradigm of care is the basis of the complications-centric AACE/ACE obesity guideline and the diagnostic term adiposity-based chronic disease (ABCD) [3].

The degree of efficacy and safety with second-generation antiobesity medications (e.g., semaglutide) and better understanding of obesity as a chronic disease has made possible a treating-to-target paradigm using percent total weight loss as a biomarker that can actively be managed within a range associated with optimal outcomes [123].

A treat-to-target approach has abundant precedent in medicine. In diabetes, clinicians treat the biomarker HbA1c to a target of ≤7.0% or ≤6.5%, because this will minimize micro- and macrovascular complications. Hypertension involves control of blood pressure levels to prevent cardiovascular and renal complications. To prevent and treat cardiovascular disease, LDL-C serves as a biomarker that is managed to a level based on patient risk estimates. In each instance, treatment to target for each biomarker (HbA1c, blood pressure, and LDL-C) is individualized based on an individual patient's overall risk, other comorbid conditions, and natural history of the disease [3].

Similarly, percent total weight loss is a more appropriate biomarker than body weight or BMI. Second-generation antiobesity medications allow clinicians to reach targets of weight loss that will predictably treat or prevent a broad spectrum of complications in ABCD [3]. Weight reductions of ≥10%, ≥15%, or 20% or more may be required for improvement in certain weight-related complications and are often more desired therapeutic goals in clinical practice [133]. Depending on the

complication profile, the target for percent total weight loss can be individualized [3].

The estimated weight reduction required to improve morbidity and mortality outcomes are [3]:

- 5% to 10% weight reduction: Improved physical and biomechanical function, type 2 diabetes prevention
- 10% to 15% weight reduction: Cardiovascular disease risk reduction and remission/reduction in obstructive sleep apnea, hypertension, type 2 diabetes hyperglycemia
- ≥16% weight reduction: Type 2 diabetes remission, NASH improvement

These figures are mostly relevant to noninvasive obesity interventions. The long-term reduction and remission of metabolic disorders attainable with bariatric surgery has led to their renaming as metabolic and bariatric surgery [126].

ANTIOBESITY MEDICATIONS

Lifestyle modification is considered the primary treatment of obesity. A meta-analysis of 31 randomized controlled trials assessing lifestyle versus control interventions showed an average 3.6-kg weight loss at one year and 2.5-kg at three years [134]. Unfortunately, most people cannot achieve sufficient weight loss or maintain it long-term without pharmacotherapy or surgery [135].

However, effective pharmacological interventions for obesity have historically been challenging to achieve. The reasons are complex and include both behavioral and biological factors, which are difficult to separate from each other. Physiologically, metabolic adaptations in response to energy deficits and weight reduction defend against sustained fat mass loss. In the CNS, redundant pathways favor a state of anabolic and orexigenic activity. Thus, efforts to develop pharmaceutical agents that can overcome these strong neurobiological defenses, while limiting adverse effects, has proven to be somewhat elusive [123].

In 1937, during clinical trials evaluating amphetamine (Benzedrine) for the treatment of depression and narcolepsy, it was noted that subjects lost weight. Amphetamines became widely used weight-loss drugs during the 1940s and 1950s but were associated with numerous side effects [136]. After World War II, researchers discovered that injecting norepinephrine into the CNS of experimental animals reduced food intake and activated thermogenesis, prompting a search for thermogenic drugs that could work through monoaminergic receptors [4]. This resulted in sympathomimetic amines, which modified the molecular structure of amphetamine to mitigate the undesirable side effects, with phentermine, diethylpropion, phendimetrazine, and benzphetamine approved for short-term weight loss and remain available for this indication [3].

The duration required of antiobesity pharmacotherapy was thought to be around 12 weeks, the length of time needed to break a bad habit or learn to ride a bicycle without training wheels [136]. Due to a limited understanding of obesity pathophysiology, it was believed that once weight was lost, ongoing treatment was unnecessary [3]. Obesity was recognized as a disease by the scientific community in 1985, but it was not until 2013 that obesity was acknowledged as a chronic disease by the American Medical Association [136].

Orlistat, which impairs intestinal fat absorption, was approved in 1999 for chronic weight management, but medications were needed for long-term use that could blunt appetite by counteracting abnormalities in the gut-brain axis. Three such medications were approved by the FDA—fenfluramine, sibutramine, and lorcaserin—were prominently serotonergic drugs, but all have been discontinued due to safety concerns [3].

Rimonabant, the first CB-1 receptor antagonist, was approved in Europe, but not by the FDA because of concerns about suicidality. Due to psychiatric side effects, marketing of rimonabant was suspended in Europe in 2008, two years after its approval as an antiobesity medication.

From 2012 to 2014, three centrally acting antiobesity medications were approved for chronic weight management that remain available: phentermine/topiramate extended-release (ER), naltrexone/bupropion ER, and liraglutide. Semaglutide was approved in 2021 [3].

Similar to several other antiobesity medications, GLP-1 receptor agonists (GLP-1 RAs) became used in obesity following observations of weight loss in other clinical populations. Liraglutide, semaglutide, and tirzepatide were approved for the treatment of type 2 diabetes before their efficacy as antiobesity medications was evaluated.

The introduction of semaglutide marks a watershed in the history of nonsurgical obesity treatment. Semaglutide essentially doubled the weight loss observed with existing obesity medications, ushering in the era of second-generation antiobesity medications [3]. Tirzepatide surpasses the weight-loss efficacy of semaglutide.

INDICATIONS FOR USE

Except for setmelanotide and metreleptin, all antiobesity medications are approved as adjuncts to a reduced-calorie diet and increased physical activity for chronic weight management in adults with obesity (BMI ≥30) or overweight (BMI ≥27) with at least one weight-related complication, such as hypertension, type 2 diabetes, or dyslipidemia [137]. All antiobesity medications are considered pregnancy risk factor category X drugs and should not be prescribed to a patient who is pregnant, breastfeeding, or trying to conceive [124].

Randomized controlled trials of antiobesity medications mirror the FDA's indications in their inclusion criteria (BMI ≥30 or ≥27 with weight-related complication) and use as adjunct to lifestyle intervention. Whether participants are randomized

to placebo or active drug, all receive a standardized lifestyle intervention: healthy meals, a deficit of 500 calories daily, 150 minutes of physical activity weekly, and regular dietitian counseling to help with meals and adherence [133; 138]. Infrequent variations are possible and are discussed later in this section.

The FDA indications may not adequately reflect current evidence. In 2018, the Endocrine Society endorsed pharmacotherapy as a first-line treatment for weight loss in patients with severe weight-related complications and removed the criteria of failed lifestyle modification [4]. A Korean obesity guideline endorses pharmacotherapy for patients with BMI ≥25, or ≥23 with weight-related complications, which may be applied to Asian populations in the United States [135; 139].

Many antiobesity medications were initially evaluated for efficacy in clinical trials of type 2 diabetes. Weight loss is considerably lower in patients with obesity and type 2 diabetes than in those without diabetes. Insulin resistance and chronic hyperglycemia correlate with diminished efficacy of GLP-1 RAs, which also argues for earlier intervention before metabolic organs are irreversibility damaged [132].

Obesity should be considered a chronic condition requiring long-term treatment, as most patients who stop pharmacotherapy are prone to weight gain. If lifestyle modification and drug therapy fail, bariatric surgery should be considered a sustainable weight loss option [135].

FDA-APPROVED AGENTS

For Monogenic Obesity Syndromes

Setmelanotide (Imcivree)

Setmelanotide is the first antiobesity medication approved specifically for the treatment of rare genetic conditions associated with obesity. The drug binds to melanocortin-4 receptor (MC4R) in the hypothalamus, downstream of the leptin signaling pathway [135]. Setmelanotide re-establishes the activity of the MC4R pathway, thus reducing hunger and promoting body weight loss by lowering caloric intake and increasing energy expenditure [140].

Setmelanotide is indicated for patients with obesity due to proopiomelanocortin (POMC), proprotein convertase subtilisin/kexin type 1 (PCSK1), or leptin-leptin receptor (LEPR) deficiency. The condition must be confirmed by genetic testing demonstrating pathogenic variants in *POMC*, *PCSK1*, or *LEPR* genes [30]. Setmelanotide is contraindicated for patients with other causes of obesity, polygenic obesity, or benign variants of the gene mutations. Dosing is subcutaneous 2 mg daily (maximum: 3 mg daily). Adverse effects include hyperpigmentation, vomiting, and nausea [135]. Setmelanotide is not associated with adverse effects on blood pressure observed with other MC4R agonists [141].

Bremelanotide

Bremelanotide is another MC4R agonist that also binds to MC3R and is FDA-approved for treatment of low sexual desire in premenopausal women. Data from two small randomized controlled trials in premenopausal women with obesity showed reduced caloric intake and weight loss with bremelanotide, without adverse effects on blood pressure, suggesting this may be an effective treatment of obesity [141].

Metreleptin

Metreleptin is a synthetic leptin analog approved by the FDA in 2014 for patients with congenital leptin deficiency or congenital/acquired lipodystrophy and is administered subcutaneously once daily. The recommended starting daily dose in adults with body weight ≤40 kg is 0.06 mg/kg (maximum: 0.13 mg/kg daily), while adults with body weight >40 kg are started on 2.5 mg or 5 mg for men or women, respectively (maximum: 10 mg daily). No leptin analog has been approved by the FDA or European Medicines Agency (EMA) as an antiobesity medication for generalized obesity [92].

For Short-Term Use: Sympathomimetic Amines

Phentermine, diethylpropion, phendimetrazine, and benzphetamine were approved for short-term use as antiobesity medications in 1959–1960, before obesity was understood as a chronic disease requiring long-term management. As a consequence, long-term (one year or longer) data on these drugs are limited [3].

All sympathomimetic amines are contraindicated in patients with hyperthyroidism, glaucoma, or in patients taking monoamine oxidase (MAO) inhibitors; all four are DEA Schedule IV controlled substances [131].

Phentermine (Adipex-P, Lomaira)

Phentermine HCl is a centrally acting sympathomimetic, with therapeutic effects mediated through increased levels of norepinephrine in the hypothalamus [123]. It was approved for short-term use in 1959 based on a 36-week trial that showed a mean placebo-subtracted weight loss of 8.2 kg [92]. Two more recent randomized controlled trials in Korea confirmed the short-term efficacy of phentermine, both showing significant weight reduction compared with placebo over 12 weeks [131].

Common adverse effects in clinical trials include dry mouth (55%) and insomnia (34%), without significant differences in systolic or diastolic blood pressure, headache, or palpitations between phentermine and placebo groups [131]. Other common side effects include dizziness, flushing, fatigue, and constipation [92]. Phentermine is not recommended for patients with cardiovascular disease, and uncontrolled hypertension is a relative contraindication. Phentermine is available in 8-mg tablets taken three times daily and in 15-mg, 30-mg, and 37.5-mg capsules taken once daily [131].

Phentermine is the most commonly prescribed antiobesity medication and is discussed further in the section on clinical use of antiobesity medications as a potential low-cost generic option to more recently approved agents.

Diethylpropion (Tenuate)

Diethylpropion and bupropion are very closely related structurally [142]. In contrast to phentermine, diethylpropion has been used infrequently in the United States. This contrasts with Mexico, Brazil, and other countries in which diethylpropion is a preferred antiobesity medication and where recent randomized controlled trials have evaluated its safety and efficacy. Outside the United States, diethylpropion is called amfepramone [143].

In one study, weight loss after 52 weeks was greater in patients randomized to diethylpropion than placebo (10.0 kg vs 3.1 kg), and more participants achieved weight loss ≥5% (71.4% vs 33.3%) [144]. Of 156 patients randomized to diethylpropion (75 mg/daily) or placebo, mean weight loss at three months (4.9 kg vs 0.7 kg) and six months (7.7 kg vs 1.1 kg) showed clinical benefit persisting beyond the short-term. Improvements in triglycerides, heart rate, and systolic and diastolic blood pressure with diethylpropion were non-significant [145].

Potential adverse effects of diethylpropion are dry mouth and somnolence (most common), constipation, anxiety, and irritability, all described as mild and nonpersistent, except dry mouth [143; 144; 145].

Diethylpropion is available in 25-mg short-acting and 75-mg extended-release tablets that are taken three times or once per day, respectively [136].

Other Medications

In analyses of two small 12-week randomized controlled trials, phendimetrazine (Obezine) appears to have similar weight-loss effects as other noradrenergic drugs [146].

Benzphetamine (Didrex) is the least prescribed among the four noradrenergic antiobesity medications, and there are few data from controlled trials evaluating its safety or efficacy [136].

For Long-Term Use

Gelesis100 Oral Hydrogel (Plenity)

Gelesis100 superabsorbent hydrogel is ingested orally, similar to drugs, but is regulated by the FDA as a class II medical device, because it acts mechanically as a transient, space-occupying device in a swallowed capsule that absorbs water to expand and fill up the stomach to induce satiety. Gelesis100 is FDA approved for patients with BMI 25–40. Recommended dosing is three capsules (2.25 g/dose) with water before both lunch and dinner [30; 123].

After 24 weeks, more patients on Gelesis100 than placebo had weight loss >5% (58.3% vs 42.3%) and >10% (27.4% vs 15.0%), but the mean weight loss difference (2.02%) did not meet the pre-determined threshold of 3%. The AGA guideline recommends the use of Gelesis100 be limited to clinical trials due to its uncertain benefit [123].

Orlistat (Xenical, Alli)

Orlistat is a pancreatic and gastric lipase inhibitor that blocks the lipase-catalysed breakdown and absorption of around 30% of dietary fats. Orlistat is the only antiobesity medication that does not exert action in the brain; its modest weight-loss effect depends mostly on diet [147].

Orlistat is available in 60-mg capsules over the counter and 120-mg capsules by prescription, both taken three times daily [131]. In the four-year XENDOS trial that randomized 3,304 subjects with obesity to orlistat (120 mg three times daily) or placebo, weight loss was significantly higher with orlistat (5.8 kg vs 3.0 kg). The study also showed a reduced progression from prediabetes to diabetes with orlistat. Adverse effects observed in ≥10% of study populations included rectal leakage, abdominal pain, abdominal stress, flatulence with discharge, fecal urgency, steatorrhea, fecal incontinence, and increased defecation [140].

Overall weight loss with orlistat is of a small magnitude (2.78%). In contrast, the adverse effects are considered very bothersome and result in high treatment discontinuation rates. Therefore, the 2022 AGA obesity guideline suggests against the use of orlistat [123].

Phentermine/Topiramate ER (Qsymia)

Topiramate is an antiepileptic drug that was approved for seizures in 1996 and migraine prevention in 2004. The weight loss observed during epilepsy treatment led to clinical trials as a treatment for obesity, but topiramate development as an antiobesity medication was discontinued due to the associated adverse effects. However, clinical observations in private practice indicated that phentermine mitigated topiramate adverse effects and increased weight-loss efficacy when used together. This led to clinical trials to approve the combination as an antiobesity medication [136].

Topiramate is thought to suppress appetite by increasing dopamine release, inhibiting glutamate receptors, and modulating neuropeptide-Y, an orexigenic hormone. Phentermine/topiramate was approved in 2012 at fixed-dose 7.5/46-mg and 15/92-mg tablets, both taken once-daily [131].

Three phase 3 randomized controlled trials assessed the efficacy of phentermine/topiramate on weight loss: EQUIP, CONQUER and SEQUEL. In EQUIP, patients with obesity (mean BMI: 42) were randomized to 3.75/23 mg, 15/92 mg, or placebo. Mean weight loss was 5.1% (low-dose), 10.9% (high-dose), and 1.5% (placebo) at 56 weeks [140].

CONQUER randomized 2,487 adults with overweight or obesity and at least two weight-related complications to placebo, 7.5/46 mg, or 15/92 mg. Mean weight loss (1.4 kg, 8.1 kg, and 10.2 kg, respectively) and patients with ≥5% (21%, 62%, and 70%, respectively) and ≥10% (7%, 37%, and 48%, respectively) weight loss at 56 weeks were significantly greater with both phentermine/topiramate dose levels [131].

SEQUEL was a 52-week extension of CONQUER involving 676 subjects [148]. At week 108, mean weight loss from baseline was 1.8%, 9.3%, and 10.5% with placebo, 7.5/46 mg, and 15/92 mg, respectively. Absolute weight loss was 2.1 kg, 9.6 kg, and 10.9 kg. Across all levels, weight loss was greater for subjects in the treatment arms than in the placebo group, with more kilograms lost among the higher dosage. After 108

weeks, 50.3% and 53.9% of patients receiving phentermine/topiramate lost at least 10% of their body weight; 9.2% and 15.3% lost 20% or greater. This compares with 11.5% and 2.2%, respectively, of participants in the placebo group. At week 108, mean waist circumference reductions were -3.6 cm for placebo, -9.8 cm for the 7.5/46-mg dose, and -10.6 cm for the 15/92-mg group. The types of adverse events in SEQUEL were similar to those in CONQUER, but the incidence was markedly lower in the second year. Drop-out due to adverse events by week 108 were 3.1%, 4.5%, and 4.4% in placebo, 7.5/46 and 15/92 treatment arms. Both systolic and diastolic blood pressure decreased from baseline by 3–5 mm Hg at 108 weeks in all three treatment arms [148].

As with phentermine monotherapy, phentermine/topiramate ER is not recommended for patients with cardiovascular disease and is contraindicated in patients with hyperthyroidism or glaucoma or in those taking MAO inhibitors [131]. Topiramate is associated with cognitive and neuropsychiatric side effects. A meta-analysis found that, compared with placebo, adverse effects associated with phentermine/topiramate included dysgeusia or altered sense of taste, paresthesia, dry mouth, disturbance in attention, irritability, hypoesthesia, constipation, and dizziness [149]. Abrupt withdrawal of topiramate increases the risk of seizures, and downward titration should be gradual over four to five days [150].

During the two-year SEQUEL trial, the incidence of reported anxiety-related adverse events increased with dose in placebo (3.1%), 7.5/46-mg (6.5%), and 15/92-mg (9.5%) arms. Most were mild in severity, but three subjects in the 15/92-mg group experienced a severe anxiety-related adverse events and one discontinued treatment [148].

Topiramate is teratogenic, posing a risk for orofacial clefts in infants exposed in utero. Women of childbearing age prescribed any topiramate formulation should be counseled to use effective contraception [124].

Naltrexone/Bupropion ER (Contrave)

Bupropion is a norepinephrine and dopamine reuptake inhibitor with FDA-approval for depression and smoking cessation and is the antidepressant least likely to induce weight gain [131]. Bupropion stimulates hypothalamic POMC neurons, releasing α-MSH (which bind MC4R), decreasing food intake, and increasing energy expenditure. When α-MSH is released, POMC neurons also release β-endorphin, a μ-opioid receptor (MOR) ligand, which inhibits further release of α-MSH by activating a negative feedback loop. Naltrexone, an opioid receptor antagonist approved for the treatment of alcohol and opioid use disorder, blocks the β-endorphin-mediated negative feedback; the subsequent increase in POMC activity may underlie the weight loss effects of naltrexone/bupropion (Contrave) [115].

Each naltrexone/bupropion tablet contains naltrexone 8 mg plus bupropion 90 mg. The target maintenance dose of 4 tablets daily (naltrexone 32 mg/bupropion 360 mg) daily is shortened with the prolonged-release formulation (NB32). The initial dose is 1 tablet daily, increased stepwise to the target of 2 tablets twice daily. Typical weight loss seen in practice is around 5% to 6% with NB32s [131].

The Contrave Obesity Trials (COR) program evaluated NB32 versus placebo over 56 weeks in patients with obesity or overweight and weight-related complication(s) (COR-I, COR-II, and COR-BMOD) and in patients with obesity and type 2 diabetes (COR-DM). Mean weight loss with NB32 compared with placebo in COR-I (6.1% vs 1.3%), COR-II (6.4% vs 1.2%), COR-BMOD (9.3% vs 5.1%), and COR-DM (5.0% vs 1.8%) showed an average 4.35% weight loss advantage over placebo [139].

Common adverse effects of NB32 include nausea (30%), headache (14%), and constipation (15%), without significant differences in depression or suicidality events, insomnia, dizziness, or dry mouth between treatment and placebo groups [131]. NB32 has been shown effective in reducing HbA1c and is safe among subjects with type 2 diabetes taking oral antidiabetic agents [151]. NB32 can increase blood pressure and pulse despite weight loss [139]. While the cardiovascular safety of NB32 was investigated in the LIGHT trial, it was terminated prematurely after the study sponsor publicly released confidential favorable interim results after only 25% of expected vascular events had accrued, making it difficult to interpret the cardiovascular safety of this combination drug [131; 139].

Contraindications include pregnancy, uncontrolled hypertension, seizure disorder, eating disorder, severe hepatic dysfunction, and concurrent administration of MAO inhibitors [131]. Naltrexone/bupropion is contraindicated in any patient prescribed opioids for pain control and in any patient receiving medication therapy for alcohol or opioid use disorder.

Glucagon-Like Peptide-1 Receptor Agonists (GLP-1 RAs)

Endogenous GLP-1 has a very short half-life due to rapid enzymatic degradation by dipeptidyl peptidase-4 (DPP-4). Synthetic analogs modify the GLP-1 structure to resist DPP-4 by amino acid substitutions in the protein structure or by attachment to large proteins such as albumin or immunoglobulin [147]. Liraglutide shares a 97% amino acid sequence similarity with human GLP-1, while semaglutide has a 94% similarity. Compared with liraglutide, the substantially longer half-life and greater weight loss efficacy of semaglutide may involve differences in the attached fatty acids [139].

Liraglutide and semaglutide are used subcutaneously once-daily and once-weekly, respectively. Liraglutide was approved for type 2 diabetes in 2010 at a dosage of 1.8 mg daily. Subsequently, liraglutide became the first GLP-1 RA approved as antiobesity medication in 2014, and in 2020, its approval was expanded to include adolescents (12 years of age or older) at a dosage of 3.0 mg/day [147]. Liraglutide acts centrally on the arcuate nucleus in the hypothalamus to suppress appetite and potentiate satiety [151].

The SCALE Obesity and Prediabetes and SCALE Diabetes were both 56-week randomized controlled trials examining the effect of daily liraglutide 3.0 mg vs placebo on normoglycemia, prediabetes, and diabetes. Both trials demonstrated significantly greater weight loss with liraglutide. In SCALE Obesity and Prediabetes, weight loss was 8.0% with liraglutide vs 2.6% with placebo; in SCALE Diabetes, weight loss was 6.0% with liraglutide vs 2.0% with placebo. In the former trial, more participants in the liraglutide group achieved weight loss of ≥5% (63.2 vs 27.1%), ≥10% (33.1 vs 10.6%), and ≥15% (14.4 vs 3.5%) [131].

Gastrointestinal adverse effects are common, including nausea (40%), diarrhea (20%), constipation (20%), and vomiting (16%), and were the most common reason for liraglutide drop-out (6.4% vs 0.7% in the placebo group). Potentially serious adverse effects include gallbladder disease (2.5%) and pancreatitis (0.4%) [131]. A 2023 analysis of data including more than 5,000 patients receiving pharmacotherapy for obesity compared the incidence of adverse events associated with GLP-1 RAs with bupropion-naltrexone. Use of GLP-1 agonists compared with bupropion-naltrexone was associated with increased risk of pancreatitis (hazard ratio: 9.09), bowel obstruction (hazard ratio: 4.22), and gastroparesis (hazard ratio: 3.67) but not biliary disease [152].

Liraglutide is initiated at 0.6 mg daily for one week, with weekly increases in dose (by increments of 0.6 mg) to the recommended 3.0 mg dose [131]. Semaglutide was initially approved for the treatment of type 2 diabetes at a dosage of 1.0 mg weekly in 2017 and at 2.0 mg weekly in 2022. It was subsequently approved at a dosage of 2.4 mg per week for chronic management of obesity in 2021 [147].

Semaglutide directly accesses the hypothalamus, brainstem, and septal nucleus and also induces activation in secondary brain areas without direct GLP-1R interaction, thus having direct and indirect effects on neutral pathways involved in homeostatic (appetite, hunger, satiety) and hedonic (food preference, cravings, control of eating) aspects of food intake and reward-related eating behaviors. Conversely, only a very small percentage of weight loss is explained by delayed gastric emptying and gastrointestinal side effects [151].

The STEP clinical trials program evaluated semaglutide 2.4 mg in patients with obesity or overweight/weight-related complication(s); patients with type 2 diabetes were excluded [30]. At 68 weeks, semaglutide led to greater mean weight loss (14.9%) compared with placebo (2.4%); further, more patients in the semaglutide group experienced weight loss of ≥10% (69.1%), ≥15% (50.5%), and ≥20% (32.0%) than those in the placebo group (12.0%, 4.9%, and 1.7%, respectively).

In an extension of this study, patients in both the treatment and control arms were engaged in intensive behavioral therapy. The therapy consisted of a reduced-calorie diet (1,000–1,200 calories/day for the first seven weeks, followed by 1,200–1,800 calories/day for the remaining study period), 200 minutes exercise per week, and 30 individual therapy sessions with a registered dietitian. The mean weight loss was 16.0% with semaglutide/intense behavioral therapy, compared with 5.7% with placebo and intense behavioral therapy. The authors concluded that intense behavioral therapy plus eight-week low-calorie diet ultimately may not confer significant weight-loss advantages beyond those achieved with semaglutide and less-intensive lifestyle interventions (i.e., 18 behavioral counseling sessions over 68 weeks) [30].

Another extension of the study, referred to as STEP 4, focused on weight-loss maintenance. All patients were initiated on semaglutide and, at week 20, were randomized to either semaglutide continuation or placebo for the remaining 48 weeks (i.e., weeks 20–68). The semaglutide continuation group further lost 8% of weight, for a total 17% weight loss. The placebo group gained 7% of weight during the same period, for a total 5% weight loss.

STEP 5 also examined the durability of weight reduction over two years. At week 104, mean weight loss from baseline was 15.2% with semaglutide compared with 2.6% with placebo (treatment difference: 12.6%).

Finally, STEP 8 was a head-to-head comparison of semaglutide 2.4 mg per week and liraglutide 3.0 mg per day over 68 weeks. Mean weight loss was 6.4% with liraglutide and 15.8% with semaglutide, a 9.4% advantage over liraglutide. While gastrointestinal adverse events were similarly common with semaglutide (84.1%) and liraglutide (82.7%), the drop-out rate due to adverse events was significantly higher with liraglutide than semaglutide (12.6% vs 3.5%) [140].

As of 2023, oral semaglutide is the only oral GLP-1 RA approved for the treatment of type 2 diabetes, at a dosage of 14 mg per day (Rybelsus). Higher doses are being investigated for weight effects in obesity without type 2 diabetes in the OASIS trials [147]. The phase 3 OASIS 1 trial assessed oral, once-daily semaglutide 50 mg in 667 adults with obesity without type 2 diabetes. After 68 weeks, participants on semaglutide had greater mean weight loss (15.1% vs 2.4%), weight loss ≥10% (69% vs 12%), ≥15% (54% vs 6%), and ≥20% (34% vs 3%) compared with placebo. Adverse effects (mostly mild-to-moderate gastrointestinal symptoms) occurred in 80% on semaglutide and 46% on placebo. These outcomes mirror those of semaglutide 2.4 mg subcutaneous [153]. Phase 3 trials have completed, and submission for FDA approval is expected in 2024. Of note, there are currently no registered clinical trials comparing oral with subcutaneous semaglutide for obesity [92].

The liraglutide, semaglutide, and tirzepatide labels carry a boxed warning regarding the risk of thyroid C-cell tumors. All three antiobesity medications are known to cause dose-dependent and treatment-duration-dependent thyroid C-cell tumors at clinically relevant exposures in rodents [20; 137]. It is unknown whether semaglutide for obesity causes thyroid C-cell tumors, including medullary thyroid carcinoma (MTC), in humans, as the human relevance of semaglutide-induced rodent thyroid C-cell tumors has not been determined. However, semaglutide for obesity is contraindicated in patients with a personal or family history of MTC or in patients with

multiple endocrine neoplasia syndrome type 2 (MEN 2) [20; 137]. All patients should be counseled regarding the potential risk of MTC and symptoms of thyroid tumors (e.g., a mass in the neck, dysphagia, dyspnea, persistent hoarseness).

In addition, acute pancreatitis, including fatal and non-fatal hemorrhagic or necrotizing pancreatitis, has been observed in patients treated with GLP-1 receptor agonists [20; 137]. These agents have not been studied in patients with a history of pancreatitis; if used as an antidiabetic agent, clinicians should consider an alternate option in such patients.

Data are lacking on use in pregnant women. However, reproduction studies in animals have shown teratogenic effects. There is no published research linking semaglutide to decreased oral contraceptive efficacy. However, any medication associated with delayed gastric emptying could theoretically impact the absorption of oral contraceptive agents.

A meta-analysis of treatment with GLP-1 RAs found liraglutide or dulaglutide associated with increased risk for gallbladder or biliary diseases; subcutaneous semaglutide and exenatide associated with non-significant increased risk; and higher-dose subcutaneous semaglutide associated with increased gallbladder or biliary diseases. Oral semaglutide, lixisenatide, and albiglutide are not associated with these increased risks [154].

GLP-1 RAs may be associated with increased risk of gallbladder or biliary diseases because GLP-1 inhibits gallbladder motility and delays gallbladder emptying by suppressing cholecystokinin secretion. The risk of gallbladder or biliary diseases was higher in trials for weight loss than diabetes control, which may relate to the greater weight loss, GLP-1 RA dose, or treatment duration [154]. When assessing potential risk to patients, prescribers should consider the denominator for essential context, when possible. The overall absolute risk increase, an additional 27 cases per 10,000 persons treated per year, was small and should be weighed against the demonstrated benefits of obesity treatment with GLP-1 RAs [154].

Tirzepatide

Tirzepatide was approved for type 2 diabetes treatment by the FDA (as Mounjaro) and the European Medicines Agency in 2022 [147]. In 2023, the FDA approved the agent for chronic weight management [155].

Tirzepatide acts as a dual incretin agonist of GLP-1R and glucose-dependent insulinotropic polypeptide (GIP) receptor and is dubbed the "twincretin" [135]. Tirzepatide has five-fold greater potency at GIPR than GLP-1R [132].

GIP was the first incretin hormone identified, but its therapeutic potential was disregarded because chronic hyperglycemia in type 2 diabetes down-regulates GIPR expression in β-cells, blunting response to GIP. Normalizing blood glucose can restore GIPR sensitivity to GIP [139; 147]. With a GIP/GLP-1 receptor agonist, GLP-1 quells the potential glucagon-stimulatory effects of GIP and (re)sensitizes β-cells to GIP's incretin effects, while potentially enhancing GIP's beneficial effects on weight regulation mechanisms [147].

GIPR agonism may have effects on adipocytes that include increasing lipoprotein lipase, promoting lipogenesis, enhancing fatty acid and glucose uptake, and inhibiting lipolysis mediated by glucagon and adrenergic receptors [139]. However, the relative contributions of GLP-1R vs GIPR agonist effects to weight loss have yet to be clearly defined [156].

SURPASS-1 compared tirzepatide (5 mg, 10 mg, or 15 mg) to placebo for 40 weeks, finding significant mean reductions in hemoglobin A1C (-1.87%, -1.89%, -2.07%) and body weight (-7.9%, -9.3%, -11.0%) for all tirzepatide doses versus placebo [131]. SURPASS-2 compared tirzepatide (5 mg, 10 mg, or 15 mg) with semaglutide 1.0 mg weekly, finding more effective and dose-dependent reductions in body weight, blood pressure, and hemoglobin A1C with tirzepatide [131]. (Note that semaglutide 1.0 mg is a subtherapeutic dose for weight-loss efficacy.)

SURMOUNT-2 randomized 1,514 adults to tirzepatide or placebo. At week 72, mean weight loss with tirzepatide 10 mg or 15 mg or placebo was 12.8%, 14.7%, and 3.2%, respectively. This translated to mean differences vs placebo of 9.6% and 11.6% for 10 mg and 15 mg. More participants had weight loss ≥5% with tirzepatide (79% to 83%) than placebo (32%). The most frequent adverse effects with tirzepatide were gastrointestinal-related, including nausea, diarrhea, and vomiting, mostly mild to moderate in severity, and few led to drop-out (<5%). Serious adverse events were reported by 7% of participants overall [157].

In the phase 3 SURMOUNT-1 trial, 2,539 patients with obesity without type 2 diabetes were randomized to weekly tirzepatide (5 mg, 10 mg, or 15 mg) or placebo [133]. Mean weight loss at week 72 was unprecedented (***Table 7***) [131]. Notably, 50% and 57% of participants in the 10- and 15-mg groups had weight loss ≥20% [131]. For the first time ever, weight loss with a medication approached levels that had only been possible with bariatric surgery.

Drop-out from adverse effects was 4.3%, 7.1%, and 6.2% with 5 mg, 10 mg, and 15 mg tirzepatide, respectively, and 2.6% with placebo. The incidence of adverse effects was similar in 10- and 15-mg groups, while the proportion of ≥10%, ≥15%, and ≥20% weight-loss was higher with 15 mg. This suggests the 15-mg dose may confer additional benefits in some patients without added safety concerns [133].

Participants treated with tirzepatide had a percent reduction in fat mass approximately three times greater than the reduction in lean mass, resulting in an overall improvement in body composition. The ratio of fat-mass loss to lean-mass loss is similar to lifestyle and surgical treatments for obesity [133].

Nearly all participants (>95%) with prediabetes initiated on tirzepatide converted to normoglycemia by 72 weeks (compared with 62% with placebo plus lifestyle changes). These improvements may translate to reduced risk of cardiovascular disease, chronic kidney disease, NAFLD, and type 2 diabetes, among other outcomes. Studies of this are still in progress [133].

SURMOUNT-1 WEIGHT-LOSS OUTCOMES AT 72 WEEKS				
Weight Loss Parameter	**Tirzepatide**			**Placebo**
	5 mg	**10 mg**	**15 mg**	
Mean weight loss	15.0%	19.5%	20.9%	3.1%
≥5% weight loss	85.1%	88.9%	90.9%	34.5%
≥10% weight loss	68.5%	78.1%	83.5%	18.8%
≥15% weight loss	48.0%	66.6%	70.6%	8.8%
≥20% weight loss	30.0%	50.1%	56.7%	3.1%
≥25% weight loss	15.3%	32.3%	36.2%	1.5%
Mean reduction in waist circumference	14.0 cm	17.7 cm	18.5 cm	4.0 cm

Source: [133] *Table 7*

The safety profile of tirzepatide was consistent with previous findings in the SURPASS trials in patients with type 2 diabetes and similar to other incretin-based therapies for the treatment of obesity. Cholecystitis was observed more frequently with tirzepatide, but the low incidence (≤0.6%) made causal conclusions difficult. Gallbladder-related events have been reported to increase in persons with considerable weight reduction and are also observed with other obesity therapies, such as bariatric surgery and treatment with GLP-1 receptor agonists [133].

Meta-analyses have variously examined the effectiveness and safety of tirzepatide compared with semaglutide in obesity. Head-to-head comparative trials have not been conducted, so indirect comparisons were used. One analysis found greater weight loss with tirzepatide 10 mg and 15 mg than semaglutide 2.4 mg [158]. Another found no significant difference from semaglutide in gastrointestinal adverse effects [159]. Together, these trials show promise for tirzepatide as an effective and safe medication for both weight reduction and glycemic control in patients with obesity with or without type 2 diabetes. Typical adverse effects are similar to GLP-1 agonists and include nausea, vomiting, and diarrhea. No clinically significant hypoglycemia was reported in any trial [131].

GLP-1 RAs provide substantial benefits in glycemic control and weight loss while improving health-related quality of life among individuals with type 2 diabetes. GLP-1 RAs have also been shown to significantly decrease the risk of cardiovascular and all-cause mortality in type 2 diabetes, producing a significant reduction in the risk for non-fatal myocardial infarction and non-fatal stroke. However, their impact on heart failure-related outcomes is nil [160].

Compared with semaglutide in subjects with type 2 diabetes, tirzepatide produced significantly more improvements in total insulin secretion and insulin sensitivity, reflecting a significant improvement in pancreatic β-cell function. Similar effects were also documented in another trial comparing tirzepatide with the GLP-1 RA dulaglutide, suggesting that dual receptor agonism might be responsible for improving insulin sensitivity, especially since the observed effect was only partially attributable to weight loss [160].

The question that inevitably arises is whether tirzepatide is more efficacious and equally safe compared with GLP-1 RAs. When tirzepatide was compared with GLP-1 RAs, it was not associated with a significant increase in the odds of nausea, vomiting, or diarrhea, except for tirzepatide 10 mg, which correlated with 51% greater odds for diarrhea compared with GLP-1 RA treatment. Tirzepatide use in subjects with type 2 diabetes did not significantly impact the incidence of any serious adverse effects compared with placebo, basal insulin, or GLP-1 RAs [160].

The cardiovascular safety of tirzepatide in type 2 diabetes was demonstrated in a meta-analysis of seven trials and 7,215 subjects randomized to tirzepatide, placebo, or an active comparator. Tirzepatide was associated with a non-significant decrease in the risk for major adverse cardiovascular events (e.g., cardiovascular death, myocardial infarction, stroke, hospitalized unstable angina) and all-cause death [161].

Current evidence suggests that tirzepatide might be more efficacious than GLP-1 RAs in terms of improvements in glycemia, body weight, β-cell function, and insulin sensitivity. Tirzepatide seems at least equally safe as GLP-1 RAs by not increasing the odds for serious adverse events [160].

Results of the ongoing cardiovascular outcome trial (SURPASS-CVOT) are awaited to answer whether tirzepatide exerts cardioprotective effects similar to that observed with GLP-1 RAs. In this trial, tirzepatide is compared with dulaglutide on major cardiovascular events in patients with type 2 diabetes and increased cardiovascular risk. Because dulaglutide has a confirmed cardioprotective effect, this head-to-head study will be particularly informative [160]. The study is expected to conclude in late 2024.

Tirzepatide is known to reduce the efficacy of oral contraceptive medications due to delayed gastric emptying. This delay is largest after the first dose, so patients should switch from oral to nonoral contraceptives for the first four weeks when tirzepatide is initiated [162]. Patients should be counseled regarding the risk of unintended pregnancy and the necessity of other contraceptive methods.

INVESTIGATIONAL ANTIOBESITY MEDICATIONS IN CLINICAL TRIALS

Given the heterogeneity and complex pathogenesis of obesity, combination therapy with multiple pathophysiologic targets is a logical approach to increasing weight-loss response with pharmacotherapy [163]. Peptide engineering, exemplified by tirzepatide, allows the development of multi-receptor agonists [139]. Other antiobesity medications in development include oral GLP-1R mono-agonists. Except where noted, the following agents are administered subcutaneously once weekly.

Cagrilintide

Amylin, a pancreatic hormone released with insulin in response to nutrient intake, acts on:

- Appetitive/energy-regulating hypothalamic neurons impacting food intake
- Dopaminergic neurons in the ventral tegmental area impacting reward and motivation
- Chemoreceptive neurons in the brainstem nucleus tractus solitarius

Pramlintide, the first amylin analog, was approved in 2005 as an adjunct to insulin for type 1 and type 2 diabetes and promotes weight loss in patients with diabetes by substituting three amino acids of human amylin with proline [139; 147]. Cagrilintide is an emerging agent that overcomes pramlintide's short half-life and frequent administration as a long-acting amylin analog. Cagrilintide is being developed in combination with semaglutide (CagriSema) to achieve sustained weight loss in persons with obesity. Both cagrilintide and CagriSema have shown promising weight loss and safety in clinical trials that supports their further development [163].

Among 706 individuals with obesity after 26 weeks, mean weight loss with cagrilintide 4.5 mg (10.6%) and 2.4 mg (9.7%) was greater than with liraglutide 3.0 mg (8.4%) and placebo (2.8%). Side effects of cagrilintide include nausea, diarrhea, constipation, fatigue, and injection-site reactions [147].

CagriSema combines cagrilintide with semaglutide to produce an additive effect on appetite reduction and weight loss [163]. In a trial of adults with obesity, mean weight loss at 20 weeks was 17.1% with CagriSema, compared with 9.8% with semaglutide 2.4 mg [147]. Among 92 adults with type 2 diabetes and BMI ≥27 randomized to once-weekly CagriSema, semaglutide, or cagrilintide (all escalated to 2.4 mg), mean weight loss at week 32 with CagriSema (15.6%) was significantly greater than semaglutide (5.1%) or cagrilintide (8.1%). Mild or moderate gastrointestinal adverse effects were common and comparable. No moderate or greater hypoglycemia was reported [164].

Retatrutide (LY3437943)

A triple agonist may provide even more effective glycemic control and weight loss compared to single or dual receptor agonists. Retatrutide is a triple agonist at GCGR, GIPR, and GLP-1R [139]. A phase 2 dose-response study evaluated retatrutide in 338 adults with obesity [165]. At 48 weeks retatrutide 1 mg, 4 mg, 8 mg, and 12 mg led to 8.7%, 17.1%, 22.8%, and 24.2% mean weight loss, compared with a 2.1% reduction with placebo. Among those who received 8 mg or 12 mg retatrutide, 91% and 93% experienced weight loss ≥10% and 75% and 83% experienced weight loss ≥15% (compared with 9% and 2% among those receiving placebo).

Dose-related mild-to-moderate nausea, diarrhea, vomiting, and constipation were the most common retatrutide adverse effects, partially mitigated with a lower starting dose (2 mg vs 4 mg). Dose-dependent increases in heart rate peaked at 24 weeks and declined thereafter [165; 166].

Survodutide (BI 456906)

Survodutide is a dual GLP-1 and glucagon receptor (GCGR) agonist developed for obesity and NASH treatment. As glucagon release from pancreatic a-cells increases blood glucose, antagonism was initially pursued as a type 2 diabetes treatment. More recent studies have localized GCGR to adipose tissue, brain, and liver and have shown that GCGR activation increased energy expenditure via thermogenesis [139; 147]. An agent combining selectively increased energy expenditure with appetite suppression is a reasonable strategy for effective weight loss or weight maintenance [139]. Hepatocytes express GCGR, but not GLP-1R, and drugs like survodutide that target GCGR may have greater benefit in improving liver fibrosis or NASH than GLP-1RAs [139].

In Phase 1 studies of survodutide, maximum placebo-corrected weight loss was 13.8% after 16 weeks, including 12.37% in Japanese men with no unexpected tolerability concerns [167; 168]. Common survodutide adverse effects included nausea, dyspepsia, vomiting, diarrhea, abdominal pain, and headache [167].

AMG-133

Co-agonism is not the only possible strategy for a unimolecular antiobesity medication. AMG-133 is a GCGR antagonist and GLP-1R agonist [25]. In one study, individuals with obesity averaged 14.3% weight loss after 12 weeks on higher-dose AMG-133. AMG-133 was associated with adverse gastrointestinal effects, but its once-monthly subcutaneous use may be advantageous to weekly tirzepatide [141]. If replicated, the rapidity and extent of this weight loss provokes questions regarding the drug's mode of action and the role of GIP and GLP-1 in physiologic weight regulation [25]. As of 2023, peer-reviewed publication of the full trial results is awaited [141].

Bimagrumab (BYM338)

Bimagrumab is a human monoclonal antibody that binds to the activin type II receptor (ActRII). Antibody blockade of ActRII signaling stimulates skeletal muscle growth, and previous studies suggest that ActRII inhibition with bimagrumab also promotes excess adipose tissue loss and improves insulin resistance [169]. A single intravenous dose of bimagrumab increased lean mass, reduced total body fat mass (by 7.9%), and ameliorated insulin sensitivity in insulin-resistant individuals during the 10-week study [92].

A phase 2 trial randomized adults with obesity and type 2 diabetes to IV bimagrumab (10 mg/kg up to 1,200 mg) or placebo every 4 weeks for 48 weeks. Body composition changes used dual x-ray absorptiometry (DEXA) and magnetic resonance imaging. At week 48, mean changes with bimagrumab vs placebo were noted in fat mass (-20.5% vs -0.5%), lean mass (3.6% vs -0.8%), waist circumference (-9.0 cm vs 0.5 cm), and body weight (-6.5% vs -0.8%) [169]. Muscle spasms and mild diarrhea were the most common adverse effects with bimagrumab. Further studies on the efficacy and safety of bimagrumab are ongoing [92].

Orforglipron (LY3502970)

Orforglipron, an oral once-daily nonpeptide GLP-1 RA, was evaluated in 272 adults randomized to orforglipron (12 mg, 24 mg, 36 mg, or 45 mg) or placebo for 36 weeks [170]. Mean weight loss with orforglipron was 9.4% to 14.7%, compared with 2.3% with placebo. In those taking orforglipron, weight loss ≥10% was noted in 46% to 75%, compared with 9% of patients taking placebo. Orforglipron led to improvement in all prespecified weight-related and cardiometabolic endpoints [170].

The most common orforglipron adverse effects were mild-to-moderate gastrointestinal events, primarily during dose escalation, and led to discontinuation of orforglipron in 10% to 17% of participants across dose cohorts. The safety profile was consistent with GLP-1RAs [170]. This trial mirrored the safety and weight reduction findings of a smaller oral orforglipron trial in patients with type 2 diabetes [171].

Danuglipron

Danuglipron is another oral GLP-1 RA under development for type 2 diabetes and obesity and is taken twice-daily with food [147]. A phase 2b trial randomized 411 adults with type 2 diabetes to placebo or danuglipron. At week 16, mean weight loss difference vs placebo was –2.04 kg and –4.17 kg with danuglipron 80 mg and 120 mg, respectively. The most common adverse effects were nausea, diarrhea, and vomiting. Only 77% of patients completed the trial [172]. In a 12-week, dose-escalation study of adults with type 2 diabetes, discontinuation from danuglipron due to adverse effects ranged from 27.3% to 72.7% [173].

Ecnoglutide

Ecnoglutide is a novel, long-acting GLP-1 analog being explored for patients with diabetes and obesity. In laboratory tests, ecnoglutide was effective at stimulating the production of cAMP, a key signaling molecule involved in glucose control and body weight regulation. In a phase 1 clinical trial, ecnoglutide was found safe and well-tolerated, with pharmacokinetic properties that support once-weekly subcutaneous injections [174].

In a phase 2 trial of 206 participants with obesity and diabetes, weekly ecnoglutide 1.2 mg, 1.8 mg, or 2.4 mg led to weight loss of 11.5%, 11.2%, and 14.7%, respectively, vs 8.8% with daily liraglutide 3.0 mg [175]. A phase 3 dose comparison trial was initiated in early 2023 [176].

Mazdutide

Mazdutide is a novel once-weekly GLP-1 and glucagon receptor dual agonist. As an oxyntomodulin analogue, mazdutide may also increase energy expenditure and improve hepatic fat metabolism through the activation of glucagon receptor. In a phase 2 trial in China, mazdutide 9 mg led to a mean weight loss of 15.4%, a weight change vs placebo of -14.7 kg, and weight loss ≥20% in 21.7% of participants (vs 0% with placebo) after 24 weeks [177].

APH-012

APHD-012 is a novel approach to address metabolic disease through the delivery of dextrose to the lower small intestines via an oral bead formulation. In the 1960s, researchers found that glucose delivered directly distal to the jejunum better stimulated insulin release and secretion of GLP-1 and GIP compared with glucose delivered higher up the tract. This agent builds on such research [178].

As of 2023, a Phase 2 trial involving 150 adult obese participants with or without endocrine/metabolic conditions is underway [179].

ARD-101

ARD-101 is a potential bitter taste receptor (TAS2R) agonist that stimulates the release of the body's natural CCK, but primarily targets vagal nerve afferents located near the gut; this in turn induces positive effects on hunger, metabolism, and inflammation through gut-brain signaling. Three phase 2 trials were initiated in 2022 to assess efficacy and safety in adults with general obesity, adults with refractory post-bariatric weight gain, and those with Prader-Willi Syndrome, a rare genetic disorder characterized by persistent hyperphagia [180].

In the general obesity trial, patients treated with ARD-101 experienced a 2.51-fold greater reduction in hunger rating vs placebo [181]. Nausea or diarrhea common among available GLP-1 drugs were not noted in the ARD-101 group.

HU6

HU6 has demonstrated inhibition of phosphodiesterase 9A in mice linked to reduced body (and myocardial) fat and stimulated mitochondrial activity, without altered activity levels or food intake [182]. In this trial, positive weight loss effects were exclusively observed in male and ovariectomized female mice, suggesting a strong sexual dimorphism in treatment response. A phase 2 trial initiated in 2023 enrolled 250 participants with type 2 diabetes at risk for NASH and will compare three doses of HU6 on weight loss and hepatic function effects [183].

Nabilone

The endocannabinoid system is involved in the regulation of body weight and metabolism throughout the body. In the CNS, endocannabinoids bind to CB1 receptors in the hypothalamus (which control appetite), gastrointestinal tract, pancreas, and adipose tissue [184]. Elevated endocannabinoid levels can lead to increased hunger and food intake.

However, a meta-analysis of data from the National Epidemiologic Survey on Alcohol and Related Conditions and the National Comorbidity Survey-Replication found a decreased prevalence of obesity among current users of cannabis (≥3 days per week) of 14.3% and 17.2%, respectively [185]. Given this decreased likelihood of obesity in current cannabis users, research has begun to explore how the endocannabinoid system can be manipulated to promote weight loss and improve metabolic health.

Nabilone is an oral synthetic Δ9–THC analog and partial CB1 agonist approved for the treatment of cancer and HIV cachexia for increasing appetite and body weight. A randomized controlled trial of cannabis-naive adults with obesity is underway to examine safety and feasibility, weight-loss effectiveness, changes in gut microbiome, and metabolic markers [186]. The results are expected in 2024–2025.

NNC9204-1177

NNC9204-1177 is a glucagon/GLP-1 receptor co-agonist that underwent three phase 1 trials. After 12 weeks, mean weight loss was 12.6% at the higher dose level. However, dose-dependent increases in heart rate (5–22 beats per minute) and decrease in reticulocyte count, increased markers of inflammation, hepatic disturbances, and impaired glucose tolerance halted further clinical development [187].

CLINICAL USE OF ANTIOBESITY MEDICATIONS

If permanent weight loss could be achieved solely with behavioral reductions in food intake and increases in energy expenditure, antiobesity medications would not be needed [120]. Unfortunately, this is not commonly the case. Thus, antiobesity medication pharmacotherapy is indicated as an adjunct to caloric restriction and physical activity in adults with obesity or overweight with weight-related complications [131].

Antiobesity medication approvals have been based on efficacy as adjunctive treatment, including 1960s phentermine trials with 1,000 calorie/day diets for both drug and placebo groups; none have been shown to be effective on their own, because such studies have not been conducted [120; 131; 188]. Patients should be educated that the addition of antiobesity medications to a lifestyle program enhances weight loss, as clinical trials have demonstrated [131]. For example, 224 adults were initiated on sibutramine (discontinued in 2020) and randomized to brief lifestyle counseling or to a comprehensive diet, exercise, and behavior therapy program. At 12 months, mean weight loss with sibutramine plus brief counseling was 4.6% compared with 11.2% among those who received sibutramine plus comprehensive intervention [189].

As of 2023, few professional organizations have independently produced practice recommendations for current antiobesity medication options. In adults for whom antiobesity medications are indicated (per FDA), the 2022 AGA guideline states that long-term pharmacologic therapy is recommended, with multiple effective and safe treatment options that include semaglutide 2.4 mg, liraglutide 3.0 mg, phentermine-topiramate ER, naltrexone-bupropion ER, phentermine, and diethylpropion [123].

Explicit first-choice recommendations have also been made. Data show that greater weight loss (≥10%) leads to greater clinical improvements in weight-related complications, including greater relative risk reduction for cardiovascular events, improvements in NASH histology, decreased disease activity in inflammatory rheumatic disease, and improvements in osteoarthritis, obstructive sleep apnea, and cancer risk [131].

Given the significantly greater weight loss with semaglutide (15%) than other currently approved antiobesity medications (6% to 10%) and with 69% and 50% of subjects attaining weight loss ≥10% and >15%, respectively, semaglutide 2.4 mg weekly is recommended as the first-line antiobesity medication for obesity management [131]. Weight-loss goals for most individuals with obesity should be at least 10% or more, which is now achievable with current antiobesity medications.

After initiating any antiobesity medication, the weight lost by 12 weeks is considered an indicator of treatment response. If adherence can be ensured and 5% weight loss is not achieved after three months, the drug can be given at an increased dose, combined with another drug, stopped altogether, or replaced with a new drug [135].

Nonetheless, long-term pharmacotherapy is still challenged by some who question whether obesity itself constitutes a disease worthy of chronic drug therapy. Lifelong pharmacologic management of chronic diseases such as hypertension might offer a relevant template for obesity treatment strategies. In these diseases, it is common practice to target multiple mechanisms to achieve optimal disease management. It seems inevitable, and with good precedent, that such a conceptual approach to lowering body weight will eventually prevail [132].

Practical Tips for Success with GLP-1 Agonists

When starting GLP-1 agonists, several strategies can promote success and decrease risk of discontinuation. Strategies to minimize adverse effects include slow dose escalation, counseling on expected adverse effects and their duration, and using a multidisciplinary team approach (including the primary care provider, pharmacists, nurses, and medical assistants) to provide regular follow-up and guidance as patients initiate the medication. It is particularly important to discuss gastrointestinal adverse effects, as patients who are not expecting these adverse effects may prematurely discontinue the medication [131].

Routine follow-up can come in many forms, including virtual visits, phone calls, pharmacist check-ins, or even portal messages at routine intervals. This type of follow-up can increase communication with the patient, normalizing expected adverse effects and allowing tighter dose titration, while also reducing the number of clinical visits a patient has to make, thereby reducing primary care provider burden and overall healthcare

FDA-APPROVED ANTIOBESITY MEDICATIONS AND RETAIL COST, 2023		
Agent	**Typical Maintenance Dose**	**Average Retail Price, 30-Day Supply**
Phentermine	8–37.5 mg daily	$11.31
Diethylpropion	75 mg daily	$48.73
Orlistat	60 mg TID (OTC) 120 mg TID (Rx)	~$45.00 (Alli) $808.06 (Xenical)
Naltrexone/bupropion ER	16/180 mg BID	$308.00
Phentermine/topiramate ER	7.5–15/46–92 mg daily	$231.07
Liraglutide 3.0 mg	Once daily	$1,064.86
Semaglutide 2.4 mg	Once weekly	$1,576.73
Tirzepatide (2.5 mg, 5 mg, 7.5 mg, 10 mg, 12.5 mg, 15 mg)	Once weekly	$1,059.87
BID = twice daily, OTC = over the counter, Rx = prescription, TID = three times daily.		
Source: [131]		*Table 8*

costs. Other strategies include a dose escalation period, with one-week dose pause when adverse effects are encountered, which may minimize nausea/vomiting. Gastrointestinal adverse effects may also be reduced by avoiding high-fat foods and focusing on small meals [131].

Demand and Supply Problems

Interest in GLP-1 RAs has expanded beyond clinicians and patients struggling to lose excessive body-fat mass. Formulations of semaglutide approved for type 2 diabetes (Wegovy and Ozempic) have gained attention as celebrities and social media influencers have described taking thee agents to lose weight in short timeframes [190]. Many people have described in the media how taking semaglutide for obesity fundamentally changed their experience of hunger and appetite [191]. Consumer demand has led to widespread supply shortages of both products and concerns that people will associate them with "vanity," not as critical medications for patients with diabetes with or without obesity [190].

Additionally, news reports have commented on the possible misuse of semaglutide and other GLP-1 analogs. The issue is facilitated by the acquisition of medications from rogue websites. Pharmacists have reported forged prescriptions and use for weight loss in patients without diabetes. Social media influencers' semaglutide promotion for weight-loss, and the associated increase in demand, have contributed to an ongoing worldwide shortage of the drug in 2023 [192].

Off-Label Prescribing of Antiobesity Medications

If all antiobesity medications could be prescribed based on individualized patient need without affordability concerns, discussion of off-label use would not be needed. Unfortunately, medication cost and insurance coverage are the primary drivers in selecting antiobesity medications for an individual patient. In a 2018 review of 136 marketplace health insurance plans, only 11% had coverage for antiobesity medications [193]. Medicare excludes drug therapy for obesity, and only 11 state Medicaid programs have full antiobesity medication coverage (California, Kansas, Minnesota, Wisconsin, Michigan, Pennsylvania, Virginia, Delaware, Rhode Island, Connecticut, and New Hampshire); a limited number of other states may offer partial coverage [131]. Even for patients with insurance, cost can be a barrier due to the lack of antiobesity medication coverage under the diagnosis of obesity [124].

In this context, off-label prescribing includes prescribing an antiobesity medication for longer than its labeled duration [194]. Phentermine as a long-term option is obviously attractive given its low cost (***Table 8***), and there are several considerations to weigh.

The original 90-day label has not been updated since 1959, despite phentermine approval for long-term treatment of obesity when combined with topiramate as Qsymia [124]. Its short-term indication is in conflict with what is now known about the nature of obesity necessitating long-term treatment [195]. When a patient shows good therapeutic response and tolerability with phentermine, the Endocrine Society states this presents a conundrum for clinicians because it is clear that weight regain will likely occur once the medication is stopped [120].

Phentermine has long been the most commonly prescribed antiobesity medication due in large measure to its low potential for CNS stimulation and abuse, its low price as a generic drug, and clinician familiarity [136]. A large proportion has been for off-label doses and durations to sustain a positive clinical response [195].

Authors of the Endocrine Society practice guideline acknowledged little evidence of any serious side effects with long-term phentermine monotherapy and concluded it was reasonable to prescribe it long-term for patients who:

- Lack serious cardiovascular disease and/or serious psychiatric or substance use disorder
- Have been informed about FDA-approved antiobesity medications shown safe and effective for long-term use while phentermine has not
- Do not show clinically significant increases in pulse or blood pressure
- Show significant weight loss on phentermine

These aspects of care should be documented in the patient's medical record, and the off-label nature of the prescribing documented at each visit [120].

Subsequent to this clinical practice guideline, an observational study of 13,972 adults with obesity, including those with hypertension (21%) and type 2 diabetes (12%), initiated on phentermine found no increase in cardiovascular risk with long-term use up to 36 months versus use 3 months of less [196].

An obesity medicine specialty clinic also examined the abuse liability of phentermine treatment in 269 patients administered validated, structured addiction medicine interviews. No evidence was found of compulsive use, cravings, unsanctioned dose escalation, or withdrawal symptoms on abrupt cessation, including at doses much higher than commonly recommended and after treatment durations of up to 21 years [197].

The AGA and the ASMBS recommend phentermine as a long-term antiobesity medication option. The OMA convened a roundtable discussion of phentermine by expert clinicians, who suggested that, while not required by the prescribing label, prescribers may obtain an electrocardiogram (ECG) before starting phentermine. In addition to finding troubling wave patterns or cardiac dysrhythmias, a baseline ECG helps bring piece-of-mind to patient and clinician. Some clinicians perform ECGs on all patients before any intensive weight loss program or antiobesity medication [198]. In addition, the experts state that phentermine can be combined with GLP-1 RAs or other antidiabetic drug classes for further weight reduction, especially in patients with a high burden of obesity. Phentermine should not be used in patients with active cardiovascular disease nor as first-line antiobesity medication with advanced age or cardiovascular disease risk factors. Patients with a history of methamphetamine use are best treated with DEA unscheduled, non-stimulant antiobesity medications or bariatric procedures [198].

It is important to pick the right drug for the right patient. A patient who tends to skip meals all day and eat large volumes late at night might not be a good match for morning phentermine, which would mainly reduce daytime hunger. If phentermine is prescribed, patients should be advised that they may have trouble sleeping for two to three nights after initiating phentermine [198].

Canagliflozin is an SGLT2 inhibitor approved for type 2 diabetes. In a randomized controlled trial of 335 subjects without type 2 diabetes (mean BMI: 37.3), the weight loss effects of once-daily canagliflozin 300 mg (Cana), phentermine 15 mg (Phen), or combined Cana/Phen were compared after 26 weeks [199]. Mean weight loss with placebo, Cana, Phen, and Cana/Phen was 1.1%, 2.6%, 4.6%, and 8.1%, respectively. Weight loss with Cana/Phen continued through week 26, with no apparent plateau. The Cana/Phen group also had greater improvements in blood pressure and heart rate. This study demonstrated the complementary renal effects with canagliflozin and CNS activity with phentermine on weight loss [199].

In commenting about the cost barrier of phentermine/topiramate ER, some have suggested prescribing phentermine and generic topiramate separately at monotherapy dosages that match Qsymia to lower the cost, noting that topiramate is not approved as an antiobesity medication but has shown benefits against weight regain following bariatric surgery [150].

Low-cost, off-label prescribing has focused on phentermine due to its extensive familiarity to obesity specialists, but diethylpropion also has low cost, comparable benefit and safety as monotherapy, and is likewise endorsed as a long-term antiobesity medication option by the AGA [123].

BARIATRIC SURGICAL PROCEDURES AND DEVICES

Bariatric approaches encompass invasive laparoscopic surgical procedures, minimally invasive endoscopic therapies that remodel the stomach using suturing/plication devices or that insert space-occupying devices to reduce gastric volume, and endoscopically placed vagal stimulation devices [125].

As discussed, the hazards of obesity are many, including a shortened life span, type 2 diabetes, cardiovascular disease, some cancers, kidney disease, obstructive sleep apnea, gout, osteoarthritis, and hepatobiliary disease, among others. Weight loss reduces all of these diseases in a dose-related manner—the more weight lost, the better the outcome [4]. Bariatric surgery is the most effective treatment for severe obesity and obesity with metabolic disease. In the majority of appropriately selected cases, substantial weight loss is sustained for years if not decades [200].

The ASMBS, the largest professional organization and recognized authority and resource on metabolic and bariatric surgery, has endorsed six surgical approaches for obesity (***Table 9***) [201]. None involve devices.

Bariatric operations increased from 158,000 in 2011 to 263,000 in 2021, including sleeve gastrectomy (153,000), Roux-en-Y gastric bypass (RYGB) (56,500), revisional (31,000), biliopancreatic diversion with duodenal switch (BPD/DS) (5,525), gastric balloon (4,100), endoscopic sleeve gastroplasty (ESG) (2,200), one-anastomosis gastric bypass (OAGB) (1,149), and single anastomosis duodenal-ileal bypass with sleeve (SADI-S) (1,025) [201].

ASMBS-ENDORSED SURGICAL APPROACHES			
Procedure	**Optimally Suited For**	**Percent Excess Weight Loss[a]**	
		At 2 years	At 10 years
Roux-en-Y gastric bypass (RYGB)	Higher BMI, GERD, diabetes	55% to 75%	52% to 69%
Sleeve gastrectomy	Metabolic disease	50% to 70%	67% to 71%
Laparoscopic adjustable gastric banding (LAGB)	Lower BMI, no metabolic disease	30% to 50%	38% to 47%
Biliopancreatic diversion with duodenal switch (BPD/DS)	Super-obesity (BMI ≥50), diabetes	63% to 80+%	68%
Single anastomosis duodenal-ileal bypass with sleeve (SADI-S)	Super-obesity	74%	NA
One-anastomosis gastric bypass (OAGB)	Higher BMI, diabetes	68% to 80%	73%
BMI = body mass index, GERD = gastroesophageal reflux disease, NA = not available. [a]Mean average.			
Source: [127; 135; 202; 203]			*Table 9*

RYGB is the prototypical bariatric surgery in use for many decades. Restrictive procedures (e.g., LAGB, vertical banded gastroplasty [VGB]) were widely used in the 1980s and 1990s as simpler alternatives to RYGB with fewer complications [204]. With malabsorption thought necessary for effective weight loss, BPD/DS was introduced as a two-stage procedure, initiated with sleeve gastrectomy. Large weight loss during sleeve gastrectomy led to its stand-alone use after 2008 and progressive replacement of VGB and LAGB [204; 205]. LAGB fell from 56,000 procedures in 2011 to just 1,121 in 2021 [201].

TERMINOLOGY

Some terminology in the bariatric literature differs from or seldom appears in the antiobesity medication literature. This includes [4; 119]:

- Metabolic and bariatric surgery (MBS): This is often preferred to the term "bariatric surgery," because these procedures are superior to intensive medical treatment for controlling and inducing remission of type 2 diabetes.
- Obesity-related complications: Replaces the term "weight-related complications," because patients with BMI <30 have not traditionally been considered MBS candidates.
- Pre-operative: The preferred term (rather than baseline) when referring to condition prior to MBS. May be notated with a p prefix (e.g., pBMI, pT2DM).

In discussion of MBS outcomes, those occurring in the 1 to 2 years following the procedure are considered short-term; medium-term outcomes are seen after 3 to 10 years, and those seen more than 10 years after surgery are considered long-term [206].

Percent excess weight loss is a more common measure of impact than percent weight loss. Excess weight is total weight above an ideal reference standard, usually BMI 25. Percent excess BMI loss uses the same concept in units of BMI. For example, in a study of 846 patients (average pBMI: 50.0) treated with RYGB, the outcomes (mean) after one year [207]:

- BMI: 33
- BMI units lost: 17
- Percent excess BMI loss: 68%
- Post-RYGB weight: 204 pounds
- Absolute weight lost: 106 pounds
- Percent weight loss: 34%
- Percent excess weight loss: 72%

Thus, for the same amount of weight loss in the same patients, percent of excess weight loss was about twice that of overall weight loss [127].

PROPOSED MECHANISMS

Considering that similar weight loss via caloric restriction provokes powerful adaptive and counter-regulatory responses (e.g., increased hunger, reduced metabolism), the sustained weight loss effects and diminished adaptive responses after MBS have sought explanation [200]. More recently, the long-term metabolic improvements have attracted investigation.

MBS is traditionally classified as restrictive, malabsorptive, or restrictive plus malabsorptive (e.g., BPD/DS) [208]. Historically, macronutrient malabsorption and restriction were considered necessary for efficacy [200; 209]. However, RYGB and sleeve gastrectomy produce large and sustained weight loss despite lower malabsorption. The weight-loss efficacy of both likely involve normal physiological mechanisms affecting energy intake, expenditure, and metabolic regulation,

significantly mediated by increased GLP-1 signaling and also by melanocortin signaling pathways, which clearly go beyond mechanical restriction and malabsorption [200].

Bypassing the duodenum via RYGB is thought to uniquely benefit metabolic parameters, independent of weight loss [210]. However, an 18% weight loss with RYGB or caloric restriction showed similar metabolic benefits due to the weight loss itself in patients with obesity and type 2 diabetes [211]. Patients attained similar type 2 diabetes remission rates after RYGB (72%) and sleeve gastrectomy (70%) in a study that established a weight-loss threshold of ≥20% for type 2 diabetes remission [212].

Thus, type 2 diabetes mitigation is dependent on weight loss and appears independent of MBS approach, although the literature is inconsistent and the underlying mechanisms of efficacy remain unclear [209]. Some inconsistency stems from retrospective versus prospective data and short-term versus long-term follow-up.

More broadly, greater clinician and patient acceptance of MBS is believed to hinge on more rigorous evidence of weight loss durability and obesity-related complication amelioration from prospective, long-term data. This includes ≥80% patient follow-up [206; 213]. However, the history of MBS shows frequent innovations, technical progress, and implementation of new approaches. The longer the timeframe of patient accrual or follow-up, the greater the odds that the procedure has been modified or replaced [214].

INDICATIONS FOR BARIATRIC SURGERY

The universally applied threshold for bariatric surgery (i.e., BMI >40 or BMI >35 with comorbidities) was set in 1991 by the National Institutes of Health. With significant advances in obesity science and safer, more effective bariatric approaches supported by three decades of evidence, this indication no longer reflects best practice and was replaced with new practice guidelines by the ASMBS in 2022 [126]. According to the ASMBS, MBS is recommended for [126]:

- Patients with BMI ≥35, regardless of presence, absence, or severity of obesity-related complication
- Patients with type 2 diabetes and BMI ≥30

MBS should also be considered in patients with BMI 30–35 who do not achieve substantial or durable weight loss or obesity-related complication improvement nonsurgically [126].

The BMI thresholds should be adjusted in Asian populations [126]. A BMI >25 suggests clinical obesity in these patients, and those with BMI >27.5 should be offered MBS.

The ABMS asserts that there is no upper age limit to MBS [126]. Older patients who could benefit from MBS should be considered after careful assessment of comorbidities and frailty.

MBS is also an effective treatment of clinically severe obesity in patients who need other specialty surgery, such as joint arthroplasty, abdominal wall hernia repair, or organ transplantation. Severe obesity is a chronic disease requiring long-term management after primary MBS, which may include revisional surgery or adjuvant antiobesity medication to achieve or sustain desired treatment effects [126].

PRE- AND POSTPROCEDURE RECOMMENDATIONS

Although safety is a concern with MBS, perioperative mortality rates (0.03% to 0.2%) have substantially improved from the early 2000s [215]. Studies consistently report that surgeon and surgical center experience are predictors of safety [4].

The OMA recommends that MBS procedures be performed at surgery centers with accreditation for quality standardization, such as the Metabolic and Bariatric Surgery Accreditation and Quality Improvement Program (MBSAQIP) administered by the ASMBS and the American College of Surgeons [127]. A multidisciplinary team can help manage the patient's modifiable risk factors to reduce perioperative complications and improve long-term outcomes [126].

Preprocedure Evaluation and Medical Clearance for Bariatric Procedures

Before undergoing bariatric surgery, a preoperative medical evaluation is optimally conducted by an obesity specialist. A bariatric surgery specialist consultation should also be performed, as well as cardiology, pulmonary, gastroenterology, and/or other specialists, as clinically indicated [127].

Potential MBS candidates should undergo a formal mental health evaluation by a qualified licensed professional to assess environmental, familial, and behavioral factors, including trauma history, suicide risk, coping mechanisms, and underlying eating, mood, and substance use disorders. Patients should receive education regarding the potential for increased suicide risk and addiction postprocedure. After RYGB and sleeve gastrectomy, high-risk groups should stop drinking due to postoperative impaired alcohol metabolism and increased risk of alcohol use disorder [125; 127].

Patients should undergo nutritional assessments by registered dietitians with expertise in MBS, who can help obtain a comprehensive weight history, identify maladaptive eating behaviors or patterns, and correct any micronutrient deficiencies prior to surgery. A registered dietitian can also provide preoperative nutrition education and prepare the patient for expected dietary changes after MBS, which include an understanding that even with bariatric surgery, lifelong adherence to healthful nutrition, physical activity, and favorable behavior modification facilitates the best chance for long-term success [127].

Other preoperative evaluations include proactive medication adjustment. While individual instructions will vary depending on the individual patient, several weeks prior to the bariatric surgery, the medical and surgical team often work together in management of medications that may increase surgical risk, such as increased bleeding risk with antiplatelet therapies (e.g., clopidogrel), anticoagulants (e.g., warfarin), and increased

thrombotic risk with sex hormone pharmacotherapies (e.g., estrogens). All herbal and over-the-counter supplements should be discontinued [127].

NSAIDs should be avoided before and after MBS, because they are implicated in the development of anastomotic ulcerations, perforations, and leaks. Alternative pain medication should be identified before the surgery [125].

Tobacco use, and cigarette smoking in particular, must be avoided at all times by all patients. Patients who smoke cigarettes should stop as early as possible, preferably one year but at the very least six weeks before MBS. In addition, tobacco use must be avoided post-MBS given the increased risk of poor wound healing, anastomotic ulcer, and overall impaired health. Structured intensive smoking cessation programs are preferable to general advice and should be implemented [125].

Postoperative Nutritional Considerations

Nutrient deficiencies are common after bariatric surgery and are carefully monitored for optimal patient health and recovery. Lower levels of vitamin D are common in patients with obesity and may worsen postoperatively without adequate supplementation. High-quality bariatric-specific multivitamin/mineral/trace element supplements are routinely recommended after MBS, with vitamin supplements often containing higher amounts of vitamin B12, iron, vitamin C (to assist with iron absorption), vitamin D, and calcium [127]. Registered dietitians can also assist postoperative patients experiencing food intolerances, malabsorption issues, micronutrient deficiencies, or weight regain [126].

Procedure Selection

Selection should be based on individualized goals of therapy (e.g., weight-loss target, improvements in specific obesity-related complication), available local/regional expertise (e.g., obesity specialists, bariatric surgeon, institution), patient preferences, and personalized risk stratification that prioritizes safety. Laparoscopic should be preferred over open procedures [125]. The decision about MBS approach should be driven primarily by informed patient preferences, but the ultimate decision for surgical readiness will be determined by the surgeon [126; 215].

Other Issues

Preoperative Predictors of Outcome

Because weight loss after surgery is heterogeneous and not entirely predictable, particularly in the long-term, there is considerable interest in identifying individuals more or less likely to benefit from MBS based on preoperative factors [208]. Although age, gender, anthropometrics, obesity-related complications, eating behavior, genetic background, circulating biomarkers (e.g., microRNAs, metabolites, hormones), and psychological and socioeconomic factors could potentially impact post-MBS weight loss, none have shown predictive utility [216].

A study of 2,022 patients with average three-year weight loss of 31% with RYGB and 16% with LAGB concluded that preoperative factors have limited predictive value for a patient's chance of a successful weight loss outcome following MBS [217]. However, surgical volume at the clinic (more than 100 per year), surgeon experience, surgery in a tertiary care center, female sex, age 55 years or older, and respiratory status all correlated with lower complications risk [208].

As genetic variants in the leptin-melanocortin pathway are associated with obesity, their effect on long-term bariatric outcomes was examined. The weight regain pattern in these patients after RYGB and sleeve gastrectomy highlights the need for proactive lifelong management to prevent relapse and careful expectation management [218]. Additionally, genotyping patients with significant weight regain after RYGB could help individualize weight-loss interventions to improve weight maintenance after surgery [219].

Preoperative Denials or Delays of Approval for Insurance Coverage

Insurance-mandated preoperative weight loss is discriminatory, arbitrary, scientifically unfounded, and contributes to patient attrition, or worse [126]. In a large study of patients medically cleared for a bariatric procedure and for whom insurance approval was requested, 22% were denied insurance coverage. For these patients, the mortality rate increased threefold during follow-up [220]. This practice by insurers leads to unnecessary delay of life-saving treatment and progression of life-threatening comorbid conditions [126].

Postoperative Esthetic Concerns

Bariatric surgery (and possibly antiobesity medication in hyperresponders) can lead to massive weight loss, resulting in excess skin and tissue that impairs hygiene, causes discomfort, and is disfiguring. Excess skin can lead to stigma due to appearance and pronounced physical and psychological impairments, but it can be mitigated by body-contouring surgery [221]. Body-contouring surgery is best pursued after weight loss has stabilized (typically 12 to 18 months after bariatric surgery) [125]. Smoking cessation is an absolute requirement before any type of body-contouring surgery [221].

Abdominoplasty can improve mobility, reduce skin fold complications, and improve psychosocial functioning. Patients who underwent body-contouring surgery after bariatric surgery had significantly better long-term weight loss than a matched cohort of patients [222]. A subsequent meta-analysis confirmed the added long-term benefits of body-contouring surgery for selected patients after massive weight loss and recommended a multidisciplinary team involving a bariatric surgeon, a plastic surgeon, nutritionists, and psychologists for the management of patients [223].

SURGICAL APPROACHES

There are several measures of procedure success. Nadir weight loss is defined as the lowest weight post-MBS, while weight recurrence is the weight regained after nadir. A case is categorized a nonresponse if the nadir excess weight loss is <50% of pre-MBS excess weight. Interventions for nonresponse and

weight recurrence include revision or conversion (to another MBS type), corrective (to resolve a complication), and antiobesity medication augmentation [125; 224].

Weight-loss success with MBS has often been defined as ≥50% excess weight loss and/or ≥25% total weight loss [212]. In the first validation of success criteria for MBS, ≥25% total weight loss exceeded 90% [225]. The quality of evidence for surgical bariatric approaches continues improving, with more prospective and longer-duration results, comparisons between MBS, and systematic reviews and meta-analyses.

Roux-en-Y Gastric Bypass (RYGB)

RYGB is the criterion-standard MBS with the longest-term safety and efficacy data [226]. In this procedure, the stomach is divided; a small gastric pouch is anastomosed (cross-connected) to a severed "roux" limb of small bowel jejunum through which food passes, bypassing the larger gastric remnant, duodenum, and proximal jejunum [227]. This approach has been found to dramatically improve type 2 diabetes and is part of the treatment algorithm for uncontrolled type 2 diabetes in patients with BMI ≥35. It is also associated with modestly greater weight loss and improvements in metabolic disease compared with sleeve gastrectomy. It also improves GERD [127; 135].

However, it is associated with more malabsorptive complications than sleeve gastrectomy, though fewer than duodenal switch. The bypassed portion of stomach cannot be viewed by conventional gastroscopy; if cancer occurs after surgery, early diagnosis is almost impossible [228]. RYGB is also not recommended for patients with Crohn disease. Potential adverse effects include marginal ulcers, internal hernia, small bowel obstruction, and vitamin and mineral deficiencies.

Efficacy

A prospective study followed 486 patients after RYGB. Average total weight loss at 2 years (36%) and 15 years (28%) showed good durability. Rates of improved or resolved obesity-related complication after one year for type 2 diabetes (99%), obstructive sleep apnea (97%), hypertension (95%), and GERD (97%) remained high through ≥10 years [226].

After RYGB, 418 patients were prospectively studied (with >90% follow-up) at 12-years. Mean total weight loss was 28.0% at 6 years and 26.9% at 12 years. Approximately 70% and 40% of patients maintained ≥20% and ≥30% total weight loss. Type 2 diabetes remission at 2, 6, and 12 years was 75%, 62%, and 51%, respectively; prevention of new-onset type 2 diabetes was 98% [229]. Evidence suggests that RYGB provides stable weight loss of more than 25% beyond 12 to 15 years that corresponds with sustainable resolution of obesity-related complications.

Sleeve Gastrectomy

Sleeve gastrectomy, also referred to as laparoscopic sleeve gastrectomy or LSG, consists of the majority of the stomach being vertically resected; a tube-shaped remnant, or "gastric sleeve," is left along the lesser curvature [227]. This procedure improves metabolic disease while maintaining small intestinal anatomy. Due to its effectiveness, relative simplicity, and low rates of margin bleeding (1.0%), leakage (1.1%), and postoperative stenosis (0.4%), sleeve gastrectomy has become the most popular MBS [228]. Micronutrient deficiencies not as frequent with sleeve gastrectomy as with some other bariatric surgeries. If necessary, these patients can be converted to RYGB at a later stage.

Despite the benefits, rates of GERD and dysphagia are high. In some cases, these effects may be severe, requiring conversion to RYGB and/or chronic medical therapy (e.g., with proton pump inhibitors) [127; 135]. Lack of bypass makes sleeve gastrectomy suboptimal for improving obesity-related complications in superobesity; other drawbacks include weight recurrence and poor diabetes control [228]. Chronic obstructive symptoms and potential strictures are additional concerns.

Efficacy

There has been concern that the popularity of sleeve gastrectomy has outpaced its long-term evidence support, especially in superseding RYGB. A systematic reviews and meta-analyses of ≥10-year sleeve gastrectomy results found 24.4% total weight loss and good remission of type 2 diabetes (45.6%) and hypertension (41.4%). However, high de novo GERD (32.3%) and 0% diabetes remission were noted in two of the reviewed studies [230].

In a randomized trial involving 240 patients with 85% follow-up at 10 years, sleeve gastrectomy led to 43.5% excess weight loss (vs 51% with RYGB), <5% weight loss in 5% of participants (vs 3% with RYGB), and similar remission of type 2 diabetes (26% vs 33%), dyslipidemia (19% vs 35%), and obstructive sleep apnea (16% vs 31%). Superior hypertension remission was noted with RYGB (8% vs 24%). The researchers found higher esophagitis rates after sleeve gastrectomy (31% vs 7%) but similar Barrett esophagus (4% vs 4%) and reoperation (15.7% vs 18.5%) rates. Longer preoperative type 2 diabetes duration was associated with lower remission, emphasizing the importance of early surgical treatment [231].

Laparoscopic Adjustable Gastric Banding (LAGB)

In LAGB, an adjustable silicone band is placed around the upper stomach and connected to a port in the subcutaneous tissue, which can be used to restrict the food-holding capacity of the stomach [127; 135]. LAGB is the considered safest bariatric surgical procedure, and it is reversible if necessary [203]. Today, LAGB is disfavored due to lack of durable long-term weight loss, limited metabolic benefits, and the risks of device complications and revisional surgery [127; 135].

Possible adverse events include band slippage, erosion, bowel obstruction, and dilatation of the esophagus. Band overfilling may underlie some LAGB problems. In one study, among 699 LAGB patients (pBMI: 41.4) with low (≤3 mL) or high (≥4 mL) band filling, low filling led to superior BMI (30.3 vs 35.8) and excess weight loss (49.1% vs 38.2%) at four to six years, and substantially lower rates of vomiting, epigastric pain, reflux, band slippage, migration, removal, and revision compared with

high filling. Using low-volume band filling and strict follow-up, the authors suggest that abandonment of LAGB should be reconsidered [232].

Efficacy

Following LAGB, excess weight loss at 10 to 20 years is approximately 47%. However, the distribution of weight loss is heterogeneous. At seven years, 62% of patients have 15% total weight loss, and equal rates have ≥35% (19%) and <5% (19%) total weight loss [233].

Due to late complications, de novo GERD in up to 70% of patients, and comparatively mediocre long-term effectiveness, trends over the past decade indicate that LAGB is managed in patients treated years or decades earlier, rather than initiated as MBS [201; 233].

Biliopancreatic Diversion with Duodenal Switch (BPD/DS)

BPD/DS involves sleeve gastrectomy, transection of the duodenum distal to the pylorus, and creation of an alimentary limb 200–250 cm long, thereby reducing anastomotic ulcers and dumping syndrome [228]. This approach is associated with the highest weight loss and metabolic disease resolution of all MBS techniques.

Technical complexity and risk of long-term nutritional deficiencies limits the acceptance of BPD/DS, which is reserved for super-obese (BMI ≥50) patients or those with nonresponse after sleeve gastrectomy without GERD, with nadir excess weight loss of 70% to 80% after two years [200; 228; 234]. Patient unwillingness or inability to follow/afford long-term nutritional recommendations, which can lead to life-threatening micronutrient deficiencies, is considered an absolute contraindication to this approach [127; 135]. Other possible adverse effects include protein malnutrition, anemia, diarrhea, stomach ulceration, duodenal dissection, and internal hernias.

Efficacy

As RYGB can lead to insufficient weight loss in patients with super-obesity (BMI >50), some surgeons advocate BPD/DS in this group [132]. In a study involving 47 patients (pBMI: 54.5) randomized to BPD/DS or RYGB (81% with 15-year follow-up), 1-, 3-, and 15-year BMI was superior with BPD/DS (28, 31, 34) compared with patients who had undergone RYGB (33, 39, 41), reflecting 20.4 vs 12.4 BMI loss and 37.5% vs 23% total weight loss [132].

Unfortunately, BPD/DS also led to greater adverse events (2.7 vs 0.9 per patient), GERD (22.2% vs 0%), and severe adverse effects (0.9 vs 0.3 per patient), including malnutrition and bowel perforation. Long-term mortality did not differ. The trial was not powered for significant differences in obesity-related complication remission.

That half of patients with RYGB remained severely obese is greatly concerning, as BMI >40 reduces life expectancy by 8 to 10 years. The benefits of BPD/DS should be weighed against the increased risk of complications, which may be severe, and the need for rigorous follow-up. However, weight and comorbidity recurrences are problematic, creating health consequences and reducing life expectancy [132].

Single-Anastomosis Duodenal-Ileal Bypass with Sleeve Gastrectomy (SADI-S)

SADI-S creates a single, end-to-side anastomosis between the created gastric sleeve pouch with preserved pylorus and distal ileum, with the division at the level of the duodenum [135]. This approach was introduced in 2010 as a simplified version of BPD/DS and is characterized by strong metabolic effects. Short-term outcomes appear similar to BPD/DS in measure of excess weight loss (BPD/DS: 81%; SADI-S: 75%), improvement of obesity-related conditions, malnutrition, and complications [228]. Potential drawbacks include micronutrient deficiencies and duodenal dissection.

Efficacy

In one study, 121 patients (pBMI: 52) had BMI ≤29, excess weight loss 80%, and total weight loss 57% after 31 months. Post-30-day adverse events (3.3%) were malnutrition or chronic diarrhea [235]. A SADI-S review noted little weight regain after 24 months, resolution of type 2 diabetes (73%), dyslipidemia (77%), and hypertension (59%) [236].

In another study, three-year total weight loss was superior with SADI-S (39%) compared with RYGB (29%). Weight loss with RYGB (30%), SADI-S (35.5%), and BPD/DS (35%) was similar in obesity with type 2 diabetes. Diabetes improved comparably with SADI-S and BPD/DS and better than RYGB [234]. For unclear reasons, longer-duration data on SADI-S are lacking.

One-Anastomosis Gastric Bypass (OAGB)

OAGB was introduced as a simplified version of RYGB, with a significantly reduced difficulty, learning curve, and operation time [228]. It consists of a single gastrojejunal anastomosis between a long gastric pouch and a jejunal omega loop [228]. It may be simpler and safer than BPD/DS, with strong metabolic effects. It may also have less micronutrient deficiencies than BPD/DS.

OAGB is suitable in patients who are elderly, with low BMI (30–35) and obesity-related complications, and high BMI (>50) as one-stage procedure. It may also be suitable for patients with large/concurrent hiatal hernia [202].

This procedure is not reversible and is not recommended for patients with GERD or esophagitis [125]. Potential adverse effects include abdominal pain, nausea, liver abscess, micronutrient deficiencies, and duodenal dissection.

Efficacy

OAGB showed substantial, durable weight loss in a trial involving 1,200 patients (pBMI: 46), with 6-, 9-, and 12-year BMI (28.5, 29.6, 29.9), excess BMI loss (83%, 78%, 76%), and excess weight loss (77%, 72%, 70%) all showing improvement. Approximately 70% of patients had data at 12 years

[237]. Patients showed remission of presurgery type 2 diabetes (94%), insulin resistance (100%), hypertension (94%), hyperlipidemia (96%), GERD (92%), obstructive sleep apnea (90%), respiratory insufficiency (100%), and fatty liver (100%). In addition, improvement/remission was noted in osteoarthritis (82%/18%) and urinary incontinence (78%/22%). All affected patients experienced improvement in polycystic ovarian disease. Complications included early severe events (2.7%), late severe events (1%), and bile reflux symptoms (2%). No followed patient required conversion for weight regain [237].

ENDOSCOPIC BARIATRIC TECHNIQUES

Endoscopic bariatric therapies have emerged as minimally invasive alternatives for patients who are not surgical candidates or who do not want to undergo surgical intervention. These approaches are expected to eventually fill the gap between conservative treatment and surgical bariatric procedures [228]. However, long-term data are needed to determine the durability of safety and efficacy.

Endoscopic Sleeve Gastroplasty (ESG)

ESG reduces gastric volume by 70% to 80%, creating a narrowed luminal sleeve—similar to sleeve gastrectomy, but without incisions or laparoscopy—using an endoscopic suturing device (OverStitch, Apollo Endosurgery, Austin, TX, USA) [238; 239]. It is approved by the FDA for patients with BMI 30–50 [238]. It acts via gastric remodeling that increases PYY and GLP-1 by decreasing leptin and preventing rising ghrelin release, which increases fullness, decreases hunger, and promotes greater weight loss [238].

ESG is associated with fewer adverse effects than other bariatric procedures, with no obvious disadvantages [239]. The most common possible adverse effects include postprocedure nausea, vomiting, and epigastric pain. Severe adverse effects are rare (0% to 2%) [228; 238].

In one study, 6-month weight loss robustly predicted 24-month weight loss, allowing early prediction of nonresponse and initiation of adjunctive therapies [238]. The MERIT trial randomized 209 participants to lifestyle modification with or without ESG. At 52 weeks, ESG showed superior excess weight loss (49% compared with 3%) and weight loss (14% compared with 0.8%) to controls. At 104 weeks, 68% of patients with ESG maintained ≥25% excess weight loss. No deaths, surgical interventions, or intensive care stays occurred [240].

In the longest prospective outcomes, weight loss at three and five years was 15% and 16%, respectively [228]. In 404 adults (pBMI: ≥40) after three years, weight loss was 20.3% and excess weight loss was 47% [62]. A meta-analysis of studies assessing efficacy of ESG found short-term and medium-term weight loss of 16.2% and 15.4%, respectively, and resolution of type 2 diabetes (55%), hypertension (63%), dyslipidemia (56%), and obstructive sleep apnea (52%) in patients with moderate obesity [241].

A study of ESG in 189 overweight patients (pBMI: 28) showed weight loss at 12, 24, and 36 months of 15%, 15.3%, and 15%, respectively. At 12 and 24 months, 76% and 86% of participants achieved normal BMI, with mean BMI reductions of 4.1 and 4.3. ESG was safe and effective in treating overweight patients, with high BMI normalization rates that could halt progression to obesity [242].

Overall, ESG looks promising as a minimally invasive bariatric procedure but needs longer-term data.

Laparoscopic Gastric Plication

Laparoscopic gastric plication is also referred to as a primary obesity surgery endoluminal (POSE) procedure. This incisionless procedure creates full-thickness plications in the gastric fundus and body using anchors that effectively reduce gastric capacity. Whereas endoscopic suturing is somewhat reversible, laparoscopic gastric plication places polypropylene anchors with baskets cinched on either end of tissue folds and is designed for permanent gastric remodeling. To accomplish this, it uses the incisionless operating platform, a medical device. As with ESG, laparoscopic gastric plication is associated with fewer adverse events compared with other bariatric procedures. The most common complaints are abdominal pain, nausea, and vomiting [127; 135; 239].

In a meta-analysis of the original laparoscopic gastric plication procedure, excess weight loss was 49% and weight loss 13% at 12 to 15 months. Severe adverse events occurred in 3% of cases and included bleeding, hepatic abscess, severe pain, nausea, and vomiting [243].

Laparoscopic gastric plication outcomes after five or more years are scarce. Among 88 patients at two and six years, weight loss was 21% and 12% and excess weight loss was 60% and 32%. The six-year weight regain of 58% led to a high revision rate (23.5%) [244].

Intragastric Balloon Devices

Intragastric balloon devices are filled with liquid or gas to reduce the effective volume of the stomach, thereby lowering the satiety threshold of meals, stimulating gut chemo-motor receptors, regulating ghrelin and other peptide hormone levels, reducing food intake, and delaying stomach emptying to achieve weight loss [228].

Three intragastric balloon devices are ASMBS-endorsed and FDA-approved for six-month dwell-time. The Orbera and Reshape balloons are both filled with methylene blue and saline. A leak or rupture releases the dye, which turns the urine blue to rapidly reveal the problem [135; 228].

Contraindications to intragastric balloon devices use include prior abdominal or weight-reduction surgery, inflammatory bowel disease, obstructive disorders, GI ulcers, severe reflux, prior GI bleeding, severe liver disease, coagulopathy, ongoing alcohol use disorder, or intestinal varices, stricture, or stenosis [239; 245].

Orbera Balloon Device

Orbera, the most widely and longest used intragastric balloon device, is an endoscopically inserted single gastric balloon filled with 400–750 mL of fluid [245]. In a meta-analysis of 1,683 patients, weight loss at 6 and 12 months was 13.2% and 11.3%, respectively. Common adverse events were pain (34%), nausea (29%), GERD (18%), gastric mucosal erosion (12%), and balloon removal due to intolerability (7.5%). Severe events included gastric ulcers (2.0%), balloon displacement (1.4%), small bowel obstruction (0.3%), perforation (0.1%), and death (0.08%). All perforations occurred in patients with prior gastric surgery; all deaths were secondary to perforation or aspiration. Thus, individualized, detailed risk assessment is necessary for patients planning to undergo intragastric balloon device placement [228]. Orbera early removal is also associated with use of selective serotonin or serotonin-norepinephrine reuptake inhibitors (SSRIs/SNRIs) [125].

Obalon Balloon System

Obalon uses up to three deflated balloons, swallowed as capsules. Gas is then injected into the balloons under x-ray observation. Weight loss typically is about 6.6%. In a registry of 1,343 patients, weight loss was 10.0% in the indicated BMI category (BMI 30–40), 10.3% in BMI 25–30, and 9.3% in BMI >40. Adverse event (14%) and severe adverse event (0.15%) rates included seven balloon deflations, none of which resulted in obstruction [246].

Common adverse effects are mainly nausea and mild abdominal pain, and serious events are rare. However, leaking occurs more easily with gas-filled than liquid-filled balloons, and leaking balloons must be removed by gastroscopy, a disadvantage with Obalon [228; 245].

ReShape Duo Balloon

With the ReShape Duo balloon device, two balloons are connected by a soft silicone rod. Each balloon is filled with 450 mL of fluid. The two-balloon design is intended to prevent premature failure, better conform to the stomach curvature, and improve patient tolerability. The ReShape device significantly reduces severe adverse effects rates compared with Orbera, but postoperative adverse event rates remain relatively high [228]. Average weight loss is approximately 6.8% [135].

AspireAssist

AspireAssist was a form of aspiration therapy via modified percutaneous endoscopic gastrostomy. In 2022, the maker of AspireAssist terminated production of this FDA-approved product [247].

OTHER OPTIONS

The TransPyloric Shuttle (TPS)

In 2019, the FDA approved the TransPyloric Shuttle (TPS) to promote weight loss in patients with BMIs 30–40 for a dwell time of 12 months. TPS provides a mechanism similar to intragastric balloon devices, with easy reversibility. The device contains a space-occupying balloon and a flexible silicone catheter that connects to a smaller bulb designed to intermittently advance through the pylorus to induce gastric outlet obstruction [239].

The initial TPS feasibility study in 22 patients demonstrated 14% weight loss at six months. The pivotal TPS trial randomized 302 patients to TPS or sham device. Weight loss at 12 months was superior with TPS (9.8 vs 2.8%). The few adverse events included esophageal rupture and gastric impaction [239].

Vagal Nerve Blocking Therapy (Vbloc)

With vagal nerve blocking therapy, a pacemaker-like implantable device is surgically placed under the skin, with lead wires placed laparoscopically around the vagus nerve just above the stomach. Activation of the device causes intermittent vagal blockade to induce a sense of satiety. It is FDA approved for weight management in patients with BMI >40 or BMI >35 with weight-related complications [127; 135]. Contraindications include cirrhosis, portal hypertension, hiatal hernia, and other implanted devices (e.g., pacemakers, defibrillators) [127; 135].

In one study, weight loss ≥10% and ≥15% at 12 months (39% and 22%) and 24 months (34% and 21%) was similar among all 123 patients. Adverse events included nausea, reflux, and pain at regulator site. No new adverse effects were noted in the second year of the two-year trial [248]. Weight loss is superior to sham-treated controls but lower than conventional MBS. Despite good safety, the modest efficacy may limit the desirability of intermittent vagal blockade [4].

Liposuction

While not a bariatric procedure, liposuction is a common esthetic procedure that can remove significant amounts of subcutaneous adipose tissue without affecting visceral adipose tissue. In a small 12-week study, women with and without diabetes had 9.1–10.5 kg body fat loss and reduced waist circumference but no improvement in blood pressure, inflammatory markers, or insulin sensitivity [4]. Removal of subcutaneous adipose tissue without reducing ectopic fat depots has little influence on the risk factors related to overweight or obesity [4].

IMPACT ON OBESITY-RELATED CARDIOMETABOLIC ENDPOINTS

MBS effects on major adverse cardiovascular events (a composite of coronary artery events, cerebrovascular events, heart failure, or cardiovascular death), major adverse liver outcomes (progression to cirrhosis, development of hepatocellular carcinoma, liver transplantation, or liver-related death), and obesity-related cancer is of considerable interest [249]. Addressing this are meta-analyses and matched-cohort studies comparing the long-term outcomes of MBS to usual obesity care (controls). Most of these data are retrospective. A noteworthy exception generating many studies is the Swedish Obese Subjects (SOS) project, which has prospectively followed 4,000 bariatric and

control patients and a random population reference group of 1,135 over more than 20 years with >98% patient follow-up [250].

In cardiovascular disease outcomes, MBS has been associated with a significantly reduced risk of cardiovascular mortality and incidence of heart failure, myocardial infarction, and stroke [129]. In a 2020 SOS study, patients who had undergone MBS were 30% less likely to die from any cardiovascular disease than controls, including myocardial infarction, heart failure, and stroke, and were 23% less likely to die from cancer. Median life expectancy of MBS patients was 3.0 years longer than controls but 5.5 years shorter than the general population [250].

A 2021 systematic review and meta-analysis found increased median life expectancy of bariatric patients of 9.3 years in those with pretreatment diabetes and 5.1 years among those with no pretreatment diabetes compared with controls. The authors responded to the shorter life expectancy gain from MBS in the 2020 SOS study by citing residual confounding and outdated procedures [251].

In a 2023 SOS study, MBS increased life expectancy by 2.1 and 1.6 years in patients with and without diabetes at a median 26-year follow-up. These authors criticized the 2021 systematic review and meta-analysis for reliance on relatively short-term retrospective data and control patients captured from registers with limited information on health status. MBS benefit in pretreatment type 2 diabetes partly depends on irreversible organ damage (more common with long diabetes duration) and whether short-term or durable remission is achieved (also affected by the severity and duration of diabetes) [252].

Among obese adults with NASH and liver fibrosis, 10-year cumulative incidence of major adverse liver outcomes was 2.3% in those who underwent MBS, compared with 9.6% in controls; major adverse cardiovascular events occurred in 8.5% of MBS participants, compared with 15.7% among controls. For patients with NASH and obesity, MBS was associated with a significantly lower risk of incident major adverse liver outcomes and major adverse cardiovascular events than nonsurgical management [249].

Ten-year outcomes significantly favored MBS in obesity-related cancer incidence (2.9% vs 4.9%) and mortality (0.8% vs 1.4%). Comparable RYGB and sleeve gastrectomy outcomes suggest the primary mechanism is weight loss itself, not procedure-specific physiological alteration. Among MBS patients, cancer incidence was highest in those with weight loss less than 24%. Dose-dependent reduction in cancer risk required substantial weight loss, and the separation of survival curves only appeared six years after the index date [130].

POSTBARIATRIC INTERVENTIONS

Greater comprehension of obesity as a chronic disease requiring long-term management has highlighted the importance of intervention in patients with primary or secondary MBS nonresponse [214]. Nonresponse has been defined as <50% excess weight loss over one to two years following intervention, and weight recurrence is defined as regaining ≥20% of nadir weight loss after MBS [224; 253]. Weight recurrence refers to secondary nonresponse [214]. Estimated rates of nonresponse (11% to 22%) and weight recurrence (16% to 37%) vary by definition used [224; 254].

Causes of weight recurrence include increased caloric intake due to increased appetite and maladaptive or dysregulated eating, inadequate physical activity, and psychosocial stresses. Weight recurrence can promote recurrence of previously controlled type 2 diabetes and other obesity-related complications, with diminished quality of life and poor emotional health. Preventing weight recurrence is a primary goal [224].

Surprisingly, nutritional, cognitive-behavioral, supportive, and other psychological and lifestyle interventions, started perioperatively or up to two years postoperatively, have not demonstrated a significant effect on overall weight loss. Systematic reviews and meta-analyses of these interventions have concluded their efficacy in preventing or reversing weight recurrence is marginal or null [224].

Intervention for patients experiencing nonresponse or weight recurrence entails revisional surgery or adjuvant antiobesity medication [126]. Because most revisional procedures carry higher morbidity than primary procedures, nonsurgical interventions should be tried first [224; 255].

Antiobesity Medication

Antiobesity medications may work synergistically with MBS, and treating patients with obesity via a multimodal approach has the potential to increase and possibly enhance MBS efficacy and durability. The ASMBS supports preoperative use of antiobesity medications for reducing perioperative risk and increasing postsurgery attainment of weight-loss goals and comorbidity resolution as well as post-MBS for ameliorating weight recurrence [124].

Phentermine is one of the most commonly used antiobesity medications in MBS patients. Pairing phentermine with topiramate may be advantageous in weight-loss efficacy through combinatory mechanisms and cost considerations in post-MBS patients. GLP-1 agonists offer high efficacy, few drug interactions, and few side effects, but cost can be a deterrent [124].

In most patients, MBS results in supraphysiological levels of circulating GLP-1. However, patients with poor postsurgery weight loss demonstrate an unfavorable postoperative gut hormone profile, including lower circulating GLP-1 levels. As such, GLP-1 analogs may benefit these patients [256].

In the BARI-OPTIMISE randomized placebo-controlled trial, patients with poor weight loss (≤20%) and suboptimal nutrient-stimulated GLP-1 response one or more years following sleeve gastrectomy or RYGB received liraglutide 3.0 mg or placebo. After 26 weeks, mean total weight loss with liraglutide was 8.82%, compared with 0.54% with placebo [256].

Patients receiving liraglutide for late weight recurrence after RYGB were prospectively followed. After 24 months, patients lost >85% of weight recurrence from nadir; hypertension and dyslipidemia also improved [257].

Weight recurrence studies of GLP-1 RAs have largely used liraglutide. However, semaglutide may be superior to liraglutide for weight recurrence, regardless of MBS procedure. In one study, semaglutide was superior on with 12-month weight loss (13% vs 9%) and odds ratio for ≥15% weight loss (2.55) compared with liraglutide [258].

Patients treated with liraglutide or semaglutide for weight recurrence after RYGB lost 67.4% of the weight regain after six months. More patients on semaglutide had total weight loss ≥10% (47.6% vs 31%) and ≥15% (24% vs 3.5%) [254].

The optimal time to initiate antiobesity medication may be at weight plateau, rather than after weight recurrence [259]. Proactive liraglutide may significantly augment ESG efficacy. Initiated five months after ESG and assessed seven months later, liraglutide/ESG showed greater reductions in weight (25% vs 20.5%) and body fat (10.5% vs 8%) compared with ESG alone at one year postprocedure [260].

Revisions/Conversions

The choice of conversion depends on the type of primary operation and the indication for conversion [125]. Patients may require reoperation (to correct/adjust) or conversion following any primary MBS, but some evidence suggests that more "restrictive" procedures (e.g., LAGB, sleeve gastrectomy) lead to higher rates of reoperation or conversion.

Conversions are the third most common MBS procedure. Of 57,683 performed between 2015 and 2017, most involved gastric band (LAGB) conversion to sleeve gastrectomy (15,433), to RYGB (10,485), or removal (14,715). It is projected that sleeve gastrectomy to RYGB conversions (8,491) will likely surpass LAGB conversions with time [261].

Weight recurrence within several years of sleeve gastrectomy is described as an emerging problem. After seven years, 28% to 30% of patients had weight recurrence and 20% had revisions, mostly due to weight recurrence (13%) and GERD (3%) [262; 263]. However, over 5 to 12 years after RYGB, up to 25% of patients experience <20% weight loss due to nonresponse/weight recurrence [256].

The ASMBS has made several suggestions concerning revisions/conversions, stating that in addition to improving weight loss, type 2 diabetes improvement and remission rates also increase [125]. It is important to consider behavioral factors, such as binge-eating, may be responsible for poor weight outcomes after LAGB reoperation. If necessary, conversions to RYGB or sleeve gastrectomy after LAGB can be performed in one or two stages. If conversion is required due to GERD, the preferred procedure is RYGB. Conversion of sleeve gastrectomy for additional weight loss can be RYGB or duodenal switch, which results in greater weight loss than RYGB but higher risk of long-term nutritional deficiencies [125].

For weight recurrence after sleeve gastrectomy, SADI-S led to greater total weight loss (30% vs 19%) and remission of type 2 diabetes and hypertension, fewer complications and reoperations after five years when compared with OAGB [264]. In one trial, OAGB for 1,075 patients with weight recurrence after various MBS led to two- and five-year excess weight loss of 68.5% and 71.6%, respectively. Adverse events included leak (1.5%), marginal ulcer (2.4%), anemia (2%), and mortality (0.3%) [265].

CONCLUSION

During 1980–2000, obesity prevalence increased roughly 100% as adults consumed less fat and sugar, became more active, and initiated more frequent weight loss attempts with diet and exercise. The obesity epidemic is unexplained by worsening diet and physical inactivity.

Today, it is acknowledged that obesity is a chronic, relapsing disease with cardiometabolic complications (e.g., insulin resistance, hypertension, type 2 diabetes, NAFLD, cardiovascular diseases) arising from adipose mass due to shared pathophysiology. The goal of obesity treatment—long-term weight loss sufficient to ameliorate cardiometabolic morbidity and premature mortality—usually requires antiobesity medications, bariatric surgery, or both.

Recently approved and emerging antiobesity medications are revolutionizing obesity treatment by achieving long-term weight loss previously unattainable without surgical intervention. Reversing the low utilization of medication and surgical treatment begins with ending the stigmatization of patients with obesity.

APPENDIX: PHYSIOLOGY AND PATHOPHYSIOLOGY

As explored throughout this course, knowledge of the mechanisms underlying obesity and advances in the understanding of how and why adiposity persists are essential in the development of new approaches in the treatment of patients with obesity. Healthcare professionals involved in the care of these patients benefit from a clear understanding of the physiology and pathophysiology involved.

NEUROHORMONAL REGULATION OF ENERGY BALANCE AND BODY WEIGHT

The biological system that regulates energy balance and body weight is dominated by a bidirectional feedback loop between the brain and periphery, sometimes called the gut-brain axis [108]. Peripheral tissue (gut, pancreas, adipose tissue) releases hormones, metabolites, and peptides to communicate infor-

mation about long-term energy stores and short-term nutrient availability to the brain. Because these molecular messengers provide homeostatic feedback of energy availability and status to the brain, they are called signals (of satiety, hunger, adiposity) [266].

These signals of energy balance reach the hypothalamus via the bloodstream and/or the brainstem via afferent vagal pathways that terminate in the nucleus tractus solitarius (nTS) [103; 267]. Brain circuits respond to this input by adjusting metabolism and behavior to acute and long-term needs and modifying energy intake and expenditure to match energy demands. Over time, this homeostatic regulation of energy balance establishes a metabolic set-point [101; 102].

Peripheral signals can be anorexigenic (appetite-suppressing) or orexigenic (appetite-stimulating) and long- or short-term. Long-term signals of energy balance circulate in proportion to fat mass to inform the brain about long-term energy storage in adipose tissue (i.e., adiposity signals) and are always (leptin) or often (insulin) anorexigenic. Short-term signals of nutrient and meal-derived energy availability (i.e., satiety and hunger signals) are gut-released and include [101; 150; 267]:

- Glucagon-like peptide-1 (GLP-1), peptide YY (PYY), glucose-dependent insulinotropic polypeptide (GIP), cholecystokinin (CCK), and oxyntomodulin (OXM), which are all anorexigenic
- Ghrelin, which is orexigenic and known as the "hunger hormone"

In obesity, this system is dysfunctional and generates and sustains excessive adipose tissue mass. Abnormal interaction between peripheral hormones and brain centers of energy homeostasis is a core feature of obesity pathophysiology [3].

The Hypothalamus

The hypothalamus, as the superordinate regulator of energy homeostasis, receives input via the bloodstream, ascending neurons from the brainstem, and descending neurons from cortical areas. It then coordinates energy balance and other homeostatic systems, integrates reciprocal orexigenic and anorexigenic responses, and governs metabolic adaptation [102; 103; 268].

The arcuate nucleus (ARC) of the hypothalamus is adjacent to the median eminence, a circumventricular organ outside the blood brain barrier, giving ARC neurons direct bloodstream access to detect circulating hormones and metabolites. Arcuate neurons are thus 'first-order' neurons, since circulating peripheral signals act directly on them [101; 102; 269].

First-order ARC neurons project to second-order neurons in the paraventricular (PVH), ventromedial, dorsomedial, and lateral hypothalamus. Second-order hypothalamic neurons project to brainstem circuits and midbrain areas [101; 102; 115; 269]. Brainstem circuits respond rapidly to gut signals to control meal size and termination. Brainstem neurons project to hypothalamic areas and communicate to the gut via parasympathetic signals. Many antiobesity medications work by activating receptors on both hypothalamic and brainstem neurons [102; 115].

The hypothalamic integrative capacity is enhanced by crosstalk with corticolimbic systems that process external sensory information, cognitive and emotional control, and reward-based decision making and mediate emotional, cognitive, and executive aspects of ingestive behavior [8].

A salience network in the frontal cortex, ventral and dorsal striatum, and amygdala, associated with motivation, desire, and craving for palatable high-energy food, is more active in obese than lean subjects. An inhibitory network in the dorsolateral prefrontal cortex is activated in subjects instructed to resist craving. This cognitive control ability is greater in patients with the highest weight loss after bariatric surgery. Connectivity between the salience and inhibitory networks (hedonic control) and the hypothalamus (homeostatic control) differs in lean versus obese subjects. The former homeostatic/hedonic ingestive dichotomy has given way to a more unified and integrative control system [8].

The Arcuate Nucleus and the Melanocortin System

In the ARC, the melanocortin system is a critical and conserved pathway of body weight homeostasis and essential to the regulatory function of the hypothalamus in energy balance and homeostasis. The melanocortin system consists of two distinct, functionally antagonistic neuron populations [150; 268; 270; 271; 272]:

Anorexigenic melanocortin neurons (POMC), which release melanocortin peptides (α- and β-MSH) that bind and stimulate melanocortin receptors (MC3R and MC4R) expressed on second-order neurons. Brain-derived neurotrophic factor, corticotropin-releasing hormone, and thyrotropin-releasing hormone mediate the downstream effects of MC4R activation on suppressing food intake.

Orexigenic agouti-related protein (AgRP) neurons, which antagonize melanocortin neurons and receptors by releasing AgRP, gamma-aminobutyric acid (GABA), and neuropeptide Y (NPY). AgRP antagonizes MC3/4R to prevent the anorexigenic effects of α- and β-MSH binding. GABA directly inhibits POMC neurons in the ARC. NPY is the most potent known short-term orexigenic stimulus.

The brainstem has a smaller number of POMC neurons. AgRP neurons solely exist in ARC and send long-distance projections throughout the hypothalamus and brainstem. AgRP neuron expression is negatively correlated with BMI [273].

POMC and AgRP neurons are tightly linked, exert opposite functions in the reciprocal regulation of downstream MC3/4R neurons, and are themselves reciprocally regulated by circulating hormones and neural inputs [274; 275].

Energy Balance and Melanocortin Activity

POMC and AgRP neurons detect and respond to circulating metabolic and hormone signals of short- and long-term deficit or surplus in energy availability [8]. Circulating hormones (e.g., leptin, insulin, ghrelin, GLP-1) bind to their respective receptors (LepR, InsR, GHSR, GLP-1R) on POMC and AgRP neurons [141]. Energy surplus stimulates POMC neurons. Heightened energy demand activates AgRP neurons [3; 276].

The PVH is a major output nucleus for the ARC and receives afferent inputs from POMC and AgRP neurons [102]. It has the highest number of MC4R-expressing neurons in the CNS [271].

POMC neurons are stimulated by positive energy balance, elevated leptin, and insulin. In contrast, AgRP neurons are inhibited by leptin and insulin deficit and activated by negative energy balance and ghrelin.

POMC and AgRP neuron projections both converge on MC4R neurons in the PVH, which anorexigenic melanocortin peptides activate to suppress food intake and enhance energy expenditure, and orexigenic AgRP neuropeptides inhibit to increase food intake [141; 277]. Also, circulating ghrelin binds its receptor on AgRP neurons, which then release NPY [3].

Negative energy balance and prolonged caloric restriction activate AgRP neurons in part by reducing plasma levels of leptin and insulin that inhibit AgRP neurons. Inactivating this inhibitory input activates AgRP neurons and increases the drive to eat, which promotes positive energy balance and recovery of lost weight [7].

Circulating levels of leptin, insulin, and other hormones serve the hypothalamus with feedback about the availability of energy. When circulating levels of these energy signals decrease during prolonged caloric deficit, increased AgRP neuron excitation recapitulates many behaviors and physiological effects associated with starvation, such as enhanced rewarding properties of food, as well as stimulating food intake [277]. Disruption of this fine-tuned control in the arcuate circuitry leads to dysregulation of energy balance and metabolism [8; 266].

Hypothalamic Regulation of Adiposity and Energy Expenditure

White adipose tissue, the dominant body fat, is comprised of fat cells (adipocytes), stores energy in the form of triglycerides, and can increase fat reserves (lipogenesis) or utilize fat as energy (lipolysis) [278]. Melanocortin signaling regulates lipid metabolism and adiposity via the sympathetic nervous system (SNS) activity; disruption promotes lipid uptake, triglyceride synthesis, and fat accumulation in white adipose tissue [150; 275].

The SNS innervates white adipose tissue, and sympathetic terminals are adjacent to more than 90% of adipocytes. The brain releases norepinephrine from sympathetic terminals, which activate α- and β-adrenergic receptors on adipocytes. This sympathetic outflow is the principal initiator of lipolysis, mediated in part by MC3/4R activity on sympathetic cholinergic neurons [271; 276].

A common frustration for individuals trying to lose weight is the marked compensatory reduction in energy expenditure associated with caloric restriction [277]. AgRP neurons, activated by negative energy balance, shift metabolism toward energy conservation by promoting lipid storage and adipogeneses, elevating carbohydrate fuel use, reducing lipolysis, and thus decreasing energy expenditure in adipose tissue, in part, by suppressing sympathetic outflow to white adipose tissue. NPY release increases food intake and decreases energy expenditure via NPY1R-mediated reduction in downstream sympathetic output to adipose tissue [268]. SNS neurons also produce NPY, which induces vasoconstriction and fat tissue expansion [150].

A key point is that through extensive bidirectional communication, adipose tissue importantly influences energy balance, while CNS and hypothalamus play an essential role in controlling systemic metabolism [279].

Hypothalamic POMC Neurons and Cannabinoids

Cannabis use represents a "wildcard" in appetite mediation by the melanocortin system. By activation of cannabinoid receptor 1 (CB1R), cannabis-induced eating is a hallmark of cannabis use [280].

POMC neurons also produce β-endorphin, an opioid peptide that binds the μ-opioid receptor (MOR). CB1R activation selectively increases β-endorphin, but not α-MSH, release by POMC neurons. Beta-endorphin inhibits AgRP neuron activity, and acute CB1R-induced eating is blocked by naloxone, a MOR antagonist [280].

Thus, cannabis stimulates a switch from α-MSH to β-endorphin release by POMC neurons and subsequently increases appetite and food intake (i.e., "the munchies"). This interesting and paradoxical finding argues against an exclusively anorexigenic role of POMC neurons [266].

Brainstem Circuits

The gut communicates information about food ingestion to the brain via vagal afferent fibers in the NTS. Most of these signals act rapidly to promote meal termination, with less impact on energy expenditure or long-term food intake [150; 281]. The NTS receives and integrates the afferent vagal information and communicates this information to other brain regions it innervates [141; 282].

POMC neurons are also expressed in the NTS, where they project to and receive inputs from brain regions that both overlap and are distinct from connections of arcuate POMC neurons [269]. NTS POMC neurons respond to, among other things, gut-secreted CCK and adipocyte-derived leptin [271].

Some NTS neurons project to the parabrachial nucleus, a central node in this ascending pathway. An anorexigenic circuit implicated in satiety and meal termination arises from calcitonin gene-related peptide (CGRP) neurons in the parabrachial nucleus. Activation of CGRP neurons by gastric distention, CCK, and GLP-1 decreases appetite, while inhibition increases meal size [7; 266].

HORMONE, METABOLIC, AND PEPTIDE SIGNALS OF SATIETY, HUNGER AND ADIPOSITY, BY PERIPHERAL TISSUE ORIGIN		
Hormone	**Receptor Locations in CNS**	**Effects on Energy Balance and Obesity**
Adipocyte origin		
Adiponectin	Hypothalamus	↓ Body weight, plasma lipids
Leptin	ARC	↓ Food intake, body weight
Pancreatic cell origin		
Amylin	ARC, AP, VTA, striatum	↑ Satiety ↓ Gastric emptying, food intake
Glucagon (GCG)	ARC, NTS	↑ Satiety, glycogenolysis, gluconeogenesis
Insulin	ARC	↓ Food intake, body weight
Pancreatic polypeptide (PP)	Hypothalamus, NTS	↑ Satiety ↓ Gastric emptying
Enteroendocrine cell origin		
Cholecystokinin (CCK)	Hypothalamus, NTS	↑ Satiety ↓ Gastric emptying/motility
Ghrelin	ARC	↑ Food consumption and reward
GIP	ARC, PVH, DMH	↓ Food intake ↑ LPL, postprandial insulin
Glucagon-like peptide-1 (GLP-1)	ARC, NTS, AP, striatum	↑ Satiety, postprandial insulin ↓ Gastric emptying/motility, food reward
Oxyntomodulin (OXM)	Hypothalamus	↑ Satiety ↓ Gastric emptying, food intake
Peptide tyrosine tyrosine (PYY)	ARC, NTS	↑ Satiety ↓ Gastric emptying/motility
AP = area postrema, ARC = arcuate nucleus of the hypothalamus, CNS = central nervous system, DMH = dorsomedial hypothalamus, GHSR, growth hormone secretagogue receptor, GIP, glucose-dependent insulinotropic polypeptide, NTS = nucleus tractus solitarius, PVH = paraventricular nucleus of the hypothalamus, VTA = ventral tegmental area.		
Source: [115; 147; 267]		*Table 10*

Arcuate nucleus signaling strongly influences CGRP neuron activity [7; 266; 274]. In the ARC, glutamate-releasing/oxytocin-receptor expressing (Vglut2/OxtR) neurons convey an excitatory, fast-acting satiety mechanism. Projections from these neurons converge with GABAergic AgRP projections on MC4R neurons in PVH, a critical second-order node in the regulation of feeding. In the PVH, MC4R neurons release glutamate and excite downstream CGRP neuron targets in the parabrachial nucleus. Thus, the parabrachial nucleus serves as a third-order node in feeding regulation. In addition, AgRP neurons project to the parabrachial nucleus; activation of AgRP neurons stimulate feeding and delays satiation by inhibiting CGRP [7].

Of note, the substantial complexity inherent in food intake regulation cannot be reduced to a small set of interacting neurocircuits, and much remains to be learned [7].

Peripheral Signals of Energy Status

As will be discussed later in this course, many novel and emerging antiobesity medications act through the hypothalamic receptors of peripherally released hormones and peptides. ***Table 10*** summarizes the effects of endogenous and pharmacological ligand-binding of these receptors.

Adipose Tissue and Pancreatic Hormones

Some peripheral signals of energy balance are released by adipocytes (leptin, adiponectin), and pancreatic α cells (GCG), β cells (insulin, amylin), and F cells (pancreatic polypeptide) [150; 282].

Leptin, the canonical signal of adipose tissue mass, is produced by white adipose tissue in approximate proportion to triglyceride stores. Adequate leptin action via its receptor (LepR) on arcuate neurons indicates sufficient energy stores; reduced leptin signaling indicates an energy deficit, promoting hunger and increasing energy intake [281]. LepR activation also decreases body weight by increasing lipolysis and energy expenditure [277]. CCK potentiates leptin effects to decrease food intake and body weight [267].

Normal body-weight maintenance requires intact leptin-regulated neurocircuits. An association of obesity with leptin resistance has been suggested, but some obese individuals may simply require more leptin to fully engage relevant neurocircuits. The primary role of leptin-responsive neurocircuits may relate more to preventing loss of body fat (by decreased leptin signaling to CNS) than defending against its increase (by increased leptin levels) [7].

Adiponectin is an adipocyte-derived protein that decreases body weight and plasma lipid levels and enhances insulin suppression of hepatic glucose production. Adiponectin levels increase following weight loss interventions in obesity, and patients with obesity show an inverse correlation between plasma adiponectin and insulin resistance [115].

Insulin and leptin both circulate in proportion to fat mass. Insulin activates its receptor (IR) expressed in the melanocortin system, which mediates its central anorexigenic effects, decreasing food intake and body weight [115]. Insulin also acts centrally to decrease hepatic glucose output, in part by inhibiting hypothalamic neurons [102]. Insulin inhibits AgRP neuron firing via IR-dependent signaling. Disruption of IR in the CNS promotes obesity with increases in body fat and leptin levels, insulin resistance, elevated insulin levels, and hypertriglyceridemia [266].

Amylin is co-released with insulin from pancreatic β-cells in response to high blood glucose levels, reduces the rate of glucose absorption and inhibits glucagon release. Amylin receptor complexes in the area postrema and brainstem NTS mediate its anorectic effects by activating a central satiety pathway. Amylin also affects hedonic eating by inhibiting reward neurocircuits [141; 267]. Amylin and leptin act synergistically, in part by amylin acting directly on AgRP neurons that co-express LepR. Amylin's ability to slow post-prandial gastric emptying also contributes to satiety [141].

Glucagon (GCG) is secreted by pancreatic α-cells and binds its receptor (GCGR) in the CNS, pancreas, adipocytes, and liver. Glucagon stimulates energy expenditure, reduces food intake, and decreases body weight through multiple mechanisms, including inducing satiety and lipolysis [147; 267]. Hypothalamic GCGR activity inhibits AgRP neuron activity to attenuate orexigenic effects, while central resistance to glucagon-induced hypophagia contributes to the development of obesity [141]. Glucagon's anorectic action seem to be mediated via the liver-vagus-hypothalamus axis [267].

Gut Peptide Hormones

Other signals of energy balance are released by enteroendocrine cells that line the gut, one of the largest hormone-producing organs. Enteroendocrine cells and their respective hormones include L-cells (GLP-1, OXM, PYY), I-cells (CCK), K-cells (GIP), and P/D1 cells (ghrelin). Gut hormones bind their receptors in CNS and on pancreatic β cells (GLP-1, GIP), pancreas (CCK, OXM), and adipocytes (GIP) [147; 267; 283].

Meal termination involves meal-induced enteroendocrine cells release of peptides (e.g., GLP-1, CCK), which promote satiety by activating vagal afferent neurons that relay GI signals to brainstem areas, including the NST [7]. Glucagon-like peptide 1 (GLP-1) increases in circulation following meals and decreases during fasting, stimulates insulin secretion and regulates energy intake, and is also produced in the NTS. GLP-1 acts on GLP-1R in the gut and brain to delay gastric emptying and decrease food intake through activation of satiety pathways and efferent pathways regulating GI function. GLP-1 also reduces glucagon secretion, inhibiting hepatic glucose production [284].

GLP-1 inhibits eating mainly by activating GLP-1R on hypothalamic and brainstem NTS neurons. GLP-1R agonists also suppress hedonic eating by interacting with the mesolimbic reward system, including the ventral tegmental area and nucleus accumbens [267]. GIP and GLP-1 are rapidly degraded by the enzyme dipeptidyl peptidase IV (DPP-IV), leading to a circulating half-life of only two minutes for GLP-1 [150].

GIP acts in concert with GLP-1 on the pancreas after meals to regulate blood glucose by stimulating insulin and glucagon release. GIP contributes to lipid metabolism by promoting lipid storage, adipose tissue blood flow, and triglyceride uptake in adipocytes [284]. The GIP receptor (GIPR) is expressed in arcuate, dorsomedial hypothalamus, and PVH neurons; GIPR activation reduces food intake [267].

Ghrelin circulates as an orexigenic signaler, promoting hunger and meal initiation by binding its receptor (GHSR) on AgRP neurons, which stimulates NPY and AgRP release and inhibits POMC neurons by increasing GABAergic signaling. Vagal afferent neurons also have ghrelin receptors [115; 267]. Compared with lean controls, individuals with obesity have lower circulating ghrelin levels and are more sensitive to its appetite-stimulating effects [115; 267].

Ghrelin and leptin have a reciprocal relationship aimed at increasing or decreasing adiposity. Fasting increases ghrelin and reduces leptin, while high leptin levels suppress gastric ghrelin release and prevent ghrelin-induced NPY neuron activation [141]. Ghrelin and GLP-1 have opposite actions on eating behaviors. Ghrelin reinforces food reward by activating ventral tegmental area dopaminergic neurons; GLP-1 attenuates various palatable food-motivated efforts [267].

Ghrelin remains the only metabolic signal that potently activates orexigenic AgRP neurons. Discovery of an endogenous antagonist of ghrelin, liver-expressed antimicrobial peptide, sparked research interest in it as a possible candidate for obesity treatment [267].

CCK is secreted postprandially and binds CCK1 receptors (CCK1R) expressed in the vagal afferents, brainstem, and hypothalamus to decrease food intake. The satiety signals of CCK are transmitted to the NTS by vagal sensory neurons. CCK activates NTS POMC neurons, and brainstem MC4R signaling is required for CCK-induced appetite suppression [267]. CCK is an acutely acting signal with a very short half-

life. Compensatory increases in meal frequency prevent CCK from producing long-term effects on total food intake or body weight [102].

OXM is secreted with GLP-1 and PYY in the postprandial state and exerts its anorectic action primarily via GLP-1R and secondarily via GCGR. The GLP-1R-mediated effects of OXM differ from those of GLP-1. OXM decreases body weight by lowering food intake and increasing energy expenditure and may act via different hypothalamic pathways than those of GLP-1 [267].

PYY is co-secreted with GLP-1 following a meal. Its major circulating form (PYY3-36) binds Y2R expressed on AgRP neurons, inhibiting these neurons and activating POMC neurons. Thus, PYY reduces appetite and body weight by increasing anorexigenic melanocortic activity in the arcuate [267].

PATHOPHYSIOLOGY

Long-term positive energy balance and increased fat mass promote pathogenic adipocyte hypertrophy and adipose tissue accumulation and dysfunction, resulting in immunopathies, endocrinopathies, increased circulating free fatty acids, and lipotoxicity. The OMA uses the term adiposopathy, or "sick fat disease," to describe pathogenic adipose tissue [128].

The consequences of adiposopathy contribute to metabolic diseases including type 2 diabetes, hypertension, dyslipidemia, cardiovascular disease, NAFLD, and cancer [18; 29]. Obesity-related metabolic and cardiovascular diseases can be termed cardiometabolic disease or metabolic syndrome.

Adiposopathy is analogous to the disease state of other organs, such as myopathy, cardiomyopathy and encephalopathy. In the disease of adiposopathy, pathogenic enlargement of fat cells and the fat organ results in anatomic and functional abnormalities, metabolic and biomechanical morbidities, and increased mortality [18; 29].

Adipose Cell and Tissue Function

Part of understanding obesity as a disease is recognizing that adipocytes and adipose tissue have vital functions beyond energy storage alone [128]. Adipose tissue is mostly comprised of adipocytes, regulates multiple body processes critical to energy and metabolic homeostasis, and is functionally classified into two types: white and brown [128; 285]. White adipose tissue is an active endocrine and immune organ that includes subcutaneous adipose tissue and visceral (abdominal) adipose tissue and primarily stores energy. However, subcutaneous adipose tissue contains brown-like inducible adipocytes that perform mitochondrial and thermogenic functions and burn fat [286].

Brown adipose tissue, comprising 1% to 2% of body fat, has more mitochondria (thus its brown appearance) and is abundant in neonates but decreases in adults and decreases further in obese adults [286]. Brown adipose tissue produces heat energy, termed thermogenesis, upon β-adrenergic stimulation [287].

Subcutaneous adipose tissue is the largest fat depot. Visceral adipose tissue is more metabolically active, vascular, and innervated than subcutaneous tissue. Ectopic fat, a third depot, is strictly pathogenic [48].

Fat depots are sexually dimorphic; on average, men have more visceral adipose tissue, and women have larger subcutaneous adipose tissue stores. Given the relative impact of fat depots on metabolic health, this sexual dimorphism may explain sex differences in metabolic disease risk until menopause, when decreased estrogen may increase low-density lipoprotein, triglycerides, visceral fat, morbidity, and mortality in women [48].

Adipocytes, which constitute the largest cell volumes in adipose tissue and are the defining fat cell type, have three important roles: lipid storage, insulin sensitivity, and secretory function. Disruption of any contributes to obesity-related metabolic disease states [288].

Some key players in adipose tissue physiology and obesity pathophysiology include glucose, glycogen, triglycerides, and insulin [289; 290]. Glucose is a carbohydrate, one of three macromolecule classes (with fats and proteins); some argue alcohol is a fourth class. Glycogen is the storage form of glucose in liver and muscle. Triglyceride, the storage form of fatty acids, is made of three fatty acids linked to glycerol. The capacity to store carbohydrates (as glycogen) is limited. What cannot be stored as glycogen, or quickly used, gets stored as triglyceride. Insulin, released by pancreatic β-cells in response to rising blood glucose, aims to store carbohydrate as glycogen or fatty acids.

Lipid Storage

During energy surplus, 60% to 80% of excess calories are stored as triglyceride by adipocytes [291]. Adipocytes can increase fat stores (lipogenesis) or release fatty acids (lipolysis) to supply other tissues with energy [278; 285]. Insulin is critically involved in these processes.

For lipogenesis, adipocytes accumulate lipid through free fatty acids from circulating triglyceride and by synthesizing triglyceride from non-lipid metabolite sources, termed de novo lipogenesis [285]. For lipolysis, enzymatic cleavage of triglyceride by lipases generates glycerol and free fatty acids, which are released into circulation for use by organs as fuel (e.g., glycerol for liver gluconeogenesis) [288]. Lipolysis is controlled by sympathetic nervous system input and norepinephrine. In the fasting state, insulin levels drop, releasing norepinephrine, which promotes lipolysis [288].

Because adipose tissue is central to the regulation of systemic lipid metabolism, a balance between lipogenesis and lipolysis within adipocytes is required to maintain insulin sensitivity and energy homeostasis. Nutrient (free fatty acids and glucose) and hormonal cues regulate both processes [288].

Insulin Sensitivity

Insulin sensitivity of adipose tissue is vital to metabolic homeostasis and systemic energy balance [285]. Insulin binds to its receptor in liver, muscle, and adipose tissue to initiate several processes [48; 292].

Insulin activates glucose transporter-4 (GLUT4) on cell surfaces, which transport glucose from the bloodstream into cells. On fat cells, insulin accelerates glucose delivery into adipocytes and induces breakdown of glucose into triglycerides for storage.

Insulin upregulates lipoprotein lipase on fat cell surfaces that bring free fatty acids into adipocytes to store them triglycerides. Insulin also increases triglyceride accumulation by inhibiting their breakdown and release as free fatty acids.

The primary source of glucose for all tissues and largest glucose storage site (as glycogen) is the liver. Hepatocytes are critical intermediaries in energy (lipid, carbohydrate) metabolism. Insulin decreases glucose output by the liver, the main target for pancreatic insulin and glucagon [292; 293].

During caloric deficit, low insulin disinhibits lipolysis, which mobilizes lipids to meet energy demand. However, elevated insulin during caloric excess stimulates glucose uptake, inhibits lipolysis, and orchestrates de novo lipogenesis. The body goes into "storage" mode of carbohydrates and fat. These normal functions of insulin help protect against the cellular and tissue toxicity caused by high circulating glucose and free fatty acids [285; 289].

Endocrine and Immune (Secretory) Function

As an endocrine/immune organ, adipose tissue releases adipokines (via adipocytes) and receives (via receptors) metabolic signals to influence and regulate adipogenesis, lipid metabolism (lipogenesis and lipolysis), appetite and energy balance, inflammatory and immune response, glucose homeostasis (insulin sensitivity), vascular homeostasis (endothelial function), blood pressure, and other processes [128; 285; 288].

Adipokines are hormones, cytokines, extracellular matrix proteins, and growth factors that transmit information from fat tissue to other metabolic organs. They can act locally (paracrine) and/or systemically (endocrine) [128; 285]. Adipocytes express receptors for nuclear and traditional hormones, adipokines, neuropeptides, lipoproteins, prostaglandins, endocannabinoids, and others [128]. Several adipokine hormones, including leptin and adiponectin, are regulators of systemic lipid and glucose homeostasis [285; 288; 294].

Accordingly, adipose tissue can release pro-inflammatory hormones (leptin), cytokines (e.g., tumor necrosis factor-alpha [TNF-a], interleukin-6 [IL-6], IL-8), acute phase response proteins (e.g., C-reactive protein [CRP]), chemokines (e.g., monocyte chemoattractant protein–1 [MCP-1]), and prostaglandins. In addition, adipose tissue can release anti-inflammatory hormones (adiponectin), interleukins (IL-10), and transforming growth factor beta 1 (TGF-beta) [128; 295; 296].

Pathogenesis of Adiposopathy and Obesity-Related Complications

An immune response appears early during adipose accumulation. With excessive fat mass, local adipose-induced inflammatory processes progress to widespread systemic inflammation that damages distant tissue and induces a host of metabolic disorders and organ tissue complications in obesity [194; 297].

Local Pathogenesis

Adipose tissue contains adipocytes, vascular cells, fibroblasts, cells of the innate (e.g., monocytes, macrophages, natural killer cells) and adaptive (e.g., lymphocytes) immune systems, and other cell types essential to its normal physiology that become abnormally altered and interact in the pathophysiology of obesity-related cardiometabolic complications [285; 296]. To expand triglyceride storage as obesity develops and fat mass increases further, adipocytes abnormally increase in number (hyperplasia), then in size (hypertrophy) [278; 285]. Hypertrophy compromises the function of adipose tissue, degrading the extracellular matrix which promotes a switch toward fibrosis that restricts adipocyte fat storage [295; 298].

Triglyceride accumulation promotes hypoxia, apoptosis, and oxidative and mitochondrial stress in adipocytes and release of pro-inflammatory factors [287; 296]. As obesity advances, lipid-laden hypertrophied adipocytes undergo necrotic and/or apoptotic cell death, contributing to the recruitment of inflammatory cells and to adipose tissue dysfunction [298].

Adipose tissue macrophages are essential for maintaining adipose tissue energy homeostasis and inflammatory response [291]. The adipose tissue macrophage phenotypic correlates to BMI and adipocyte size [296]. The obesity-induced M1 phenotype is associated with inflammation and tissue destruction; M1 may comprise 50% of all adipose tissue cells (compared with 10% to 15% in lean adults) [298; 299].

As adipose tissue expands, angiogenesis lags. The hypoxic state triggers an inflammatory response, which initiates monocyte recruitment and differentiation into M1 adipose tissue macrophages [299]. Circulating macrophages infiltrate adipose tissue, producing MCP-1, which recruits more inflammatory cells to adipose tissue and TNF-a and further promotes MCP-1 production by adipocytes, recruiting yet more immune cells to adipose tissue. The M2 to M1 shift aggravates a vicious cycle of chronic low-grade inflammation [128; 285].

Systemic Pathogenesis

The inflammatory adipose tissue microenvironment diffuses systemically and to remote organ sites. MCP-1 recruitment and proliferation into liver, adipose, pancreatic islet, intestine, and muscle tissue induces a pro-inflammatory M1 state [299]. Cytokines (TNF-a, IL-1b, IL-6) and adipokines (leptin) activate systemic and organ-specific inflammatory signaling pathways, impairing β-cell function, suppressing insulin secretion, and promoting accumulation of ectopic fat, insulin resistance and hyperglycemia [287; 297; 298; 300].

Adiposopathic tissue pumps free fatty acids into circulation, leading to ectopic pathogenic deposition of fatty acids into pericardial and perivascular fat depots, within/around the liver, muscle, heart, pancreas, and kidney [128]. Ectopic fat intensifies local inflammatory activity and promotes lipotoxicity [300].

Insulin resistance in adipocytes impedes fat storage, accelerates lipolysis and further increases plasma free fatty acids, promoting insulin resistance in liver and muscle, hepatic steatosis and dyslipidemia, and contributing to β-cell failure. Insulin resistance in muscle and fat is marked by impaired glucose transport from circulation due to M1 inhibition of GLUT4, leading to hyperglycemia [301].

Increased ectopic fat deposition, lipotoxicity from excess circulating free fatty acids, glucose toxicity, along with β-cell resistance to GLP-1, cause progressive failure of β-cell functioning. Increased glucagon and enhanced liver sensitivity to glucagon lead to excessive hepatic glucose production. Increased renal glucose reabsorption by sodium/glucose co-transporter 2 (SGLT2) helps maintain hyperglycemia.

Insulin resistance in obesity leads to chronic compensatory hyperinsulinemia, which in turn promotes further weight gain [302]. This is exacerbated by resistance to the anorexigenic effects of insulin, leptin, GLP-1, amylin, and PYY [303].

Insulin resistance, hyperglycemia, and hyperinsulinemia in obesity promote hypertension, dyslipidemia, endothelial dysfunction, and a prothrombotic state, leading to NAFLD and type 2 diabetes [304]. NAFLD increases the risk of liver cirrhosis and hepatocellular carcinoma and is strongly correlated with cardiovascular disease and type 2 diabetes [305].

Type 2 diabetes, the predominant consequence of insulin resistance accounting for more than 90% of all diabetes cases, can lead to disabling and life-threatening microvascular (retinopathy, nephropathy, and neuropathy) and macrovascular (cardiovascular disease) complications [304; 306].

Biomechanical Consequences of Obesity

Local biomechanical stress due to excessive fat mass and body weight (e.g., on the joints, respiratory tract, blood vessels or within the abdominal compartment) causes and/or exacerbates morbidities common in patients with obesity, such as knee osteoarthritis, back pain, restrictive lung disease, obstructive sleep apnea, gastroesophageal reflux disease (GERD), hernias, and chronic venous insufficiency. These complications are further aggravated by the adverse metabolic profile and chronic inflammatory state in obesity, amplifying the overall burden of the disease and creating a vicious cycle that can be effectively broken only by sustained weight loss [302].

"Metabolically Healthy" Obesity

The concept of metabolically healthy obesity has been described in the literature. In general, it is defined as obesity in the absence of type 2 diabetes, hypertension, and hypercholesterolemia. Some have questioned the cardiovascular disease risk of persons with metabolically healthy obesity, suggesting this as a low-risk phenotype [307]. However, a large cohort demonstrated that obesity is a risk factor for cardiovascular disease regardless of whether the individual remained metabolically healthy over long periods [308]. Furthermore, a study of 270 patients who met strict inclusion criteria for metabolically healthy obesity found that even with strict criteria to eliminate all patients with any metabolic problems, a significant proportion had unsuspected NAFLD (35.5%); some had steatohepatitis (8.2%) and liver fibrosis (4.4%) [305].

Psychiatric Disorders

The neuropathological processes that lead to psychiatric disorders share common brain pathways with those that lead to obesity, metabolic syndrome, and cardiovascular disease risk factors, each of which can influence the risk for the others. Evidence points to a critical role for two major pathways: inflammatory processes that induce alterations of brain functions, and chronic stimulation of the hypothalamic-pituitary-adrenal (HPA) axis [87].

Psychiatric disorders are often characterized by a chronic HPA axis activation and sustained cortisol elevation, both of which are linked to abdominal obesity, hepatic steatosis, insulin resistance, and cardiovascular disease. Conversely, increased adiposity leads to chronic low-grade activation of inflammatory processes, which plays a potent role in the pathophysiological brain alterations associated with psychiatric disease. Thus, adiposity-driven inflammation may contribute to the growing prevalence of mood disorders [87].

Customer Information/Evaluation insert located between pages 60–61.

COURSE TEST - #94280 PHARMACOLOGIC AND MEDICAL ADVANCES IN OBESITY MANAGEMENT

This is an open book test. Please record your responses on the Answer Sheet.
A passing grade of at least 70% must be achieved in order to receive credit for this course.

This 15 contact hour activity must be completed by November 30, 2026.

1. **A Black patient with a body mass index of 26 is considered overweight.**
   A) *True*
   B) *False*

2. **Increasing activity levels may bring diminishing returns due to compensatory responses in nonactivity energy expenditure.**
   A) *True*
   B) *False*

3. **The biological pressure to gain weight is a consequence of both increased appetite and suppressed energy expenditure as the body attempts to restore energy homeostasis.**
   A) *True*
   B) *False*

4. **Paroxetine is considered to be a weight-reducing antidepressant.**
   A) *True*
   B) *False*

5. **Each naltrexone/bupropion tablet contains naltrexone 90 mg plus bupropion 8 mg.**
   A) *True*
   B) *False*

6. **Given this decreased likelihood of obesity in current cannabis users, research has begun to explore how the endocannabinoid system can be manipulated to promote weight loss and improve metabolic health.**
   A) *True*
   B) *False*

7. **Semaglutide 2.4 mg weekly is recommended as the first-line antiobesity medication for obesity management.**
   A) *True*
   B) *False*

8. **Sleeve gastrectomy is optimally suited for a patient with lower BMI and no metabolic disease.**
   A) *True*
   B) *False*

9. **Orbera is an ASMBS-endorsed intragastric balloon device FDA-approved for six-month dwell-time.**
   A) *True*
   B) *False*

10. **Ghrelin increases food consumption and reward.**
    A) *True*
    B) *False*

Be sure to transfer your answers to the Answer Sheet insert located between pages 60–61.
PLEASE NOTE: Your postmark or facsimile date will be used as your test completion date.

Course Availability List

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POSTOPERATIVE COMPLICATIONS

UPDATE

#30764 • 15 ANCC Hours / 1 Pharm Hour

Book By Mail – $98 • ONLINE – $90

Purpose: The purpose of this course is to provide nurses and all allied health professionals who care for postsurgical patients the knowledge necessary to recognize and manage common postoperative complications, improving patient care and outcomes.
Faculty: Susan Engman Lazear, RN, MN
Audience: This course is designed for all nurses and allied professionals involved in the care of patients who undergo surgical procedures, especially those who work in the preoperative area, the operating room, or the postanesthesia unit in hospitals or free-standing surgical centers.
Additional Approval: AACN Synergy CERP Category A

COMMUNICATION AND SOFT SKILLS IN NURSING PRACTICE

NEW!

#31350 • 3 ANCC Hours

Book By Mail – $26 • ONLINE – $18

Purpose: The purpose of this course is to provide nurses with strategies to support the soft skills needed to provide optimal patient care and enhance professionalism in health care.
Faculty: Mary Franks, MSN, APRN, FNP-C
Audience: This course is designed for nurses in all practice settings.
Additional Approval: AACN Synergy CERP Category C

MULTIMODAL PHARMACOTHERAPY FOR PAIN MANAGEMENT

NEW!

#35270 • 5 ANCC Hours / 5 Pharm Hours

Book By Mail – $38 • ONLINE – $30

Purpose: The purpose of this course is to provide healthcare providers with a clear understanding of the concept of multimodal pharmacotherapy for pain relief, including available classes of analgesics.
Faculty: Richard E. Haas, BSN, MSN, EdM, PhD, CRNA (Retired), LTC US Army Nurse Corps (Retired)
Audience: This course is designed for nurses involved in the care of patients with pain.
Additional Approval: AACN Synergy CERP Category A

CARING FOR THE GERIATRIC PATIENT

#39101 • 3 ANCC Hours

Book By Mail – $26 • ONLINE – $18

Purpose: The purpose of this course is to provide nurses with an overview of the physical and psychosocial considerations necessary when providing care to geriatric patients.
Faculty: Alice Yick Flanagan, PhD, MSW; Allan G. Hedberg, PhD
Audience: This course is designed for nurses in a variety of practice settings who work with older patients.
Additional Approval: AACN Synergy CERP Category A

PULMONARY EMBOLISM

NEW! NP LEVEL

#90120 • 2 ANCC Hours / 1 Pharm Hour

Book By Mail – $23 • ONLINE – $15

Purpose: The purpose of this course is to provide healthcare professionals with the knowledge and clinical strategies necessary to optimally triage and treatment patients with pulmonary embolism.
Faculty: Dalia Saha, MD
Audience: This course is designed for physicians, PAs, and nurses involved in assessing, triaging, and managing patients with suspected pulmonary embolism.
Additional Approval: AACN Synergy CERP Category A

BOTULINUM TOXIN AND DERMAL FILLERS FOR FACIAL AGING

NP LEVEL

#90200 • 10 ANCC Hours / 5 Pharm Hours

Book By Mail – $68 • ONLINE – $60

Purpose: This course is designed to provide clinicians with the knowledge necessary to provide minimally invasive aesthetic procedures and to care for patients who have undergone these procedures.
Faculty: Mark Rose, BS, MA, LP
Audience: This course is designed for physicians, nurses, and other healthcare professionals who may administer or care for patients who have undergone aesthetic procedures.
Additional Approval: AACN Synergy CERP Category A

If you are an APRN seeking an Autonomous license, please see the special offers located on the inside back cover of this booklet.

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Course Availability List *(Cont'd)*

MATERNAL HEALTH DISPARITIES

#93010 • 4 ANCC Hours

Book By Mail – $32 • ONLINE – $24

NEW! NP LEVEL

Purpose: The purpose of this course is to provide healthcare providers with the knowledge and skills necessary to improve maternal outcomes in all races, ethnicities, and marginalized groups.
Faculty: Mary Franks, MSN, APRN, FNP-C
Audience: This course is designed for all healthcare providers who may intervene to improve peripartum and postpartum health care and reduce health disparities.
Additional Approval: AACN Synergy CERP Category B

LOW BACK PAIN

#94102 • 15 ANCC Hours / 10 Pharm Hours

Book By Mail – $98 • ONLINE – $90

UPDATE NP LEVEL

Purpose: The purpose of this course is to provide healthcare professionals with a greater understanding of the pathophysiology and differential diagnosis of low back pain conditions so they may effectively treat or manage low back pain, resulting in improved patient health, quality of life, and satisfaction.
Faculty: Mark Rose, BS, MA, LP
Audience: This course is designed for physicians, physician assistants, nurses, and other healthcare professionals involved in the care of patients with back pain.
Additional Approval: AACN Synergy CERP Category A

DIABETES CARE AND PATIENT EDUCATION

#94394 • 15 ANCC Hours / 3 Pharm Hours

Book By Mail – $98 • ONLINE – $90

Expiration Date: 10/31/25

Purpose: The purpose of this course is to provide nurses and behavioral health professionals with the information and resources needed to develop proficiency in teaching and caring for the patient with diabetes.
Faculty: Susan Semb, MSN, RN, CDE
Audience: This course is designed for all nurses and behavioral health professionals involved in the care of patients with diabetes.
Additional Approval: AACN Synergy CERP Category A

AUTOIMMUNE DISEASES

#94454 • 15 ANCC / 10 Pharm Hours

Book By Mail – $98 • ONLINE – $90

NP LEVEL

Purpose: The purpose of this course is to provide healthcare professionals with the information necessary to diagnose and treat the most common autoimmune disorders according to evidence-based or guideline-endorsed recommendations in order to improve patient quality of life.
Faculty: Lori L. Alexander, MTPW, ELS, MWC; John M. Leonard, MD
Audience: This course is designed for physicians, physician assistants, nurses, and other healthcare professionals involved in the diagnosis, treatment, and care of patients with autoimmune diseases.
Additional Approval: AACN Synergy CERP Category A

OSTEOARTHRITIS

#94954 • 10 ANCC / 5 Pharm Hours

Book By Mail – $68 • ONLINE – $60

New Guidelines NP LEVEL

Purpose: The high prevalence of osteoarthritis and its substantial burden at both the individual and healthcare system levels demands sound knowledge and clinical skills in diagnosing and managing the disease. The purpose of this course is to provide healthcare professionals with the information necessary to adequately assess osteoarthritis symptoms, treat osteoarthritis patients based on evidence-based guidelines, and appropriately refer to specialists.
Faculty: Lori L. Alexander, MTPW, ELS, MWC
Audience: This course is designed for physicians, physician assistants, nurses, and other healthcare professionals involved in the care of patients with osteoarthritis.
Additional Approval: AACN Synergy CERP Category A

MANAGING DRUG INTERACTIONS WITH DIRECT ORAL ANTICOAGULANTS

#95010 • 1 ANCC / 1 Pharm Hour

Book By Mail – $23 • ONLINE – $15

NEW! NP LEVEL

Purpose: The purpose of this course is to provide prescribers and other healthcare professionals with the knowledge and skills necessary to identify and act to avoid or address drug-drug interactions that occur in patients taking direct oral anticoagulants.
Faculty: Jeff Langford, PharmD
Audience: This course is designed for physicians, physician assistants, and nurses involved in the care of patients who require anticoagulation therapy.
Additional Approval: AACN Synergy CERP Category A

PSYCHOPHARMACOLOGY

#95230 • 10 ANCC Hours / 10 Pharm Hours

Book By Mail – $68 • ONLINE – $60

NP LEVEL

Purpose: The purpose of this course is to provide members of the interprofessional healthcare team with the information necessary to appropriately prescribe, administer, and dispense psychopharmacotherapy, with the ultimate goal of improving patient care and public health.
Faculty: Carol Whelan, APRN
Audience: This course is designed for nurses and pharmacy professionals involved in the care of patients with mental health conditions.
Additional Approval: AACN Synergy CERP Category A

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Course Availability List *(Cont'd)*

FRONTOTEMPORAL DEMENTIA

UPDATE NP LEVEL

#96102 • 2 ANCC Hours / 1 Pharm Hour

Book By Mail – $23 • ONLINE – $15

Purpose: The purpose of this course is to provide healthcare professionals with current information on frontotemporal dementia (FTD). Understanding the epidemiology, pathology, clinical features, diagnostic process, genetics, symptom treatment/management, role of brain autopsy, and current research provides a foundation for the care of patients with FTD and support for their families.

Faculty: Ellen Steinbart, RN, MA; Lauren E. Evans, MSW

Audience: This course is designed for physicians, nurses, and allied health and mental health professionals who may intervene to support patients with frontotemporal dementia and their families.

Additional Approval: AACN Synergy CERP Category A

ATTENTION DEFICIT HYPERACTIVITY DISORDER

NEW! NP LEVEL

#96213 • 5 ANCC Hours / 2 Pharm Hours

Book By Mail – $38 • ONLINE – $30

Purpose: Attention deficit hyperactivity disorder (ADHD) has a significant effect on day-to-day functioning and quality of life; however, it often goes unrecognized. The purpose of this course is to educate healthcare professionals about the epidemiology, diagnosis, and management of ADHD.

Faculty: John J. Whyte, MD, MPH; Paul Ballas, DO

Audience: This course is designed for all physicians, nurses, and social work/counseling groups involved in the care of patients with attention deficit hyperactivity disorder.

Additional Approval: AACN Synergy CERP Category A

ANXIETY DISORDERS IN OLDER ADULTS

NP LEVEL

#96690 • 3 ANCC Hours / 1 Pharm Hour

Book By Mail – $26 • ONLINE – $18

Purpose: Older adults are the fastest growing demographic in the world, and anxiety disorders are the most common mental disorder in this age group. The purpose of this course is to provide clinicians with the knowledge and skills necessary in order to improve the assessment and treatment of anxiety disorders in older adults.

Faculty: Beyon Miloyan, PhD

Audience: This course is designed for the benefit of a broad range of allied health professionals, including but not limited to physicians, nurses, medical assistants, and nursing home administrators.

Additional Approval: AACN Synergy CERP Category A

PSYCHEDELIC MEDICINE AND INTERVENTIONAL PSYCHIATRY

NEW! NP LEVEL

#96790 • 10 ANCC Hours / 8 Pharm Hours

Book By Mail – $68 • ONLINE – $60

Purpose: The purpose of this course is to provide medical and mental health professionals with the knowledge and skills necessary to effectively treat mental disorders using emerging psychedelic and interventional techniques.

Faculty: Mark S. Gold, MD, DFASAM, DLFAPA

Audience: The course is designed for all members of the interprofessional team, including physicians, physician assistants, nurses, and mental health professionals, involved in caring for patients with mental disorders resistant to traditional treatment approaches.

Additional Approval: AACN Synergy CERP Category A

INTERCULTURAL COMPETENCE AND PATIENT-CENTERED CARE

NEW! NP LEVEL

#97510 • 4 ANCC Hours

Book By Mail – $32 • ONLINE – $24

Purpose: The purpose of this course is to provide members of the interprofessional healthcare team with the knowledge, skills, and strategies necessary to provide culturally competent and responsive care to all patients.

Faculty: Alice Yick Flanagan, PhD, MSW

Audience: This course is designed for all members of the interprofessional healthcare team.

Additional Approval: AACN Synergy CERP Category B

CANNABINOID OVERVIEW

NEW! NP LEVEL

#98010 • 3 ANCC Hours / 3 Pharm Hours

Book By Mail – $26 • ONLINE – $18

Purpose: The purpose of this course is to provide healthcare professionals in all practice settings the knowledge necessary to increase their understanding of the various cannabinoids.

Faculty: Chelsey McIntyre, PharmD

Audience: This course is designed for healthcare professionals whose patients are taking or are interested in taking cannabinoid products.

Additional Approval: AACN Synergy CERP Category A

THE SCOOP ON COLLAGEN

NEW! NP LEVEL

#98070 • 1.5 ANCC Hours

Book By Mail – $23 • ONLINE – $15

Purpose: The purpose of this course is to provide healthcare professionals in all practice settings the knowledge necessary to increase their understanding of the various collagen products.

Faculty: Chelsey McIntyre, PharmD

Audience: This course is designed for healthcare professionals whose patients are taking or are interested in taking collagen products.

Additional Approval: AACN Synergy CERP Category A

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FL24

Answer Sheet

(Completion of this form is mandatory)

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Please note the following:

- A passing grade of at least 70% must be achieved on each course test in order to receive credit.
- Darken only one circle per question. **A = True, B = False**
- Use pen or pencil; please refrain from using markers.
- **Information on the Customer Information form must be completed.**

#91334 MEDICAL ERROR PREVENTION AND ROOT CAUSE ANALYSIS—2 HOURS

Please refer to page 13.

Expiration Date: 08/31/25 *May be taken individually for $15*

	A	B		A	B
1.	❍	❍	6.	❍	❍
2.	❍	❍	7.	❍	❍
3.	❍	❍	8.	❍	❍
4.	❍	❍	9.	❍	❍
5.	❍	❍	10.	❍	❍

#31253 LAWS AND RULES FOR FLORIDA NURSES—2 HOURS

Please refer to page 31.

Expiration Date: 10/31/25 *May be taken individually for $15*

	A	B		A	B
1.	❍	❍	6.	❍	❍
2.	❍	❍	7.	❍	❍
3.	❍	❍	8.	❍	❍
4.	❍	❍	9.	❍	❍
5.	❍	❍	10.	❍	❍

#97111 RECOGNIZING AND REPORTING HUMAN TRAFFICKING IN FLORIDA—2 HOURS

Please refer to page 56.

Expiration Date: 08/31/25 *May be taken individually for $15*

	A	B		A	B
1.	❍	❍	6.	❍	❍
2.	❍	❍	7.	❍	❍
3.	❍	❍	8.	❍	❍
4.	❍	❍	9.	❍	❍
5.	❍	❍	10.	❍	❍

#94280 PHARMACOLOGIC AND MEDICAL ADVANCES IN OBESITY MANAGEMENT—15 HOURS

Please refer to page 116.

Expiration Date: 11/30/26 *May be taken individually for $90*

	A	B		A	B
1.	❍	❍	6.	❍	❍
2.	❍	❍	7.	❍	❍
3.	❍	❍	8.	❍	❍
4.	❍	❍	9.	❍	❍
5.	❍	❍	10.	❍	❍

#97923 DOMESTIC VIOLENCE: THE FLORIDA REQUIREMENT—2 HOURS

Please refer to page 23.

Expiration Date: 07/31/25 *May be taken individually for $15*

	A	B		A	B
1.	❍	❍	6.	❍	❍
2.	❍	❍	7.	❍	❍
3.	❍	❍	8.	❍	❍
4.	❍	❍	9.	❍	❍
5.	❍	❍	10.	❍	❍

#31112 RECOGNIZING IMPAIRMENT IN THE WORKPLACE: THE FLORIDA REQUIREMENT—2 HOURS

Please refer to page 39.

Expiration Date: 10/31/25 *May be taken individually for $15*

	A	B		A	B
1.	❍	❍	6.	❍	❍
2.	❍	❍	7.	❍	❍
3.	❍	❍	8.	❍	❍
4.	❍	❍	9.	❍	❍
5.	❍	❍	10.	❍	❍

#91152 STRATEGIES FOR APPROPRIATE OPIOID PRESCRIBING: THE FLORIDA APRN REQ.—3 HOURS

Please refer to page 71.

Expiration Date: 08/31/25 *May be taken individually for $18*

	A	B		A	B
1.	❍	❍	6.	❍	❍
2.	❍	❍	7.	❍	❍
3.	❍	❍	8.	❍	❍
4.	❍	❍	9.	❍	❍
5.	❍	❍	10.	❍	❍

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