PHARMACIST CE:

The Pharmacists Role in Combating Statewide Epidemics

by Cody J Wenthur, PharmD, PhD, Laurel Legenza, PharmD, MS, Nicole Weinfurter, 2019 PharmD Candidate, Ashley Lorenzen, PharmD, BCPS, Dean Bowen, 2020 PharmD Candidate

CE FOR **PHARMACISTS**

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Learning Objectives

- Summarize the CDC's definition of an epidemic
- Describe the impact of the opioid, *Clostridium difficile* infection (CDI), and obesity epidemic in Wisconsin and the United States
- Identify tools and education pearls to provide patients related to epidemics affecting Wisconsin residents
- Recommend evidence-based treatments to help combat each the opioid, *Clostridium difficile* infection (CDI), and obesity epidemic.

The word "epidemic" carries a lot of weight. It is a word that can instill fear and a sense of urgency in a population. It ultimately means there is a serious issue that is negatively affecting a high proportion of that population and needs to be addressed immediately. The Centers for Disease Control and Prevention (CDC) defines an epidemic as, "an increase, often sudden, in the number of cases of a disease above what is normally expected in that population in that area."[1] The CDC has also quantified an "epidemic threshold" for pneumonia and influenza deaths that could be applied to other healthcare issues.[2] The "epidemic threshold" is met when there is an increase of 1.645 standard deviations above the seasonal baseline of pneumonia and influenza deaths.[2]

The United States (US) has dealt with various epidemics in the past. Examples of diseases causing epidemics which have been eradicated include polio, with the last case in the US occurring in 1978, and smallpox, which was eradicated from North America in 1952.[3,4] Currently in Wisconsin and the US, there are a number of epidemics affecting vast amounts of people. Three examples were pharmacists have the opportunity to get involved and assist with epidemic mitigation include opioid misuse, *Clostridium difficile* (*C. diff*), and obesity. Pharmacists are very accessible healthcare providers and may see patients up to a monthly basis. Pharmacists can recommend optimal antibiotic and pain management therapy, educate patients on how to use their medications properly, and provide diet and lifestyle interventions. The objective of this article is to describe the scope of each epidemic, how pharmacists can play a role in mitigating the epidemic, and present tools that pharmacists can recommend or use.

Background and Epidemiology of the Opioid Misuse Epidemic

Balancing the risks and benefits of opiate receptor agonists as analgesics has been a challenge in pain management for thousands of years, beginning with the use of products derived from the opium poppy, papaver somniferum.[5] As modern medicine promoted the increased availability and rapid expansion of semi-synthetic opioids, the need for proper management of this risk-benefit profile has likewise expanded to cover hundreds of millions of acute and chronic pain patients worldwide.[6] This growth has been especially dramatic in the US.[7,8] Opioid prescribing rates in the US peaked in 2012, with a rate of 81.3 prescriptions written for every 100 individuals. Although rates have recently declined, Wisconsin remains above the national average with 62.2 opioid prescriptions written per 100

individuals.[9] Although the expansion of access to appropriate pain control is a desirable public health outcome overall, the specific increase in opioid pain reliever utilization as a means to this end has unfortunately been a major driving force in the continuation of a general drug overdose epidemic and resurgence of broader opioid misuse.[10,11] Indeed, the magnitude of the problem has increased to the point where the US Department of Health and Human Services declared the opioid crisis to be a public health emergency.[12] In 2016, there were about 63,600 deaths nationwide due to drug overdose – a more than four-fold increase since 1999.[13] Within Wisconsin, there were approximately 20,600 individuals diagnosed with opioid use disorder (OUD) and 827 deaths due to opioid-associated overdose in 2016.[14] This corresponds to a rate of approximately 20 opioid overdose deaths per 100,000 people; drug overdose accounted for 15.5% percent of deaths amongst individuals 18-25 and 7.1% of deaths in 26-64 year old individuals in 2015.[15]

In response to the opioid crisis, the US government issued the Comprehensive Addiction and Recovery Act (CARA) in 2016, which was the first major legislation to address substance use disorder in over forty years.[16] This act contained measures to respond to the opioid overdose crisis across six distinct areas: law enforcement, criminal justice reform, prevention, treatment, recovery, and overdose reversal. The Heroin, Opiate, Prevention and Education (HOPE) agenda was instituted in Wisconsin in 2013 to address many of these same concerns, and expansion on this agenda through a dedicated task force and special legislative session has resulted in 28 enacted pieces of legislation to date.[17] Several of these laws directly impact the daily practice of pharmacy in the state, including a requirement to view and record identifying information from patients picking up a schedule II or III drug, a requirement to have a prescription for codeine cough syrup, and implementation of a statewide standing order for naloxone pharmacist dispensing.[18-21] Other laws have an indirect impact on pharmacist counselling and referral strategies, such as those expanding good Samaritan coverage and legal protections for individuals reporting or experiencing opioid overdose, and those funding additional medically assisted treatment (MAT) centers in underserved areas.[22-24]

TABLE 1. Risk Factors for Opioid Overdose

Medication-Related Factors	*Patient-Related Factors*
Combining opioids and benzodiazepines	Age ≥ 65 years
Daily dose ≥ 100 morphine mg equivalents	Sleep-disordered breathing
Long-acting or extended release opioid formulation	Renal or hepatic impairment
Long term opioid use for ≥ 3 months	Major depressive disorder
≤ 2 weeks since initiating long-acting opioid formulation	Substance use disorder
	History of drug overdose

Role of Pharmacists in Reversing the Opioid Misuse Epidemic

As the primary point of care for medication therapy expertise, pharmacists are optimally positioned to take advantage of these tools and help end the opioid misuse epidemic. At a broad level, the CDC identify a four-fold role for pharmacists in vigilance for signs of opioid misuse: assessment, verification, consultation, and communication.[25] Assessment is focused on identifying red flags associated with misuse, such as forged or altered prescriptions and inconsistent or early refills. Verification is used to validate proper therapeutic use, check prescriptive authority through the Drug Enforcement Administration (DEA), and confirm proper patient identification. Consultation with available patient records and prescribing databases is then recommended to identify possible misuse. Finally, communication with the patient and prescriber and submission of relevant information to the written record should be incorporated in order to allow for ongoing monitoring and risk-assessment by all parties.

However, individual pharmacists are ultimately responsible for applying these general vigilance roles in a way that leads to meaningful improvements in patient outcomes. Fortunately, multiple tools are available to support both preemptive opioid misuse risk reduction and interventional harm mitigation, while still preserving compassionate therapeutic care. Pharmacist-driven resolution of the opioid misuse epidemic would take maximum advantage of these tools by concurrently addressing multiple areas of need, including consistent risk and harm screening, expanded public education on proper opioid use, ongoing promotion of best-practice opioid prescribing, effective support for medication-assisted recovery from opioid use disorder, and reliable dispensing of pharmacological protection against fatal opioid overdose.[26]

Reducing Likelihood of Opioid Misuse in At-risk Patients

Although open-ended, empathetic, and non-judgmental questioning regarding opioid medication use is often an appropriate and sufficient method to perform a simple assessment for patient risk of misuse, there are also a number of risk screening tools available when formal metrics are desired.[27,28] These include the opioid risk tool (ORT), screener and opioid assessment for patients with pain (SOAPP), diagnosis, intractability, risk, efficacy score (DIRE), the brief risk interview (BRI), brief risk questionnaire (BRQ), and screening instrument for substance abuse potential (SISAP). Although the SOAPP tool is among the most well validated, there is little evidence of superior performance between any of these screening measures, so selection of the appropriate tool is contingent upon considerations such as prior experience and ease of access.[29] Specific assessment of patients for elevated

TABLE 2. Treatment Options for Opioid Withdrawal Symptoms

Withdrawal Symptoms	*Common Treatment Choices*
Autonomic Hyperactivity	clonidine, tizanidine, lofexidine
Muscle Cramps / Pain	ibuprofen, ketorolac tromethamine
Diarrhea	bismuth subsalicylate
Nausea / Vomiting	prochlorperazine, ondansetron
Insomnia	Non-pharmacologic treatments preferred

risk of overdose can be undertaken by providing patients with a self-screening checklist generated by the Wisconsin Department of Health Services.[30] This document allows pharmacists to identify common medication- and patient-related risk factors (Table 1), providing a platform to initiate discussion of how to safely and correctly use opioid medications in the event that such risk factors are identified.

Published guidelines on opioid prescribing are effective tools for verification and implementation of proper therapeutic use.[31] The predominant, current guidelines at the national and local levels are the CDC Guideline for Prescribing Opioids for Chronic Pain and the Wisconsin Medical Examining Board Opioid Prescribing Guidelines.[32,33] Overall, these guidelines espouse four key principles for safe opioid prescribing for the treatment of adults with non-cancer pain: identify and treat the cause of pain, use non-opioid therapies when possible, start with a low dose and increase dosage slowly, and provide close follow-up. Adherence to these key principles should be considered for every opioid prescription that is processed. Additional recommendations from the Wisconsin guidelines include the use of short-acting opioids for initial dose titration, avoiding oxycodone as a first-line therapy, discouraging methadone prescribing by inexperienced or inexpert practitioners, and writing new prescriptions for treatment of acute pain to less than three days in most cases. Pharmacists should communicate with prescribers to clarify and correct when deviations from these recommendations are identified, remembering that the desired outcome is to support safe use of opioids overall, rather than to simply limit access.[34]

Consultation of the enhanced Wisconsin Prescription Drug Monitoring Program (ePMDP) will now identify more cases of potential opioid misuse due to an administrative rule change allowing e-prescribing for Schedule II controlled substances and recent legislation mandating practitioner review upon initial prescription of a schedule II drug.[35-36] This law resulted in dramatically increased overall use of the ePDMP in 2017, although pharmacist use remained relatively steady at round 70,000 queries per month.[37] The same legislation also decreased the time requirement for submission of dispensing information from 7 days to 24 hours, to make the database more timely and accurate. In addition to multiple prescriber and/or dispenser alerts, the ePDMP also provides safety alerts regarding specific actionable scenarios that increase risk of overdose, such as concurrent opioid and benzodiazepine overlap.[38]

In terms of risk communication, the provision of proper storage and disposal instructions to patients using opioids remains an important pharmacist task. The majority of misused prescription medications are given by, bought from, or taken from a friend or relative.[39] Therefore, pharmacists should continue to counsel patients to store opioids in a secure, preferably locked, location, and offer self-disposal instructions for opioids. These options include trashing them with coffee grounds or kitty litter, or flushing unused medications down the toilet, as many opioids are on the approved Food and Drug Administration (FDA) flush list.[40] Furthermore, the increasing availability of community resources for returning or destroying unused or unwanted opioid medications should also be emphasized. These resources include a growing network of drug takeback locations such as local police or fire stations, expansion of mail-back programs, and periodic statewide drug take-back days.

Mitigating Harms for Patients with Opioid Use Disorder (OUD)

While the Diagnostic and Statistical Manual of Mental Disorders (DSM-5) is the prevailing standard for providers to identify OUD, there are also several screening tools available for pharmacists to quickly identify concerning opioid misuse patterns in the absence of information regarding a formal OUD diagnosis.[41] These include the current opioid misuse measure (COMM), the drug abuse screening tool-20 (DAST-20), and the National Institute on Drug Abuse-modified Alcohol, Smoking, and Substance Involvement Screening Test (NM-ASSIST) screen.[28,29] Although more evidence is needed to determine their validity in pharmacy settings, these tools can still support preliminary stratification of patients with, lower, moderate, or high risk opioid misuse, providing the opportunity to advise on proper medication use, assess patient readiness to change, offer assistance with the process of changing, and arranging a referral for specialty OUD assessment and treatment, if necessary.

Amongst patients diagnosed with OUD, pharmacists have a direct role in the management of current opioid therapy, including initiation of a dose taper regimen and associated withdrawal symptom support. The recommended rate of taper in patients experiencing harms from opioid use is a 25% reduction in morphine milligram equivalents (MME) per week, although this range can vary between 2 – 50%, depending on setting and patient needs.[33,42] If patients need pharmacologic support for autonomically-mediated withdrawal symptoms such as lacrimation, rhinorrhea, sweating, chills, hypertension, tachycardia, or mydriasis during this taper, pharmacists can recommend use of an appropriate agent, such as oral clonidine or tizanidine.[33] Ancillary symptoms

arising from withdrawal should be treated supportively as needed (Table 2).[43] Options for ongoing medication assisted treatment (MAT) should also be communicated to patients with OUD and their providers, including monthly naltrexone intramuscular injections, daily methadone oral tablets, and daily buprenorphine-containing sublingual preparations.[44] When selecting an appropriate MAT regimen, the potential for precipitation of withdrawal symptoms with naloxone and buprenorphine should be considered, as should the dose accumulation and elevated risk of overdose with methadone. Integration of appropriate non-opioid and non-pharmacologic pain control methods in individuals experiencing ongoing pain is also a crucial consideration for compassionate treatment of these patients.

Mitigating Harms in Cases of Opioid Overdose

Education of members of the public to recognize and respond to opioid overdose symptoms is an effective method by which mortality due to opioid misuse can be reduced.[45,46] Opioid overdose is characterized by respiratory depression, manifesting as slow, shallow, or absent breathing. An overdosing individual will be difficult to rouse, including by yelling or painful stimuli, such as a sternal knuckle rub. They may make snoring, gurgling, or choking noises while asleep or nodding off. Additionally, they may be vomiting, have blue or pale lips, skin, or fingernails, and the individual's face may appear pale or clammy. Incorporating a frank discussion of these symptoms alongside other potential adverse effects of opioid medication is recommended, especially in patients with risk factors that increase the likelihood of overdose. When overdose is suspected, individuals should call 911, open the airway and give one rescue breath every five seconds if the individual is not breathing and has a pulse, give naloxone if available, place the person on their side with the top leg and arm crossed over the body, and stay with the individual until help arrives, re-administering naloxone as directed.[47]

As a component of this response, administration of the opioid receptor antagonist naloxone is the most effective method to avoid a fatal opioid overdose, reversing 89% of cases where it is used.48 Pharmacists in Wisconsin may now dispense naloxone without a prescription pursuant to a statewide standing order. Consistent application of this authority by pharmacists has the potential to drastically alter the trajectory of the opioid misuse epidemic in the state and significantly reduce opioid overdose mortality, as one life can be saved for every 227 naloxone kits dispensed.[49] Unfortunately, the stigma associated with opioid use disorder currently results in very high rates of patient resistance to hear about or accept naloxone.[50,51] Therefore, in order to maximize the impact of this intervention, pharmacists need to be cognizant of this stigma and take steps to actively mitigate its impact. This includes avoiding terms like 'addict' during discussion and normalizing naloxone dispensing as a measure that is undertaken as a matter of course to maximize the benefits of opioid use while limiting its potential risks.

Specific naloxone products available for dispensing include intramuscular injections (manual or auto-injector) and intranasal sprays (single-step or multistep). The single-step nasal spray is a simple, widely-available, and easily-

transportable method suitable for use by most individuals who have received basic administration information. The auto-injector is a useful option where the individual administering the naloxone is likely to have limited experience or information about the situation and patient, as it provides audible step-by-step instructions for use; however, these instructions are only provided in English.[52] All naloxone containing products should be protected from light and prevented from undergoing extreme temperature fluctuations. Products with needles should be placed in a puncture-proof container upon use, and any unused or expired naloxone should be returned using a drug take-back program. Naloxone dispensing records under the statewide standing order need to be reported quarterly using prescriber number 1346552668, including the number of doses dispensed, number of refills dispensed, number of different dosage forms dispensed, and any challenges or barriers encountered.[20,21] Patient counselling on any of these naloxone products should cover overdose risk factors, overdose signs/symptoms, and overdose response measures, along with administration, storage, and disposal instructions. If the individual being counseled on naloxone rescue is also the one taking an opioid medication, they should be instructed to communicate this naloxone use information with a caregiver or other responsible individual, as the patient would likely be unresponsive or too confused to take action themselves in the event of an overdose.

Summary Statement

The tragic impact of the opioid misuse epidemic continues to be felt throughout the country and within the state of Wisconsin, especially through fatal opioid overdose. However, recent legislative changes have provided pharmacists with direct access to life-saving pharmacological tools to address this problem, as well as improved screening measures to recognize and correct misuse. Furthermore, specific guidelines are available to optimize opioid therapy at a population level, and access to MAT options for patients with OUD continues to expand. By employing these tools, pharmacists have the opportunity to build upon recent gains in this high-need area, directly saving patient lives across the state of Wisconsin.

Background on *Clostridium difficile*

Clostridium difficile is the most common pathogen causing healthcare-associated infections.[53] *C. difficile* is a spore forming bacteria that can cause diarrheal infections ranging from mild-moderate to life threating colitis and sepsis. Patients will usually present with diarrhea and abdominal cramps and other signs of infection including, increased white blood cell count; CDI is diagnosis by a stool test.

At the turn of the century *C. difficile* infection (CDI) caused massive outbreaks in hospitals across North America and Canada that were associated with highly virulent *C. difficile* strains.[54] Since then CDI bundle approaches for appropriate prevention, treatment and diagnosis, along with antibiotic stewardship programs have halted what was a rapid increase in infection rates.[55,56] Nonetheless, the CDC continues to classify CDI as an urgent threat. CDI is also occurring without recent healthcare exposure or as community onset CDI, in recently discharged patients, and in long-term care facilities.[57]

Epidemiology of *Clostridium difficile*

According to the CDC *C. difficile* is associated with 453,000 infections per year and about 15,000 of these infections result in death directly attributable to CDI.[58] *C. difficile*, transmitted via a fecal oral route, can be toxigenic or non-toxigenic. Non-toxigenic strains can colonize the gut of individuals without infection. The toxigenic form can lead to active infection, especially in the setting of antibiotic use that kills normal gut flora, but not *C. difficile*, allowing it to overgrow. The toxins cause intestinal enterocytes to loose integrity and subsequently cause an inflammatory response, associated with the severity of the infection.[59] CDI incidence and severity increased rapidly, including fatal outbreaks in the early 2000s. These outbreaks were associated with the hypervirulent *C. difficile* BI/NAP/027 strain. However, a recent CDI epidemiology study conducted across Veterans Affairs Medical Centers (2011-2016) found a decrease in the overall BI/NAP/027 strain prevalence from a high of 26.2% in 2013 to 16.9% in 2016.[56] The recently revised Infectious Diseases Society of America (IDSA) guideline classifies CDI by severity and setting/timing of onset, including healthcare associated (healthcare facility onset [>3 days after admission] or community-onset/healthcare associated [within 12 weeks of healthcare facility discharge]) and community associated.[60]

Antibiotic exposure is the most critical and modifiable CDI risk factor. Antibiotics associated with high CDI risk are those that are broad spectrum and affect normal gastrointestinal flora. A meta analysis of antibiotic classes and community-associated CDI risk found clindamycin, fluoroquinolones, and a combined group of cephalosporins, monobactams, and carbapenems had a high CDI risk. Macrolides, sulfonamides-trimethoprim, and penicillins had a lower CDI risk. Tetracycline had no association with CDI in this study.[61] Prolonged antibiotic durations and multiple antibiotics also increase risk. In a study of cumulative antibiotic exposure patients who received 1st-2nd generation cephalosporins (HR 2.4), 3rd-4th generation cephalosporins (HR 3.1), quinolones (HR 4.5), and sulfa drugs (HR 1.8), intravenous vancomycin (HR 2.6) were more likely to develop CDI relative to patients who did not receive these antibiotics, independent of other antibiotics received. The minimal gastrointestinal exposure from intravenous vancomycin exposure is thought to disrupt normal flora enough for *C. difficile* to overgrow without killing it. Patients who received two antibiotics had a 2.5-fold increase in risk compared to those who received one antibiotic.[63] The increased risk of CDI persists during antibiotic therapy and three months following therapy discontinuation. Even a prophylactic single dose of an antibiotic can increase a patient's risk of CDI.[60]

Additional CDI risk factors are advanced age, female sex, gastrointestinal tract surgery, immunosuppression from a medication such as chemotherapy or disease, and proton pump inhibitors. In the US and high resource settings, the majority

of deaths (80%) are associated with patients aged 65 or older.[64] This finding is likely attributable to the age at which healthcare exposure, antibiotic use, and comorbid conditions and complexity increases. For example, a recent epidemiology study in South Africa found the average age of patients testing positive for *C. difficile* was 46.5 years and the study identified tuberculosis as a novel risk factor for CDI, in a population with high HIV and tuberculosis prevalence.[62]

Treatment Considerations and Guideline Updates of *Clostridium difficile*

Historically metronidazole and vancomycin were associated with similar clinical cure and recurrence rates (metronidazole 500 mg by mouth three times daily for ten days, vancomycin 125 mg by mouth four times daily for ten days). IDSA clinical practice guidelines for CDI were updated in early 2018. These guidelines and recent evidence support initial CDI treatment with either vancomycin or fidaxomicin (fidaxomicin 200 mg by mouth twice daily for 10 days). Metronidazole shifted from previously a first line agent for mild-moderate CDI to only be used when other therapies are contraindicated or unavailable in non-severe cases (WBC ≤15000 cells/mL and a serum creatinine level <1.5 mg/dL). Similar to the previous 2010 guidelines metronidazole is not recommend for severe CDI episodes.[56,60]

Recent evidence supports the new guidelines. For severe CDI infections, vancomycin is associated with a significant reduced risk of all cause 30-day mortality compared to metronidazole.[65] Furthermore, a 2017 Cochrane review of all severity found vancomycin was more effective than metronidazole for achieving symptomatic cure (79% vs. 72%, RR 0.90, 95% CI 0.84 to 0.97). Fidaxomicin was found to be more effective than vancomycin for achieving symptomatic cure (71% vs. 61%, RR 1.17, 95% CI 1.04 to 1.31). The authors noted the differences between the antibiotics are not great, while the cost differences between options are substantial. Ten-day CDI treatment courses were reported as: metronidazole $13, vancomycin tablets $1779, and fidaxomicin tablets $3453.[66] The cost associated with administration of the intravenous formulation of vancomycin orally is less than the capsules. A liquid vancomycin formulation was approved in 2018 and costs much less than the capsules.

Approximately 20% of successfully treated patients experience CDI recurrence, due to re-exposure or reactivation of spores, and this risk increases with each recurrence.[60,67] Recurrence risk is similar when patients are treated with vancomycin compared to metronidazole. However, clinical trials comparing fidaxomicin to vancomycin found fidaxomicin reduced risk of recurrence (15.4% vs. 25.3%) while clinical cure rate was similar. While fidaxomicin is significantly more expensive, it may be of greater benefit for patients experiencing recurrence. For patients with multiple CDI recurrences and treatment failures, fecal microbiota transplantation (FMT) is recommended and has proven to be highly effective with cure rates often greater than 90%.[60] FMT may have a role in initial CDI therapy in the future.

Additionally CDI management should include discontinuation of any antibiotics that may be contributing to CDI if clinically appropriate as soon as possible. Loperamide is contraindicated in CDI due to containment of the *C. difficile* toxins and should be discontinued if used. As with any diarrheal illness adequate rehydration and electrolyte balance is imperative. *C. difficile* spores can withstand alcohol hand sanitizer and can be transmitted between hospitalized patients and healthcare providers. Therefore, healthcare providers providing care to CDI patients should use contact precautions, gowns and gloves, and hand washing with soap and water to prevent transmission to other patients.

Role of Pharmacists in *Clostridium difficile*

Pharmacists can play a key role in CDI prevention, identification, and treatment. One of the most important roles is advocating for antimicrobial stewardship, the appropriate antibiotic use of antibiotics to reduce CDI risk and development of antimicrobial resistance. Pharmacists can review the appropriateness of antibiotic therapy and ensure antibiotics are only used when necessary. When possible, pharmacists can recommend lower risk antibiotics to reduce CDI risk. Pharmacists can also play a key role in antimicrobial stewardship programs. Stewardship interventions can include reducing the use and duration of high-risk antibiotics through formalized antibiotic restrictions and other measures. Stewardship interventions have been associated with significant reductions in CDI incidence in hospitals after epidemic outbreaks and overtime.[68]

Pharmacists should consult patients receiving an antibiotic on the risks associated with that antibiotic, including association with CDI. Pharmacist should advise patients to contact their doctor if they experience severe diarrhea or watery diarrhea that occurs three or more times per day and is not resolving. The pharmacist can also educate patients on why appropriate antibiotic use is important; antibiotic use increases the risk of antibiotic resistance development that may affect both the patient and their community.[69] Pharmacists working in transitions of care roles can ensure CDI contact precautions and treatment are continued if patients are transitioning from a hospital to long-term care setting.

CDI primary prevention vaccines are currently in development. Once approved, pharmacists can play a key role in CDI prevention by identifying patients who meet vaccination criteria and achieving high vaccination rates.[70] A phase III clinical trial is currently recruiting subjects with expected completion in 2020 (NCT03090191).

Pharmacists are commonly asked about the benefits of probiotics. While several studies have evaluated the role of probiotics in CDI, the updated IDSA guidelines state "there are insufficient data at this time to recommend administration of probiotics for primary prevention of CDI outside of clinical trial".[60] The statement reflects the limitations of the meta analyses and evidence quality suggesting probiotics may be effective for preventing CDI. A Cochrane analysis concluded short-term probiotic use appears to be safe and effective, but should not be used in immunocompromised or severely

TABLE 3. Adiposity-Based Chronic Disease[73]

Diagnostic Criteria	*Disease Stage*	*Suggested Therapy*
BMI <25 kg/m2 (BMI <23 kg/m2 for certain ethnicities)	Healthy weight (no obesity)	**Primary prevention** (Healthy lifestyle)
BMI 25-29.9 kg/m2 with no complications* (BMI 23-24.9 kg/m2 for certain ethnicities)	Overweight stage 0	**Secondary prevention** (Lifestyle therapy)
BMI >30 kg/m2 with no complications* (BMI >25 kg/m2 for certain ethnicities)	Obesity stage 0	**Secondary prevention** (Lifestyle therapy; add weight-loss medications if needed for BMI >27)
BMI >25 kg/m2 with 1 or more mild to moderate complications* (BMI >23 kg/m2 for certain ethnicities)	Obesity stage 1	**Tertiary prevention** (Lifestyle therapy; add weight loss medications if needed for BMI >27)
BMI >25 kg/m2 with at least 1 severe complication* (BMI >23 kg/m2 for certain ethnicities)	Obesity stage 2	**Tertiary prevention** (Lifestyle therapy; add weight loss medications if needed for BMI >27; may consider bariatric surgery if BMI >35)

BMI – Body Mass Index
Mild/Moderate – conditions generally well controlled
Severe – conditions generally uncontrolled

**Complications include metabolic syndrome, prediabetes, type 2 diabetes, dyslipidemia, hypertension, cardiovascular disease, nonalcoholic fatty liver disease, polycystic ovary syndrome, female infertility, male hypogonadism, obstructive sleep apnea, asthma/reactive airway disease, osteoarthritis, urinary stress incontinence, gastroesophageal reflux disease, or depression*

debilitated.[71]

Pharmacists can also identify patients at risk for CDI and ensure timely testing and management. Pharmacists ensure CDI treatment prescriptions and orders are effective. For example, vancomycin CDI therapy must be administered by mouth to reach site of infection as intravenous vancomycin gut penetration is negligible. Renal adjustment is not necessary for oral vancomycin because it is not systemically absorbed. Often the intravenous formulation is administered in water orally as the oral capsules may be cost prohibitive.

Background and Epidemiology of Obesity

The national rate of obesity has been on the rise in the US over the last 40 years for adults and children.[72] National data regarding obesity rates is collected annually via the National Health and Nutrition Examination survey (NHANES). In 2015-2016, national averages indicated that 39.6 percent of adults and 18.5 percent of children were considered obese. Differing rates of obesity are seen among different demographic groups when analyzed by race and ethnicity, gender, age, socioeconomic status, highest level of education, and residential setting (urban versus rural). In the state of Wisconsin, the most recent rates of obesity collected are 32.0 percent in adults (2017), 14.7 percent in 2- to 4- year-old WIC participants (2014), and 14.3 percent in 10- to 17-year-old adolescents (2016-2017).[73]

Obesity is defined as an unhealthy level of body fat.1 Previously, obesity was determined by measuring a patient's body mass index (BMI), which is calculated as follows:

$$\text{BMI} = \frac{(\text{weight (kg)}}{[\text{height (m)}]^2}$$

In adults, patients with BMI measurements over 30 kg/m2 were considered to be obese, with patients with a BMI measuring over 40 kg/m2 classified as severely obese. For children and adolescents, obesity is determined by comparing a child's own BMI to BMI-for-age charts produced by the CDC to determine which percentile they fall in when compared to children of the same age and gender. Children in the 95th percentile and above are classified as obese, with those measuring at 120 percent of the 95th percentile and above being classified as severely obese. However, BMI is not a direct measurement for body fat, prompting more recent guidelines to further define how obesity is classified. The American Association of Clinical Endocrinologists (AACE) and American College of Endocrinology (ACE) released a set of clinical practice guidelines for the diagnosis and management of patients with obesity in 2016, replacing the term obesity with the more medically-defined diagnostic term adiposity-based chronic disease (ABCD).[73] This set of guidelines also recommends that waist circumference and the related risk of comorbid conditions be evaluated, in addition to BMI, when assessing patients for the diagnosis and staging of ABCD. The staging criteria for ABCD are located in Table 3.

Primary prevention of ABCD involves promoting lifestyle factors that prevent weight gain, such as following a healthy meal plan, engaging in regular physical activity, and behavior modification.[73] Secondary prevention of patients who are diagnosed with ABCD aims to promote weight loss, prevent further weight gain, and prevent the development of weight-related comorbid conditions. Patients with obesity are at a higher risk for the development of many chronic conditions such as type 2 diabetes, hypertension and other cardiac diseases, stroke, sleep apnea, and kidney disease.[72] Lifestyle modifications are also the first-line

TABLE 4. Obesity Medications Compared[74-81]

Generic Name	Brand Name(s)	Starting Dose	Maximum Dose	Common Adverse Effects	Contraindications
Orlistat	Xenical®; Alli®	120mg three times daily; 60mg three times daily	120mg three times daily	increased defecation, fecal urgency, flatus, oily spotting, steatorrhea	chronic malabsorption syndrome, cholestasis
Lorcaserin	Belviq®, Belvix XR®	10mg twice daily; 20mg XR once daily	10mg twice daily; 20mg XR once daily	constipation, headache, hypoglycemia, nausea, dizziness, fatigue	pregnancy
Phentermine	Adipex-P®; Lomaira™	37.5mg once daily, 15mg once daily; 8mg three times daily	37.5mg once daily, 30mg once daily; 8mg three times daily	insomnia, constipation, diarrhea, headache, dry mouth	cardiovascular disease, monoamine oxidase inhibitor use, hyperthyroidism, glaucoma, history of drug abuse, pregnancy
Phentermine/ Topiramate ER	Qsymia®	3.75mg/23mg once daily	15mg/92mg once daily	constipation, dizziness, abnormal taste, insomnia, paranesthesia, dry mouth	cardiovascular disease, monoamine oxidase inhibitor use, pregnancy, glaucoma, hyperthyroidism
Naltrexone/ Bupropion	Contrave®	8mg/90mg once daily	8mg/90mg - 2 tablets twice daily	headache, dizziness, insomnia, nausea, vomiting, diarrhea, constipation, dry mouth	uncontrolled hypertension, seizure disorder, chronic opioid use, monoamine oxidase inhibitor use. Black box warning: increased suicidal thoughts or behaviors.
Liraglutide	Saxenda®	0.6mg once daily	3mg once daily	gastrointestinal upset, tachycardia, headache, dizziness, fatigue, local injection site reactions, hypoglycemia, new or worsening depression	medullary thyroid carcinoma, multiple endocrine neoplasia syndrome, pregnancy

treatment for secondary prevention, but may be supplemented with prescription medications if progress is not seen after using lifestyle modifications alone for 6 months.[73] Patients that meet predefined criteria may also be candidates for bariatric surgery; however, this topic is not a focus of this article.

Available Medications for Obesity Management

A variety of medications with varying mechanisms of action have received FDA approval for chronic weight management, many of which are newer agents that have only been introduced to the market within the last decade. As stated above, it is important to keep in mind that weight-loss medication is a second-line therapy, and lifestyle modifications should be continued in conjunction with starting any of these pharmaceutical products.

Orlistat (Xenical®) is a serotonin 2C receptor agonist indicated for chronic weight management in adults and adolescents age 12 years and older with a baseline BMI >30 kg/m2, or with a baseline BMI >27 kg/m2 with at least one weight-related comorbid condition (e.g., hypertension, type 2 diabetes mellitus, and/or dyslipidemia).[74] This medication works to inhibit the activity of lipases in the stomach and small intestine and therefore prevents the absorption of dietary fats. Patients should take one 120 mg capsule orally three times daily during or up to one hour after a fat-containing meal in conjunction with a dietary management plan. An over-the-counter orlistat product, called Alli, is available as a 60 mg capsule.[75] The OTC packaging instructs patients to take one 60 mg capsule orally with a fat-containing meal, not to exceed more than three capsules daily (180 mg). Patients taking orlistat concomitantly with cyclosporine or levothyroxine should separate these medications by three and four hours from doses of orlistat, respectively. The most common adverse effects seen during use of this medication are increased defecation and fecal urgency, flatus, oily spotting and steatorrhea.

Lorcaserin (Belviq®) is another serotonin 2C receptor agonist approved for use in weight management in adults with a baseline BMI >30 kg/m2, or with a baseline BMI >27 kg/m2 with at least one weight-related comorbid condition.[76] The recommended dose of the immediate-release formulation is 10 mg orally twice daily. Lorcaserin is also available as an extended-release formulation (Belviq XR®), which is available as a 20 mg oral tablet that is taken once daily. Either formulation may be taken with or without food, and the extended-release tablets should not be crushed or chewed. Lorcaserin is classified as a class IV controlled substance in the US based on its potential for abuse; therefore, its use should be avoided in patients with a history of substance abuse. Patients who have not seen greater than or equal to 5 percent weight loss compared to baseline after 12 weeks of therapy should discontinue use (either formulation). This medication should be used with caution in patients with renal or hepatic impairments, but no specific dose adjustments are recommended by the manufacturer. Lorcaserin and lorcaserin extended-release should not be used during pregnancy (category X). The most common side effects of this medication are constipation, headache, hypoglycemia (in diabetic patients), nausea, dizziness, and fatigue. Patients should also be cautious and monitor for signs and symptoms of serotonin syndrome if using lorcaserin/

lorcaserin extended-release concomitantly with other serotonergic agents (bupropion, monoamine oxidase inhibitors, serotonin reuptake inhibitors, serotonin and norepinephrine reuptake inhibitors, triptans, etc.).

Phentermine (Adipex-P®) is a noradrenergic agent approved for short-term treatment of obesity in adults and adolescents age 16 years and older in combination with lifestyle modifications.[77] Phentermine is available as generic 37.5 mg tablets (37.5 mg taken orally once daily in the morning) or 15 mg capsules (15-30 mg taken orally once daily in the morning). An 8 mg oral tablet is also available (Lomaira™) and should be taken orally three times daily.[78] Phentermine works to increase endogenous norepinephrine and dopamine, which promotes weight loss through an increased resting metabolic rate and suppressed appetite. Dose adjustments should be provided for patients with renal impairment, and should not be used in pregnancy. Phentermine is classified as a class IV controlled substance in the US based on its potential for abuse; therefore, its use should be avoided in patients with a history of substance abuse. The most common adverse effects seen with use of this medication are insomnia, constipation, diarrhea, headache and dry mouth.

Phentermine is also available as a combination product with a second noradrenergic agent, topiramate extended-release (ER; Qsymia®), for chronic weight management in adults with a baseline BMI >30 kg/m2, or with a baseline BMI >27 kg/m2 with at least one weight-related comorbid condition.[79] Patients are initiated on the medication by taking one phentermine 3.75 mg/topiramate ER 23 mg capsule orally once daily for 14 days, and are then increased to a maintenance dose of one phentermine 7.7 mg/topiramate ER 46 mg capsule once daily. After 12 weeks, if patients have not lost at least 3 percent of baseline weight, use should be discontinued or increased to one phentermine 11.25 mg/topiramate ER 69 mg capsule once daily for 14 days, and then increase further to one phentermine 15 mg/topiramate ER 92 mg capsule once daily for 12 weeks. If at least 5 percent of baseline body weight has not been lost since dose escalation, therapy should be discontinued by de-escalating the dose to one capsule every other day for one week. Dose adjustments should be performed in the setting of renal and/or hepatic impairments. The most common adverse effect seen with this combination therapy are constipation, dizziness, abnormal taste, insomnia, paresthesia and dry mouth. Patients with a history of cardiovascular disease, including coronary artery disease, stroke, arrhythmias, congestive heart failure or uncontrolled hypertension should not be prescribed any product containing phentermine.[79]

A combination product containing naltrexone (an opioid antagonist) and bupropion (a norepinephrine and dopamine reuptake inhibitor) is indicated for chronic weight management in adults with a baseline BMI >30 kg/m2, or with a baseline BMI >27 kg/m2 with at least one weight-related comorbid condition.[80]

Although the exact mechanism of this product is not understood, it is likely that it exerts effects on multiple areas of the brain, including the reward system, to regulate appetite and aid in weight loss. Available as brand name Contrave®, this medication is initiated at one naltrexone 8 mg/ bupropion 90 mg tablet orally in the morning for one week. Then, doses are increased to one tablet twice daily for one week; then, two tablets in the morning and one tablet in the evening for one week. A maintenance dose of two tablets in the morning and two tablets in the evening is taken daily thereafter. Patients who do not see a weight loss of at least 5 percent from baseline after using the maintenance dose for 12 weeks should discontinue use. Dose adjustments should be performed for patients using this medication in the setting of renal or hepatic impairment. Patients should be advised that this product carries a black box warning for the potential to cause increased suicidal thoughts or behaviors. The most common adverse effects of this medication are headache, dizziness, insomnia, nausea, vomiting, diarrhea, constipation and dry mouth.

Liraglutide (Saxenda®) is a human glucagon-like peptide-1 (GLP-1) receptor agonist that has received FDA approval for the management of obesity in adult patients with a baseline BMI >30 kg/ m2, or with a baseline BMI >27 kg/m2 with at least one weight-related comorbid condition.[81] Liraglutide is also approved for use in the management of type 2 diabetes (Victoza), but the products are not interchangeable between indications. In terms of weight management, endogenous GLP-1 works in the body to slow gastric emptying, which decreases caloric intake by promoting feelings of satiety. Liraglutide is used as a once-daily subcutaneous injection, initiated at a starting dose of 0.6 mg daily. The daily dose should be increased by 0.6 mg increments at weekly intervals until a maintenance dose of 3 mg daily is achieved. Daily injections should be administered into the abdomen, thigh or upper arm without regards to meals. Patients that do not see greater than or equal to 4 percent weight loss compared to baseline after 16 weeks should discontinue use. Since liraglutide delays gastric emptying, the potential for impacts on absorption of oral medications should be monitored. Common adverse effects include gastrointestinal upset (such as nausea, vomiting, diarrhea or constipation, abdominal pain, decreased appetite, and/ or dyspepsia), tachycardia, headache, dizziness, fatigue, local injection site reactions (such as redness, itching or rash), hypoglycemia (especially when used in combination with sulfonylureas in patients with diabetes), and new or worsening depression or suicidal behaviors. This medication carries a Black Box Warning for the risk of development of thyroid t-cell tumors, and should not be used in patients with a personal or family history of medullary thyroid carcinoma or multiple endocrine neoplasia syndrome type 2. Liraglutide use is also contraindicated in pregnancy and should be used with caution in patients with renal or hepatic impairments.

The Pharmacist's Role in Obesity Management

Pharmacists are often considered one of the most accessible healthcare providers due to their presence in the retail setting and are adequately trained to assist patients in achieving their weight loss goals. One of the ways that pharmacists can help patients looking to lose weight is to assist them in the development of healthy eating and exercise plans. First, patients should be engaged in motivational interviewing to determine their readiness to make a change. Once a patient is ready to implement lifestyle modifications, pharmacist can assist patients with development of their plan. The current set of AACE and ACE guidelines recommend that patients attempting weight loss begin a reduced-calorie meal plan, participate in 150 minutes of aerobic physical activity over three to five days per week, and modify their behaviors (such as self-monitoring of food intake and goal setting) to achieve weight loss.[67] Pharmacists are also in a great position to provide ongoing support and encouragement to patients throughout their weight loss journey, as most pharmacists will see patients every one to three months when they visit the pharmacy to obtain medication refills.

Pharmacists are also able to provide patients initiating weight loss medication therapy with appropriate medication counseling to supplement information that their provider may have already shared with them. Medication counseling for these types of medications should always include administration directions (i.e. with or without food, or injection technique for liraglutide), adverse effects and how to manage them, and monitoring parameters (i.e. when they should expect to see results, or certain parameters that should be monitored for safe and effective use). Pharmacists in both the inpatient and outpatient setting may also receive postoperative medication inquiries from patients or other healthcare providers when patients undergo weight loss surgeries. For example, the absorption of certain medications may be affected and a patient's medication regimen may need substituting and/or adjusting of therapies to accommodate these physiological differences. Nutritional supplements are also an area in which pharmacists can provide support to postoperative patients, as they will also be less able to obtain these nutrients from their diet after surgery.

Summary of Obesity Epidemic

Obesity rates have continued to climb to alarming rates in the US, with national rates mirrored in Wisconsin. Recently updated guidelines promote well-defined methods for diagnosing, classifying and managing ABCD. There are many different medication options available to patients that are not able to be managed through lifestyle modifications alone. Pharmacists are the most accessible healthcare providers in the community and are adequately trained to provide patients with education and support as they work towards accomplishing their weight management goals.

Conclusion

Opioid abuse, CDI and obesity are three epidemics that are currently affecting the State of Wisconsin and the US. This article has shown ways in which pharmacists are uniquely positioned to help combat these epidemics through a variety of mechanisms.

Cody Wenthur is an Assistant Professor at the University of Wisconsin-Madison School of Pharmacy in Madison, WI. Laurel Legenza is the Director of Global Health & Assistant Scientist at the University of Wisconsin-Madison School of Pharmacy in Madison, WI. Nicole Weinfurter is a 4th Year Doctor of Pharmacy Candidate and Dean Bowen is a 3rd Year Doctor of Pharmacy Candidate at the University of Wisconsin-Madison School of Pharmacy in Madison, WI.

Disclosure: The author declares no real or potential conflicts or financial interest in any product or service mentioned in the manuscript, including grants, equipment, medications, employment, gifts and honoraria.

References

1. Lesson 1: Introduction to Epidemiology. Centers for Disease Control and Prevention. https://www.cdc.gov/ophss/csels/dsepd/ss1978/lesson1/section11.html. Published May 18, 2012. Accessed November 3, 2018.
2. Overview of Influenza Surveillance in the United States . https://www.cdc.gov/flu/weekly/pdf/overview.pdf. Published October 5, 2012. Accessed November 3, 2018.
3. Minor P. Vaccine-derived poliovirus (VDPV): Impact on poliomyelitis eradication. Vaccine. 2009;27(20):2649-2652. doi:10.1016/j.vaccine.2009.02.071
4. Smallpox. Centers for Disease Control and Prevention. https://www.cdc.gov/smallpox/history/history.html. Published August 30, 2016. Accessed November 3, 2018.
5. Stefano GB, Pilonis N, Ptacek R, Kream RM. Reciprocal Evolution of Opiate Science from Medical and Cultural Perspectives. *Med Sci Monit*. 2017;23:2890-2896.
6. Trang T, Al-Hasani R, Salvemini D, Salter MW, Gutstein H, Cahill CM. Pain and Poppies: The Good, the Bad, and the Ugly of Opioid Analgesics. *J Neurosci.* 2015;35(41):13879-13888. doi:10.1523/JNEUROSCI.2711-15.2015
7. del Portal DA, Healy ME, Satz WA, McNamara RM. Impact of an Opioid Prescribing Guideline in the Acute Care Setting. J Emerg Med. 2016;50(1):21-27. doi:10.1016/j.jemermed.2015.06.014
8. Paulozzi L, Jones C, Mack K, Rudd R. Vital Signs: Overdoses of Prescription Opioid Pain Relievers --- United States, 1999--2008. *CDC Morb Mortal Wkly Rep*. 2011;60(43):1487-1492.
9. U.S. Opioid Prescribing Rate Maps. https://www.cdc.gov/drugoverdose/maps/rxrate-maps.html. Published 2018.
10. Jalal H, Buchanich JM, Roberts MS, Balmert LC, Zhang K, Burke DS. Changing dynamics of the drug overdose epidemic in the United States from 1979 through 2016. *Science.* 2018;361(6408). doi:10.1126/science.aau1184
11. Cicero TJ, Ellis MS, Surratt HL. Effect of abuse-deterrent formulation of OxyContin. *N Engl J Med*. 2012;367(2):187-189. doi:10.1056/NEJMc1204141
12. Hargan E. Determination That a Public Health Emergency Exists. Washington, DC; 2017. https://www.hhs.gov/sites/default/files/opioid PHE Declaration-no-sig.pdf.
13. Hedegaard H, Warner M, Minino AM. Drug Overdose Deaths in the United States, 1999-2016. *NCHS Data Brief.* 2017;(294):1-8.
14. Wisconsin Dept of Health Services Division of Public Health Office of Health Informatics. Wisconsin Interactive Statistics on Health (WISH) data query system. Opioid-Related Hospital Encounters Module. https://www.dhs.wisconsin.gov/wish/index.htm. Published 2016.
15. Wisconsin Department of Health Services. Annual Wisconsin Death Report.; 2015: 5, 25.
16. The Comprehensive Addiction and Recovery Act (CARA). United States of America; 2016. https://www.congress.gov/bill/114th-congress/senate-bill/524/text.
17. Jackson L. Legislation to Combat the Opioid Crisis in Wisconsin. Madison, WI; 2018. https://docs.legis.wisconsin.gov/misc/lrb/lrb_reports/lrb_reports_2_6.pdf.
18. 2013 Wisconsin Act 199. A.B. 445. 2014 Asm; 2014.
19. Wisconsin Act 25. A.B. 4. 2017 Asm Special Session; 2017.
20. Wisconsin Act 200. A.B. 446. 2014 Asm; 2013.
21. Wisconsin Act 115. A.B. 427. 2015 Asm; 2015.
22. Wisconsin Act 33. A.B. 3. 2017 Asm Special Session; 2017.
23. Wisconsin Act 194. A.B. 447. 2017 Asm; 2013.
24. Wisconsin Act 195. A.B. 701. 2014 Asm; 2013.
25. Pharmacists: On The Front Lines. Atlanta, GA; 2018. https://www.cdc.gov/drugoverdose/pdf/Pharmacists_Brochure-a.pdf.
26. Strand MA, Eukel H, Burck S. Moving opioid misuse prevention upstream: A pilot study of community pharmacists screening for opioid misuse risk. *Res Social Adm Pharm*. July 2018. doi:10.1016/j.sapharm.2018.07.011
27. Jones T, Moore T, Levy JL, et al. A comparison of various risk screening methods in predicting discharge from opioid treatment. *Clin J Pain.* 2012;28(2):93-100. doi:10.1097/AJP.0b013e318225da9e
28. Moore TM, Jones T, Browder JH, Daffron S, Passik SD. A comparison of common screening methods for predicting aberrant drug-related behavior among patients receiving opioids for chronic pain management. *Pain Med*. 2009;10(8):1426-1433. doi:10.1111/j.1526-4637.2009.00743.x
29. Lawrence R, Mogford D, Colvin L. Systematic review to determine which validated measurement tools can be used to assess risk of problematic analgesic use in patients with chronic pain. *Br J Anaesth.* 2017;119(6):1092-1109. doi:10.1093/bja/aex316
30. Screening Checklist.; 2017. https://www.dhs.wisconsin.gov/publications/p01572.pdf%0A.
31. Bohnert ASB, Guy GPJ, Losby JL. Opioid Prescribing in the United States Before and After the Centers for Disease Control and Prevention's 2016 Opioid Guideline. *Ann Intern Med*. 2018;169(6):367-375. doi:10.7326/M18-1243
32. Dowell D, Haegerich T, Chou R. CDC Guideline for Prescribing Opioids for Chronic Pain — United States, 2016. *MMWR Recomm Rep*. 2016;65(No. RR-1):1-49. doi:10.15585/mmwr.rr6501e1
33. Simons K, Westlake T, Capodice M. Wisconsin Medical Examining Board Opioid Prescribing Guideline. 2018. https://dsps.wi.gov/Documents/BoardCouncils/MED/20180321MEBGuidelinesv8.pdf.
34. Juurlink DN. Critiquing the CDC Opioid Guideline: Some Light From the Heat. *Clin Pharmacol Ther.* 2018;103(6):966-968. doi:10.1002/cpt.1061
35. Clearinghouse Rule CR 13-075. Wisconsin Pharmacy Examining Board. 2014.
36. Wisconsin Act 266. A.B. 364. 2015 Asm; 2015.
37. PDMP 2017 Report.; 2017.
38. Karaca-Mandic P, Meara E, Morden NE. The growing problem of co-treatment with opioids and benzodiazepines. *BMJ.* 2017;356:j1224.
39. Center for Behavioral Health Statistics and Quality. 2016 National Survey on Drug Use and Health. Rockville, MD; 2017.
40. US Food and Drug Administration. Medicines Recommended for Disposal by Flushing Listed by Medicine and Active Ingredient. https://www.fda.gov/downloads/drugs/resourcesforyou/consumers/buyingusingmedicinesafely/ensuringsafeuseofmedicine/safedisposalofmedicines/ucm337803.pdf. Accessed October 23, 2018.
41. American Psychiatric Association. Diagnostic and Statistical Manual of Mental Disorders. 5th ed. Washington, DC: American Psychiatric Association; 2013.
42. US Department of Veterans Affairs. Opioid Taper Decision Tool.; 2016.
43. Kleber HD. Pharmacologic treatments for opioid dependence: detoxification and maintenance options. *Dialogues Clin Neurosci.* 2007;9(4):455-470.
44. Substance Abuse and Mental Health Services Administration. Medication-Assisted Treatment of Opioid Use Disorder.
45. Alexandridis AA, McCort A, Ringwalt CL, et al. A statewide evaluation of seven strategies to reduce opioid overdose in North Carolina. *Inj Prev.* 2018;24(1):48-54. doi:10.1136/injuryprev-2017-042396
46. Behar E, Santos G-M, Wheeler E, Rowe C, Coffin PO. Brief overdose education is sufficient for naloxone distribution to opioid users. *Drug Alcohol Depend*. 2015;148:209-212. doi:10.1016/j.drugalcdep.2014.12.009
47. Wisconsin Dept of Health Services. Opioids: Overdose. https://www.dhs.wisconsin.gov/opioids/overdose-response.htm. Published 2018. Accessed October 23, 2018.
48. Enteen L, Bauer J, McLean R, et al. Overdose prevention and naloxone prescription for opioid users in San Francisco. *J Urban Health.* 2010;87(6):931-941. doi:10.1007/s11524-010-9495-8
49. Coffin PO, Sullivan SD. Cost-effectiveness of distributing naloxone to heroin users for lay overdose reversal. *Ann Intern Med*. 2013;158(1):1-9. doi:10.7326/0003-4819-158-1-201301010-00003
50. Green TC, Case P, Fiske H, et al. Perpetuating stigma or reducing risk? Perspectives from naloxone consumers and pharmacists on pharmacy-based naloxone in 2 states. *J Am Pharm Assoc.* (2003). 2017;57(2S):S19-S27.e4. doi:10.1016/j.japh.2017.01.013

51. Winstanley EL, Clark A, Feinberg J, Wilder CM. Barriers to implementation of opioid overdose prevention programs in Ohio. *Subst Abus.* 2016;37(1):42-46. doi :10.1080/08897077.2015.1132294
52. PrescribetoPrevent. Naloxone Product Comparison. http://prescribetoprevent.org/wp2015/wp-content/uploads/Naloxone-product-chart.17_04_14.pdf Published 2017. Accessed Jan 7, 2019.
53. Magill SS, Edwards JR, Bamberg W, Beldavs ZG, Dumyati G, Kainer MA, et al. Multistate point-prevalence survey of health care-associated infections. *N Engl J Med*. 2014;370(13):1198-208.
54. Vindigni SM, Surawicz CM. *C. difficile* Infection: Changing Epidemiology and Management Paradigms. *Clin Transl Gastroenterol.* 2015;6:e99.
55. Abbett SK, Yokoe DS, Lipsitz SR, Bader AM, Berry WR, Tamplin EM, et al. Proposed checklist of hospital interventions to decrease the incidence of healthcare-associated *Clostridium difficile* infection. *Infect Control Hosp Epidemiol.* 2009;30(11):1062-9.
56. Giancola SE, Williams RJ, Gentry CA. Prevalence of the *Clostridium difficile* BI/NAP1/027 strain across the United States Veterans Health Administration. *Clin Microbiol Infect.* 2017.
57. Depestel DD, Aronoff DM. Epidemiology of *Clostridium difficile* infection. *J Pharm Pract.* 2013;26(5):464-75.
58. Lessa FC, Mu Y, Bamberg WM, Beldavs ZG, Dumyati GK, Dunn JR, et al. Burden of *Clostridium difficile* infection in the United States. *N Engl J Med.* 2015;372(9):825-34.
59. Abt MC, McKenney PT, Pamer EG. *Clostridium difficile* colitis: pathogenesis and host defence. *Nat Rev Microbiol.* 2016;14(10):609-20.
60. McDonald LC, Gerding DN, Johnson S, Bakken JS, Carroll KC, Coffin SE, et al. Clinical Practice Guidelines for *Clostridium difficile* Infection in Adults and Children: 2017 Update by the Infectious Diseases Society of America (IDSA) and Society for Healthcare Epidemiology of America (SHEA). *Clin Infect Dis*. 2018.
61. New reference for this addition: Brown KA, Khanafer N, Daneman N, Fisman DN. Meta-Analysis of Antibiotics and the Risk of Community-Associated *Clostridium difficile* Infection. *Antimicrob Agents Chemother.* 2013;57(5):2326-2332.
62. Stevens V, Dumyati G, Fine LS, Fisher SG, van Wijngaarden E. Cumulative antibiotic exposures over time and the risk of *Clostridium difficile* infection. *Clin Infect Dis.* 2011;53(1):42-8.
63. Legenza L, Barnett S, Rose W, Bianchini M, Safdar N, Coetzee R. Epidemiology and outcomes of *Clostridium difficile* infection among hospitalised patients: Results of a multicentre retrospective study in South Africa. *BMJ Global Health*. 2018;3(4).
64. CDC. (2015). CDC Press Releases. [online] Available at: https://www.cdc.gov/media/releases/2015/p0225-clostridium-difficile.html [Accessed 30 Jan. 2019].
65. Stevens VW, Nelson RE, Schwab-Daugherty EM, Khader K, Jones MM, Brown KA, et al. Comparative Effectiveness of Vancomycin and Metronidazole for the Prevention of Recurrence and Death in Patients With *Clostridium difficile* Infection. *JAMA Intern Med.* 2017;177(4):546-53.
66. Nelson RL, Suda KJ, Evans CT. Antibiotic treatment for *Clostridium difficile*-associated diarrhoea in adults. *Cochrane Database Syst Rev.* 2017;3:Cd004610.
67. Leffler DA, Lamont JT. *Clostridium difficile* infection. *N Engl J Med.* 2015;372(16):1539-48.
68. Valiquette L, Cossette B, Garant MP, Diab H, Pepin J, Impact of a Reduction in the Use of High-Risk Antibiotics on the Course of an Epidemic of *Clostridium difficile*-Associated Disease Caused by the Hypervirulent NAP1/027 Strain. *CID* 2007:45 (Suppl 2) S112-S12.
69. Carling P, Fung T, Killion A, Terrin N, and Barza M. Favorable impact of a multidisciplinary antiobiotic management program conducted during 7 years. *Infection Control and Hospital Epidemiology.* 2003;24(9): 699-706.
70. Legenza LM, Barnett SG, Rose WE. Vaccines in development for the primary prevention of *Clostridium difficile* infection. *J Am Pharm Assoc* (2003). 2017;57(4):547-9.
71. Goldenberg JZ, Yap C, Lytvyn L, Lo CK, Beardsley J, Mertz D, Johnston BC. Probiotics for the prevention of *Clostridium difficile*-associated diarrhea in adults and children. *Cochrane Database Syst Rev.* 2017 19;12:CD006095. doi: 10.1002/14651858.CD006095.pub4.
72. Robert Wood Johnson Foundation. The State of Obesity. Available at: https://stateofobesity.org. Accessed November 30, 2018.
73. Garvey WT, Mechanick JI, Brett EM, et al. American association of clinical endocrinologists and American college of endocrinology comprehensive clinical practice guidelines for medical care of patients with obesity. *Endocr Pract.* 2016;22(Suppl 3):1-203. DOI:10.4158/EP161365.GL.
74. Xenical® (orlistat) [package insert]. Montgomery, AL: H2-Pharma, LLC; August 2017.
75. Alli® (orlistat) [package insert]. Warren, NJ: GlaxoSmithKline; April 2018.
76. Belviq/Belviq XR (lorcaserin hydrochloride) [package insert]. Woodcliff Lake, NJ; May 2017.
77. Adipex-P (phentermine) [package insert].
78. Lomaira (phentermine) [package insert].
79. Qsymia (phentermine/topiramate ER) [package insert].
80. Contrave (naltrexone/bupropion) [package insert].
81. Saxenda® (liraglutide) [package insert]. Plainsboro, NJ: Novo Nordisk; November 2018.

Assessment Questions

1. The CDC defines an epidemic as, "a gradual and often minor increase in the number of cases of a disease above what is normally expected in that population area."
   a. True
   b. False

2. What was the approximate mortality rate per 100,000 individuals due to opioid overdose in Wisconsin in 2016?
   a. 26.2
   b. 20
   c. 20,600
   d. 827

3. A key principle of current guidelines for opioid prescribing is 'start with a low dose and increase dosage rapidly'.
   a. True
   b. False

4. Patient counseling on naloxone kits for opioid overdose should include which of the following topics?
   a. Overdose risk factors
   b. Overdose response measures
   c. Administration instructions
   d. All of the above

5. What class of antibiotics is associated with a high CDI risk?
   a. Fluoroquinolones
   b. Macrolides
   c. Sulfonamides-trimethoprim
   d. Penicillins

6. According to the CDC, CDI is associated with 453,000 infections per year and about 15,000 of these infections result in death directly attributable to CDI.
   a. True
   b. False

7. Which of the following is NOT a way pharmacists can help combat the CDI epidemic?
   a. Recommend lower risk antibiotics
   b. Educate patients receiving an antibiotic on the risks associated with that antibiotic, including association with CDI
   c. Become involved with antimicrobial stewardship
   d. Always recommend probiotics

8. What was the rate of obesity for adults in the state of Wisconsin in 2017?
   a. 14.7%
   b. 18.5%
   c. 32.0%
   d. 39.6%

9. What is the most common monitoring parameter to measure efficacy of prescription weight loss medications?
   a. Body-mass index (BMI)
   b. Percentage of weight loss from baseline after a specified time period
   c. Development of weight-related complications
   d. Daily calorie intake

10. Which of the following are common side effects of medications available for chronic weight management?
    a. Gastrointestinal upset (nausea/vomiting, constipation and/or diarrhea)

b. Dizziness or fatigue
c. Headache
d. All of the above

11. Which of the following are ways that a pharmacist can help patients reach their personal weight management goals?
    a. Provide adequate medication counseling for medications used in chronic weight management
    b. Engage patients using motivational interviewing techniques to assess readiness to make lifestyle modifications
    c. Provide education and aid patients in monitoring for other weight-related health complications (e.g. diabetes, hypertension, etc.)
    d. All of the above

12. Did the activity meet the stated learning objectives? (if you answer no, please email sarahs@pswi.org to explain)
    a. Yes
    b. No

13. On a scale of 1 – 10 (1-no impact; 10-strong impact), please rate how this program will impact the medication therapy management outcomes or safety of your patients.

14. On a scale of 1 – 10 (1-did not enhance; 10-greatly enhanced), please rate how this program enhanced your competence in the clinical areas covered.

15. On a scale of 1 – 10 (1-did not help; 10-great help), please rate how this program helped to build your management and leadership skills.

16. How useful was the educational material?
    a. Very useful
    b. Somewhat useful
    c. Not useful

17. How effective were the learning methods used for this activity?
    a. Very effective
    b. Somewhat effective
    c. Not effective

18. Learning assessment questions were appropriate.
    a. Yes
    b. No

19. Were the authors free from bias?
    a. Yes
    b. No

20. If you answered "no" to question 19, please comment (email info@pswi.org).

21. Please indicate the amount of time it took you to read the article and complete the assessment questions.

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March/April 2019
The Pharmacists Role in Combating Statewide Epidemics

ACPE Universal Activity Number: 0175-0000-19-095-H01-P

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3) a b
4) a b c d
5) a b c d
6) a b
7) a b c d
8) a b c d
9) a b c d
10) a b c d
11) a b c d
12) a b
13)_____
14)_____
15)_____
16) a b c
17) a b c
18) a b
19) a b
20)_____
21)_____

Name_____Designation (RPh, PharmD, etc.)_____

CPE Monitor #_____ DOB (MMDDYY)_____

Preferred Mailing Address_____

City_____State_____ Zip _____

Is this your home ☐ or work ☐ address?