Pharmacy Today
An official publication of the **American Pharmacists Association**
NOVEMBER 2023

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Study finds pharmacist intervention improved diabetes control for Hispanic patients

A new study published September 28, 2023, in *JAMA Network Open* found that an intervention involving patient assessments by trained pharmacists in conjunction with primary care physicians led to better glycemic control among Hispanic patients with T2D.

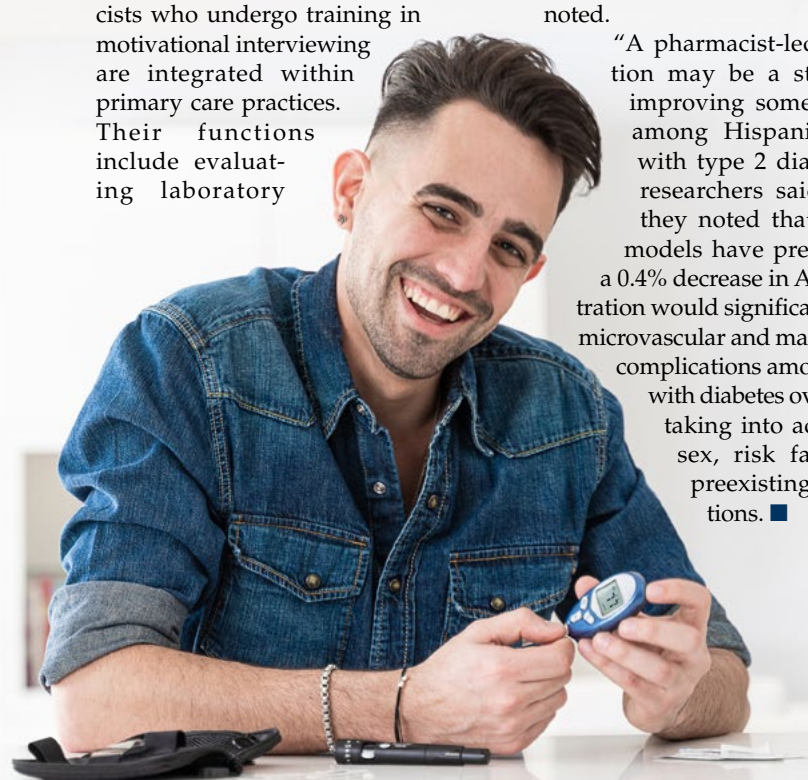
The patients' blood glucose levels fell by a mean of 0.46% within a year of participating in at least one visit with a UCMyRx-trained pharmacist from a UCLA program, according to the research.

The UCMyRx program was launched in 2012 in the Los Angeles area across 38 primary care clinics. Under the program, clinical pharmacists who undergo training in motivational interviewing are integrated within primary care practices. Their functions include evaluating laboratory results and vital signs, performing medication reconciliation, and gauging medication adherence using a standardized measure.

In the study, the researchers noted a sensitivity analysis revealing that just one pharmacist intervention visit was linked with notably lower blood glucose levels. However, visits in excess of the median number of visits did not appear to have a significant effect.

The study did not identify a major difference in systolic BP change, but this co-primary endpoint measure was at a comparatively low level among study participants from the onset, with a mean of 136 mm Hg, the researchers noted.

"A pharmacist-led intervention may be a strategy for improving some outcomes among Hispanic patients with type 2 diabetes," the researchers said. Further, they noted that economic models have predicted that a 0.4% decrease in A1C concentration would significantly reduce microvascular and macrovascular complications among patients with diabetes over 25 years, taking into account age, sex, risk factors, and preexisting complications. ■



Adult obesity prevalence remains high, prevention and treatment needed

According to the most recent population data from CDC, 22 states have an adult obesity prevalence at or above 35%, up from 19 states in 2021. In contrast, no state had an adult obesity prevalence at or above 35% a decade ago.

The 2022 Adult Obesity Prevalence Maps point to the need for population-based strategies to help individuals have access to safe areas for physical activity, healthy foods, health care services such as surgery and medication, and obesity treatment and prevention programs without stigma.

The data came from state-based, self-reported height and weight information in the Behavioral Risk Factor Surveillance System. Adults with obesity are more vulnerable to such health conditions as heart disease, stroke, T2D, certain cancers, worse COVID-19 outcomes, and mental health issues.

"Our updated maps send a clear message that additional support for obesity prevention and treatment is an urgent priority," said Karen Hacker, MD, MPH, director of CDC's National Center for Chronic Disease Prevention and Health Promotion in a CDC press release. "However, we know the key strategies that work include addressing the underlying social determinants of health such as access to health care, healthy and affordable food, and safe places for physical activity." ■

Postnatal SSRI treatment could benefit both mother and child

Findings from a study published August 29, 2023, in *JAMA Network Open* suggest that postnatal SSRI treatment may bring benefits in the long term to not only mothers, but also their offspring.

A total of 61,000 mother and child pairs participated in the cohort study. Participating women were recruited in weeks 17 to 18 of pregnancy from 1999 to 2008 and were prospectively followed after childbirth. Data analysis was performed between December 2021 and October 2022.

Researchers found that postnatal SSRI treatment reduced the risk of postnatal depression that related to maternal mental health, relationship satisfaction, and externalizing behaviors within the child's early years.

According to the study, 10% to 15% of women are affected with postnatal depression, which is different from postpartum depression because it's characterized by reoccurring depressive episodes that lead to a higher display of depression in the years after childbirth. Postpartum depression occurs immediately following childbirth. Postnatal depressive episodes not only affect a mother, but also the child, and can lead to long-term partner relationship issues, as well.

SSRIs are the preferred treatment for postnatal depression compared to other antidepressants, said study authors.

They also noted that their research could provide valuable information for clinicians and women with postnatal depression to make informed treatment decisions. ■

USPSTF's new PrEP recommendation aims for more choices, greater impact

According to a new recommendation statement published in *JAMA*, the U.S. Preventive Services Task Force (USPSTF) recommends that those at high risk of contracting HIV receive newer antiretroviral drug options for PrEP, including a long-acting option.

Truvada was the first medication approved for HIV prevention in 2012. In 2019, Descovy was added as a PrEP option, and the first injectable PrEP (Apretude) became available in 2022.

USPSTF recommends that sexually active adults and adolescents be considered for PrEP if they have had anal or vaginal sex in the previous 6 months and/or a sexual partner living with HIV, an STI in the past 6 months, or a history of inconsistent or no condom use as well as if they inject drugs or have a partner who injects drugs.

No PrEP medications have FDA approval for the indication of reducing the risk of acquiring HIV via injectable drug use, but CDC guidelines note that people who inject drugs are likely to benefit from PrEP with any FDA-approved PrEP medication.

Practice laws in 17 states allow pharmacists to provide patients with PrEP or PEP and, in some cases, reimbursement for these services.

The USPSTF's new recommendation is consistent with the 2019 recommendation that clinicians offer PrEP with effective antiretroviral therapy to individuals who are at high risk of HIV infection. ■

CDC: Overdose deaths from counterfeit drugs on the rise

A new report from CDC finds that in recent years, the number of people who overdosed and died from counterfeit prescription drugs has more than doubled. From mid-2019 to the end of 2021, overdose deaths involving counterfeit drugs increased from 2% to 4.7%.

Many individuals who didn't obtain drugs legally from pharmacies assumed they were taking oxycodone (OxyContin) or alprazolam (Xanax), according to CDC. But counterfeit drugs contain a variety of unknown substances, and in many cases are tainted with harmful levels of fentanyl.

In the majority of all overdose deaths (93%) involving counterfeit drugs, illicit fentanyl was detected. Overall, nearly 107,000 people died from drug overdoses in 2021, and early estimates for 2022 put that figure at 105,000 deaths, according to CDC.

The researchers found that counterfeit oxycodone was most prevalent in western states, while counterfeit alprazolam was found most frequently in the South. In the western states, overdose deaths from counterfeit drugs more than tripled, from 4.7% in 2019 to 14.7% as of late 2021, likely because of an increase in the illegal and counterfeit drug supply. ■

Psilocybin may be safe and effective as treatment for MDD

Results from a new study published August 31, 2023, in *JAMA* found that among patients with major depressive disorder (MDD), a single 25-mg dose of psilocybin led to a steady reduction in depressive symptoms and helped improve psychosocial functioning. The goal of the research was to examine the safety and efficacy of using psilocybin in patients with MDD.

The randomized, double-blind, placebo-controlled, Phase II trial was conducted at 11 research sites across the United States between December 2019 and June 2022 and was comprised of 104 adults diagnosed with MDD.

Participants received either a single 25-mg dose of psilocybin or a placebo of 100-mg dose of niacin, both administered along with psychological support. Primary and secondary outcomes were evaluated at different time points up to 43 days after dosing.

Treatment with psilocybin was associated with a notable reduction in Montgomery-Asberg Depression Rating Scale scores compared with niacin from baseline to day 8 and baseline to day 43.

In addition, psilocybin treatment reduced Sheehan Disability scores significantly compared with niacin from baseline to day 43. Additional measures showed improvements in such areas as global disease severity, self-reported depressive and anxiety symptoms, and improved quality of life. Psilocybin treatment did not lead to emotional blunting, which is an adverse effect of standard antidepressant medications.

The researchers concluded that psilocybin may be a possible intervention for MDD, as it helped reduce a variety of depressive symptoms and also improved overall functioning, anxiety symptoms, and quality of life for study participants. ■

CDC develops antibiotic policy for reducing STIs

In proposed guidance published October 2, 2023, in the Federal Register, CDC advised clinicians to offer gay and bisexual men and transgender women more access to doxycycline, a widely used tetracycline antibiotic.

As PEP, individuals could use the drug after engaging in unprotected sex to reduce their risk of contracting gonorrhea, chlamydia, or syphilis. Research studies indicate that a treatment regimen known as "doxy PEP," consisting of a single, 200-mg dose of doxycycline taken no more than 72 hours after unprotected sex, can curb the transmission of chlamydia and syphilis by nearly 80%, and gonorrhea by roughly 50%.

"Doxy PEP is moving STI prevention efforts into the 21st century," said Jonathan Mermin, director of CDC's National Center for HIV, Viral Hepatitis, STD, and TB Prevention, in a statement. "We need game-changing innovations to turn the STI epidemic around, and this is a major step in the right direction."

CDC has been developing the guidance for more than a year and wants feedback on the proposed guidance within 45 days.

In the DoxyPEP trial, researchers divided men who have sex with men and transgender women into two groups, with one group receiving doxycycline following unprotected sexual activity and a second group of those who did not. Among people who did not receive the antibiotic, their STI rate was 30% per quarter. Participants in the doxycycline arm received a median of four doses of the drug over the course of a month, while some received as many as 10 doses. ■

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CPE

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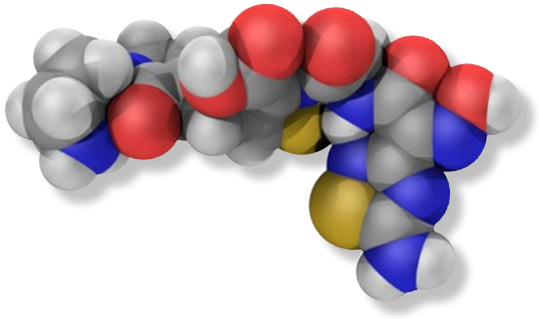

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Pharmacists are key to caring for older adults with dementia

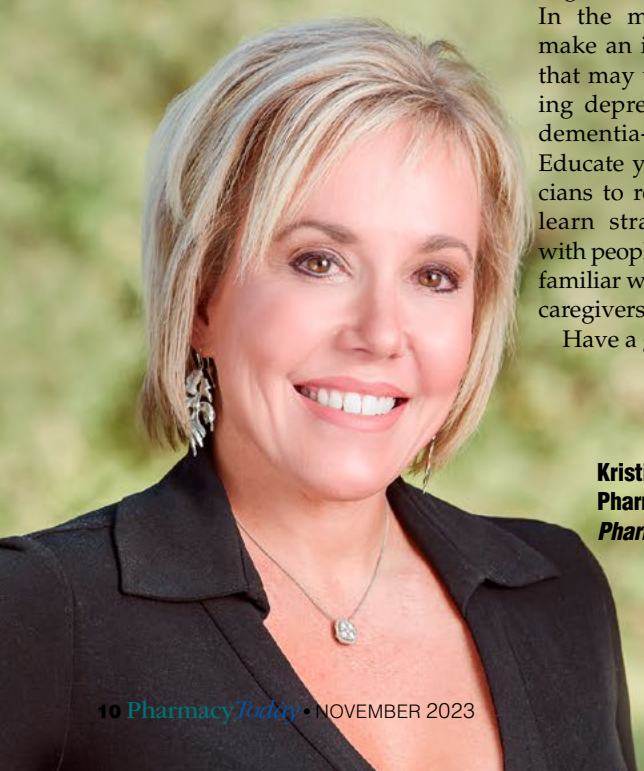
Alzheimer disease is the most common form of dementia, with as many as 6.7 million Americans living with the disease in 2023. Nearly 15.7 million additional U.S. adults provide care for a family member with dementia. Pharmacists play an essential role in assisting these patients and their caregivers. This is especially true for community pharmacists, considering that approximately 70% of adults with dementia live outside of a residential facility.

This month's *Pharmacy Today* cover story provides essential information for pharmacists caring for patients with Alzheimer disease or dementia. While some steps seem intuitive to pharmacists — for example, staying on the lookout for medications that worsen dementia such as anticholinergics or benzodiazepines — others require pharmacists to take a more holistic approach. According to Kirby Lee, PharmD and Professor Emeritus in clinical pharmacy at UCSF School of Pharmacy, who developed a multidisciplinary Care Ecosystem model for dementia care, pharmacists do not focus on memory drugs alone in the care of dementia patients. "We focus on the whole patient and whatever medical conditions they are dealing with." This type of approach allows for optimal care of the patient and considers their caregivers' needs as well. UCSF's Care Ecosystem model was shown in a recent study to decrease the use of high-risk or inappropriate medications in patients with dementia. Check out the cover story to learn more.

You'll find more critical news in this issue of *Today*, including the latest on FDA's actions on phenylephrine, potential changes on the horizon for nonprescription CBD products, and an update on FDA's recent approval of the first oral drug for postpartum depression. You'll also find new information on medication changes in updated coronary disease guidelines and stay current with your CPE credit with this month's article on cannabis for pharmacists.

While nearly 150 drugs are currently in clinical trials for Alzheimer disease, with recent novel approvals of disease-modifying agents that target aggregated forms of amyloid, we have a long way to go in developing effective treatments. In the meantime, pharmacists can make an impact by identifying drugs that may worsen dementia, encouraging deprescribing, and developing a dementia-friendly care environment. Educate your pharmacists and technicians to recognize signs of dementia, learn strategies for communicating with people with dementia, and become familiar with resources for patients and caregivers.

Have a great *Today*!



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Chaos or a symphony in the making?

Recently, I attended a performance of the musical *Moulin Rouge* at The John F. Kennedy Center for the Performing Arts in Washington, DC. As we got comfortable in our seats, the audience buzzing about the theater, I could hear the instrumentalists from the orchestra warming up their instruments.

The cacophony made absolutely no sense—there wasn't a melody, they weren't running scales together—just playing and making noise. And the crowd in the theatre was attempting to carry on hundreds of conversations over the tuning of the instruments. As the crowd built, so did the chaos of the noise. This went on for about 15 minutes or so before everything went silent, and then moments later the curtain was raised.

Those very same musicians who didn't seem to be in unison were suddenly playing beautiful music together, which wouldn't be denied its crescendo! It was a fantastic, relaxing evening.

For someone watching our profession from the sidelines, it might seem that there is nothing but chaos happening in pharmacy and health care. But I know what is happening. Pharmacy is warming its instruments, and even inventing new ones that haven't been played before. External pressures and forces largely out of pharmacists' control such as staffing models, payment systems, and laws and regulations are all in need of a serious tune up, and are growing louder in an attempt to drown out the voice of the pharmacist.

But pharmacists will not be denied—our calling is to care for patients across the entire health care system. We won't stop practicing and tuning and adjusting to do our best by our patients—even if the forces and sounds around us are sometimes deafening.

At the annual meetings of the National Community Pharmacists Association and Academy of Managed Care Pharmacy, I've been inspired by the stories of pharmacists with incredible hope, and I've also heard of dramatic challenges that are threatening to destroy our profession.

Sometimes corporations make business decisions and engage in business practices that none of us like—and yet despite that, the pharmacist stays true to the patient. Pharmacists get up every day, no matter the practice setting, with the goal of helping patients get the best use of medicines. And this is fundamentally the sound of hope ringing out. Our patients deserve our focused attention no matter how loud the noise gets around us.

Am I concerned about the current practice environment and the negative forces facing our profession? Absolutely, and we'll fight those forces every day. Why? Because I know that shortly silence will come, the curtain will rise, and the most beautiful symphony–that of pharmacists practicing at the top of their training with full scope, properly supported with well-trained staff, and compensated based upon the quality of care provided—is about to be heard.

Keep fighting. Keep the faith. We are right beside you. For every pharmacist. For all of pharmacy. ■

Michael D. Hogue
PharmD, FAPhA, FNAP, FFIP
Executive vice president and CEO of APhA

NEW DRUGS

MOTIXAFORTIDE
(Aphexda—BioLineRx)

Drug class: Aphexda is a hematopoietic stem cell mobilizer.

Indication: Aphexda is indicated in combination with filgrastim to mobilize hematopoietic stem cells to the peripheral blood for collection and subsequent autologous transplantation in patients with multiple myeloma.

Recommended dosage and administration: Initiate Aphexda treatment after filgrastim has been administered daily for 4 days. The recommended dosage is 1.25 mg/kg actual body weight by S.C. injection 10 to 14 hours prior to initiation of apheresis. A second dose of Aphexda can be administered 10 to 14 hours prior to a third apheresis.

Common adverse effects: The most common adverse reactions are injection site reactions, injection site pain, injection site erythema, injection site pruritus, flushing, and back pain.

Warnings and precautions: Aphexda is contraindicated in patients with a history of hypersensitivity reaction to Aphexda. Premedicate all patients with a combination of an H1-antihistamine, an H2 blocker, and a leukotriene inhibitor prior to each Aphexda dose. Administer Aphexda in a setting where personnel and therapies are available for immediate treatment. Observe patients for signs and symptoms of anaphylaxis and manage promptly.

The addition of analgesic premedication is recommended for injection site reactions. Aphexda may mobilize leukemic cells and should not be used in leukemia patients. Increased circulating leukocytes have been observed. Monitor white blood cell counts during Aphexda use.

Tumor cells may be released from marrow during hematopoietic stem cell mobilization with Aphexda and filgrastim. The effect of reinfusion of tumor cells is unknown. Aphexda may cause fetal harm. Advise patients of reproductive potential of the potential risk to a fetus and to use effective contraception. Advise patients not to breastfeed during treatment.

MOMELOTINIB
(Ojjaara—GlaxoSmithKline)

Drug class: Ojjaara is a kinase inhibitor.

Indication: Ojjaara is indicated for the treatment of intermediate or high-risk myelofibrosis (MF), including primary MF or secondary MF, in adults with anemia.

Recommended dosage and administration: The recommended dosage is 200 mg orally once daily with or without food. In severe hepatic impairment, reduce the starting dose to 150 mg orally once daily.

Common adverse effects: The most common adverse reactions are thrombocytopenia, hemorrhage, bacterial infection, fatigue, dizziness, diarrhea, and nausea.

Warnings and precautions: Do not initiate Ojjaara in patients with an active infection. Monitor for signs and symptoms of infection, including reactivation of hepatitis B, and initiate appropriate treatment promptly. Manage thrombocytopenia and neutropenia by dose reduction or interruption. Obtain liver tests before initiation of and periodically throughout treatment with Ojjaara. Monitor for symptoms of major adverse cardiovascular events and evaluate and treat promptly. Evaluate and treat symptoms of thrombosis promptly. Monitor for development of secondary malignancies, particularly in current or past smokers. Monitor for adverse reactions when used concomitantly with organic anion transporting polypeptide (OATP)1B1/B3 inhibitors. If taken concomitantly with rosuvastatin, reduce rosuvastatin dosage. Follow approved product information recommendations if Ojjaara is taken concomitantly with other breast cancer resistant protein substrates. Ojjaara may cause fetal harm if used during pregnancy and patients should be advised not to breastfeed during treatment.

GEPIRONE
(Exxua—Fabe-Kramer Pharmaceuticals)

Drug class: The mechanism of the antidepressant effect of Exxua is not fully understood but it is thought to be related to its modulation of serotonergic activity in the central nervous system through selective agonist activity at 5HT1A receptors.

Indication: Exxua is indicated for the treatment of major depressive disorder in adults.

Recommended dosage and administration: Correct electrolyte abnormalities and perform an electrocardiogram (ECG) prior to initiating treatment with Exxua. Do not initiate therapy if the QTc is >450 msec. Perform ECGs during dosage titration and periodically during treatment. The recommended starting dose is 18.2 mg administered orally once daily with food at approximately the same time each day. Depending on clinical response and tolerability, the dosage may be increased to 36.3 mg once daily on day 4. Dosage may be further titrated to 54.5 mg once daily after day 7 and to 72.6 mg once daily after an additional week. In geriatric patients, the recommended starting dosage is 18.2 mg once daily and the dosage may be increased to 36.3 mg after 7 days. In patients with moderate hepatic impairment, dosage may be increased to 36.3 mg once daily after 7 days. Adjust Exxua dose by 50% when a moderate CYP3A4 inhibitor is administered.

Common adverse effects: The most common adverse reactions were dizziness, nausea, insomnia, abdominal pain, and dyspepsia.

Boxed warning: There is an increased risk of suicidal thinking and behavior in pediatric and young adult patients taking antidepressants. Closely monitor for worsening and emergence of suicidal thoughts and behaviors. Exxua is not approved for use in pediatric patients.

Other warnings and precautions: Exxua is contraindicated in known hypersensitivity to gepirone or components of Exxua, prolonged QTc interval of >450 msec at baseline, congenital long QTc syndrome, concomitant use of strong CYP3A4 inhibitors, severe hepatic impairment, and use with an MAOI or within 14 days of stopping treatment with Exxua. Do not use Exxua within 14 days of discontinuing an MAOI.

Exxua prolongs the QTc interval. Correct electrolyte abnormalities. Perform ECGs prior to initiation, during dose titration, and periodically during treatment with Exxua. Monitor ECGs more frequently when Exxua is used concomitantly with drugs known to prolong the QTc interval, in patients who develop QTc intervals of ≥450 msec during treatment, or are at significant risk of developing torsade de pointes. Do not escalate dosage if QTc interval is >450 msec. There is an increased risk of serotonin syndrome when co-administered with other serotonergic agents. If serotonin syndrome occurs, discontinue Exxua and initiate supportive measures. Screen patients for bipolar disorder as activation of mania/hypomania can occur. Avoid concomitant use with strong CYP3A4 inducers as this reduces Exxua exposure. Use of Exxua in the third trimester may increase the risk for persistent pulmonary hypertension and symptoms of poor adaptation (e.g., respiratory distress, temperature instability, feeding difficulty, hypotonia, irritability) in the neonate.

NEDOSIRAN
(Rivfloza—Novo Nordisk)

Drug class: Rivfloza is an LDHA-directed small interfering RNA.

Indication: Rivfloza is indicated to lower urinary oxalate levels in children 9 years and older and adults with primary hyperoxaluria type 1 (PH1) and relatively preserved kidney function (eGFR ≥30 mL/min/1.73 m^2).

Recommended dosage and administration: The recommended dosage in adults and adolescents 12 years and older weighing ≥50 kg is 160 mg once monthly. The recommended dosage in adults and adolescents 12 years and older weighing <50 kg is 128 mg once monthly. The recommended dosage in children between the ages of 9 years and 11 years ≥50 kg is 160 mg once monthly. The recommended dosage in children between the ages of 9 years and 11 years weighing <50 kg is 3.3 mg/kg once monthly, not to exceed 128 mg.

Common adverse effects: The most common adverse reaction is injection site reactions.

Warnings and precautions: There are none reported at this time.

NEW INDICATIONS

TEMOZOLOMIDE
(Temodar—Merck Sharp & Dohme)

Drug class: Temodar is an alkylating drug.

Indication: Temodar is indicated for the treatment of adults with newly diagnosed glioblastoma concomitantly with radiotherapy and then as maintenance treatment, as an adjuvant treatment for adults with newly diagnosed anaplastic astrocytoma, and for the treatment of adults with refractory anaplastic syndrome.

Recommended dosage and administration: Temodar should be administered either orally or intravenously. For the treatment of newly diagnosed glioblastoma, the recommended dosage is 75 mg/m^2 for 42 to 49 days concomitant with focal radiotherapy followed by initial maintenance dose of 150 mg/m^2 once daily for days 1 to 5 of each 28-day cycle for 6 cycles. The maintenance dose may be increased to 200 mg/m^2 on cycles 2 to 6 based on toxicity. Provide pneumocystis pneumonia (PCP) prophylaxis during concomitant phase and continue in patients who develop lymphopenia until resolution to Grade 1 or less.

For adjuvant treatment of newly diagnosed anaplastic astrocytoma, Temodar is administered orally beginning 4 weeks after the end of radiotherapy in a single dose on days 1 to 5 of a 28-day cycle for 12 cycles. The recommended dosage for cycle 1 is 150 mg/m^2 per day and for cycles 2 to 12 is 200 mg/m^2 if the patient experienced minimal or no toxicity in cycle 1. For the treatment of refractory anaplastic astrocytoma, the initial dose is 150 mg/m^2 once daily on days 1 to 5 of each 28-day cycle.

Common adverse effects: The most common adverse reactions are alopecia, fatigue, nausea, vomiting, headache, constipation, anorexia, convulsions, decreased lymphocytes, decreased platelets, decreased neutrophils, and decreased leukocytes.

Warnings and precautions: Monitor absolute neutrophil count and platelet count prior to each cycle and during treatment. Geriatric patients and women have a higher risk of developing myelosuppression. Fatal and severe hepatotoxicity have been reported. Perform liver tests at baseline, midway through the first cycle, prior to each subsequent cycle, and approximately 2 to 4 weeks after the last dose of Temodar.

Closely monitor all patients, particularly those receiving steroids, for the development of lymphopenia and PCP. Myelodysplastic syndrome and secondary malignancies, including myeloid leukemia, have been observed. Temodar can cause fetal harm. Advise patients of reproductive potential of the potential risk to a fetus and to use effective contraception. Temodar capsules should not be opened, chewed, or dissolved but should be swallowed whole with a glass of water. Patients should be advised not to breastfeed during treatment. ■

FDA approves cancer testing panel

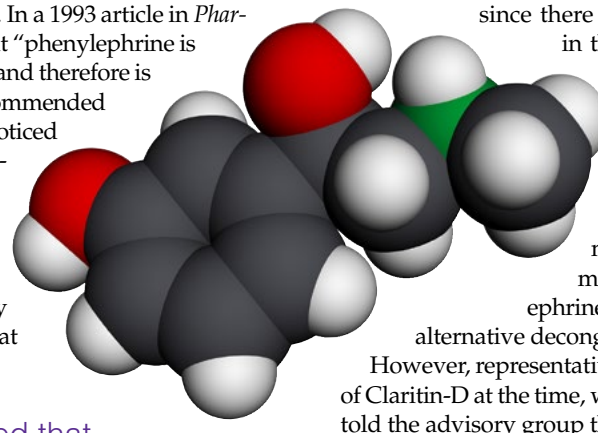
In September 2023, FDA approved the first marketing authorization for the Invitae Common Hereditary Cancers Panel. This diagnostic test has the ability to test for hundreds of genetic variants that are associated with an elevated risk of developing certain cancers. Additionally, the test can be used to detect hereditary variants that are potentially associated with cancer in individuals who have already been diagnosed with cancer. The panel utilizes DNA extracted from a blood sample to identify variants in 47 different genes that are known to be associated with a higher risk of developing cancer. It is important that the results of the Invitae Common Hereditary Cancers Panel are reviewed with a health care professional to prevent patients from misunderstanding the results. Patients should be advised that this test is not intended to identify all known genes that are associated with a predisposition for cancer and that genetics are not the only factor in the development of cancer. ■

Phenylephrine: The story of an ineffective nasal decongestant

Mary Warner

On September 12, 2023, the FDA Nonprescription Drugs Advisory Committee unanimously agreed that oral phenylephrine is ineffective, setting the stage for FDA to require its removal from hundreds of nonprescription products. But why did it take so long for a decongestant that patients claimed didn't work to be brought to the committee for evaluation?

Leslie Hendeles, PharmD, and Randy Hatton, PharmD, faculty members at the University of Florida College of Pharmacy, have been advocating for the removal of oral phenylephrine from the market for many years. In a 1993 article in *Pharmacotherapy*, Hendeles wrote that "phenylephrine is subject to first-pass metabolism and therefore is not bioavailable in currently recommended doses." Ten years later, Hatton noticed an increase in calls to the University of Florida Drug Information and Pharmacy Resource Center hotline asking about the efficacy of phenylephrine. Pharmacists were asking why patients consistently claimed that phenylephrine didn't work.



FDA has not yet directed that oral products containing phenylephrine be removed from store shelves, and over the coming months, or even years, there will likely be much debate about how to move forward.

Those calls led him to Hendeles and the two began a collaboration that eventually included two Citizen Petitions (endorsed by APhA), based upon research to determine if phenylephrine was effective at the dosage available over the counter, and a Freedom of Information Act request for unpublished data, as well as multiple studies that confirmed their skepticism about phenylephrine's effectiveness.

Market forces

Until early 2006, when the Combat Methamphetamine Epidemic Act (CMEA) forced pseudoephedrine behind the pharmacy counter, phenylephrine was in very few products, as pseudoephedrine dominated the market. But pseudoephedrine is a primary ingredient used by illegal methamphetamine synthesis labs, and when the CMEA forced restriction of pseudoephedrine sales, requiring identification and maximum purchase amounts, pharmaceutical manufacturers turned to their only other option to not lose OTC sales: phenylephrine.

Hendeles and Hatton convinced U.S. Representative Henry Waxman of California to support their efforts to remove phenylephrine from OTC medications and Waxman wrote four letters during late 2006 to FDA's acting commissioner asking for "a thorough scientific review of phenylephrine's effectiveness at the monograph dose of 10 mg." FDA replied by restating the findings of its 1976 decision that both pseudoephedrine and phenylephrine are generally recognized as safe and effective (GRASE). Phenylephrine is now in hundreds of nonprescription medications, from Sudafed PE, to Nyquil, to Benadryl Cold, to Tylenol Cough and Cold.

The two professors then filed a Citizen Petition requesting the agency to determine if doses higher than 10 mg were effective and to remove approval for children <12 years since there were no data on safety or efficacy in this age group. Congressman Waxman's persistence led to an FDA advisory hearing in 2007 where both Hatton and Hendeles made presentations. The Consumer Healthcare Products Association, the group representing the manufacturers of nonprescription medication, maintained that phenylephrine worked, likely because they had no alternative decongestants to use in their formulations.

However, representatives for Schering Plough—the maker of Claritin-D at the time, which contained pseudoephedrine—told the advisory group that they had studied phenylephrine and found it ineffective. The advisory committee voted 11 to 1 that "evidence is supportive" that phenylephrine "may be effective," and called for more research on higher doses, as the petition requested.

Proving the point

According to Hatton, the systematic review and meta-analysis that he and his colleagues published in *Annals of Pharmacotherapy* in 2007 revealed the limitations of the data that FDA used decades ago to designate phenylephrine as effective. The study included unpublished data from the 1960s and 1970s that had not undergone peer review. "The FDA review did not apply meta-analytic methods and focused primarily on expert opinion in the interpretation of conflicting data. Thus, phenylephrine lacks adequate data to support its efficacy at the FDA-approved dose," noted Hatton and Hendeles in the article.

"My resident and I reviewed every study on phenylephrine, revealing much about the data quality and phenylephrine's effectiveness," said Hatton. "The study also led to a forensic analysis of one laboratory with the most dominant positive data [Elizabeth Biochemical], which suggested a methodologic

problem at that lab—or worse, possible fraud. Without that suspect data, the data used by FDA in 1976 to approve phenylephrine would have definitely shown it to be ineffective."

Finally, after pandemic legislation expanded FDA staffing and changed the process for approving nonprescription drugs to align more closely with those for prescription drugs, FDA produced an 89-page review of phenylephrine that not only confirmed Hendeles and Hatton's earlier conclusions, but also noted the apparent bias in some of the original data that led to the initial approval.

The briefing document

FDA noted in the introduction to the review (i.e., the briefing document for the committee) that the study includes all available clinical pharmacology and clinical data. This includes significant new data that were not available at the time the original decision was made to include oral phenylephrine in the OTC monograph, as well as a detailed evaluation of each of the original studies that supported that decision. The briefing document further stated that "we have now come to the initial conclusion that orally administered phenylephrine is not effective as a nasal decongestant at the monographed dosage (10 mg of PE hydrochloride every 4 hours) as well as at doses up to 40 mg (dosed every 4 hours)."

Finally, FDA stated that there were a number of potential benefits to changing the GRASE status of oral phenylephrine, including avoiding the unnecessary costs and delay in care of taking a drug that has no benefit, avoiding the risks of potential allergic reactions or other adverse effects related to use of phenylephrine in combination products, avoiding the inherent risks (especially for combination therapies) of taking more medication in order to seek some benefit, avoiding the risks of medication use in children, lowering overall health care costs, and avoiding missed opportunities for use of more effective treatments (including seeing a doctor if needed). However, a significant impact on industry would be inevitable, FDA noted, and could lead to significant supply chain issues.

Vote dissent

Although the committee's vote was unanimous, there have been some vocal disagreements with the outcome. Notably, former FDA commissioner Scott Gottlieb said of the vote, "This is a shame. At FDA we looked closely at this question in 2005 when pseudoephedrine was forced behind the counter, concluding phenylephrine was active. Now cold sufferers may have even fewer accessible options, driving up health care costs." Gottlieb has close ties to industry, which may have played a role in his comments. And, said Hatton, "it appears his perspective is that it is okay to have ineffective drugs on the market because the market will sort it out. This contradicts the 1962 Kefauver-Harris Amendments to the Food, Drug and Cosmetic Act, which requires all drugs, prescription and nonprescription, to be safe and effective." Gottlieb may also have been unaware of the comprehensive investigation conducted by the FDA team, added Hendeles.

Pharmaceutical manufacturers are also pushing back on any action that would remove phenylephrine from the market, saying that it's safe, even if it isn't as effective as previously claimed. The Consumer Healthcare Products Association issued a statement defending the use of phenylephrine and stating that "it is important to integrate new data within the broader framework of existing evidence rather than viewing it as a complete substitute for the previous body of evidence," clearly taking issue with FDA's recent evaluation of earlier data.

But it's unlikely that anything will happen anytime soon. FDA must still review the panel's recommendation and will almost certainly solicit public comments and give manufacturers time to adjust their formulas to remove phenylephrine. Oral phenylephrine is safe, though one of the Advisory Committee members expressed concern that patients taking products containing multiple ingredients may increase the dose or repeat the dose and get toxicity from one of the other ingredients, such as acetaminophen that can cause liver failure. Patients should be aware that they should not expect relief from these drugs.

Alternatives to phenylephrine

Oral phenylephrine is ineffective because 99% of each dose is inactivated by first-pass metabolism, allowing insufficient concentrations to reach systemic circulation. However, phenylephrine delivered via a nasal spray is effective. Other alternatives for nasal stuffiness include

- Oxymetazoline nasal spray
- Oral pseudoephedrine
- Nasal steroids (fluticasone, mometasone, triamcinolone)
- Nasal antihistamine/mast cell stabilizer (azelastine)

Patients should understand that phenylephrine and oxymetazoline should only be used for stuffiness caused by a cold and not for allergic rhinitis. In contrast, neither nasal steroids nor azelastine are effective for virus-induced stuffiness but are very effective for nasal stuffiness associated with allergies.

Future developments

The decision by FDA (and confirmed by the Nonprescription Drugs Advisory Committee) that oral phenylephrine is ineffective as a decongestant has been a long time coming (close to 40 years), but it's not the end of the discussion. FDA has not yet directed that oral products containing phenylephrine be removed from store shelves, but on October 20, 2023, CVS Health said it would remove all oral products that contain phenylephrine as the only ingredient from its stores. Over the coming months, or even years, there will likely be much debate about how to move forward.

However, what is clear is that Hendeles and Hatton will remain a part of the discussion. "The FDA Briefing Document was a joy to read," said Hendeles, who added "Nothing was as exciting and exhilarating as the vote." Hatton added, "We feel vindicated for something that we worked on for a long time. But it's not over." ■

Psyllium husk and weight loss

Mickie Cathers

Weight loss is big business, and the popularity of Ozempic, the FDA-approved prescription T2D drug, was boosted by those using it off-label for weight loss. Called "the poor man's Ozempic," psyllium husk is enjoying a rise in interest as an affordable alternative to semaglutide. But does it deliver on the promise of weight loss?

Background

Semaglutide and psyllium husk are very different. Semaglutide is a GLP-1 receptor agonist that prompts the body to produce more insulin, which in turn reduces blood glucose. Higher amounts of GLP-1 interact with parts of the brain that suppress appetite and signal a feeling of fullness.

Psyllium husk doesn't cause weight loss but can aid in weight loss as a supplement to a healthy, balanced diet, and regular exercise.

Psyllium husk can induce the same feeling of fullness as it contains more fiber than barley, beans, legumes, oat bran, and some fruits and vegetables. A single teaspoon of ground psyllium husk provides nearly 8 times more soluble fiber by weight compared with oat bran. Psyllium is a shrub-like herb (*Plantago ovata*) most commonly found in the Mediterranean and India. Psyllium husk is a popular dietary fiber supplement widely used as a gentle bulk-forming laxative and probably best known as the main ingredient in Metamucil. Also found in cereal, used in gluten-free and low-carb baking, management of GI issues, and a way to curb appetite, psyllium husk has recently been a hot-selling supplement with 249 new products introduced between 2018 and 2022.

In the small intestine, fiber drives metabolic effects such as lowering cholesterol and improving glycemic control. In the large intestine, fiber provides a laxative effect by binding with water and digestive fluids, to soften or bulk stool.

Psyllium is also a prebiotic that promotes healthy colonies of probiotics to grow in the gut, improving digestion and strengthening the immune system.

Psyllium husk supplements are a concentrated hit of soluble fiber that have been studied extensively and been proven to help lower cholesterol, relieve constipation and diarrhea, regulate blood glucose levels, and treat GI issues. But what about weight loss?

Is there a benefit?

Many studies have shown that psyllium husk can help maintain a healthy glycemic balance and affect body weight through increased satiety. Psyllium husk doesn't cause weight loss but can aid in weight loss as a supplement to a healthy, balanced diet and regular exercise.

Several studies showed that people with T2D who add 10 grams of psyllium daily saw improved blood glucose levels. A 2019 critical review by Jane and colleagues in *Nutrition* showed that the addition of psyllium improved blood lipid profiles, glycemic response, and increased satiety. One study showed sustained weight loss of an average of 3.3 kg in the treatment group supplementing their diet with 3.5 grams psyllium husk twice a day before breakfast and dinner.

Finally, a review published in the *Journal of the American Association of Nurse Practitioners* by Gibb and colleagues performed a comprehensive meta-analysis of randomized, controlled clinical studies designed to assess psyllium husk's impact on body weight, BMI, and waist circumference in overweight and obese participants.

Results of the meta-analysis showed that psyllium husk at a mean dose of 10.8 g/day taken just before meals, over the mean duration of 4.8 months, was effective for decreasing body weight by 2.1 kg, BMI by 0.8 kg/m^2, and waist circumference by 2.2 cm in overweight and obese populations.

Dosage

Psyllium husk is widely available in a variety of forms such as a capsule, tablet, or powder meant to be mixed with water.

Recommended dosages for adults suffering from constipation and IBS range from 3.5 grams to 7 grams mixed in 8 ounces of water 1–3 times daily. Psyllium husk is an easy way to increase daily fiber on occasion or regularly promote overall digestive health.

What to tell your patients

For patients using psyllium husk for weight loss, it's important to note that this supplement should be used in addition to a healthy diet and regular exercise. Psyllium husk is considered safe but does have laxative effects. Potential adverse effects include gas, bloating, and abdominal cramps. Caution patients taking psyllium husk to start slowly and monitor reactions.

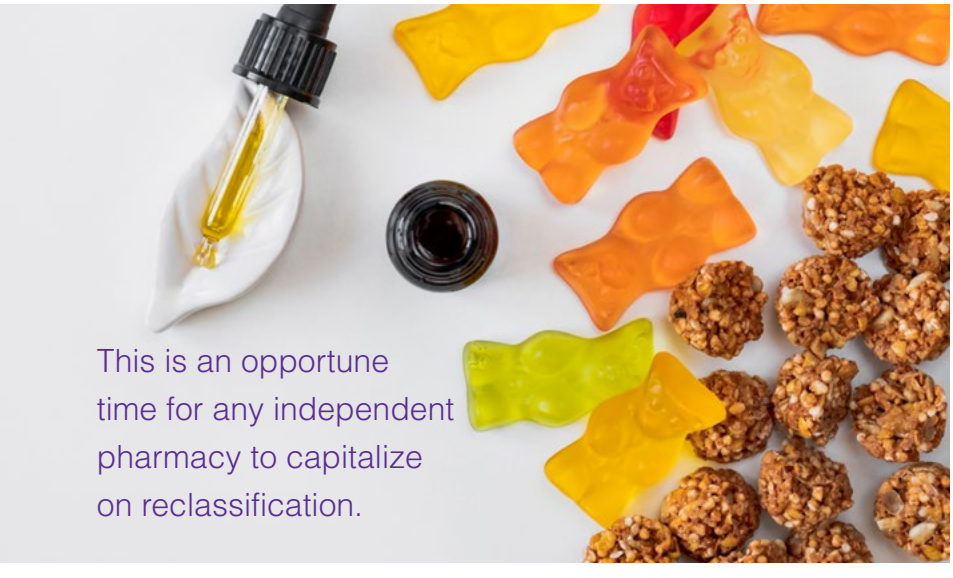
Advise patients to follow the directions on the package and drink at least 6 to 8 glasses of water daily when taking psyllium husk. Patients with trouble swallowing, or esophageal or GI issues, should not take psyllium husk and those with kidney disease should speak with their health care provider before using the supplement. Patients taking antidepressants, carbamazepine, diabetes medications, cholesterol-lowering medications, digoxin, and lithium should avoid using psyllium husk. ■

Potential changes coming for nonprescription CBD products

Ariel L. Clark, PharmD

Over a decade has passed since the first states, Colorado and Washington, legalized cannabis for recreational use. Another 5 years have gone by since the Farm Bill allowed for the sale of hemp and its derived products. And over the past several years, many states have passed legislation allowing cannabis to be used medically. But questions remain.

Recently, FDA announced plans to begin research into a new regulatory framework for cannabidiol (CBD)-containing products sold over the counter. HHS also issued a new recommendation to FDA to reclassify cannabis from a Schedule I to Schedule III drug. Cannabis, which contains tetrahydrocannabinol (THC) and CBD, has been investigated in the treatment of multiple disease states, yet federally, remains a Schedule I drug and is therefore considered to be a "drug(s) with no currently accepted medical use."



This is an opportune time for any independent pharmacy to capitalize on reclassification.

Both of these potential actions by FDA and HHS could mean major changes for the cannabis industry and pharmacists alike.

CBD-containing products

Today, you can find CBD-containing products, derived from hemp, anywhere from local gas stations to pharmacies to grocery stores. This is because the Farm Bill, legislation passed by Congress in 2014 and reaffirmed in 2018, removed hemp (i.e., cannabis sativa L., with <0.3% w/w Δ-9 THC) from the DEA Controlled Substance Act as a Schedule 1 drug.

After more than 5 years of investigation, FDA remains concerned over the safety of OTC CBD products, particularly with long-term use.

In January 2023, FDA's Office of the Commissioner made an announcement that the current regulatory framework for OTC CBD-containing products was ineffective. With the aim of ensuring that products are safe, they called for clear product labeling and for products to be unadulterated, which is not guaranteed currently. Epidiolex, the only FDA-approved CBD product, indicates some potential for liver damage, which would likely be a risk in OTC CBD products.

Further, FDA specifically noted that CBD cannot be sold as a dietary supplement. Even though hemp-derived OTC CBD products are available, it is federally illegal for them to be marketed as a food additive similar to a dietary supplement, beverage, or other food, according to Cynthia Solomon, PharmD, and Glen Solomon, MD, from Wright State University Boonshoft School of Medicine in Dayton, OH.

Cannabis reclassification

On September 13, 2023, HHS issued a recommendation to reclassify cannabis as a Schedule III drug. Members of the Congressional Research Service, who authored the recommendation, stated that this reclassification would "allow for medical use of marijuana while maintaining federal criminal control."

Reclassification would also result in implications for states that have medical cannabis programs, including compliance with the Controlled Substance Act, and the potential for federal income tax deductions. As cannabis is a Schedule I drug currently, research is inherently limited due to roadblocks in place by DEA.

Blair Curless, PharmD, PhD, who is involved with cannabis education in Georgia, said this is an opportune time for any independent pharmacy to capitalize on reclassification by being among the first to provide prescription cannabis programs.

Reclassification could also open up an avenue for further research.

"Researchers would face less strict regulatory controls in researching cannabis as a Schedule III controlled substance, which may in turn promote further research on cannabis," noted authors of the HHS recommendation. Next steps toward the change to Schedule III will include a review by DEA, followed by a federal rulemaking process, if rescheduling is to move forward.

Changes to the regulation of CBD products and to the schedule of cannabis may better help pharmacists understand what is safe for patients and how the products can be sold or advertised in an appropriate and legal way. ■

FDA approves first oral medication for postpartum depression

Sonya Collins

In August 2023, FDA approved zuranolone (Zurzuvae), the first oral medication for postpartum depression. Until now, the only treatment specifically for postpartum depression was brexanolone, a 60-hour I.V. infusion administered in a health care facility.

Postpartum depression affects as many as one in five new mothers, typically within the first 6 weeks after giving birth. Untreated, it can prevent mother–child bonding, lead to thoughts of harming oneself or the baby, and result in ongoing depressive disorder for the mother. Treatment can prevent these serious consequences, but stigma and other barriers, such as cost and convenience, have kept many women from seeking care.

This new pill for postpartum depression, a neuroactive steroid, could eliminate some of these barriers.

"It seems to be a game changer," said Kathleen Vest, PharmD, professor of pharmacy practice at Midwestern University College of Pharmacy in Downers Grove, IL. "As a 14-day oral medication that can be taken in the comfort of your own home—where nobody has to know about it—this becomes a really significant thing that will help improve access. Now it's just a matter of raising awareness that postpartum does exist and that we have this medication."

New neuroactive steroid

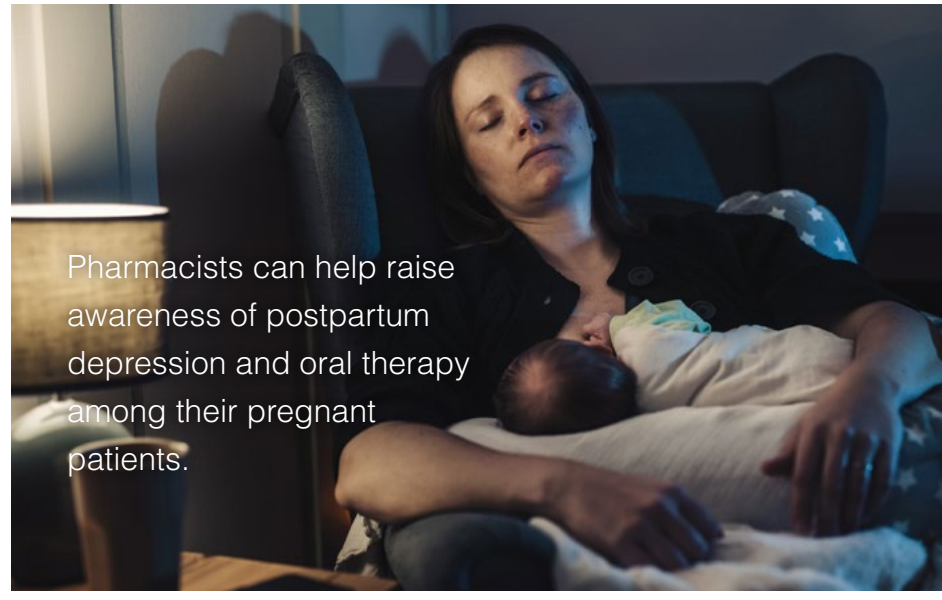
During pregnancy, levels of the neuroactive steroid allopregnanolone, a metabolite of progesterone, are high. This substance mimics endogenous neurosteroids that are thought to modulate GABA—a relaxatory neurotransmitter that helps regulate mood. After childbirth, allopregnanolone plummets.

"That's thought to be a contributing factor in the onset of postpartum depression," Vest said.

Zuranolone mimics allopregnanolone and helps compensate for that sudden drop.

In two double-blind, placebo-controlled clinical trials, women with postpartum depression who took 40 mg to 50 mg of zuranolone every evening for 14 days had significant improvement in symptoms at day 15 compared to women who took the placebo.

"Some of the trials are showing benefit even within the first few days of use," Vest said.



In the trials, the drug's effects continued through 42 days of follow-up.

Counseling points

Pharmacists can help raise awareness of postpartum depression and oral therapy among their pregnant patients. "It's really important to let them know before delivery that this is a significant but common condition and that if they do notice symptoms to report them to their doctor," Vest said.

Pharmacists may also familiarize themselves with the Edinburgh Postnatal Depression Scale and ask postpartum patients whether they are experiencing any of these symptoms.

"You might say something like, 'Have you talked with your provider about postpartum depression?' or 'Do you mind if I ask you a few questions today?'" Vest suggested.

Pharmacists should stress the significant central nervous system depressive effects of the drug, including drowsiness and confusion, to patients who pick up a prescription for zuranolone. Ideally, the 50-mg dose should be taken in the evenings, with fatty foods for optimal absorption, and patients should not drive for 12 hours after their dose. If the depressive effects are too severe, alert patients that health care providers can lower doses to 40 mg per day.

Women may continue to breastfeed while taking zuranolone. According to LactMed, the National Library of Medicine Drug and Lactation Database, very low amounts of the drug are found in breast milk, and it is not expected to cause any adverse effects in breastfed infants.

"Pharmacists can discuss risks and benefits with the patient—of both the clinical need for the medication and also the benefits of breastfeeding," Vest said. If women are concerned, Vest added, "There's always the option of withholding breast milk for those 14 days—pumping and discarding for up to a week after." ■

Updated chronic coronary disease guidelines factor in new drug therapies

Loren Bonner

Taking into consideration specific recommendations on several new classes of medications as well as placing an emphasis on social determinants of health, the American Heart Association, the American College of Cardiology, and other associations issued updated guidelines on managing chronic coronary disease.

"Our understanding of how to manage patients with chronic coronary disease both in terms of diagnosis and management has evolved considerably," said Salim Virani, MD, chair of the guideline writing committee. "Several recent clinical trials have provided a better understanding of therapies recommended in the past as well as newer therapies that did not exist at the time of prior guideline publication."

The last guideline on the topic was published in 2012, with an update in 2014.

Medication adherence is a problem area for patients with chronic coronary disease, but pharmacists can engage in dialogue with patients to understand what their barriers to medication adherence may be.

The updated recommendations as they relate to medications apply to nonstatin lipid lowering therapies, dual antiplatelet therapy use and its duration, anticoagulants, SGLT-2 inhibitors, as well as GLP-1 receptor agonists. Recommendations on the use of beta-blockers in patients with chronic coro-

Key perspectives from the 2023 multisociety guideline for the management of patients with chronic coronary disease

1. The chronic coronary disease guideline emphasizes team-based, patient-centered care that considers social determinants of health along with associated costs while incorporating shared decision-making in risk assessment, testing, and treatment.
2. Lifestyle modification and nonpharmacologic therapies, including healthy dietary habits and exercise, are recommended for all patients with chronic coronary disease.
3. Patients with chronic coronary disease who are free from contraindications are encouraged to participate in habitual physical activity, including activities to reduce sitting time and to increase aerobic and resistance exercise.
4. Cardiac rehabilitation for eligible patients provides significant cardiovascular benefits, including decreased morbidity and mortality outcomes.
5. Use of SGLT-2 inhibitors and GLP-1 receptor agonists are recommended for select groups of patients with chronic coronary disease, including groups without diabetes to improve outcomes.
6. Long-term beta-blocker therapy is not recommended to improve outcomes in patients with chronic coronary disease in the absence of myocardial infarction in the past year, left ventricular ejection fraction ≤50%, or another primary indication for beta-blocker therapy.
7. Either a calcium channel blocker or beta-blocker is recommended as first-line antianginal therapy.
8. Statins remain first line for lipid lowering in patients with chronic coronary disease. Several adjunctive therapies (e.g., ezetimibe, proprotein convertase subtilisin/kexin type 9 [PCSK9] inhibitors, inclisiran, bempedoic acid) may be used in select populations, although clinical outcomes data are not yet available for novel agents

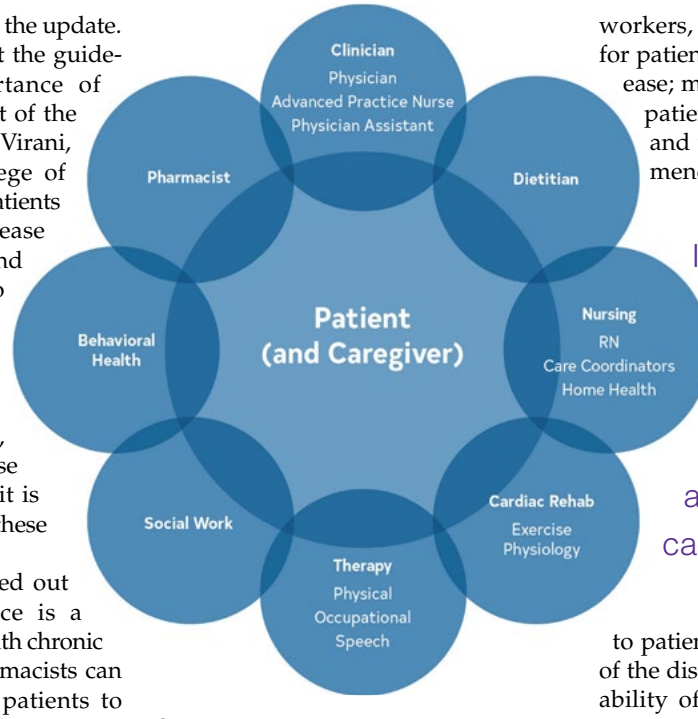
nary disease are also part of the update.

"I would emphasize that the guideline endorses the importance of having pharmacists as part of the cardiovascular team," said Virani, who is from Baylor College of Medicine. "We know that patients with chronic coronary disease have a high pill burden and that their adherence to guideline-directed medical therapy is low. Pharmacists can play a pivotal role in ensuring that patients are on the correct medications, they understand what those medications do, and why it is important for them to take these medications regularly."

Virani specifically pointed out that medication adherence is a problem area for patients with chronic coronary disease, but pharmacists can engage in dialogue with patients to understand what their barriers to medication adherence may be.

"I believe pharmacists can play an important role in addressing this gap," he said.

Besides being mindful of how social determinants of health affect care, Virani said other important takeaways from the new guideline include fully leveraging all members of the team—such as nurses, pharmacists, social workers, and others—who are caring for patients with chronic coronary disease; making sure practitioners help patients understand their disease and why therapy is being recommended; and lastly emphasizing to patients that as the understanding of the disease advances with the availability of new therapies, living with chronic coronary disease is much more manageable in terms of quality of life and overall prognosis.



Source: Virani et al. 2023 Multisociety guideline for managing chronic coronary disease: key perspectives. *J Am Coll Cardiol.* 2023.

> I would emphasize that the guideline endorses the importance of having pharmacists as part of the cardiovascular team.

For busy clinicians, Virani recommends taking a look at the "Top 10 take home messages" section of the guideline. Visit apha.us/CCDGuidelines to access the full guideline. ■

such as inclisiran and bempedoic acid.

9. Shorter durations of dual antiplatelet therapy are safe and effective in many circumstances, particularly when the risk of bleeding is high and the ischemic risk is not high.

10. The use of nonprescription or dietary supplements, including fish oil and omega-3 fatty acids or vitamins, is not recommended in patients with chronic coronary disease given the lack of benefit in reducing cardiovascular events.

11. Routine periodic anatomic or ischemic testing without a change in clinical or functional status is not recommended for risk stratification or to guide therapeutic decision-making in patients with chronic coronary disease.

12. Although they increase the likelihood of successful smoking cessation, because of the lack of long-term safety data and risks of sustained use, e-cigarettes are not recommended as first-line therapy.

13. In patients with chronic coronary disease and lifestyle-limiting angina despite guideline-directed management and therapy and with significant coronary artery stenoses amenable to revascularization, revascularization is recommended to improve symptoms.

14. In patients with chronic coronary disease who require revascularization for multivessel coronary artery disease with complex and diffuse coronary artery disease (e.g., SYNTAX score >33), it is reasonable to choose coronary artery bypass grafting over percutaneous coronary intervention to improve survival.

15. Finally, studies are needed to assess which interventions lead to effective guideline implementation in clinical practice. Similarly, research is needed to assess the effect of a new guideline release at the patient, clinic, hospital, health care system, and community levels. ■

Pictured (left to right): Shane Naeole, PharmD; Tasha Caulford; Malie Leauanae; Khanh Vy Tran, PharmD; and Anjel Cultura, PharmD.

Pharmacists on the ground after Maui wildfires provide biggest medical need: medications

Loren Bonner

After deadly wildfires ripped through Lahaina, located on the western edge of Maui, pharmacists quickly mobilized to get displaced residents their medications.

The fires left over 2,200 buildings damaged in Lahaina. More than 5,000 people were displaced, and most lost everything. Hawai'i Governor Josh Green described the fires as likely the "largest natural disaster in Hawai'i's state history."

After the acute care needs of the wildfire victims were addressed, a select group of pharmacists—including those from Kaiser Permanente, the Veterans Health Administration, and an independent pharmacy—were allowed to come into the area. It was apparent to everyone that one of the greatest medical needs would be getting people their medications.

"I'd say by day two we were trying to get meds to people—the critical ones at first," said Ross Takara, PharmD, executive director for the pharmacy department at Kaiser Permanente in Honolulu. Kaiser's main location for Hawai'i is in Honolulu, but they operate Maui Health System on the island of Maui, as well as several clinics, with pharmacies, on Maui. Their clinic in Lahaina burned down and was completely destroyed.

Crystal Tsuda, PharmD, a pharmacy manager at Kaiser Permanente in Honolulu, was physically on the ground in Lahaina working with providers to get people, who were being housed in temporary shelters, their medications.

Because Kaiser is an integrated health system, Tsuda could access patients' records on file to look up their medications and dosages. But during the initial crisis phase, she was helping non-Kaiser members as well.

"For the rest of the community—the non-Kaiser members—the doctors on the ground were trying to do their best to figure out what dose to give them, to at least get them some meds in the interim. It was difficult, but patients were grateful," said Tsuda.

Since cell towers had burned down, getting any kind of signal was nearly impossible and made communication hard. Physicians were handwriting prescriptions. Medications were fulfilled outside of Lahaina, and Tsuda and her team needed rental cars to go back and forth to deliver the medications.

Ayman Alholail, PharmD, a Veterans Affairs pharmacist based in Maui, was also on the ground in Maui getting medications to the veteran population.

"As soon as we got word of fires, we pulled everyone in our system with a Lahaina-based address and tried to figure out how we could get medications to them," said Alholail. "I can also prescribe independently and that was so helpful in streamlining the process of getting veterans their medications."

"Since phone lines were down, we'd advertise that the VA will be here at this location at this time," said Alholail. But that didn't work for everyone. Alholail had to track some patients down and meet them somewhere—sometimes that was at a relief station, but in some cases, he had to deliver medications right to a patient's door.

With only two VA pharmacists on Maui, Alholai focused on medication distribution on the ground while the other pharmacist remained in the VA clinic.

Through an emergency proclamation signed by Hawai'i's governor, a mobile clinic with a pharmacy was set up in Lahaina weeks after the wildfire hit.

An independent pharmacy is perfectly positioned

CVS and Walgreens were part of the initial response team to help expand telehealth processing from the mainland, according to Corrie Sanders, PharmD,

president of the Hawai'i Pharmacists Association (HPhA).

But, in fact, an independent community pharmacy—Mauliola Pharmacy in nearby Wailuku—became the most essential pharmacy to help those in need.

"We were part of the initial response—not necessarily by choice but because the primary shelter is literally across the street from our flagship pharmacy," said Corey Lehano, PharmD, owner of Mauliola Pharmacy, which has two locations in Wailuku. Most temporary shelters—including the main one called War Memorial—were located in Wailuku.

"Everything was being worked out of the War Memorial gym those initial 12 hours. When we first arrived, it was just a lot of volunteers and medical professionals. It was chaotic and intense," said Lehano. "A lot of providers were there but there was no workflow or system. They were writing paper scripts, but there was no one to fill them and no way for the patients to get to the pharmacies. That's where we started."

Lehano said they were perfectly set up to meet the needs of the community.

"We already had free delivery service, people trained to deliver medications, and a workflow already in place," he said. "We were able to utilize both our sites in town and were tag teaming to get things done."

His team performed medication reconciliation for patients the first couple of days.

"At one point, I had three to four pharmacists doing med rec and calling pharmacies and providers and from there acquiring orders to fill for them," said Lehano.

Over time, bigger organizations stepped in and Lehano handed off the service to them and moved on to what else was needed for patients. Lehano's staff began point-of-care testing next, bringing the service to patients because their CLIA-waived laboratory is registered as a mobile lab. Most recently, Lehano has been asked to help facilitate and coordinate education classes to train culturally competent behavioral health specialists as wildfire victims struggle with mental health care needs in the aftermath.

Through an emergency proclamation signed by Hawai'i's governor, a mobile clinic with a pharmacy was set up in Lahaina weeks after the wildfire hit. Displaced patients, who have moved to temporary housing in resorts, are shuttled back and forth to the clinic to get their medications.

"I have never seen anything where in such a short amount of time, you have pharmacists from every avenue of practice all moving collectively together to get patients care."

Hawai'ian culture

Lehano noted that one of their state senators said something that has stuck with him: "Often times in a disaster, one of the things that is overlooked are all the casualties that occur after the immediate disaster due to medications or things like that. She said she didn't hear any of that."

"I think that's a testament to the collective partnerships and networks that were created over this short period of time to support the immediate and now long-term needs," said Lehano.

Tsuda from Kaiser noted that even though the wildfires occurred on the island of Maui, the entire state of Hawai'i came together.

"Everybody stepped in and that just reflects our culture," she said. "You also have to understand that to help out another island you have to fly everything in."

Or get it over by jet ski or boat—as Jodi Lyn Nishida, PharmD, noticed in the immediate aftermath.

"People from other parts of Maui as well as neighboring islands pooled their resources to get people what they needed," said Nishida. "This is Hawai'ian culture—we take care of our own."

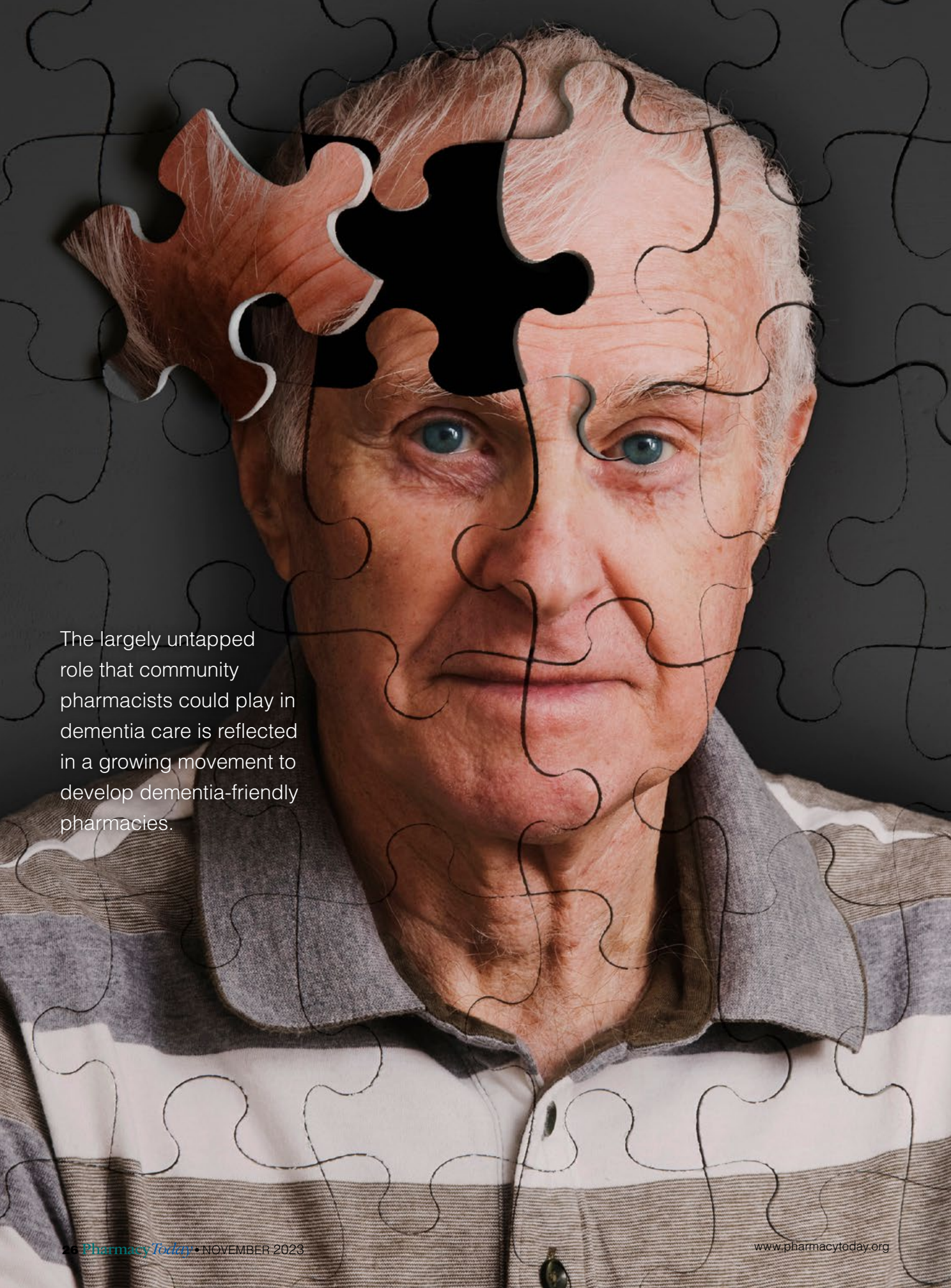
Nishida, who is the founder of a keto-based diet medical practice, helped by cooking, preparing, and shipping meals to those displaced in Lahaina.

Sander from HPhA said she has never seen so many pharmacists from various groups come together. On a daily basis, she said, pharmacists and leaders spoke by phone to figure out the logistics of getting medications to displaced residents.

"I have never seen anything where in such a short amount of time, you have pharmacists from every avenue of practice all moving collectively together to get patients care," she said. "We had drug suppliers on those calls asking how they could get manufacturers' drug donations—it was everything from drug supply to regulations to how do we get this to Corey [Lehano]."

For Lehano, this whole experience reminded him of the depths he'd go for his community.

"As a pharmacy we will live and die by the community," he said. "If we are not there for them, it doesn't make sense for us to operate." ■



The largely untapped role that community pharmacists could play in dementia care is reflected in a growing movement to develop dementia-friendly pharmacies.

FROM THE COMMUNITY TO THE CLINIC, PHARMACISTS HAVE A CRITICAL ROLE TO PLAY IN DEMENTIA CARE

Sonya Collins

"George" had chronic constipation. But as an older adult living with advanced Alzheimer disease, he couldn't talk to his doctors about what might be triggering the problem or work with them to help determine the best care plan. Instead, the constipation worsened, and George would become agitated and aggressive. When his behavior became too difficult to control, his family caregivers asked the physician for help. He was prescribed antipsychotics to calm him down, which came with added adverse effects and did nothing to address the underlying constipation.

That's when George's family caregiver reached out to the Care Ecosystem team at the University of California San Francisco (UCSF). Coordinated by a navigator, the telephone-based, multidisciplinary collaborative dementia care model, which includes medical specialists, social workers, pharmacists, and other experts, augments existing health care services by lending expertise in dementia care directly to family caregivers and to their health care providers.

"We were able to help the patient take the medications to manage the underlying problem and avoid these other medications that come with unwanted adverse effects," said Kirby Lee, PharmD, professor emeritus in clinical pharmacy at UCSF School of Pharmacy, who led pharmacists on the Care Ecosystem team.

George's story is not unusual. An estimated 6.7 million Americans over the age of 65—or about 1 in 9 older adults—are living with Alzheimer disease. Some 15.7 million U.S. adults care for a family member with dementia. As treatment options increase, patients and their caregivers need more support. Pharmacists can play a critical role in supporting patients, caregivers, and other health care providers from the community pharmacy to the clinic.

Counsel on risk and prevention

Before patients ever show the first signs of dementia or mild cognitive impairment, their charts reveal health conditions they have or medications they take that might raise their risk.

Anticholinergics, benzodiazepines, proton pump inhibitors, and certain pain medications are associated with an increased risk for Alzheimer disease, as are some chronic conditions. Numerous other medications are known to induce Alzheimer-like symptoms. When patients pick up these medications, or medications for risk-associated conditions, pharmacists may seize the opportunity to counsel patients on these links and on lifestyle factors that might lower risk.

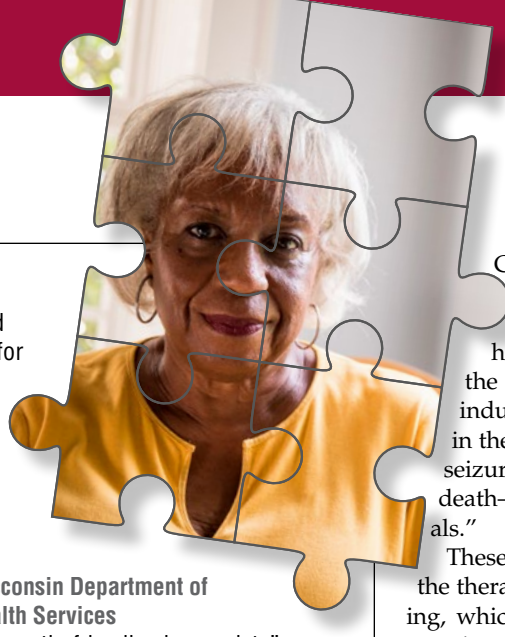
"One of the big things we overlook is preventive care," said Emily Peron, PharmD, an associate professor at the Virginia Commonwealth University School of Pharmacy, who works with an interprofessional team of faculty and students to provide care coordination and wellness services for community-dwelling older adults through the Richmond Health and Wellness Program. "We can be thinking more about what we are doing in terms of lifestyle education, diabetes prevention, and all of those things that we know to be potentially reversible causes of dementia."

Educate on available drugs

Recent years have seen FDA approvals for two Δ-amyloid-targeted, disease-modifying monoclonal antibodies for Alzheimer disease. Aducanumab (Adulhelm) earned accelerated approval in 2021 followed by lecanemab (Leqembi), which also received accelerated approval and, ultimately, traditional approval in 2023. A third drug in this class, donanemab, is in the pipeline. The medications entered a drug landscape that had not changed in 20 years, and which consisted only of therapies that treat symptoms but do not modify disease.

"A big need in Alzheimer care that pharmacists can address is to educate patients and caregivers on the available drugs and reasonable expectations of these drugs," said Jeff Sherer, PharmD, a clinical professor at the University of Houston College of Pharmacy.

As disease-modifying agents, the newest drugs for Alzheimer disease target aggregated forms of amyloid, which experts believe underlies the progress of the disease. Aducanumab targets soluble oligomers and fibrils. Lecanemab targets oligomers and protofibrils. Donanemab targets fat.



Helpful resources

Experts interviewed for this story recommended the following resources for pharmacists caring for patients with dementia.

Health In Aging
"Ten medications older adults should avoid or use with caution."
apha.us/TenMedsToAvoid

Journal of the American Geriatrics Society
"American Geriatrics Society 2023 updated AGS Beers Criteria® for potentially inappropriate medication use in older adults."
apha.us/AGSInappropriateMeds

Alzheimer's Association
"Medical management and patient care."
apha.us/MedMgt

HHS
"Role of the pharmacist in the care of persons living with dementia."
apha.us/PharmRole

Wisconsin Department of Health Services
"Dementia-friendly pharmacists"
apha.us/DementiaFriendly

Texas Health and Human Services
"Improving dementia care: Strategies for pharmacists in long-term care facilities."
apha.us/LongTermCare

CMS
"Guiding an improved dementia experience model."
apha.us/InnovationModel

But, as the newest tools in the toolbox, the data on the two FDA-approved drugs come from just 18 months of research.

"We don't know what the changes in endpoints seen in clinical trials mean for patients in the real world," said Kristin Zimmerman, PharmD, an associate professor in the Department of Pharmacotherapy and Outcomes Science at Virginia Commonwealth University School of Pharmacy. "We don't understand the long-term clinical significance."

On the other side of the coin, mainstays such as cholinesterase inhibitors and memantine lessen some of the symptoms of the disease but do not interfere with its progress.

"In the past, commercials showed an unhappy grandma who has Alzheimer disease and then she gets put on Aricept and now she's back to her old self, but the drugs just don't work that way, unfortunately," Sherer said. Pharmacists can help patients and their caregivers have more reasonable expectations of these therapies.

Research also identifies gaps in some pharmacists' knowledge of the common adverse effects that come with these older Alzheimer drugs. According to a 2018 study in the *Journal of Rural Health,* pharmacists in the most remote areas of Northern California, Southern Oregon, North and South Dakota, and West Virginia, were less likely to be able to name two or more adverse GI effects of donepezil (Aricept). They were also less likely to stock metamine and certain other Alzheimer drugs.

Though finding effective disease-modifying agents is considered the holy grail of Alzheimer disease research, these older therapies aren't expected to go anywhere anytime soon. The new drugs are only approved for early stages of Alzheimer disease and many questions about them still remain.

"We don't know what the central nervous system (CNS) adverse events seen in clinical trials mean for patients in the real world," Zimmerman said. "Amyloid-related imaging abnormalities are considered indicative of CNS-related adverse events, like edema and micro hemorrhage. We're not sure if it hastens cognitive decline in the long term, whether it might induce a hemorrhage-prone state in the brain, whether it can induce seizures, and in rare cases cause death—as we've seen in clinical trials."

These concerns mean patients on the therapy require frequent monitoring, which puts pressure on patients, caregivers, health systems, and payers to cover multiple MRIs and adds to the costs of already expensive therapy. It's still unknown how patients will pay for disease-modifying agents and whether access will be equitable across socioeconomic groups.

"Only lecanemab is currently accessible—and I won't even say easily accessible—but CMS will pay for 80%. But when you're talking about a drug that costs upwards of $30,000 a year plus imaging and infusion centers, 20% is still going to be a lot of money for a lot of people," Sherer said.

The clinical benefits, risks, and out-of-pocket costs of new Alzheimer drugs will become clearer over time. New drugs will also continue to come to the market. Some 150 drugs—both new and repurposed older ones including metformin and semaglutide—are currently in clinical trials for Alzheimer disease.

"There's amyloid-targeting agents and biologics, but also more traditional small molecule drugs with novel targets like sigma receptors and tyrosine kinase inhibitors and more traditional targets like NMDA, which is what metamine targets," Zimmerman said.

Given that older drugs address symptoms only and new drugs are not yet readily accessible, pharmacists might call patients' and caregivers' attention to clinical trials and point them toward channels for enrollment.

Eliminate dangerous drugs

Patients living with dementia or mild cognitive impairment and those who are at risk stand to benefit from a pharmacist's intervention on other medications that can cause or exacerbate

cognitive symptoms.

"This is something that every pharmacist can do," said Shalini Lynch, PharmD, a professor in the department of clinical pharmacy at UCSF School of Pharmacy and a member of the Care Ecosystem team. "Whether we're in the hospital or the pharmacy, we have medication lists. Take a look at the list and see if anything jumps out at you as being potentially risky or inappropriate."

Pharmacists from the community pharmacy to the clinic can make a major impact in this area by identifying and potentially eliminating drugs that may exacerbate dementia symptoms.

Research led by UCSF's Lee and coauthored by Lynch adds to a large and growing body of evidence that medication oversight by a pharmacist benefits complex older patients in general and those living with dementia in particular.

The study, published in the May 2023 issue of *Alzheimer's & Dementia: The Journal of the Alzheimer's Association*, used a randomized controlled clinical trial to demonstrate the benefits of including pharmacists in the Care Ecosystem model. Compared to patients who got usual care, those who had access to a Care Ecosystem pharmacist were less likely to be prescribed high-risk or inappropriate medications. Due to the successes of UCSF's Care Ecosystem model, CMS recently reported plans to reimburse for care provided through these types of comprehensive and collaborative models (see resource in sidebar).

Care Ecosystem pharmacists developed a questionnaire for patients and caregivers to screen for medication problems that can trigger a referral to a pharmacist for a comprehensive medication review. All medications that undergo review, not only those for dementia, are scrutinized for potential interactions and cognitive adverse effects.

"Our pharmacists specialize in dementia, sure, but with our background in geriatric pharmacy, we're also addressing hypertension, osteoporosis, diabetes, drug interactions, and adverse effects," Lee said. "We don't focus just on memory drugs. We focus on the whole patient and whatever medical conditions they're dealing with."

Pharmacists from the community pharmacy to the clinic can make a major impact in this area by identifying and potentially eliminating drugs that may exacerbate dementia symptoms.

"We can all brush up on our knowledge of and ability to identify med-related problems," Zimmerman said. "We can take a sense of ownership of more comprehensive med reviews and feel empowered to take action on med-related problems."

See signs, recommend resources, make referrals

Because some 70% of adults with dementia live outside of a facility setting, there may be a greater role for community pharmacists than many appreciate.

"There's a lot that can be done in the community pharmacy where you're getting a lot of touch points with folks," said Peron. "The pharmacist, especially in a community, is going to have relatively frequent interaction compared to other providers a lot of times."

Pharmacists can get a sense of patients' cognitive state, Peron said, through routine interactions at the community pharmacy. They can take note of whether patients of concern are getting their prescriptions filled regularly and their demeanor when they do so. "Even things like someone asking the same questions repeatedly, seeming more confused, withdrawn" can provide clues to a patient's cognitive state.

Pharmacists also have the opportunity to gauge caregivers' concerns about changes in their loved one's condition. "We can think about drug formulations, adherence devices, and offering referrals to a geriatrician or a neurologist."

Become a dementia-friendly pharmacy

The largely untapped role that community pharmacists could play in dementia care is reflected in a growing movement to develop dementia-friendly pharmacies. Countries including the United States, the UK, Australia, and Austria have resources on the value of and how to become a dementia-friendly pharmacy.

Clinicians and staff in these pharmacies have special training to recognize the unique needs and abilities of people with dementia and their caregivers and better communicate with and serve them. The pharmacies may also make changes to lighting, signage, and other aspects of the environment in order to facilitate patients with cognitive impairment.

The Wisconsin Department of Health Services offers a two-page handout on dementia-friendly pharmacy (see resource in sidebar), which includes a link to a free 20-minute online training module for pharmacy staff members and links to other training resources. The dementia-friendly model focuses on continuing to treat the whole person and offer person-centered care throughout the course of dementia.

"Just because someone has a diagnosis of mild cognitive impairment or even dementia," Peron said, "doesn't mean that they can't make decisions for themselves, doesn't mean that they can't play a role in their health care and doesn't mean that they don't deserve to be spoken to directly about their care." ■

For pharmacists, requirements for reporting abuse vary

Elizabeth Briand

Pharmacists are among the most accessible health care providers, working with patients outside of traditional clinical environments and in highly visible and trafficked settings. As such, they are uniquely positioned to provide assistance to individuals who may be experiencing abuse or violence.

"It's important to understand state regulations, and pharmacists are interested in guidance on this," said Marie Barnard, PhD, assistant professor of pharmacy administration at the University of Mississippi, who led a 2020 study published in the Nov/Dec issue of *JAPhA* on this topic. Barnard and fellow researchers examined the reporting requirements for pharmacists in all 50 states and two territories with regard to intimate partner violence, child abuse, and elder abuse. They also looked at statutes to determine if pharmacists were considered mandatory reporters for each type of abuse.

Examining the requirements

Results showed that pharmacists are specifically named as mandatory reporters of intimate partner violence in 10 states and territories, of child abuse in 12, and of elder abuse in 20, according to Barnard's research paper in *JAPhA*.

In conducting the research, Barnard and colleagues used three key resources to identify existing laws: the Futures Without Violence compendium, funded by HHS; the mandatory reporting laws for child abuse published by HHS' Children's Bureau; and a policy database maintained by the Rape, Abuse & Incest National Network. Statutes identified were then further studied to determine specific requirements and who were designated as mandatory reporters of abuse.

Many states use the broad term "health care provider" to indicate a mandatory reporter while others require that anyone—health care provider or not—who is aware of or suspects abuse must report it. The number of states or territories in which pharmacists would be expected to report abuse stands at 31 for intimate partner violence, 45 for child abuse, and 47 for elder abuse.

> "You can just talk to your pharmacist. For individuals experiencing abuse, this is a really positive thing."

Barnard has long been interested in issues of domestic violence and, as part of her dissertation prior to this study, surveyed pharmacists across the country to ask if cases of abuse had ever been disclosed to them. "Almost all of them said they had, but they had never received training on what to do," said Barnard. "Every other health care discipline is required to have training, but pharmacists are left out of that."

This is a significant missed opportunity, according to Barnard. Because many pharmacists work in settings such as supermarkets, they are easily accessible and can be visited by victims without undue attention from their abuser. This was especially true during the pandemic, when many people stopped going to their physician's offices but could still see their pharmacist.

"Every other health care provider requires appointments but not pharmacists," said Barnard. "You can just talk to your pharmacist. For individuals experiencing abuse, this is a really positive thing. But pharmacists have not been at the table for this. Patients see their pharmacists more often than their physicians, and we're not leveraging that relationship."

How more pharmacists can help

To be a better ally and serve as a resource for victims of abuse, pharmacists can take the initiative to learn about and stay abreast of their state's reporting requirements. Clear corporate policies on how best to meet state guidelines also would benefit pharmacists, providing a well-defined plan of action should difficult situations arise.

Pharmacists can directly help by preparing in advance and practicing the CARD method: Care, Assess for Safety, Refer patients to local resources, and Document as appropriate for the practice setting. It includes learning what local referral services are available for victims of abuse and how to reach them; learning what mechanisms are required for reporting; preparing to hear disclosures safely and in private; and prominently displaying screening and education materials, including the National Domestic Violence Hotline (1-800-799-SAFE [7233]), which offers free and confidential help to victims in a multitude of languages 24 hours a day. ■

To bolster pharmacy workforce and well-being, groups agree on strategies for technician roles

Loren Bonner

Beyond just naming the issues, APhA and other organizations recognize that change needs to happen in the pharmacy workplace. Workplace conditions continue to be the primary reason cited for prolonged stress and burnout submitted to the Pharmacy Workplace and Well-being Reporting (PWWR) portal, a confidential and anonymous way pharmacy personnel can report positive and negative experiences in pharmacy practice.

In collaboration with the National Association of Boards of Pharmacy (NABP) and ASHP, APhA released a report called "Implementing Solutions Summit: Building a Sustainable, Healthy, Pharmacy Workforce and Workplace," which came out of a summit held in June 2023 with a variety of pharmacy professionals gathered together to identify solutions to address workplace conditions. Across the board, there was strong support to expand the role of pharmacy technicians.

"Participants supported establishing uniform educational and practice standards for pharmacy technicians, with the idea that assigning more complex duties to pharmacy technicians would make them feel more highly valued and, at the same time, free pharmacists to utilize the full extent of their training and provide better service to patients," the report stated.

Specifically, participants recommended establishing a new higher professional level for technicians and developing a corresponding academic curriculum for advanced-level pharmacy technicians. In some chain community pharmacy settings, technicians serve as pharmacy operations managers. Advanced-level technicians manage the supply chain or work in informatics in certain health systems.

William Schimmel, executive director and CEO of the Pharmacy Technician Certification Board (PTCB), sees both short-term and long-term solutions for the role of pharmacy technicians.

Across the board, there was strong support to expand the role of pharmacy technicians.

"When talking about pharmacist well-being, I would reframe that to be technician and pharmacist well-being," said Schimmel. "The best teams are

APhA, NASPA release latest well-being survey findings

According to the most recent Pharmacy Workplace and Well-being Reporting (PWWR) portal findings, based on 85 submitted reports from April to June 2023, harassment from patients or caregivers and the lack of open staff–supervisor communication channels are real and continue to be reported this cycle, APhA noted.

"Reports of threats and abuse by patients, harassment by colleagues or other health care providers, and feelings of hopelessness permeate the submissions," said Brigid Groves, PharmD, APhA vice president of pharmacy practice. "Individual reporters cite going beyond the typical above-and-beyond in community-based settings to assure that their patients' needs are met, yet are not receiving the recognition they deserve for the time and effort invested."

APhA said that from this latest report, there are two primary learnings: First, training is needed to enhance pharmacy staff's knowledge on how to de-escalate or "walk away" from abusive or aggressive patient situations. The second is the importance of nonpharmacy management training on supporting pharmacy staff when faced with harassment from patients or caregivers.

Groves said negative submissions continue to be submitted in greater numbers than positive examples.

Some positive experiences reported for this most recent cycle ranged from working with a patient to help him understand how to use a new medical device to navigating medication payment coverage when moving from a jail to a rehabilitation facility. Those who submitted positive experiences indicated that those experiences would have a long-term effect on their well-being.

going to feed off of each other."

In the long term, he believes techs should do more. But right now, they have to be trusted within the regulatory framework of what they are allowed to do in their respective state.

He said employers can do a lot in the short term.

"I'd tell employers hold onto the techs you have—invest in them, provide good benefits, education, training, recognition, and a defined career path—which is best of all," said Schimmel.

"I'd tell employers hold onto the techs you have—invest in them, provide good benefits, education, training, recognition, and a defined career path—which is best of all."

According to PTCB's 2022 national pharmacy technician workforce survey, most technicians viewed their job as a career. Responses may be biased, however, as the majority of respondents were certified technicians, according to Schimmel. However, that potential bias is more evidence to encourage or require technicians to be certified. It's more likely to set them on a career path.

He noted that most techs have a fragmented career path, whereas pharmacists enter pharmacy school and take the NAPLEX. "Pharmacists have a pipeline," said Schimmel.

A longer-term goal for PTCB is to have a more defined career path for techs and to get the word out that being a pharmacy technician is a great job, said Schimmel.

Contributors to the "Implementing Solutions Summit" report noted that schools and colleges of pharmacy could provide curricula for pharmacy technicians, such as by offering an associate degree program in pharmacy education.

Many participants advocated for boards of pharmacy to assess, increase, or eliminate pharmacy technician ratios to allow for adequate and redundant staffing levels if staff members are out sick or on break. To provide a basis for continuity, participants called for universal minimum practice standards for pharmacy technicians in every state.

Discussions and solutions in the report focused on five workplace themes: practice advancement, mental health, workforce, regulations and requirements, and technology and workflow efficiencies.

"We cannot delay in enacting these solutions," said Michael D. Hogue, PharmD, FAPhA, FNAP, FFIP, executive vice president and CEO of APhA. "It is imperative that we continue to prioritize the well-being of our pharmacy personnel now to usher in positive changes that not only elevate their workplace experiences but also reinvigorates the profession."

The full report can be accessed at apha.us/ImplementingSolutions. ■

Kroger wants pharmacists to revisit their passion of serving patients

Kroger's Project Passion is a new opportunity for Kroger pharmacists to step outside of their normal routine and be reminded of the reasons they serve patients.

The 12-week program, open to all Kroger pharmacists, is focused on well-being, recognition, connection, development, communication, and better ways of working as teams.

"At a time when the world was coming out of the pandemic, experiencing the 'Great Resignation' and increased burnout in the health care industry, the Kroger Health team looked at how to better care for our workforce and specifically our pharmacists," said Colleen Lindholz, president of Kroger Health. "We wanted to reignite the passion that motivates our teams to live out the Oath of a Pharmacist and provide the best patient care every day."

"Project Passion essentially provides our pharmacists with a leadership foundation and professional development for them to provide the best patient care, lead high-performing teams, and foster a culture that embodies Kroger Health's mission and vision," she said.

Gastroenterology

Common GI complaints that can generally be managed with nonprescription treatments and self-care include belching, heartburn, indigestion, acid reflux, sour stomach, and nausea. Patients also seek quick relief from other common and bothersome intestinal and bowel symptoms and conditions such as bloating, flatulence, diarrhea, and constipation. Constipation leads to at least 2.5 million physician visits per year in the United States, with older adults (>65 years) 5 times more likely to experience constipation than younger adults.

Gastrointestinal

Diarrhea relief
Imodium....1

Fiber supplement
Metamucil....1
Benefiber....2

Gas relief
Gas-X....1

Heartburn relief
Tums....1
Pepcid....2

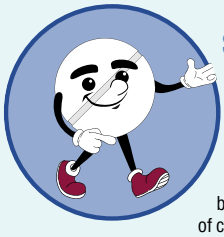
Hemorrhoid relief
Preparation H....1

Laxative
Dulcolax....1
MiraLAX....2

Nausea treatment/Relief
Dramamine-N....1
Emetrol....1
Pepto Bismol....2

Stool softener
Colace....1
Dulcolax....2

Upset stomach relief
Pepto Bismol....1
Tums....2



Self-care survey redux

This section of *Pharmacy Today*'s Self-Care Product Survey is reprinted from the full survey results published in the August 2023 issue of the magazine and available online at pharmacytoday.org.

The current survey was conducted by BrandSpark/Newsweek International using a scientifically valid methodology, the survey determines those nonprescription products most often recommended by pharmacists in the United States to consumers.

The winners were selected based on a survey of 1,716 pharmacists practicing in the United States who gave their unaided write-in opinions on which brands they'd recommend to patients in 86 categories. The highest share of citations as Most Trusted in the category determined the winner. If the margin of citation share between the leading brands did not exceed the estimate of sampling error at 90% statistical confidence, then a tie was declared.

Please also see APhAs *Handbook of Nonprescription Drugs*, the definitive source of professional information about OTC products. The *Handbook* is available online at PharmacyLibrary.com.

Massachusetts court allows lawsuit against pharmacy for breach of patient records system

David B. Brushwood, BSPharm, JD

Patient confidentiality is a cornerstone of the professional duty owed by pharmacists to their patients.

In times past, pharmacies maintained minimal information about patients. Patient information was recorded on paper and was difficult to access. The medication record was often nonspecific, because the relatively few drugs available for therapy did not disclose the precise condition for which the patient was being treated. As long as caution was used in the language of both spoken and written communications, pharmacists could meet confidentiality responsibilities.

Pharmacists today dispense and monitor the use of many different medications with very specific indications that can reveal extremely private information about a patient's health status. Pharmacy records also contain extensive data about a patient's medical history. All of this confidential information is organized in a computerized database. The key confidentiality responsibility today is to prevent access to the pharmacy's computer records by computer hackers.

A court in Massachusetts recently declined to dismiss a lawsuit brought by patients who alleged that their pharmacy should be held liable for a data breach that resulted in the release of patient information.

Background

The plaintiffs alleged that as-yet unidentified hackers breached the defendant's patient record system that contained a vast amount of patient information. They claimed that they suffered "anxiety, sleep disruption, stress, and fear" as a result of this information disclosure. Their lawsuit was based primarily on two legal theories: professional negligence and the breach of fiduciary duty.

The pharmacy moved for dismissal of the lawsuit, contending that neither of these legal theories could support the plaintiffs' lawsuit.

Rationale

The court first examined the pharmacy's argument that contract law, and not professional liability, would be the appropriate legal theory on which to base a lawsuit of this kind.

The court acknowledged that in a case asserting professional negligence, the plaintiffs must allege the breach of a duty of care. A lawsuit based on poor business practices must be evaluated under contract law. Nevertheless, the court ruled that the plaintiffs had alleged a professional negligence claim, because they contended that the pharmacy's "security procedures were deficient, permitting an inference that it breached its duty of care."

The court then turned to the breach of fiduciary duty theory of liability. The court noted that such a claim must allege: "(1) the existence of a duty of a fiduciary nature, based on the relationship of the parties, (2) breach of that duty, and (3) a causal relationship between the breach and some resulting harm to the plaintiff."

The court examined precedent from prior Massachusetts legal cases that had "twice considered whether the law imposes a fiduciary duty on a pharmacist to keep confidential a patient's information and had both times concluded that such a fiduciary relationship exists." The court concluded that the plaintiff's lawsuit successfully alleged the breach of the pharmacy's fiduciary duty to protect the confidentiality of patient information, and that the plaintiffs were harmed as a result.

The pharmacy's motion to dismiss was denied. Although the outcome of this lawsuit has yet to be determined, the basic principles of legal liability for a breach of pharmacy records have been established.

Takeaways

The commitment to patient confidentiality serves two important purposes in pharmacy.

First, there is a practical purpose, because pharmacists must know sensitive information about patients to facilitate their provision of effective pharmaceutical case services. If patients withhold sensitive information from pharmacists, for fear of public disclosure, then the quality of pharmaceutical care will be diminished.

Second, there is a relational purpose, because confidentiality demonstrates how pharmacists differ from other providers of commercial products. The fiduciary relationship recognized by this legal case reflects the mutuality of trust between pharmacists and patients.

Pharmacies must establish and maintain effective cybersecurity systems to promote quality patient care and to respect the fiduciary nature of the pharmacist–patient relationship. ■

Ensure appropriate dosing instructions and devices are provided for injectable medications

Institute for Safe Medication Practices, Horsham, PA

When patients are prescribed injectable medications to self-administer at home, it is critical that they receive education from both the prescriber and pharmacist on proper injection technique, with clear verbal and written instructions on the dose volume to measure and administer, and are provided appropriate syringes, needles, and ancillary supplies (e.g., alcohol swabs) to administer the dose.

In a recent case reported by a patient, many of these steps did not occur when they started a new injectable medication.

A patient received a prescription for methotrexate injection for the first time. The prescriber and pharmacy provided administration instructions in terms of the mg dose rather than the mL dose volume. The pharmacy dispensed vials of methotrexate injection (50 mg/2 mL) labeled with the directions to "Inject 2.5 mg subcutaneously once weekly for 2 weeks then increase to 5 mg once weekly. May increase up to 10 mg once weekly." When the patient picked up the prescription, they were not offered counseling by the pharmacist.

The pharmacy did not provide syringes and needles to administer the methotrexate. The patient's roommate, who happened to be a student pharmacist, helped interpret the instructions, provided the correct initial dose volume of 0.1 mL (and each subsequent dose increase—0.2 mL [5 mg] and 0.4 mL [10 mg]), and informed the patient that they would need to return to the pharmacy to obtain 1 mL syringes to measure and administer the medication.

At the time of a subsequent refill of the methotrexate prescription, the pharmacy dispensed 3-mL syringes with 1-inch needles. While the syringe had markings for each tenth of an mL, it would be difficult for any patient to accurately measure their current 0.4 mL dose much less their earlier doses of 0.2 mL or 0.1 mL. Also, a 1-inch needle is appropriate for I.M., not S.C. injections. S.C. injections require 1/2- to 5/8-inch long needles.

When prescribing and dispensing injectable medications for patients to self-administer, whether they come in a prefilled device (e.g., pen device) or a vial, it is critical that prescribers and pharmacists provide patient education and injection training. This includes how to use the device (e.g., syringe) to measure and administer the medication.

Use the teach-back method to verify that the patient understands, and can demonstrate, how to properly prepare and administer the medication. Ensure the patient instructions printed on the pharmacy label include the dose in the unit of measure used for administration, which in the above case would be mL. Printing only the mg dose or even both the mg and mL dose on the pharmacy label can increase the risk of confusion for the patient.

Dispense metric-only syringes, with needles of appropriate length and gauge for the route of administration, in volumes that most closely match the prescribed dose volume. Ensure the patient is provided with a sufficient quantity of syringes based on the frequency of injections and is educated on the appropriate single-use nature of syringes and needles to avoid syringe re-use and potential contamination of multiple dose vials. CDC's One & Only Campaign, available at apha.us/OneAndOnly, offers resources to help educate patients. ■

Figure. The pharmacy dispensed a 3-mL syringe with a 1-inch needle, which is not appropriate to measure doses of 0.1 mL, 0.2 mL, or 0.4 mL, or for S.C. administration.

Inpatient*Insights*

Is tighter blood glucose control better for ICU patients?

Hyperglycemia is common in critically ill patients, but randomized, controlled trials have shown both benefit and harm from tight blood-glucose control in patients in the ICU, resulting in unclear treatment protocols. In a new study published in *NEJM* on September 28, 2023, researchers participating in the TGC-Fast trial investigated whether variation in the use of early parenteral nutrition and in insulin-induced severe hypoglycemia could explain these inconsistent results.

TGC-Fast was an investigator-initiated, prospective, multicenter, randomized, controlled, parallel-group trial, in which patients were randomly assigned on ICU admission to liberal glucose control (insulin initiated only when the blood glucose level was >215 mg/dL) or to tight glucose control (blood glucose level targeted with the use of the LOGIC-Insulin algorithm at 80 to 110 mg/dL). Parenteral nutrition was withheld in both groups for 1 week. The primary outcome was the length of time that ICU care was needed.

Of 9,230 patients who underwent randomization, 4,622 were assigned to liberal glucose control and 4,608 to tight glucose control. The median morning blood-glucose level was 140 mg/dL for patients on liberal glucose control and 107 mg/dL with tight glucose control. Severe hypoglycemia occurred in 31 patients (0.7%) in the liberal-control group and 47 patients (1.0%) in the tight-control group, and the length of time that ICU care was needed was similar in the two groups. In addition, analyses of eight prespecified secondary outcomes suggested that the incidence of new infections, the duration of respiratory and hemodynamic support, the time to discharge alive from the hospital, and mortality in the ICU and hospital were all similar in the two groups, whereas severe acute kidney injury and cholestatic liver dysfunction appeared less prevalent in patients with tight glucose control.

The authors noted that the primary outcome may have been affected by variable discharge policies related to shortage of ICU beds during the COVID-19 pandemic. They also noted that hyperglycemia was less pronounced in this trial compared with previous trials in which patients received early parenteral nutrition, which suggests that avoiding such nutrition could lead to better outcomes in both treatment groups. ■

Does the risk for CDI vary by type of prior antibiotic use?

Prior antibiotic use is an important risk factor for *Clostridioides difficile* infection (CDI), but does the antibiotic type and class affect the risk? A recent study in the August 2023 issue of *Open Forum Infectious Diseases* expanded on previous studies of aggregated antibiotic use to evaluate CDI risk across individual antibiotic types. Researchers from the University of Iowa conducted a matched case–control study using a large database of insurance claims capturing longitudinal health care encounters and medications to identify antibiotics associated with CDI.

More than 150,000 patients with CDI were each matched to five control patients by age, sex, and enrollment period, and antibiotics prescribed within 30 days before CDI diagnosis, along with other risk factors, including comorbidities, health care exposures, and gastric acid suppression. The authors were able to differentiate and order the 27 individual antibiotics studied in terms of their relative level of associated risk for CDI and found wide variation in CDI risk within and between classes of antibiotics. The greatest risk for CDI was associated with clindamycin and later-generation cephalosporins, with the lowest risk associated with minocycline and doxycycline.

They note that future work is needed to further assess the time since exposure and the associated level of risk for CDI. ■

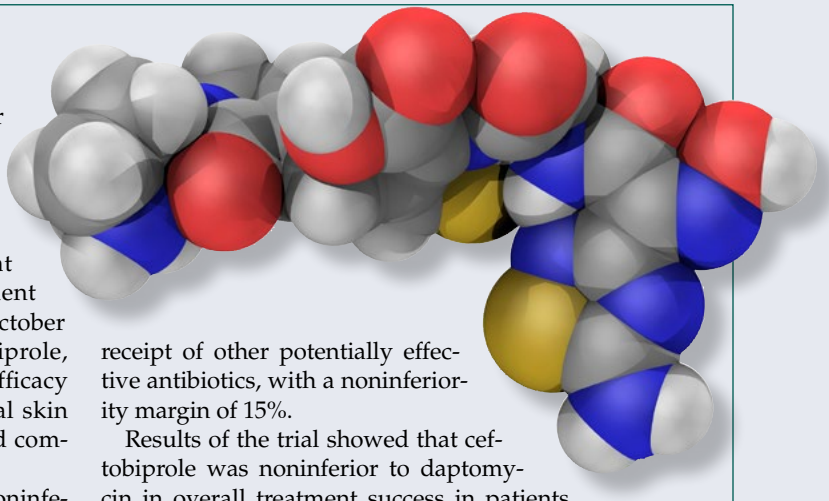
Lactated ringers may improve outcomes for patients with acute pancreatitis

Previous trials have found that use of lactated ringers (LR) may result in decreased risk of acute pancreatitis compared with normal saline, but the small size of these studies limits their strength. Researchers at The Ohio State University, along with colleagues from health systems around the world, conducted a multicenter prospective study to investigate these preliminary results.

Close to 1,000 patients directly admitted to 22 international sites with a diagnosis of acute pancreatitis between 2015 and 2018 were prospectively enrolled in the study. Demographics, fluid administration, and disease severity data were collected and mixed-effects logistic regression analysis was performed to determine their relationship with the type of fluid administered during the first 24 hours.

Results of the study, published ahead of print in the *American Journal of Gastroenterology* in July 2023, showed that use of LR during the first 24 hours was associated with reduced odds of moderately severe/severe acute pancreatitis compared with normal saline after adjusting for region of enrollment, etiology, BMI, and fluid volume and accounting for the variation across centers. Similar results were observed in sensitivity analyses eliminating the effects of admission organ failure, etiology, and excessive total fluid volume. The authors note that a large-scale randomized clinical trial is needed to confirm these findings. ■

Ceftobiprole shows potential for treatment of complicated *S. aureus* bacteremia



Antibiotic treatment options are limited for patients with methicillin-resistant *Staphylococcus aureus* (MRSA) bacteremia, a serious and frequently lethal infection. Few randomized trials have been conducted to inform treatment of *S. aureus* bacteremia, including one trial that supported approval of daptomycin for treatment of this indication. A new study published on October 12, 2023, in *NEJM*, compared the use of ceftobiprole, a cephalosporin that has been shown to have efficacy for patients with pneumonia and acute bacterial skin infections, with daptomycin in patients who had complicated *S. aureus* bacteremia.

In the Phase 3, double-blind, double-dummy, noninferiority trial, adults with complicated *S. aureus* bacteremia were randomly assigned to receive 500 mg ceftobiprole intravenously every 6 hours for 8 days and every 8 hours thereafter, or 6 to 10 mg/kg body weight daptomycin intravenously every 24 hours plus optional aztreonam (at the discretion of the trial-site investigators). The primary outcome was overall treatment success 70 days after randomization, defined as survival, bacteremia clearance, symptom improvement, no new *S. aureus* bacteremia–related complications, and no receipt of other potentially effective antibiotics, with a noninferiority margin of 15%.

Results of the trial showed that ceftobiprole was noninferior to daptomycin in overall treatment success in patients with *S. aureus* bacteremia. In the ceftobiprole group, 69.8% of patients had overall treatment success compared with 68.7% of patients in the daptomycin group. Findings also appeared to be consistent between the two groups with regard to secondary outcomes, including mortality and occurrence of microbiologic eradication. Adverse events were reported in 63.4% of patients who received ceftobiprole and 59.1% of patients who received daptomycin. Gastrointestinal adverse events (primarily mild nausea) were more frequent with ceftobiprole. ■

Researchers develop new PIRRT antimicrobial dosing recommendations

Corey Diamond, PharmD

Prolonged intermittent renal replacement therapy (PIRRT)—dialysis sessions given over 6 to 12 hours—is an increasingly used treatment strategy for critically ill patients with acute kidney injury. A compromise between intermittent hemodialysis (IHD) and continuous renal replacement therapy (CRRT), PIRRT may have better hemodynamic tolerability compared to IHD and lower costs compared to CRRT.

Until now, there's been an absence of clear guidance regarding antimicrobial dosing for patients undergoing PIRRT. A new systematic review, published online in *Pharmacotherapy* on August 19, 2023, now offers clinicians an evidence-based antimicrobial dosing guideline for critically ill patients on PIRRT.

Grewal and colleagues' systematic review had three objectives: To identify and describe the pharmacokinetics of antimicrobials used in critically ill adults receiving PIRRT; to evaluate the quality of evidence supporting the collected data; and to propose dosing recommendations based on the synthesis of the collected data.

Thirty-nine studies enrolling 452 patients met criteria for inclusion and provided PK and/or PD data for 20 antimicrobials in critically ill adults receiving PIRRT. The quality of evidence was deemed strong for 7 out of 20 antimicrobials, and strong dosing recommendations were determined for 9 out of 20 antimicrobials studied.

Dosing recommendations

For each antimicrobial included in the report, the authors evaluated the body of evidence using a standardized framework. This included data from previous studies, how often and how long the PIRRT was given, the risk of adverse effects, and if computer simulations showed the right dose would be reached. The physiochemical properties of the antimicrobials were also considered.

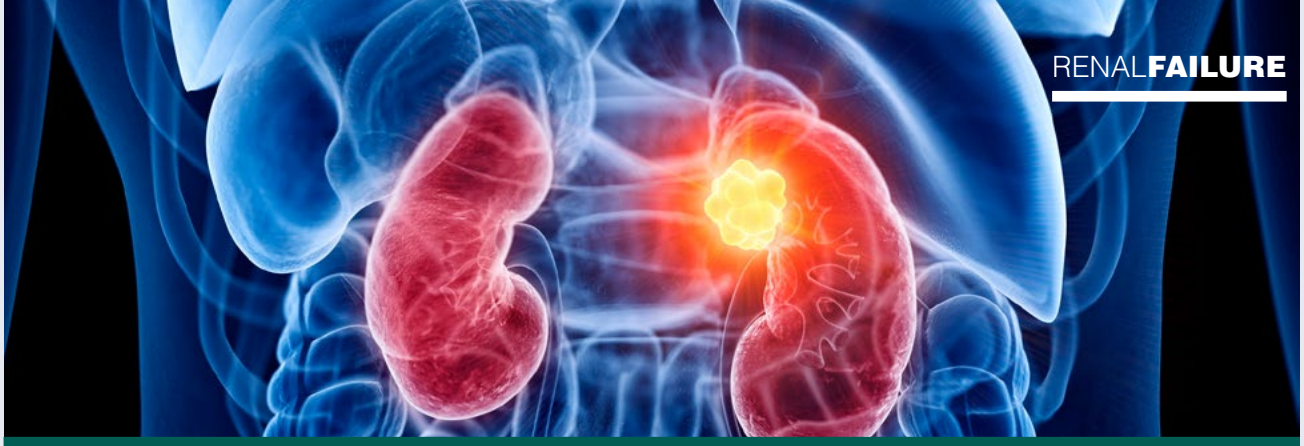
If there were multiple pharmacodynamic targets used between studies for an antimicrobial, the most aggressive target was used in the dosing recommendation. Additionally, all dosing recommendations were intended for critically ill patients of an average weight of roughly 187 lbs (85 kg) receiving PIRRT daily for 8 hours.

Ultimately, the GRADE method was used to score the strength of the dosing recommendation for each antimicrobial.

The authors noted that despite an overall low quality of evidence, strong recommendations were able to be made for almost half of the identified antimicrobials. However, knowledge gaps persist for many antimicrobials, they continued, and higher quality studies (i.e., population PK studies with assessment of PD target attainment) are needed to address these gaps.

> "It must be recognized that the dosing recommendations are based on the likelihood of achieving a pharmacodynamic target, rather than a clinical outcome such as clinical cure or microbiological cure."

Finally, the authors state that the dosing recommendations are based on the likelihood of achieving a pharmacodynamic target, rather than a clinical outcome and the dosing recommendations may not be applicable if the local operational characteristics of PIRRT, minimum inhibitory concentrations of the organisms being targeted, or the pharmacodynamic targets differ from those used in original studies. ■



PIRRT antimicrobial dosing guidance

Antimicrobial	Dosing recommendation	Recommendation strength
Ampicillin/ Sulbactam	3 g I.V. every 6 hours	Weak
Cefepime	Loading dose of 2 g I.V. followed by 1 g I.V. every 6 hours on PIRRT days. On non-PIRRT days, 1 g I.V. daily	Weak
Ceftazidime	2 g I.V. daily, with an additional 2 g I.V. post-PIRRT on PIRRT days	Strong
Ciprofloxacin	400 mg I.V. twice daily	Weak
Colistin	Loading dose of 300 mg I.V. followed by 60 mg I.V. every 8 hours	Weak
Daptomycin	8 mg/kg I.V. daily for daily PIRRT, 8 mg/kg I.V. every 48 hours for every other day PIRRT	Weak
Ertapenem	1 g I.V. daily	Strong
Fluconazole	Daily PIRRT: loading dose of 800 mg I.V.; maintenance dose of 400 mg I.V. twice daily with the second dose after PIRRT Non-daily PIRRT: loading dose of 800 mg I.V., maintenance dose of 400 mg I.V. daily	Weak
Fosfomycin	Loading dose of 8 g I.V.; maintenance dose of 5 g I.V. every 8 hours	Strong
Gentamicin	6 mg/kg I.V. 1 hour before PIRRT every 48 hours, using levels to confirm clearance	Strong
Imipenem	Daily PIRRT: Avoid imipenem use in PIRRT but, if necessary, loading dose of 1 g I.V. followed by 500 mg I.V. every 6 hours; we also suggest a continuous or prolonged infusion Non-daily PIRRT: use a different agent	Weak
Isavuconazole	200 mg I.V. every 8 hours for the first 48 hours followed by 200 mg I.V. daily	Weak
Levofloxacin	500 mg I.V. daily	Weak
Linezolid	All pathogens except *S. aureus:* 600 mg I.V. every 12 hours *S. aureus:* avoid linezolid if possible or 600 mg I.V. every 12 hours with an extra 600 mg I.V. post-PIRRT on PIRRT days	Strong Weak
Meropenem	Loading dose of 2 g I.V. followed by 1 g I.V. every 8 hours For a patient with residual diuresis >300 mL/day or a highly resistant organism with minimum inhibitory concentration >2 µg/mL, 2 g I.V. every 8 hours	Strong Weak
Moxifloxacin	400 mg I.V. daily post-PIRRT	Strong
Piperacillin/ Tazobactam	Daily PIRRT: 3.375 g–4.5 g I.V. every 8 hours for most infections. For septic shock or resistant organisms (e.g., *Pseudomonas*), 3.375 g I.V. every 6 hours as a continuous infusion Non-daily PIRRT: Same dose as above for PIRRT days, 2.25 g dose at the same interval on off days	Strong
Vancomycin	Loading dose 25 mg/kg I.V. prior to PIRRT followed by 15–20 mg/kg I.V. post-PIRRT. Utilize and adjust dose based on levels	Strong

A strong recommendation indicates author confidence that the benefits of a proposed dosing regimen (pharmacodynamic target achievement) outweigh its drawbacks (toxicity or inefficacy). A weak recommendation indicates author confidence that the benefits of a proposed dosing regimen (pharmacodynamic target achievement) probably outweigh its drawbacks (toxicity or inefficacy). Per the authors, not all critically ill patients on PIRRT may benefit from these recommendations.

Adapted from *Pharmacotherapy,* August 19, 2023.

Specialty pharmacies step up to successfully manage patients with multiple sclerosis

Olivia C. Welter, PharmD

A recent study conducted across multiple health-system specialty pharmacy sites found that pharmacist interventions can be beneficial for patients with multiple sclerosis (MS) who are on disease-modifying therapies (DMTs).

Published online in *AJHP* on August 9, 2023, the study sought to identify rates of patient-reported outcomes, including relapse; impacted productivity—framed as missing work, school, or planned activities—and hospitalization. Additionally, investigators evaluated the associations within patient-reported outcomes, pharmacist outcomes, and patient and medication characteristics.

"The most important piece of this study is that health-system specialty pharmacies were able to collaborate to demonstrate that pharmacists in the health-system specialty pharmacy care model play an important role in educating patients and managing DMTs resulting in positive clinical outcomes for patients with MS," said lead author Autumn Zuckerman, PharmD, from Vanderbilt Specialty Pharmacy.

Study background and findings

Zuckerman and colleagues conducted this multisite study at Vanderbilt University Medical Center, University of Rochester Specialty Pharmacy, Fairview Specialty Pharmacy, and WVU Medicine Specialty Pharmacy Services, Allied Health Solutions. Because the sites were affiliated with separate health systems, researchers standardized patient-reported outcome assessments and defined pharmacist actions into 6 categories: general medication education, safety, effectiveness, adherence, nonfinancial coordination of care, and financial coordination of care.

Patients were prospectively enrolled in the study if they had at least one fill of a self-administered DMT on record at the health-system specialty pharmacy. Once enrolled, patients were followed for 12 months and were asked to respond to patient-reported outcome assessments. A total of 968 patients were enrolled and nearly 7,000 patient-reported outcome assessments were collected during the study period. Patients reported that productivity was affected most often, with 141 patients experiencing this patient-reported outcome 239 times; 45 patients experienced MS-related relapse; and 18 experienced MS-related hospitalization. Investigators noted that these were low rates compared with prior studies.

A total of 3,683 pharmacist actions were documented with a median of four actions per patient. The most common action category was general medication education totaling 1,570 actions, followed by safety with 1,226 actions, and adherence at 479 actions. Overall, glatiramer acetate accounted for 31.6% of fills, fingolimod for 18.2%, dimethyl fumarate for 17.8%, and teriflunomide for 12.5%.

Across medication classes, rates of general medication education actions were similar, but the actions happened frequently. The study found that glatiramer acetate was associated with a lower rate of safety actions than the other medication classes, and fumarates were associated with higher rates of adherence actions than the other classes. Effectiveness actions were not as frequent, with authors indicating that patients taking drugs such as fingolimod had a rate of this action once every 4.3 person-years on the treatment and those taking teriflunomide had a rate of once every 8.5 person-years. Similarly, nonfinancial coordination of care actions were not very frequent with rates of these equaling once per 4 to 5 person-years, and financial coordination of care rates at once every 5 person-years for fumarates and up to once every 27.7 person-years for teriflunomide.

Overall, more pharmacist actions were performed for patients with impacted productivity, indicating that health-system specialty pharmacies can better guide their staffing initiatives by anticipating that these patients may require more education or safety monitoring interventions from their pharmacist.

Notably, the study authors acknowledged that the landscape of brand versus generic DMTs is evolving, potentially foreshadowing a higher need for financial coordination actions from pharmacy teams. The first generic fumarate was approved and launched during the study period, which could explain why this study found that the rates for financial coordination actions were much higher for fumarates than any other DMT class.

> "If we could expand this standardization as an industry, we could better compare practice models and more effectively use data to build best practices in caring for patients on DMT."

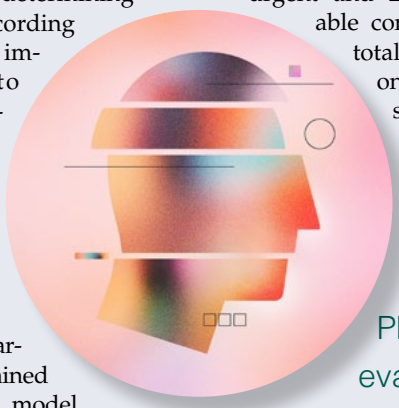
The study is the first to successfully standardize patient-reported outcome assessments across all sites, which Zuckerman noted is a significant achievement. "If we could expand this standardization as an industry, we could better compare practice models and more effectively use data to build best practices in caring for patients on DMT," Zuckerman said. If future research identifies which interventions are most impactful, health-system specialty pharmacy can focus on standardizing them profession-wide. ■

Pharmacists take active role in setting up pharmacogenomics programs

Olunife Akinmolayan, PharmD

A recent report published online July 21, 2023, in the *American Journal of Health-System Pharmacy* highlighted what it takes to put a pharmacist-driven pharmacogenomics model into practice.

The aim of the report by Mitaly and colleagues was to give pharmacy leadership an idea of what's needed to create a pharmacogenomics program led by a pharmacist. A Mayo Clinic model created a process for pharmacists to interpret pharmacogenomics results and provide electronic consults to providers while determining staffing needs. According to the authors, an important factor to consider when implementing any model is the expected patient volume, "as this greatly impacts estimated hiring needs."



A total of 395 pharmacists were trained using this program model, also known as the Mayo Clinic experience. Pharmacists completed over 2,500 e-consults with an average time spent per consult of around 24 minutes. The pharmacist's time was self-documented and was a requirement of consultation completion. Over the course of 11 months, the average number of e-consults per pharmacist was 7 with the most common gene pair for semi-urgent consultation being *CYP2C19*-clopidogrel.

To put this model into practice, the clinic used biobank samples from the RIGHT 10K Study to get pharmacogenomic results, which sequenced 77 genes from 10,077 patients making it easier to determine which consults were deemed semi-urgent and clinically actionable. Semi-urgent phenotypes were defined as those with the potential to cause serious harm while clinically actionable phenotypes were defined as those with the potential to affect the risk of adverse drug reactions or drug therapy effectiveness.

Each pharmacist had 5 days to complete a clinically actionable consult and 48 hours to complete a semi-urgent consult. Over the course of the study, there were a total of 61 semi-urgent and 2,782 clinically actionable consults completed. The total amount of time spent on completing all consults was 1,159 hours over the course of the entire study.

> Pharmacy leadership will need to evaluate how to overcome common program barriers including lack of financial resources, infrastructure, and staff to provide services.

Training the trainer

Typically, the interpretation of pharmacogenomic results is completed by a pharmacogenomic pharmacist, but new models can open the door to training more pharmacists to provide these services in multiple practice settings.

Pharmacogenomic pharmacists developed a quick reference guide and a series of competency modules to make training of the trainer a more structured process. The Mayo Clinic experience offers a 16-hour continuing education pharmacogenomics online certification course based on lessons learned and training activities.

An effective training experience can be created in other institutions by using an internal resource that provides specific recommendations for guidelines based on pertinent gene–drug pairs, supported by routine updates and reevaluation, according to study authors.

The authors go on to say that pharmacy leadership will need to evaluate how to overcome common program barriers including lack of financial resources, infrastructure, and staff to provide services. Although the model outlined in the report is better suited for "institutions looking to expand pharmacogenomics implementation system-wide," the authors said there are still many takeaways for various interested institutions who are looking to start programs.

Tailored response

"[Pharmacists'] knowledge of pharmacogenomics impacts patient medications and adeptness in offering alternative therapies consistent with patient needs and have made them a ready resource in clinical application of the science," said study authors.

Delivery of personalized health care is not a new concept, but the role of the most accessible health care provider—the pharmacist—is evolving rapidly. Pharmacists are well known as medication experts with backgrounds in pharmacokinetics, pharmacodynamics, and now pharmacogenomics. Pharmacists can add more value to the health care team by increasing communication with a patient's primary care provider. ■

A minute with ...

Elizabeth Yett, PharmD, BCACP, TTS, clinical assistant professor, University of Texas at Tyler, and clinical pharmacist, UT Health East Texas Tyler Cardiovascular Consultants, Tyler, TX

Member since 2014

"Against almost everyone's advice, I joined and was active in almost every student organization while in pharmacy school. I did not know yet what I wanted to do as a pharmacist, but I did know I did not feel like I fit in with my heavily inpatient-focused colleagues. When I decided to focus on community pharmacy as a PGY-1 and ambulatory care and academia as a PGY-2, I realized APhA was the right place for me all along!

As a new practitioner, I have been involved in the Preceptor Special Interest Group (SIG), am the co-advisor for our school's APhA–ASP chapter, and attended my first APhA Annual Meeting & Exposition in Spring 2022. I now practice in a cardiology clinic and encourage any of my students with an interest in outpatient pharmacy to get involved and stay involved in APhA. I am proud to be a part of this group of pharmacists with a collective desire to optimize medication use and health for all."

What excites you about the profession of pharmacy?

I spent a lot of time with the president of our student group over this past year. This student pharmacist displayed true joy and perseverance in organizing, planning, and hosting events to benefit her community, her classmates, and her patients.

That is what excites me about pharmacy—students who demonstrate an understanding of their professional identity as a pharmacist and recognize there is more to the profession than good grades and an interest in working in health care. Joining in their excitement and dedication to represent all of us for all of pharmacy is what encourages me in my own career.

How has APhA helped you establish meaningful connections?

My involvement in the Preceptor SIG was one of the first experiences I had as part of a national organization. It was the perfect group of passionate, engaged, and enthusiastic pharmacists and preceptors who helped me start building my network as a new practitioner.

We each had different practice sites and job responsibilities, but ultimately wanted to provide the best resources for other preceptors and to our students.

Can you share a meaningful story about a time you interacted with a patient?

I recently got back from a weeklong medical outreach trip to Guatemala. All the patients there speak Spanish or a local indigenous language and have a low health literacy. I got to be the "pharmacist in charge" of our makeshift pharmacy. I counseled each member of the family when they would come pick up their prescriptions.

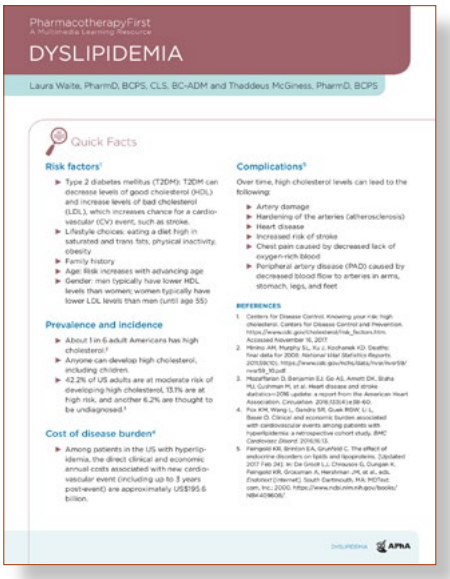
I am not fluent in Spanish but quickly settled into my counseling routine with the help of the Guatemalan experts and my APhA book, *Essential Spanish for Pharmacy.* One family included many small children who each needed ibuprofen and antibiotics. When the last child came through, the mother handed me a beautiful drawing of a bird that the children had colored. They had written "gracias" and "tancks"—the best interpretation of "thanks" I've ever seen. The gratitude they showed is universal in any language, and truly made me appreciate the impact we can have as pharmacists, no matter the setting.

How does APhA help you thrive in your everyday practice?

It is a seemingly simple thing, but when the "APhA's *Pharmacy Today*" email arrives in my inbox, it always makes me feel more prepared to take on the day.

Whether I need to catch up on CE hours, cannot remember the latest change in COVID-19 vaccine schedules, or seek guidance in implementing tobacco cessation services at my practice site – I'm confident that I have a great place to start at APhA. ■

Did you know?


PharmacotherapyFirst
A Multimedia Learning Resource
DYSLIPIDEMIA
Laura Waite, PharmD, BCPS, CLS, BC-ADM and Thaddeus McGinness, PharmD, BCPS
Quick Facts
Risk factors[1]
Type 2 diabetes mellitus (T2DM): T2DM can decrease levels of good cholesterol (HDL) and increase levels of bad cholesterol (LDL), which increases chance for a cardiovascular (CV) event, such as stroke.
Lifestyle choices: eating a diet high in saturated and trans fats, physical inactivity, obesity
Family history
Age: Risk increases with advancing age
Gender: men typically have lower HDL levels than women; women typically have lower LDL levels than men (until age 55)
Prevalence and incidence
About 1 in 6 adult Americans has high cholesterol.[2]
Anyone can develop high cholesterol, including children.
42.2% of US adults are at moderate risk of developing high cholesterol, 13.1% are at high risk, and another 6.2% are thought to be undiagnosed.[3]
Cost of disease burden[4]
Among patients in the US with hyperlipidemia, the direct clinical and economic annual costs associated with new cardiovascular event (including up to 3 years post-event) are approximately US$195.6 billion.
Complications[5]
Over time, high cholesterol levels can lead to the following:
Artery damage
Hardening of the arteries (atherosclerosis)
Heart disease
Increased risk of stroke
Chest pain caused by decreased lack of oxygen-rich blood
Peripheral artery disease (PAD) caused by decreased blood flow to arteries in arms, stomach, legs, and feet
REFERENCES
APhA

Pharmacotherapy First is a unique, digital-only, peer-reviewed resource focused on disease state management and patient care. Learning therapeutics is more than memorization and cramming for exams. This innovative tool is designed to teach therapeutics to the modern learner by incorporating concise evidence-based content, assessment tools, and instructor resources.

A complementary feature of Case-Based Learning contains

- Mini cases with questions
- Cases following steps of the Pharmacists' Patient Care Process
- Detailed patient case with expert SOAP note and justification for assessment and plan

The goal of PharmacotherapyFirst is to help learners—students and practitioners alike—expand their knowledge and to help instructors facilitate the process. Please see apha.us/PharmacotherapyFirstDyslipidemia to preview PharmacotherapyFirst. ■

Practice Resources

Pulse On Practice & Policy Open Forum

As the voice of pharmacy, APhA's monthly Pulse on Practice and Policy Open Forum Series creates a platform where all of pharmacy can come together to share perspectives and be informed of key practices and policies impacting the profession. Please join us each month as we welcome pharmacy leaders who will cover the latest practice and policy topics and what they mean for you, your practice, and your patients.

This open forum series will be conducted the second Thursday of each month from 1:00 pm to 2:00 pm ET.

Each open forum will be moderated by APhA President Valerie Prince. We welcome all of pharmacy to join us for the upcoming live webinars using the registration links at www.pharmacist.com/Practice/Practice-Resources/Pulse-On-Practice-Policy. ■

Get involved in APhA

Compounding SIG

The mission of the APhA–APPM Compounding Special Interest Group (SIG) is to provide a professional network for compounding pharmacists and student pharmacists. The Compounding SIG focuses on education, communication, collaboration, advocacy, and sharing of ideas in compounding pharmacy practice. "I am immensely proud to be a part of the Compounding SIG, a group of dedicated experts at the forefront of a vital and historic pharmacy practice," said Natalie Young, PharmD, FACVP, at Brava Care, in Raleigh, NC, and SIG Coordinator. "The intricacies involved in delivering personalized medication solutions tailored to individual patient needs are not challenges any professional should face alone. Our group provides a platform for members to share insights, refine practices, and collaborate with esteemed colleagues."

Interested in getting involved in the Compounding SIG? Visit apha.us/CompoundingSIG to learn more. ■

A joint effort: Cannabis update for pharmacists

Mark Garofoli, PharmD, MBA, BCGP, CPE, CTTS, WVU School of Pharmacy, Morgantown, WV

It's natural! Yet, as with any substance, chemical, and medication on this planet, it comes with its own baggage. Hence the circular and polarized conversations emanating across our country and globe. Here we will clear the smoke by diving deeper into the weeds of all things cannabis and cannabinoids to immediately impact your patient care and communities.

Words matter

As is the case with so very many health care–related terms, our society can benefit from a recalibration of cannabis and cannabinoid terminology. Even though the word "opiate" refers to morphine, codeine, or thebaine, the term is commonly used when referring to other opioids such as hydrocodone, oxycodone, fentanyl, and even diacetylmorphine (i.e., heroin). Likewise, when one intends to discuss cannabidiol (CBD), yet uses the word "marijuana"—which actually refers to all cannabis species including the plant containing the psychoactive constituent tetrahydrocannabinol (THC)—imprecise language creates confusion.

Botanical naming includes the genus of cannabis followed by the species including sativa, indica, ruderalis, and so on, even accommodating for hybrids. To best facilitate conversations regarding cannabis, refer to the terminology with its respective description in Table 1.[1]

The next distinction includes "cannabis-based medication" in comparison to "medical cannabis." Cannabis-based medication, also referred to as cannabis-derived medications, includes registered products with defined and/or standardized cannabinoid content, such as FDA-approved prescription cannabinoids which will be discussed later. Medical cannabis includes the cannabis plant, flowers, buds, leaves, and any extracts or other

Table 1. Terminology

Terminology	Species
Hemp	Sativa
Marijuana	All species
Weed	All species
THC	Indica and ruderalis (not sativa)
Cannabidiol (CBD)	Sativa
Cannabinoids	All species
Semisynthetic cannabinoids	Derived from CBD within sativa

Learning objectives

At the conclusion of this knowledge-based activity, the pharmacist will be able to

- Compare and contrast current legislation around cannabis at the federal and state levels.
- Interpret clinical studies discussing the efficacy of cannabis for treating various syndromes.
- Discuss safety concerns with cannabis, including adverse effects, drug–drug and drug–disease interactions.
- Identify resources about cannabis available for pharmacists and patients.

Preassessment questions

Before participating in this activity, test your knowledge by answering the following questions. These questions will also be part of the CPE assessment.

1. **What is the term for registered cannabis products with defined and standardized cannabinoid content (e.g., FDA-approved cannabinoids)?**
   a. Cannabis-based medication
   b. Hemp
   c. Medical cannabis
   d. Medical marijuana

2. **Hemp is legally allowed to have less than what concentration of THC in the United States?**
   a. 0.01% THC
   b. 0.10% THC
   c. 0.03% THC
   d. 0.30% THC

3. **According to a major American Heart Association 2020 *Circulation* review, which medical conditions have known cannabinoid utilization based on conclusive/substantial evidence?**
   a. Anxiety, depression, obesity, diabetes mellitus, Parkinson's, and sleep
   b. Long-term opioid utilization, dystonia, and glaucoma
   c. Epilepsy, multiple sclerosis, nausea/vomiting, and pain
   d. Glaucoma, multiple sclerosis, nausea/vomiting, and pain

formulations derived directly from the cannabis plant to be used for medical reasons.

At the corner of botany and chemistry

Cannabinoids are most commonly found in cannabis (genus) plants including cannabis sativa, cannabis indica, cannabis ruderalis, and various hybrids. Cannabis sativa plants tower higher than other cannabis species and have main leaves with nine smaller leaves. Cannabis indica plants are wider than other cannabis plant species with a medium height and main leaves which include smaller leaves. Cannabis ruderalis plants are the shortest of the core cannabis species, along with being more narrow, and have main leaves with only four smaller leaves. Cannabinoids are also found in more plants than merely cannabis, including some common landscaping plants such as the rhododendron (e.g., the West Virginia state flower).[2–3]

Chemically speaking, a cannabinoid is an oxygenated 21 carbon atoms skeleton, with a common fragment that includes the dibenzopyran ring and a hydrophobic alkyl chain, or in other words, an isopropenyl section, a resorcinol core, and an alkyl side chain. Another manner of describing the chemical structure is as a dibenzopyran ring surrounded by two "R" groups and two hydroxyl (OH) groups.[4]

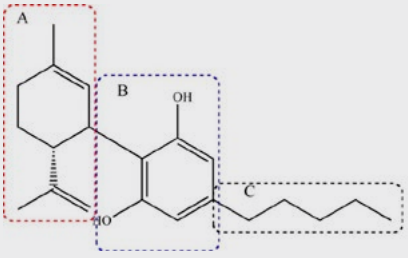
Cannabis plants can yield industrial products more robustly than other cash crops such as cotton. For instance, cannabis plants can grow to maturity in approximately 4 months compared to 20 years for some trees yielding fiber. Cannabis plant meat and cake can be utilized as food; shells can be utilized as flour and baking products; oils as personal care, cooking, fuel, and paint products; fiber as fabric, insulation, carpeting, and paneling; and hurds as fiber board, compost, mortar, paper filler, among other utilizations (Figure 1).[5]

History, taxes, and regulation

Cannabis plants have naturally existed and been cultivated for centuries. The American history of cannabis began the moment our ancestors arrived on the continent. Presidents Washington, Jefferson, and Adams were known growers of cannabis sativa (i.e., hemp), which was also legal tender in Pennsylvania, Virginia, and Maryland at those times. In the seventeenth century, cannabis was found in many U.S. tinctures and medicines.

In the 1920's, 6% of all medications contained cannabis extract intended for medical use. At the same time, our southern neighboring country of Mexico and 29 of our states outlawed "marijuana." The 1937 Marihuana (not a typo) Tax Act taxed transfers of cannabis in the same

Figure 1. Cannabinoid



fashion as narcotic substances, including a $1 tax stamp for farmers to grow the plant. Prescribers and dispensers were also taxed on sales.

In 1996, California became the first state to legalize "medical marijuana." In 2014, legislatures provided DEA a one-dollar budget for federal enforcement of cannabis as a class one con-

trolled substance. The 2018 Agriculture Improvement Act (Farm Bill) allowed CBD derived from cannabis sativa to be sold legally as a cosmetic as long as the THC content was less than 0.3%.[6] In 2023, only 7 out of 50 states have not enacted some type of legislation in respect to medical or recreational cannabis.[7] The court of public opinion has witnessed the ship having already set sail. What regulation lies ahead is on the tip of everyone's tongue in many conversations across the United States.

In respect to substance regulation and net benefit or loss, Nora Volkow, MD, director of the National Institute on Drug Abuse (NIDA), said, "Legal drugs (alcohol and tobacco) offer a sobering perspective, accounting for the greatest burden of disease associated with drugs, not because they are more dangerous than illegal drugs, but because their legal status allows for more widespread exposure."[8] Drugs (collectively speaking) account for just over 100,000 related deaths annually, while alcohol-related deaths reach almost 150,000; and tobacco related deaths resonate at 500,000 annually.[9]

Beyond regulation lies taxation, which is not unique to cannabis plants and products. On one side of the coin, medical and recreational cannabis has facilitated millions of dollars of revenue for states. On the other side of the coin, no state has yielded more than 1% of a respective state budget from any form of cannabis to date.[10] Same verifiable information, different viewpoints.

Endocannabinoid system

Regardless of cannabis regulation and tax status, education on the endocannabinoid system (ECS) is foundational to a better understanding of our human bodies, whether initiated at the middle school level in health classes where other body systems are introduced, or at the graduate level. The ECS interacts with other body systems, just as other bodies systems overlap each other and affect the body. The ECS most commonly interacts and has overarching effects with the immune system and central nervous system (CNS), two body systems that frequently interact with other body systems as well.

Table 2. Cannabinoid receptors

Receptor	Description
CB1	Primarily CNS (analgesia, euphoria, and anticonvulsive)
CB2	Primarily in immune system and GI tract
TRPV1	Transient receptor potential subfamily V member 1
GCPRs	G-coupled protein receptors
PPARs	Peroxisome proliferator-activated receptors
FABPs	Fatty acid binding proteins

The ECS involves many receptors and enzymes, which ultimately are strategic targets for cannabinoid pipeline pharmacotherapy. The most commonly known cannabinoid receptors are CB1 and CB2, yet there are many more including TRPV1, CGPRs, PPARs, and FABPs, as described in Table 2.[12–14] CB1 receptors are primarily in the CNS, which can be recalled by realizing that the number one digit is relatively narrow, just as the CNS is in the central narrow part of the human body, whereas CB2 receptors are typically in the periphery, just as the number two digit is wider. There are four main ECS enzymes including two "building" biosynthesis enzymes known as DAGL-alpha and NAPE-PLD, along with two degradation enzymes known as MAGL and FAAH, as described in Table 3.[13,15,16]

The two primary endocannabinoids in our human bodies are anandamide (AEA) and 2-Arachidonylglyercol (2-AG). Anandamide's name is derived from ananda which is Sanskrit for "bliss, joy, delight" and amide, meaning nitrogen-containing. Arachidonylglyercol is a structural combination of arachidonic acid and diacylglycerol and acts as a CB1 and CB2 agonist.[11]

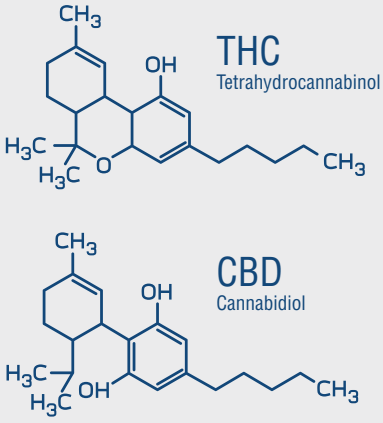
Table 3. ECS enzymes

Enzyme	Description
DAGL-alpha	Biosynthesis of DAG → 2-AG
MAGL	Degradation of 2-AG to arachidonic acid and glycerol
NAPE-PLD	Biosynthesis of NAPE → AEA
FAAH	Degradation of AEA to arachidonic acid and ethanolamine

All natural cannabinoids

Phytocannabinoids are those cannabinoids formed within plants including cannabigerolic acid (CBGA), cannabigerol (CBG), cannabidiolic acid (CBDA), CBD, tetrahydrocannabinolic acid (THCA), THC, and cannabinol (CBN). CBGA is the main origin of phytocannabinoid; all other main cannabinoids are directly or indirectly developed in the plant from it. CBGA becomes CBG, along with being transformed into CBDA and THCA. THCA then becomes THC and CBN, while CBDA naturally transforms to CBD in the plant.[12]

Figure 2. THC and CBD structures



The two primary and most well-known phytocannabinoids are THC and CBD, with relatively similar two-dimensional chemical structures, only differing in that THC contains a cyclic ring and CBD contains a hydroxyl group (Figure 2).[13]

THC is a CB1 partial agonist and CB2 partial agonist. CBD is a CB1 antagonist, CB2 negative allosteric modulator, along with being an agonist at the transient receptor potential cation channel subfamily V member 1 (TRPV1) and serotonin 1A (5-HT_{1A}) receptors.[14] Antagonists physically

block access of an agonist to a receptor, whereas negative allosteric modulators bind at a secondary receptor site to diminish agonist effects. Thus, THC and CBD have relatively opposite mechanisms of action at the CB1 and CB2 receptors, naturally translating to differing effects.

Cannabinoid products

Cannabinoid products are typically extracted from cannabis plants with the utilization of solvents such as ethanol, butane, propane, hexane, petroleum ether, methyl tertbutyl ether, diethyl ether, carbon dioxide (CO_2), and olive oil. Some solvent extraction methods such as the utilization of ethanol and hydrocarbon processing can result in products containing undesired ingredients of remaining alcohol or heat byproducts, respectively. Product processing involving supercritical CO_2 involves simply pushing CO_2 through cannabis plant material to extract specific cannabinoids, which is similar to, and preferred, pharmaceutical product processing methods.[15]

THC products

THC products are available in different formulations including those meant for inhalation and those meant for oral consumption. Inhalation formulations include joints, blunts, and spliffs. Joints are created by placing cannabis inside thin paper that is then rolled and sealed. Blunts are rolled tobacco leaves with cannabis inside. Spliffs mix tobacco and cannabis together within a rolling paper. Hashish is isolated marijuana resin typically in a formulation of dark colored gummy balls. Hash oil is attained through a process of first boiling the cannabis plant, then filtering out undesired solids, and vaporizing the remaining liquid.[16,17]

Perhaps the most important patient safety aspect, to avoid overuse, is to educate those choosing to use a THC oral formulation product that the onset of effects should be expected to be significantly delayed (i.e., one hour compared to seconds or minutes), compared with inhalation products.

CBD products

CBD products are available in different formulations including those meant for inhalation, oral consumption, and topical utilization. Inhalation formulations (e.g., smoking, vaping, hookah) have an immediate onset with peak effects dissipating within 30 minutes. Oral consumption formulations (e.g., edibles, capsules, tablets, oils, tinctures, sprays) have an onset of approximately 15 minutes (as seen in sublingual sprays) and 1 to 6 hours for other oral formulations. Oral formulations are recommended to be taken with water after meals as food delays the absorption and fat increases peak concentrations.

Topical formulations (e.g., creams, gels, ointments) have very low human skin absorption, with CBD having relatively higher skin absorption than THC. Higher concentration CBD topical products and applying topical CBD products generously can aid in absorption, and patients must remain wary of overuse of a product.[24,25] As is the case with THC products, an important patient safety aspect is to educate those choosing to use a CBD oral formulation product that the onset of effects will be expected to be significantly delayed compared to inhalation products.

CBD products are classified as one of three types including full spectrum, broad spectrum, and isolate as depicted in Figure 6.[18] One of the most important factors to discuss with patients is whether there is concern of a CBD product potentially including THC, in respect to employment drug screenings or tests, and general effect concerns.

Another pivotal patient care concern is CBD product labeling accuracy. A 2019 FDA study evaluated 14 CBD products and found that 71% were not within 20% of the CBD amount on the label.[19] A 2022 *Journal of Cannabis Research* study evaluated 80 CBD products and found that 46% were not within 10% of the CBD amount on the label.[20] A 2022 *JAMA* study evaluated 105 topical CBD products and found that 18% were over-labeled, 58% were under-labeled, and only 24% were accurately labeled.[21] CBD product labeling accuracy has generally improved over the last decade, yet is still not at an appreciable point considering the results of these studies.

Consumers commonly look for guidance in the decision to use a cannabinoid product and in the product selection process. *Consumer Reports* developed a 2018 guide for those deciding to purchase CBD products,[22] which can be a functional resource for patients. One of the main recommendations within that guide is to ask for lab testing results including the frequency and amount of product being tested. The New York Office of Cannabis Management developed a patient-friendly guide for CBD product discernment which includes various product testing aspects, such as concerns for contaminants (e.g., microorganisms, heavy metals, pesticides, solvents, moisture, and foreign substances). CBD products should have a certificate of analysis available which is a certified lab report that provides CBD product testing results in a manner that allows one to easily access testing result details. Certificates of analysis are typically available via a QR code on a CBD product label and will provide one with the total amount of each cannabinoid present along with any contaminants.[23]

Synthetic cannabinoids

In contrast to phytocannabinoids being produced naturally, synthetic cannabinoids are developed either chemically from scratch or semi-synthetically from phytocannabinoids (primarily CBD). Synthetic CBD derivatives include hydrogenated, dimethylheptyl, c4′-alkyl chain modifications, halogenated (Cl, Br, Fl, and I), hydroxyl, diacetylated, and quinone chemicals. Synthetic THC derivatives are categorized as first, second, or third generation. First generation THC derivatives include Sterling-Winthrop Aminoalkylindoles (WIN-X), John Williams Huffman (JWH-X), Hebrew University (HU-X), and Charles Pfizer (CP-X) chemicals. Second generation THC derivatives include alkyl, N-methylpiperidine, and benzoindole chemicals. Third generation THC derivatives include indole and indazole chemicals. Synthetic THC derivatives are often referred to by nicknames (i.e., product names) such as Scooby Snax, K2, Spice, Legal

Table 4. Types of CBD

CBD product	Cannabinoids
Full spectrum	All cannabinoids
Broad spectrum	All cannabinoids except THC
Isolate	Only CBD

Funk, Arizona, Black Mamba, Bombay Blue, Genie, Banana Ice Cream, Nuke, Krypton, and Lava Red.[24] An area for improved patient confidence in CBD and THC product safety and efficacy is a revision of the product naming process to include less puerile names.

One particular synthetic THC derivative has been increasingly observed in recent years, THC-O-acetate (pronounced "Oh," not "zero"). THC-O-acetate is developed by starting with converting CBD to Delta-8 THC and combining it with another chemical to form THC-O-acetate. The addition of acetate allows the substance to more easily cross the blood–brain barrier, and once the acetate dissipates, the remaining cannabinoid can interact with cannabinoid receptors in the brain.[25] This is the same chemical foundational effect of the addition of two acetyl groups to morphine for diacetylmorphine (i.e., heroin). Delta-8-THC is another more commonly observed synthetic cannabinoid in recent years, which involves a subtle chemical change from Delta-9-THC (a psychoactive phytocannabinoid commonly found in cannabis), as an attempt to skirt the legal system (Table 4).[26]

In contrast to controlled substance prescription product tracking, cannabis products sales have no monitoring program comparable to prescription drug monitoring programs in the United States. The concern that arises from this gap is the opportunity for bad actors to purchase the maximum allowed amount of cannabis products at a dispensary, and then go to dispensary after dispensary doing the same, which is commonly referred to as "looping."

Prescription cannabinoids

Despite the non-health care supply chain for cannabis and cannabinoid products, FDA-approved prescription cannabinoids are readily available in the United States, with some available by prescription for decades. Dronabinol is available as two synthetic THC prescription product formulations including capsules and liquid. FDA-approved for chemotherapy-induced nausea and vomiting, dronabinol also aids in treatment for anorexia. Dronabinol capsules are a controlled substance class three medication available in 2.5 mg and 5 mg doses while dronabinol liquid is a controlled substance class two medication available as a 150 mg bottle (5 mg/mL). CBD is available as an extracted CBD FDA-approved noncontrolled substance prescription product (10,000 mg bottle; 100 mg/mL) for pediatric epilepsy conditions.[27]

Cannabinoid utilizations

An initial patient care concern regarding the utilization of nonprescription cannabis and cannabinoid products is the determination of an appropriate dosage. Regardless of the methodology deployed in these scenarios, one should always recall the patient-specific factors that go into general dosage determination efforts including body weight, age, condition severity, other medical conditions (e.g., hepatic, renal, etc.), similar pharmaceutical product dosages, formulation and administration route, and product potency.

Given the reality that certain cannabinoids are FDA-approved for certain medical conditions, it seems only natural to consider that cannabinoids can be potentially effective for various medical conditions beyond those already within FDA labeling. There are numerous studies venturing into the clinical applicability of cannabis and cannabinoids (primarily THC and/or CBD) worthy of discussion.

A 2020 *Circulation* article reviewed many studies ascertaining the clinical utilization of cannabis and cannabinoids in various common medical conditions. This prominent review by the American Heart Association discerned medical conditions warranting the utilization of cannabis and cannabinoids into three categories including inconclusive evidence (i.e., lacking randomized controlled trials), possible safety and efficacy (i.e., moderate evidence), and known safety and efficacy (i.e., conclusive and substantial evidence). The medical conditions identified as having inconclusive evidence included Alzheimer disease, anxiety, depression, tumors, Crohn's, ulcerative colitis, heart failure, ischemia, hepatitis C, Huntington disease, metabolic syndrome, obesity, diabetes mellitus, Parkinson's, and sleep. The medical conditions identified as having possible safety and efficacy included long-term opioid utilization, dystonia, and glaucoma. The medical conditions identified as having known safety and efficacy included pain (e.g., neuropathic pain, fibromyalgia, cancer), cachexia, nausea and vomiting, multiple sclerosis (MS), and epilepsy.[28]

In respect to MS, a 2018 review of 32 studies concluded that there was sufficient evidence that cannabinoids may be effective for symptoms of pain and/or spasticity in MS.[29] Regarding epilepsy, a 2018 review of 36 studies concluded that CBD was more effective than placebo at reducing seizure frequency by over 50% with a number needed to treat of 8, while also being more effective than placebo at achieving complete seizure freedom.[30]

Perhaps one of the most discussed potential clinical utilizations of cannabis and cannabinoids in present day is pain management. A 2018 *Cochrane Review* of 16 studies, including a total of 1,750 participants with painful conditions, had four primary outcomes: participant-reported pain relief of 50% or greater; patient global impression of

change much or very much improved; withdrawals due to adverse events; serious adverse events. Results illustrated that cannabis-based medicines may increase the number of people achieving 50% or greater pain relief compared with placebo. There was low quality evidence for improvement in patient global impression of change with cannabis; more participants withdrew from the studies due to adverse events with cannabis-based medicines than with placebo; and there was not enough evidence to determine if cannabis-based medicines increase the frequency of serious adverse events compared with placebo. The study authors concluded that the potential benefits of cannabis-based medicine in chronic neuropathic pain might be outweighed by potential harms; there is a lack of good evidence that any cannabis-derived product works for any chronic neuropathic pain; and that all cannabis-based medicines pooled together were better than placebo for substantial and moderate pain relief, global improvement, pain intensity, sleep problems, and psychological distress.[31]

Patient concerns

Drug–drug interactions are one of the main patient care concerns regarding cannabis and cannabinoids use. Cannabinoids have hundreds of drug–drug interactions and, as is the case with all medications, determining clinical significance is paramount to patient care. When a health care professional attempts to identify and discern drug–drug interactions for a patient utilizing cannabis or cannabinoids, it can be beneficial to proceed—as is a best practice for any medication review—by utilizing online medication databases to check respective drug interactions. Some databases allow simple keyword searches of "CBD" or "THC" into the application, while others only enable the utilization of prescription cannabinoids to be entered into the application. Either way, one should always identify and mitigate any and all cannabinoids drug–drug interactions for patients.

The determination of clinical significance for cannabis and cannabinoid drug–drug interactions is often as arbitrary as any other drug–drug interaction determination. Although drug–drug interactions will be highlighted by various database reports, the true art is in the deciphering of clinical significance for any particular patient. CBD is a CYP-450 substrate for the 2C19 and 3A4 enzymes, while also being an inhibitor of 2C9, 2C19, 2D6, and 3A4. THC is a CYP-450 substrate for the 2C9 and 3A4 enzymes, while also being an inhibitor of 2C9 and 2D6.[38–40] Studies of THC, CBD, and CBN inhibition and induction of major human CYP-450 isoforms generally reflect a low risk of clinically significant drug interactions with most use, but specific human data are lacking. Smoking cannabis induces CYP1A2, although the role of cannabinoids specifically in eliciting this effect is questionable.[40]

Additionally, cannabinoids are universally highly protein-bound, which provides another avenue for potential drug–drug interaction concerns.[32–33] However, not every single medication that is a substrate inhibitor or inducer of those CYP-450 enzymes or is highly protein-bound will yield a clinically significant change in serum concentrations or effects. Narrow therapeutic index medications stand out as key medications of concern for any cannabinoid drug–drug interactions to review with a relatively keener eye given the nature of their respective dosage concerns. THC also exhibits potential sedative drug–drug interaction concerns given its respective cognitive effects. Along those same lines, one should evaluate the potential overlapping effects of cannabis and cannabinoid utilization for patients with medical conditions that involve the same body systems in which cannabis and cannabinoids exhibit their effects. Thus, patients with any neurological conditions (e.g., epilepsy, depression, anxiety, etc.), inflammatory conditions (e.g., irritable bowel syndrome, arthritis, etc.), or immunological conditions should be carefully reviewed when considering cannabis or cannabinoid utilization.[41]

A commonly referred to drug–drug interaction in this realm is warfarin and cannabis (when the drug is smoked). Although there are not many case reports, one case report illustrated that cannabis may increase warfarin's anticoagulant effect by inhibiting its metabolism, and to a lesser extent, displacing warfarin from protein-binding sites. This single case study involved a patient with an evolving INR level of 10.41 upon initial hospital admission, which decreased to 1.8 the next day. Upon the patient's return to the hospital 15 days' post-discharge, his INR was 11.55. The patient stated that in the time in between hospital stays, he smoked cannabis due to his depression. After consultation with a pharmacist, the patient ceased smoking cannabis, and his INR remained relatively stable.[34]

As with all medications and substances, another main patient care

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concern when cannabis and cannabinoids are being utilized is adverse drug events. Prescription dronabinol (THC) products include labeling stating possible acute adverse effects of mood changes, delusions, tachycardia, memory loss, feelings of unreality, and possible long-term depression and anxiety. The prescription CBD product includes labeling stating possible acute adverse effects of tiredness or—conversely—insomnia, decreased appetite, diarrhea, and asthenia, among others.[35]

Cannabis products resonate with the most concerning potential effects including eventual cannabis use disorder, abnormal brain development, progression to utilization of other substances (i.e., gateway drug), schizophrenia, depression, anxiety, diminished life achievement, chronic bronchitis symptoms, lung cancer (seen with inhalation products), and indirect motor vehicle accidents, which all can increase in occurrence and intensity with escalating doses.[35]

A unique condition observed particularly in recent years is cannabinoid hyperemesis syndrome (CHS), which is a condition in which one experiences cyclical nausea, vomiting, and abdominal pain after cannabis utilization. CHS may result from chronic overstimulation of CB1, CB2, and TRPV1 receptors. CHS is associated with a peculiar bathing behavior of repeated and prolonged hot baths or showers. CHS relief is typically attained by a sustained cessation of cannabis utilization although multiple treatments have been studied including serotonin antagonists, tricyclic antidepressants, anticholinergics, and capsaicin.[36]

Paracelsus, known as the father of toxicology, stated "sola dosis facit venenum," which translated from Latin means "the dose makes a poison."[37] THC product potency, detected in confiscated samples, steadily increased from the 1980's to the past decade—3% to 12%, respectively—which significantly raises concerns while also explaining the almost paralleled increase in emergency department visits due to cannabis utilization.[46]

A path forward: Perception and education are key

There is an inverse correlation between cannabis utilization and its respective perception of risk among adolescents: when perceived risk is down, utilization is up, and vice versa. Thus, as with any patient care or public health effort, education is key in forging perception,[38] along with having the most appropriate resources.

There needs to be a clear distinction between prescription cannabinoids versus other cannabinoid products versus cannabis itself. Current (and future) FDA-approved cannabinoids will safely treat medical conditions, while the market for other cannabinoid products hopefully improves labeling accuracy. Cannabis utilization, particularly with ever products entering the market with increasing potency, has been associated with substantial adverse effects. Almost all states have some form of cannabis or cannabinoid legislation differing from prohibition. It is incumbent on health care professionals, particularly pharmacists as medication experts, to educate our public in unbiased manners to steer public perceptions. As Volkow stated, "The effects of a drug (legal or illegal) on individual health are determined not only by its pharmacologic properties but also by its availability and social acceptability." Our public needs our pharmacist knowledge and skills more than ever to avoid getting lost in the weeds.

Resources for cannabis and cannabinoid health care–related concerns

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CPE information

To obtain 1 hour of CPE credit for this activity, complete the CPE exam and submit it online at www.pharmacist.com/education. A Statement of Credit will be awarded for a passing grade of 70% or better. You have two opportunities to successfully complete the CPE exam. Pharmacists and technicians who successfully complete this activity before November 1, 2026, can receive credit. Your Statement of Credit will be available online immediately upon successful completion of the CPE exam.

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CPE assessment

This assessment must be taken online; please see "CPE information" in the sidebar on the previous page for further instructions. The online system will present these questions in random order to help reinforce the learning opportunity.

There is only one correct answer to each question.

1. **What is the term for registered cannabis products with defined and standardized cannabinoid content (e.g., FDA-approved cannabinoids)?**
   a. Cannabis-based medication
   b. Hemp
   c. Medical cannabis
   d. Medical marijuana

2. **Hemp is legally allowed to have less than what concentration of THC in the United States?**
   a. 0.01% THC
   b. 0.10% THC
   c. 0.03% THC
   d. 0.30% THC

3. **According to a major American Heart Association 2020 Circulation review, which medical conditions have known cannabinoid utilization based on conclusive/substantial evidence?**
   a. Anxiety, depression, obesity, diabetes mellitus, Parkinson's, and sleep
   b. Long-term opioid utilization, dystonia, and glaucoma
   c. Epilepsy, multiple sclerosis, nausea/vomiting, and pain
   d. Glaucoma, multiple sclerosis, nausea/vomiting, and pain

4. **A well-known 2018 review of 32 studies involving cannabinoid utilization in MS concluded that cannabinoids**
   a. May be effective for symptoms of MS pain and/or spasticity
   b. May be effective only for the MS symptom of pain
   c. May be effective only for the MS symptom of spasticity
   d. Is not effective for symptoms of MS pain nor spasticity

5. **A well-known 2018 review of 36 CBD utilization studies in epilepsy concluded that**
   a. CBD was more effective than placebo at reducing seizure frequency by at least 50% and provided complete seizure freedom.
   b. THC was more effective than placebo at reducing seizure frequency by at least 50% and provided complete seizure freedom.
   c. CBD was less effective than placebo at reducing seizure frequency by at least 50% and provided complete seizure freedom.
   d. THC was less effective than placebo at reducing seizure frequency by at least 50% and provided complete seizure freedom.

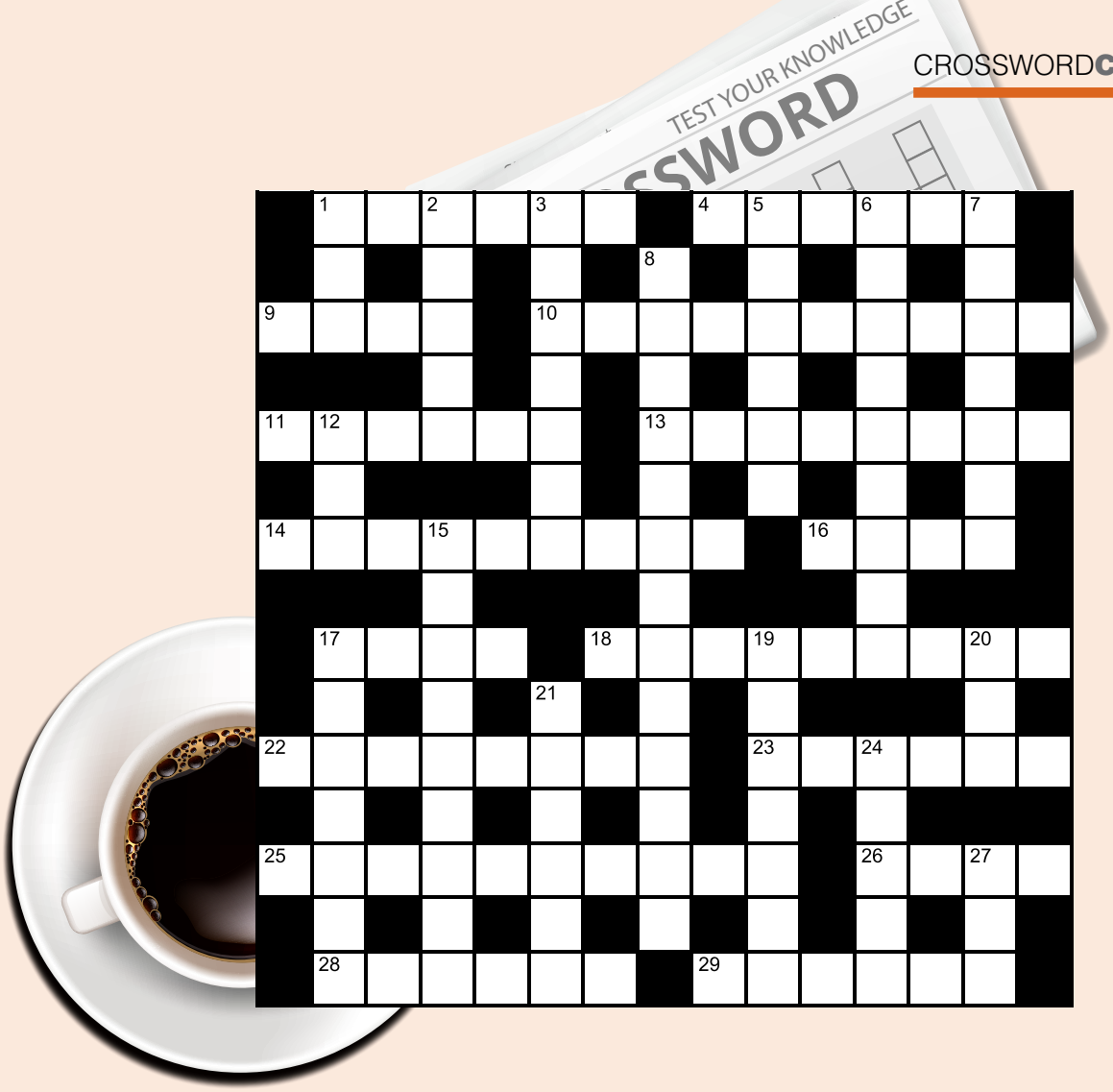
6. **Which of the following is available as an FDA-approved synthetic oral capsule THC medication for chemotherapy-induced nausea and vomiting?**
   a. Cannabidiol
   b. Dronabinol
   c. Tetrahydrocannabinol
   d. Tetrahydrocannabis

7. **Which of the following is available as an FDA-approved extracted oral liquid medication for various specific pediatric seizure conditions?**
   a. Cannabidiol
   b. Dronabinol
   c. Tetrahydrocannabinol
   d. Tetrahydrocannabis

8. **Which of the following CYP-450 enzymes have shown in vitro interactions with cannabinoids?**
   a. 2B6, 2C9, and 2C19
   b. 2B6, 2C9, 2C19, and 2E1
   c. 2C9, 2C19, 2D6, and 2E1
   d. 2C9, 2C19, 2D6, and 3A4

9. **What is the typical onset of effects for edible cannabis products?**
   a. 5 minutes
   b. 10 minutes
   c. 20 minutes
   d. 60 minutes

10. **Which of the following is a textbook resource for evidence-based cannabis information for health care professionals?**
    a. Cannabis in Medicine
    b. Cannabis Dictionary
    c. Cannabinoid Medications
    d. Cannabinoid Substances



Across

1 Dermatitis often treated with corticosteroids
4 Alias
9 The "O" in P.O.
10 Often a consequence of long shifts
11 Referring to the kidney
13 These patients often need the most care
14 Pharmacists can make pediatric medicines more _____by adding flavors
16 Short comedy sketch
17 The proper ____ needle is critical for injections
18 CNS stimulant that can be used to prevent low blood pressure during anesthesia
22 Exceptional rating
23 Error allowance
25 Amphetamines, caffeine, and nicotine, for example
26 This and exercise are important for a healthy lifestyle
28 _____ tunnel syndrome
29 Opposite of cancerous

Down

1 Common site of infections for infants
2 Nada
3 Plasma cell cancer
5 Common adverse effect of many medications
6 Faultfinder extraordinaire
7 Horizon happening
8 OTC decongestant determined by FDA to be ineffective
12 Govt. agency that regulates pesticides
15 Neuropathologist who identified "presenile dementia"
17 Nerves that run from the lower back down each leg
19 All together
20 NIH org. devoted to cancer research
21 And others, in Latin
24 Forearm bones
27 Very long time

Solution is available online at pharmacytoday.org.