Chairman’s Note

Pharmacists Support Women’s Health

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PHARMACY TIMES®

PHARMACISTS CAN HELP PROVIDE OPTIMAL HEALTH CARE TO WOMEN to improve the quality of their lives by offering advice and education on important areas. Among these are cancer, chronic respiratory disease, depression, diabetes, heart disease, HIV/AIDS, pregnancy, and smoking.

In this issue of Pharmacy Times®, we focus on women’s health, including the cover feature article by Kathleen Kenny, PharmD, RPh, that explores how women may experience heart disease differently than men. Although heart disease is the leading cause of death for both men and women, she reports that just 56% of women recognize that it can be as deadly for them as it can be for men, according to the CDC.1 Kenny provides information on risk factors for the disease and how to help patients take steps to maintain cardiovascular health.

In terms of family planning, pharmacists can help women take control of their reproductive health. Ashley Walsh, PharmD, writes in this issue’s Patient Focus article that pharmacists ready to exercise prescriptive authority have the education and tools to successfully provide birth control to women. In fact, 49 states have awarded some form of prescriptive authority to pharmacists with variable prescriber oversight and restrictions.2

For more essential and timely coverage of women’s health issues, visit the resource center on the Pharmacy Times® website (https://www.pharmacytimes.com/clinical/womens-health).

Meanwhile, on the COVID-19 front, though infection rates are still high in many countries, notably India and Malaysia, there is light at the end of the tunnel in the United States. About half of all US adults had been vaccinated as of May 25, 2021, according to the Biden administration.3 Nearly 130 million adults have completed their COVID-19 vaccine regimens, and another 700 million vaccine doses are in the distribution pipeline, according to the CDC.4

The agency now says that “fully vaccinated people can resume activities without wearing a mask or physically distancing, except where required by federal, state, local, tribal, or territorial laws, rules, and regulations, including local business and workplace guidance.”5

Jeannette Y. Wick, MBA, RPh, FASCP, in this issue’s Rx Focus article, provides an update on the COVID-19 vaccines and urges pharmacists to expect changes related to the vaccines as new ones are approved, vial sizes change, storage conditions improve, and data sets accumulate.

We wish you a great start to summer.

Thanks for reading!

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Study: Combining Minimally Invasive Bariatric Surgery With Semaglutide Increases Weight Loss

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The Value of the Pharmacist in Supporting Patients' Health, Wellness

Postmenopausal, Vitamin D-Deficient Women May Experience More Pain After Total Knee Replacement

Identifying Causes of Pharmacist Burnout
On social media, you recently talked about the important roles pharmacists play in educating patients, especially about COVID-19 vaccines.

Ron C.: People who have gotten the vaccine should be vigilant of symptoms, the FDA and CDC say. If you received the Johnson & Johnson vaccine and develop severe headache, abdominal pain, leg pain, or shortness of breath within 3 weeks of vaccination, contact your health care provider.

Esther H.: Since pharmacists are one of the most accessible and trusted health care professionals, we can do so much to help these areas. ❤️🙏🏼😊

Tell us why you’re proud to be a pharmacist and why the profession is so important. Use #APharmacistIs on social media or email submissions to Aislinn Antrim at aantrim@pharmacytimes.com.
Editor’s Note

Social Determinants and Vulnerability Affect Health Outcomes

Post Pandemic, These Concepts Are Hitting the Mainstream in the Payer, Policymaker Environments

By Troy Trygstad, PharmD, PhD, MBA, Editor in Chief

Building Codes and Construction Innovations in many coastal communities have improved dramatically over the past few decades. From elevating living quarters above storm surge reach to strengthening structure joints with hurricane ties that withstand the most extreme forces to building with water-resistant materials, beach homes are made to survive severe weather events. Coastal communities and mortgage lenders alike also require and lobby for continued government-backed flood insurance, making it compulsory for most homeowners with residences in areas of risk.

However, not far from the coast are older structures subject to little or no code enforcement. They have scarce resources to carry out updates and are susceptible to Mother Nature’s tantrums, particularly flooding. Off-coast or inland communities in places such as the Carolinas are often economically impoverished, racially segregated, or even devastated by increasingly frequent and intense storms. These primary residences are occupied during all types of weather, with families having no other place to go. Many in these communities are also underinsured or have multigenerational ownership without a mortgage or the requirement to purchase homeowner’s insurance.

Statisticians Armed With Geo Mapping Take Notice

In the 1980s, a mix of new and old satellite capabilities gave us the Global Positioning System (GPS). This eventually enabled scientists to combine mapping and spatial capabilities with other data sets that had been digitized, such as education, income, and education. Now, by using cell-phone positioning, one’s average miles traveled can be monitored for social distancing purposes during a pandemic, for example.

People love maps, and statisticians love data. Public health officials love having the 2 blended to identify risk and risk-reduction opportunities, the ethos of public health. Knowing which areas of the country are most likely to be adversely affected as a result of a natural or unnatural disaster allows for better preparation and resource allocation, especially prior to the event occurring, so that mitigation efforts can be put into place. Responding to this need, scholars began to apply statistical models to predict human suffering and lack of resilience resulting from an event.

CDC Introduces Country to Social Vulnerability Index

The CDC/Agency for Toxic Substances and Disease Registry Social Vulnerability Index (SVI) has become the gold standard for mapping communities at risk. The SVI has 4 core components that determine risk:

- Household composition and disability (65 years or older, 17 years or younger, older than age 5 with a disability, or single-parent households)
- Housing type and transportation (crowding, group quarters, mobile homes, multi-unit structures, no vehicle)
- Minority language and status (minority and/or does not speak English well)
- Socioeconomic status (below poverty line, no high school diploma, unemployed)

Pandemic Unmasks Social Vulnerability Nationwide

The CDC has relied heavily on the SVI to aid pharmacy partners receiving

AUTHOR BIO

TROY TRYGSTAD, PHARMD, PHD, MBA, is vice president of pharmacy provider partnerships for Community Care of North Carolina, which works collaboratively with more than 2000 medical practices to serve more than 1.6 million Medicaid, Medicare, commercially insured, and uninsured patients. He received his PharmD and MBA degrees from Drake University and a PhD in pharmaceutical outcomes and policy from the University of North Carolina. He also serves on the board of directors of the American Pharmacists Association Foundation and the Pharmacy Quality Alliance.
COVID-19 vaccine doses so they can identify communities at particular risk. These include low-income individuals, who tend to be essential workforce employees; minority and non-English speaking individuals, who tend to have legitimate rationales for being vaccine hesitant; people living in households with the very old or young individuals, who are more susceptible to disease; those living in multifamily and multigeneration households, who are at greater risk of exposure to infectious disease; and those without transportation, who are less likely to access health care or testing.

Social Determinants of Health Linked to Poor Patient Outcomes
Cousins to SVI, social determinants of health (SDoH) continue to gain recognition and funding and generate action. SDoH concepts use statistical models at the patient level to determine the factors driving health and wellness.

Multiple peer-reviewed and published statistical models corroborate a sobering reality: Just 20% of patient outcomes are due to health care intervention, with genetic predisposition and social determinants making up the balance. SDoH factors such as domestic violence, employment, food insecurity, housing, social stability, and transportation influence health outcomes to a greater extent than clinicians, diagnostic capabilities, and the latest drug to market.

Policymakers, Public, and Health Care System Are Beginning to React
One can reasonably ask why we would spend $3.6 trillion on health care in the United States, more than twice the rest of the industrialized world, when behavioral health providers, nurses, pharmacists, and physicians have little influence on global outcomes. Most citizens would rather have that money for better-tasting food, cars, housing, and smart phones.

Health Care System Starting to Sit Up Straight
Nothing will get an industry to rethink its posture faster than customers and taxpayers rethinking the value of the entire sector. If the public starts to realize that no matter how good a plan, cardiology group, or pharmacy is, they do not really influence health, the industry will start to shift attention and resources to factors that do. Insurance companies, particularly in the Medicaid managed care space, are leading the charge. Not only are they starting to make assessments of SDoH for their members, they are also increasingly partnering with community-based organizations or providing solutions directly to enrollees instead of begging health care providers to change their stances. In other words, address SDoH or become irrelevant versus other agencies, vendors, and government-provided solutions.

Pharmacies Are Well Positioned
Pharmacies are in an advantageous and unique position to respond to the SDoH and SVI movements, but it will require a mindset change. Pharmacist academics often push the notion that it is the comprehensive and unique training in therapeutics that separates pharmacists from other care team members when it comes to providing value. But it is also pharmacists’ placement in communities as accessible frontline sentinels and first responders for disease recognition, management, and triage that allow that training to be meaningful. Yes, pharmacists with clinical capabilities and superior therapeutic knowledge are found in many great institutions of higher learning and advance care delivery, but the data show that those institutions do not play a huge part in the big picture. As a son, parent, or relative of a sick patient, I want those pharmacists there to optimize therapy. But as an individual and taxpayer living in an upper-class neighborhood who feels responsible for investing in the well-being of all Americans, I applaud the SDoH and SVI movements on both economic and moral grounds.

These movements represent an enormous opportunity for community pharmacies to reposition themselves. Pharmacies are the front door to the health care system, but they can also be the entrance and major contributors to the infrastructure regarding physical location and personnel, for screening, education, referral, and direct support to address SDoH in highly vulnerable communities and populations.

Critical-Access Pharmacies
Critical-access hospitals serve rural communities that are often at risk for poor outcomes because of their location, geography, social fragility, and, sometimes, poor economic circumstances. With respect to communities with high social vulnerability and prevalent social determinants of poor health outcomes, policymakers should consider a similar model of cost-based reimbursement, grants, regulatory flexibility, and expanded scope of practice. The COVID-19 pandemic highlighted the need for an essential pharmacist workforce in communities of need. Let’s learn from that to ensure those communities have access to local pharmacies.
## FDA Approvals

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<tr>
<td>Naloxone hydrochloride nasal spray (Kloxxado)</td>
<td>Indicated for the emergency treatment of known or suspected opioid overdose in adult and pediatric patients</td>
<td>Hikma Pharmaceuticals</td>
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<td>Dapagliflozin (Farxiga)</td>
<td>Indicated for the treatment of chronic kidney disease in patients at risk of progression either with or without type 2 diabetes</td>
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<td>Pembrolizumab (Keytruda)</td>
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<td>Merck</td>
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<td>Nivolumab (Opdivo)</td>
<td>Indicated for the adjuvant treatment of completely resected esophageal or GEJ cancer with residual pathologic disease in patients who have received neoadjuvant chemoradiotherapy</td>
<td>Bristol Myers Squibb</td>
<td>5/20/21</td>
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<td>Amivantamab-vmjw (Rybrevant)</td>
<td>Indicated for adults with non–small cell lung cancer whose tumors have epidermal growth factor receptor exon 20 insertion mutations</td>
<td>Janssen</td>
<td>5/21/21</td>
</tr>
<tr>
<td>Remingepant (Nurtec ODT)</td>
<td>Indicated for dual therapy of acute migraines and the preventative treatment of migraines in adults</td>
<td>Biohaven Pharmaceutica Holding Company Ltd</td>
<td>5/27/21</td>
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<tr>
<td>Sotorasib (Lumakras)</td>
<td>Indicated for adult patients with non-small cell lung cancer whose tumors have the KRAS G12C genetic mutation and who have received at least 1 prior systemic therapy</td>
<td>Amgen</td>
<td>5/28/21</td>
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<tr>
<td>Ozanimod (Zeposia)</td>
<td>Indicated for adults with moderately to severely active ulcerative colitis</td>
<td>Bristol Myers Squibb</td>
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For the full FDA approvals list, go to pharmacytimes.com.
Understanding How a Virus Binds to Human Cells Is Key to Vaccine Development

As new variants of SARS-CoV-2 necessitate the development of more vaccine options, research into the way in which the virus binds to human cells could provide a key to the development process.

Michael Cho, PhD, a professor of biomedical sciences at Iowa State University College of Veterinary Medicine in Ames, is investigating ways to develop COVID-19 vaccines that target SARS-CoV-2’s receptor-binding domain (RBD), which docks with the angiotensin-converting enzyme 2. Cho and his team have developed an experimental vaccine that produced antibodies that attack the virus’ RBD. The RBD is the portion of the viral spike protein that binds to host cells to initiate infection, he said in a statement, likening the spike protein to a key. The RBD is the part of the key that enters the lock, he said.

This approach differs from that used for the 3 vaccines approved in the United States. The messenger RNA vaccines from Moderna and Pfizer-BioNTech work by teaching the immune system to make the entire spike protein that triggers an immune response. The Johnson & Johnson vaccine uses a modified version of a different virus to induce an immune response.—Aislinn Antrim

Study: Dapagliflozin Fails to Improve Outcomes in Hospitalized Patients

New research results have shown that dapagliflozin (Farxiga) did not significantly reduce death or organ dysfunction among noncritically ill hospitalized patients with COVID-19. Furthermore, it did not improve recovery.

The DARE-19 trial (NCT04350593) aimed to assess the efficacy and safety of dapagliflozin among eligible hospitalized patients with COVID-19, according to results presented at the 2021 American College of Cardiology Annual Scientific Session. Dapagliflozin is a sodium-glucose cotransporter 2 inhibitor commonly used for patients with chronic kidney disease, heart failure, and type 2 diabetes (T2D).

In the trial, 1250 eligible patients were randomized 1:1 to receive either dapagliflozin 10 mg daily or a placebo. Participants were hospitalized with confirmed or suspected SARS-CoV-2 for 4 days or longer and had an oxygen saturation of 94% or greater on 5 L/min or less. They also had at least 1 risk factor, such as atherosclerotic cardiovascular disease (ACSVD), chronic kidney disease, heart failure, hypertension, or T2D.

Exclusion criteria included critical illness on presentation, an estimated glomerular filtration rate of less than 25 mL/min/1.73 m², prior diabetic ketoacidosis, and T1D.

The study results showed that 16% of participants had ASCVD and 51% had T2D. The mean systolic blood pressure was 127 mm Hg.

The primary end point of death or organ failure was 11.2% for those receiving dapagliflozin compared with 13.8% for those who received the placebo, according to a statement.—Aislinn Antrim

Study Finds Symptoms of Post–COVID-19 Syndrome

Findings from a new study from Mayo Clinic show that patients who received a diagnosis of post–COVID-19 syndrome (PCS), also known as COVID-19 long-haul syndrome and postacute sequalae of SARS-CoV-2, experience symptoms such as fatigue, mood disorders, and perceived cognitive impairment that can negatively affect their return to work and resumption of normal activities.

The study reports on the first 100 patients to participate in Mayo Clinic’s COVID-19 Activity Rehabilitation Program (CARP), which is among the first multidisciplinary programs to evaluate and treat patients with PCS. Sixty-eight percent of the patients were female, with a mean age of 45 years. They were evaluated a mean of 93 days after infection and treated between June 1 and December 31, 2020.

In patients seeking evaluation for PCS, the most common symptom was fatigue. Eighty percent reported unusual fatigue, 59% had respiratory complaints, and a similar percentage had neurologic complaints. More than one-third had difficulty performing basic activities of daily living, and only 1 in 3 had returned to unrestricted work activity.

“Most patients in the study had no preexisting comorbidities prior to COVID-19 infection, and many did not experience symptoms related to COVID-19 that were severe enough to require hospitalization,” Greg Vanichkachorn, MD, MPH, medical director of CARP and first author of the study, said in a statement.

Patients’ symptoms often resulted in significant negative effects when they tried to return to normal daily activities, including work. Most needed physical therapy, occupational therapy, or brain rehabilitation to address the cognitive impairment, Vanichkachorn said.

Mayo Clinic developed CARP in June 2020 to care for patients experiencing persistent symptoms after COVID-19 infection. The organization is conducting intensive research on PCS, partly to better determine how it presents across different socioeconomic ethnicities and groups.—Jill Murphy
ALLERGIES

Survey: Nearly 1 in 4 Americans With Nasal Congestion Has Symptoms Daily

THE RESULTS OF A HARRIS On Demand survey show that chronic nasal congestion is a common problem among US adults, with nearly 1 in 4 experiencing it every day and 85% reporting the congestion negatively affecting daily activities.

According to the survey, although most individuals who have chronic nasal congestion know about allergies as a potential cause, more than half are unaware that nasal polyps—noncancerous growths that occur with chronic inflammation deep and high in the nasal passages—are a common cause of nasal symptoms that last more than 12 weeks. Further, fewer than half of individuals who have chronic nasal congestion seek help from a specialist to look deeper at the cause of their chronic problem, according to the survey.

Additional survey findings include the following:

• Approximately 90% of individuals reported aspects of their daily lives are negatively affected when they experience chronic nasal congestion, including their ability to get a good night’s sleep (60%), properly taste or enjoy food (48%), or enjoy outdoor activities (33%).
• Ninety-five percent of those surveyed experience additional symptoms with their chronic congestion, including more than half who have headaches and one-third who feel fatigued.
• Half of those surveyed are uncertain as to whether symptoms they experience are because of their chronic nasal congestion worsening or from COVID-19.

“Despite their high prevalence, nasal polyps are largely underdiagnosed, and as the survey showed, most people with chronic congestion don’t know that nasal polyps deep in the nose might be causing their symptoms,” Neal Jain, MD, an allergist-immunologist, said in a statement.—Jill Murphy

COGNITIVE HEALTH

Short-Term Exposure to Air Pollution Can Impede Cognition; Aspirin May Help

THE RESULTS OF A NEW STUDY led by investigators at Columbia University’s Mailman School of Public Health found that exposure to air pollution, even over a few weeks, can impede mental performance.

Even with these data, the adverse effects were lessened in individuals taking nonsteroidal anti-inflammatory drugs (NSAIDs), such as aspirin.

The investigators examined the relationship between exposure to fine particulate matter (PM2.5) and black carbon, a component of particulate matter, with cognitive performance in 954 older White men from the greater Boston, Massachusetts, area enrolled in the Normative Aging Study. Further, they explored whether taking NSAIDs could modify this relationship. Cognitive performance was assessed using the global cognitive function (GCF) and mini–mental state examination (MMSE) scales with air pollution levels obtained from a site in Boston.

Elevated average PM2.5 exposure over 28 days was associated with declines in GCF and MMSE scores.

Participants who took NSAIDs experienced fewer short-term adverse effects of air pollution exposure on cognitive health than those who didn’t take NSAIDs, although there were no direct associations between cognitive performance and recent NSAID use.—Jill Murphy

MENTAL HEALTH

Sleep Disorders Connected to Increased Medical Visits, Prescriptions

SLEEP DISORDERS ARE ASSOCIATED WITH significantly higher rates of health care use, according to the results of a study published in Journal of Clinical Sleep Medicine.

The investigators found the number of medical visits and prescriptions filled were nearly double in individuals with sleep disorders such as insomnia and sleep apnea when compared with similar individuals without these conditions. Additionally, affected patients were also more likely to visit the emergency department and have more comorbid medical conditions.

The study examined differences in health expenditures in similar patients with and without a sleep disorder diagnosis, as determined by their ICD-10 diagnosis code.

The investigators used data from the 2018 Medical Expenditure Panel Survey, a nationally representative survey of more than 22,000 Americans administered by the US Department of Health & Human Services’ Agency for Healthcare Research and Quality. They found that 5.6% of respondents had at least 1 sleep disorder, which translated to an estimated 13.6 million US adults.

The individuals affected by sleep disorders accumulated approximately $7000 more in overall health care expenses per year than those without a sleep disorder, resulting in approximately 60% more in annual costs. This equates to an estimated $94.9 billion in health care costs per year attributable to sleep disorders.

Individuals with certain sleep disorders experience decreased daytime functionality that relates to an increased risk of motor vehicle accidents, drowsiness, and mental fog.—Skylar Kenney
Women May Experience Heart Disease Differently Than Men

Help Female Patients Stay Informed About Prevention Strategies, Symptoms, and Treatment of This Potentially Deadly Condition

Heart disease is the leading cause of death in the United States for both men and women. Approximately 655,000 Americans die every year from heart disease. That equates to 1 person every 36 seconds. The condition costs the United States about $219 billion annually in health care services, lost productivity, and medications.¹
Despite increased awareness over the past few decades, only a little over half (56%) of women recognize that heart disease is as deadly for them as it is for men, according to the CDC.

In 2017, 299,578 women died from the disease.²

**Gender Disparities**

It is important to recognize that women sometimes experience heart disease differently than men. Women are less likely than men to experience chest pain. But they are more likely to experience back or stomach pain, chest pressure or tightness, dizziness, fatigue, indigestion, nausea, or shortness of breath.³⁻⁵

Survival rates after a heart attack are lower in women than in men. Compared with men, women are less likely to get advice about quitting smoking or receive potentially beneficial treatment, such as aspirin therapy and cholesterol-lowering medications.³ Doctors are less likely to refer women for certain diagnostic tests, such as an initial electrocardiogram, and younger women are more likely than men to receive a wrong diagnosis and be sent home after cardiac events.³

**Pregnancy**

Preeclampsia, or high blood pressure (BP) during pregnancy, is a heart disease risk factor that increases the chances for blood vessel and heart problems later in life. In addition, having heart disease before pregnancy may raise the risk of pregnancy complications.⁴

**Menopause**

In middle age, risk factors for heart disease increase partially because of decreased estrogen production and weight gain. Women who go through early menopause, especially if they have had hysterectomies, have a higher risk of developing heart disease than those of the same age who have not gone through menopause. Hormone replacement therapy immediately after a hysterectomy may reduce the risk of heart disease. However, treatment later in life may increase the risk of heart disease.¹

**Keeping Healthy**

Although some risk factors cannot be changed, such as age and family history, women can take steps at every stage of life to maintain heart health. These include the following:

**Knowing the risk factors.** Patients should be aware of the various health conditions that increase the risk of developing heart disease. These include, but are not limited to, diabetes, hyperlipidemia, hypertension, and obesity.⁶

**Managing health conditions.** The health conditions listed above should be managed with lifestyle changes and/or medications. Hypertension is a major risk factor for heart disease. This occurs when the pressure of the blood in the arteries and blood vessels is too high. Primary hypertension has no identifiable cause and tends to develop gradually over time. Secondary hypertension is caused by adrenal gland tumors, certain medications, congenital blood vessel defects, kidney disease, obstructive sleep apnea, and thyroid problems. Secondary hypertension tends to appear suddenly and increase BP more than primary hypertension.⁷

Hyperlipidemia can cause fat deposits to build up in arteries, thereby narrowing the diameter the blood has to flow through, which then raises BP. Patients should have their cholesterol levels checked regularly and keep their numbers under 200 mg/dL total cholesterol.⁸

Individuals with diabetes are more than twice as likely to develop heart disease as those without diabetes. When insulin cannot properly manage glucose levels in the blood, the circulating glucose builds up and can damage blood vessels and the nerves that control them.³

Obesity causes the heart to work much harder than the heart of an average weight person. This raises BP and can contribute to heart disease through atherosclerosis, atrial enlargement, and ventricular enlargement.¹⁰

**Recognizing symptoms.** Not all heart problems come with warning signs. Some heart symptoms do not even happen in or around the heart. Common symptoms include chest discomfort; dizziness; getting easily winded; heartburn; indigestion; irregular heartbeat; jaw, stomach, or throat pain; lightheadedness; nausea; pain that spreads down the arm; persistent cough; snoring; sudden fatigue; sweating; and swelling in the lower extremities.¹¹
**Engaging in regular physical activity.** Exercise can help keep the heart healthy by boosting one’s mood, helping maintain a healthy weight, improving sleep, lowering BP, reducing stress, and strengthening the heart.12

**Maintaining a healthy weight.** Maintaining a healthy weight can also help manage cholesterol levels, diabetes, and hypertension.

**Eating a healthy diet.** Following the Dietary Approaches to Stop Hypertension diet includes eating beans, fish, fruit, low-fat dairy products, nuts, poultry, vegetables, and whole grains. It also means limiting foods that are high in saturated fat, sodium, and sugar or other sweeteners.13

**Avoiding smoking.** Chemicals in tobacco smoke, as well as flavorings found in vaping products, can damage the blood vessels, heart, and lungs. Even second-hand smoke can have these effects.14

**Managing stress.** Chronic stress can have negative effects on the heart. Stress can lead to hypertension, which can lead to heart disease. Stress can also contribute to other cardiovascular risk factors, such as increased alcohol intake, lack of physical activity, poor sleep, overeating, and smoking.15

**Getting enough sleep.** Most adults need 7 to 8 hours of sleep every night. Unfortunately, about one-third of American adults report not getting enough sleep. Not getting enough sleep or regularly getting poor-quality sleep increases the risk of heart disease, hypertension, and other medical conditions.16

Treatment of heart disease is similar in men and women. It can include angioplasty and stenting, coronary bypass surgery, and medications. Women are more likely to have complications after coronary bypass surgery than men.17

It is important to note that aspirin therapy is not recommended in women, unless they have already had a heart attack. Once they have a heart attack, daily aspirin therapy may help prevent another.17

**REFERENCES**

VITAMIN D IS CLASSIFIED AS A FAT-SOLUBLE VITAMIN and is synthesized in the skin from dietary or endogenous cholesterol when an individual is exposed to sunlight or ultraviolet radiation.¹

The primary biologic function of vitamin D is to maintain normal blood levels of calcium and phosphorus.¹,² Vitamin D is added to some foods, available in dietary supplements, and presents naturally in some foods. Study results have shown a link between low levels of vitamin D and certain medical conditions such as autoimmune disorders, cardiovascular disease, dementia, depression, infectious disease, musculoskeletal decline, and some types of cancer.¹,³

Some health experts disagree that vitamin D has a role in clinical outcomes of COVID-19 cases. Nonetheless, the use of vitamin D supplements increased at the beginning of the pandemic due at least in part to study results suggesting that lower levels of the vitamin are associated with elevated rates of serious COVID-19 infections and mortality rates.

An estimated 42% of Americans have a vitamin D deficiency, according to statistics presented by the Cleveland Clinic in 2018.⁴ In study results published in March 2021 in *Journal of Clinical Endocrinology and Metabolism*, 80% of more than 200 patients hospitalized with COVID-19 had a vitamin D deficiency.⁵

In another March 2021 publication, Meltzer et al noted that in a cohort study of 4638 individuals with a measured vitamin D level in the year before undergoing COVID-19 testing, the risk of having positive results in Black individuals was 2.64-fold greater with a vitamin D level of 30 to 39.9 ng/mL than a level of 40 ng/mL or greater, decreasing by 5% per 1 ng/mL increase in level among individuals with a level of 30 ng/mL or greater.⁶

There were no statistically substantial correlations between vitamin D levels with COVID-19 positivity rates in White individuals. Investigators concluded that randomized clinical trials should be conducted to ascertain whether increasing vitamin D levels to greater than 30 to 40 ng/mL affects COVID-19 risk, especially in Black individuals.⁶ The investigators are recruiting...
participants for 2 separate clinical trials to test the efficacy of vitamin D supplements in preventing COVID-19. More information on these trials can be found at https://chess.uchicago.edu/vitd/.

In a May 2021 publication, Ma et al examined the prospective correlation between the habitual use of vitamin D supplements and the risk of COVID-19 infection and assessed whether such an association differed according to patients' levels of circulating and genetically predicted vitamin D. The investigators discovered that after adjustment for covariates, the habitual use of vitamin D supplements was substantially correlated with a 34% lower risk of COVID-19 infection. Circulating vitamin D levels at baseline or genetically predicted vitamin D levels were not linked with the risk of COVID-19 infection. The correlation between the use of vitamin D supplements and the risk of COVID-19 infection did not vary according to the different levels of circulating or genetically predicted vitamin D ($P = .75$ and $.74$, respectively). The investigators concluded that their findings imply that habitual use of vitamin D supplements is related to a lower risk of COVID-19 infection, although they could not rule out the possibility that the inverse relationship is because of residual confounding or selection bias. Further clinical trials are necessary to validate these results, they noted.

Results from a study presented at the Endocrinology Society 2021 Annual Meeting held virtually in March indicated that hospitalized patients with COVID-19 and low vitamin D levels could have a decreased risk of dying or needing mechanical ventilation if they obtain at least 1000 units of vitamin D supplementation weekly.

CONCLUSION

Pharmacists are likely to encounter patients seeking guidance on the selection and use of vitamin D supplements. Pharmacists should remind patients to adhere to the recommended dosages as directed by their primary health care providers or indicated by the manufacturer. Pharmacists also serve as excellent resources in identifying possible drug-micronutrient contraindications and interactions. Patients taking other medications and those with chronic medical conditions should always consult their primary health care provider before taking any supplements.

REFERENCES

Multicapsule Supplement Line
Marketed by SmartyPants Vitamins

For patients looking for an alternative to gummies or a sugar-free vitamin option, the new SmartyPants Vitamins Multi Capsule line includes prenatal vitamins, vitamins for men and women, and vitamins for individuals aged 50 and older. The vitamins are a blend of fruit and vegetables, and feature plant-based omega-3 DHA from algal oil; vitamins A, B6, B12, C, and D3; and zinc to support brain, heart, bone, eye, and immune health. The vitamins are free of the 8 major food allergens and genetically modified organisms and are vegetarian, according to a statement.

FOR MORE INFORMATION:
smartypantsvitamins.com

Envive Probiotic Supplement
Marketed by Bausch Health Companies

To help reduce the frequency and severity of 5 common gastrointestinal symptoms, Bausch Health Companies is launching the Envive daily probiotic supplement. The probiotics tackle bloating, constipation, diarrhea, discomfort, and gas, and also strengthen the digestive symptom and gut barrier. Results from a 4-week study showed that the supplements can reduce the frequency and severity of these symptoms at both 2 and 4 weeks of daily use, with 85% of participants reporting overall improved gastrointestinal well-being, according to a company statement.

FOR MORE INFORMATION:
envive.com

Bonny Fiber Supplement
Marketed by Bonny

Bonny, a female-founded health and wellness brand, offers a new line of supplements aimed at helping patients meet their daily fiber needs with natural, organic supplements. The prebiotic fiber supplements contain a proprietary blend of fiber powder that is gluten- and sugar-free, as well as vegan, and has more than 7 g of fiber per serving. Nearly 95% of Americans are not getting enough fiber, and many supplements lack natural ingredients and sustainable packaging, according to the company. The supplements are available in 3 flavors: Chocolate Hazelnut Dream, Extremely Unflavored, and Vanilla Berry Bliss.

FOR MORE INFORMATION:
trybonny.com

Extra-Strength CBD Topicals
Marketed by LeafLine Wellness

To meet high demand for cannabidiol (CBD) topical products, LeafLine Wellness is launching a range of extra-strength CBD topicals under its Happy Place brand. The new products include the CBD Cooling Pain Relief Roll-On, with 250 mg of CBD isolate; CBD Healing Balm, with 500 mg of CBD; CBD Hydrating Cream, with 500 mg of CBD isolate; and the CBD Muscle & Joint Patch, with 50 mg of CBD isolate. Like the company’s gummies, the topical CBD products are priced under $20 and will be available online and in stores.

FOR MORE INFORMATION:
discoverhappyplace.com
Ear Infections

BY RUPAL PATEL MANSUKHANI, PHARMD, FAPHA, NCTTP; AND AMMIE J. PATEL, PHARMD, BCACP, BCPS

CASE 1: Labyrinthitis

**Q** PJ is a 7-year-old boy with complaints of ringing in his ears followed by trouble hearing with a sudden onset. His mother, ET, reported that he had a cold this past week and that he appears to have poor balance when walking. She asks about ear wax removal kits to improve the hearing problems. What should the pharmacist recommend?

**A** PJ’s symptoms are consistent with common presentation of labyrinthitis, and the pharmacist should refer him to his PCP for further evaluation and treatment. The symptoms of hearing loss and poor balance, especially in a child with a recent common cold, suggest viral etiology. Viral infections are a common trigger for labyrinthitis. PJ’s PCP may conduct testing and refer the child to a specialist. In some cases, corticosteroids or antiviral medications may be prescribed.1,2

CASE 2: Otic Suspension

**Q** MT, a 42-year-old man, has a prescription for ciprofloxacin and dexamethasone (Ciprodex). He has not used ear drops since he was a child, and his mother would pull his ear canal downward to apply the treatments. MT asks the pharmacist to walk him through the application for adults. How should the pharmacist instruct him to use the medication?

**A** MT should first wash his hands with soap and water. He should then warm the ciprofloxacin and dexamethasone bottle in his hands for 1 to 2 minutes prior to administration, as dizziness may occur if a cold otic suspension is instilled in the ear canal. The pharmacist should then instruct MT to remove the cap and place it on a clean dry surface. Unlike how children are administered ear drops, MT should tilt his head sideways and pull his affected ear up and back. He should then administer the ear drops using the applicator but avoid having the applicator tip enter the ear canal. To maximize the ciprofloxacin and dexamethasone exposure, he should lie down on his side with the affected ear up for 5 minutes or place a piece of cotton ball at the end of the outer ear canal of the affected ear for 20 minutes. Remind MT not to share this medication with others.3
**CASE 3: Acute Otitis Media (AOM) in Children**

**Q** JP is a 3-year-old, 35-lb boy with mild to moderate ear pain who has had a 38 °C fever for the past 24 hours. His mother, MO, calls the pharmacy with questions about unilateral AOM. She noted that upon consultation, JP’s pediatrician recommended initial observation with pain control but without antibiotics. MO is concerned about the pediatrician’s recommendation and asks for the pharmacist’s input and what pain medications JP should take. What advice can the pharmacist give her?

**A** Given that JP is an immunocompetent child older than age 2 without craniofacial abnormalities and ear discharge and with a temperature of less than 39 °C, study results support the approach of either immediate antibiotic treatment or initial observation. If his pain and symptoms worsen or do not improve after 48 to 72 hours, the pediatrician should give JP antibiotics. Typically, a pediatrician will choose either amoxicillin or amoxicillin-clavulanate antibiotic treatment for AOM if no recent allergies, antibiotic use, or resistance are noted. If JP’s symptoms improve in 48 hours, he should follow up with the pediatrician at the next health maintenance visit.4-9

In terms of pain control, study results show that patients with AOM who received acetaminophen or ibuprofen experienced pain relief at 48 hours compared with a placebo. There are insufficient data to support the use of both acetaminophen and ibuprofen together. If using acetaminophen, give 160 mg oral liquid every 4 to 6 hours as needed, with a maximum of 5 doses per day and a maximum daily dose of 75 mg/kg or 4000 mg, whichever is less. If using ibuprofen, administer 100 mg oral liquid every 6 to 8 hours, with a maximum single dose of 400 mg and a maximum daily dose of 40 mg/kg per day.10,11

**CASE 4: Swimmer’s Ear**

**Q** HP is a 68-year-old man who asks about a nonprescription product to help with painful, water-clogged ears with discharge. He just returned from a family trip to an all-inclusive beach resort, where he spent much of the time in the pool. HP’s temperature has been running high for the past 2 days since his return, and he is having trouble hearing on the phone, which is a necessity for his work-from-home job. His coworker mentioned that OTC ear drops relieve discomfort. What advice should the pharmacist give HP?

**A** The symptoms of discharge, ear pain, and fever, combined with a lot of time swimming recently are consistent with the common presentation of swimmer’s ear. Given the virulent nature of swimmer’s ear, refer HP to his primary-care provider (PCP) for further evaluation and treatment. In the meantime, HP should be instructed to avoid using cotton swabs. The PCP will likely first clean HP’s ear canal using an otoscope and then treat the infection and inflammation with a topical steroid and/or an oral or topical antibiotic. The PCP may recommend an OTC analgesic such as ibuprofen or naproxen to treat the ear pain. Throughout the duration of treatment for swimmer’s ear, HP should protect his ears from water using petroleum jelly–coated cotton balls when bathing and avoid swimming for 7 to 10 days.12,13

If HP had had water-clogged ears without discharge, fever, or pain, he could have self-treated with a cerumen removal kit, such as carbamide peroxide. To reduce the risk of swimmer’s ear in the future, he should use ear plugs when swimming, and if water does enter his ears, tilt his head to each side to shake his ears dry. HP can also consider blow drying his ears at the lowest heat setting after water exposure by holding the dryer 1 foot away from his ears.14
Potassium Citrate Extended-Release Tablets
Marketed by Camber Pharmaceuticals

Compare to: Urocit-K
Patients with renal tubular acidosis (RTA), a kidney stone condition, have a new generic option with Camber’s launch of potassium citrate extended-release tablets. RTA occurs when the kidneys fail to excrete acids into the urine, causing patients’ blood to remain too acidic. Symptoms include confusion, decreased alertness, fatigue, impaired growth in children, and kidney stones. Potassium citrate tablets produce an alkaline load that increases urinary pH. Common adverse effects include diarrhea, nausea, stomach pain, and vomiting.

FOR MORE INFORMATION:
camberpharma.com

Sapropterin Dihydrochloride Powder for Oral Solution
Manufactured by Dr. Reddy’s Laboratories

Compare to: Kuvan
Indicated to lower blood phenylalanine (Phe) levels in adults and children over 1 month of age with phenylketonuria, the new generic sapropterin dihydrochloride powder from Dr. Reddy’s Laboratories is available in 100-mg unit-dose packets in a 30-count carton. Phenylketonuria is an inborn error of metabolism that results in decreased metabolism of the amino acid Phe, which can lead to behavioral problems, intellectual disability, mental disorders, and seizures if left untreated. Sapropterin dihydrochloride hydroxylates Phe through an oxidative reaction to form tyrosine, thereby improving the normal oxidative metabolism of Phe. Adverse reactions can include cough, diarrhea, headache, nasal congestion, and vomiting.

FOR MORE INFORMATION:
dreddys.com
Potassium Chloride Extended-Release Tablets
Manufactured by Aurobindo

Compare to: Merck Potassium Chloride Extended-Release Tablets
The FDA has approved Aurobindo’s generic potassium chloride extended-release tablets in dosage strengths of 10, 15, and 20 mEq. They are indicated for the treatment of patients with hypokalemia with or without metabolic alkalosis, in digitalis intoxication, and in patients with hypokalemia familial period paralysis. They can also be used for the prevention of hypokalemia in patients who would be at particular risk if it were to develop. Potassium chloride is an electrolyte replenisher intended to slow the release of potassium and reduce the likelihood of a high localized concentration of potassium chloride in the gastrointestinal tract.

FOR MORE INFORMATION:
aurobindousa.com

Azelastine HCI Nasal Spray 0.1%
Manufactured by Aurobindo

Compare to: Astelin
With the launch of azelastine hydrochloride (HCI) nasal spray 0.1%, Aurobindo has introduced its first product in the United States with a pump nasal spray delivery system. The medication is used to relieve nasal symptoms caused by allergies or other conditions and works by blocking histamines. Adverse effects can include a bitter taste in the mouth, a burning feeling in the nose, drowsiness, cough, dry mouth, headache, nausea, nose bleeds, runny nose, and sneezing fits.

FOR MORE INFORMATION:
aurobindousa.com
IT HAS BEEN ABOUT A YEAR since the federal government initiated Operation Warp Speed, a program to develop, manufacture, and distribute COVID-19 vaccines with the lofty goal of producing and distributing 300 million doses by January 2021.¹

This gigantic program—its funding included $10 billion from the CARES Act and access to $95.5 billion in as-needed funding from the Biomedical Advanced Research and Development Authority for countermeasure development and the National Institutes of Health for research—is the largest of its kind in history. The SARS-CoV-2 pandemic necessitated 3 actions¹:

• Running clinical trials simultaneously, rather than sequentially
• Manufacturing the vaccines concurrently with trials, so they would be ready if effective
• Authorizing vaccines under “emergency use”

The results have been astonishing to people familiar with the slower, more measured pace of traditional drug research and development. The normal vaccine approval process, described in the FIGURE,² involves 7 sequential steps that can take years.² Prior to the FDA’s Emergency Use Authorization (EUA) that allowed the use of the Pfizer-BioNTech COVID-19 vaccine, the fastest vaccine developed was that for mumps. Maurice R. Hilleman of Merck created that vaccine in 1967 after a decades-long search for a mumps cure became a priority during World War II. During World War I, mumps was the leading cause of missed days among US army active duty personnel in France. During the 1940s and 1950s, investigators made constant small breakthroughs in lab techniques. It took Hilleman 4 years

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**FIGURE.** Normal Vaccination Approval Process²

BLA, biologics license application.
to attenuate the Jeryl Lynn strain of mumps that he had cultured from his daughter until it was an effective and safe vaccine. That vaccine remains an MMR vaccine component.3

Now, with EUA awarded to 3 vaccines, pharmacists are at the forefront of the race to vaccinate as many Americans as possible. Let’s look at 3 questions concerning the COVID-19 vaccines and pharmacist efforts:

1. Why don’t we use this approval process all the time? Many people, pharmacy staff members included, wonder why all vaccine development is not this fast. The answer is that the pandemic galvanized the development and review process for these particular vaccines. But this approach consumes resources, and in many companies, federal agencies, and state governments it redirects efforts away from existing projects into 1 project. The approach also has a high level of risk: Manufacturing vaccines while running trials with no guarantee of FDA approval could result in large inventories that cannot be used. Additionally, such an approach requires fast clinical trial enrollment, which is a challenge unless a sense of urgency is present.1,3

2. Is everyone happy with the pharmacist as vaccinator? Many have lauded pharmacies and pharmacists for their efforts to increase vaccination rates. Certainly, many Listservs and social media outlets have provided a platform for complaining about lack of appointment availability and that some neighborhood pharmacies seem to be more likely to have vaccines available while others lag behind. But overall, people have been grateful and receptive. Pharmacists should note that, as always, there is room for improvement. The results of a recent study (N = 642) show that most physicians perceive pharmacist vaccinators as helpful and convenient for patients but also worry about pharmacists’ lack of access to sufficient patient information or vaccination history.4 Physicians also indicated that pharmacists do not tell them when they administer vaccinations (69%) and that they do not enter vaccinations into an immunization information system (57%). These findings suggest that collaboration between pharmacists and primary-care physicians needs improvement.4

3. What have pharmacists found noteworthy? Many pharmacists report that, as expected, processes behind the scenes have sometimes been confusing but have improved and streamlined rapidly. They also report that procedures were different even between sites in the same organizations. And although pharmacists are accustomed to patients having anxiety or crying before vaccinations, they have been surprised to see many being moved to tears after receiving a vaccine. Such is the joy and relief of receiving a shot of hope.5

Table: Good Immunization Technique: Points to Remember7-10

<table>
<thead>
<tr>
<th>Points to Remember</th>
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<tbody>
<tr>
<td>Do not aspirate when injecting into the deltoid.</td>
<td></td>
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<tr>
<td>Hold (stretch) the skin around the area the injection will be given. Do not bunch or pinch skin.</td>
<td></td>
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<tr>
<td>Immunizers who sit and administer vaccines to seated patients, using needles of appropriate length, reduce the risk of SIRVA.</td>
<td></td>
</tr>
<tr>
<td>To prevent SIRVA, avoid administering vaccines in the top one-third of the deltoid.</td>
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</table>

SIRVA, shoulder injury related to vaccine administration.

CONCLUSION

Expect changes related to the vaccines as new ones are approved, existing vaccine vial sizes change and storage conditions improve, and data sets accumulate. The best approach to stay current is to read the FDA-approved product labeling. ■
Cabotegravir and Rilpivirine Combination (Cabenuva)

Manufactured by ViiV Healthcare

Cabotegravir extended-release injectable suspension and rilpivirine extended-release injectable suspension is the only once-monthly complete treatment for HIV-1. It is available through AllianceRx Walgreens Prime for adults who are virologically suppressed on a stable antiretroviral regimen with no history of treatment failure and no known or suspected resistance to either of the drugs’ components. The combination treatment provides an alternative for patients who previously relied on a daily oral treatment regimen.

FOR MORE INFORMATION:
cabenuva.com

Spinosa Topical Suspension, 0.9% (Natroba)

Manufactured by ParaPRO

The FDA has recently approved spinosad topical suspension, 0.9% for scabies infestations in both adult and pediatric patients 4 years and older. The drug was previously approved for the topical treatment of head lice in January 2011. This new approval represents the first important pharmacological advancement in scabies treatments in decades, according to a statement from William Culpepper III, president of ParaPRO. According to clinical trial results, spinosad is highly effective and well tolerated following a single application, and it could represent a new standard of care for scabies treatment.

FOR MORE INFORMATION:
parapro.com

Drospirenone and Estetrol (Nextstellis)

Manufactured by Mayne Pharma

FDA officials have approved a new combined oral contraceptive tablet of 3 mg drospirenone and 14.2 mg estetrol. It is the first and only contraceptive pill containing estetrol, making it the first new estrogen product to be introduced in the United States in more than 50 years. In phase 3 clinical trials conducted in 3725 women, the contraceptive was found to be effective and safe and demonstrated excellent bleeding and cycle control, safety, and tolerability.

FOR MORE INFORMATION:
maynepharma.com

Omalizumab (Xolair)

Manufactured by Genentech

Patients with certain allergic and inflammatory conditions have increased flexibility in their treatment regimens with the recent FDA approval of omalizumab prefilled syringe for self-injection across all approved indications. Omalizumab is the only FDA-approved antibody that targets and blocks IgE, downregulating high-affinity IgE receptors and limiting mast cell degranulation to treat moderate to severe persistent allergic asthma, chronic urticaria, and nasal polyps. Patients starting therapy with omalizumab will begin with administration by a health care provider, who will then determine whether they are eligible for prefilled syringe self-injections.

FOR MORE INFORMATION:
gene.com
NANCY PETERSON, RPH, FIRST FELL IN LOVE with the pharmacy profession in high school, when she worked as a soda jerk at a local independent pharmacy. She then attended pharmacy school at the University of Kansas School of Pharmacy in Lawrence. After graduating, Peterson gained a variety of experience working in chain, hospital, and independent pharmacies. She was hired to open Clearwater Pharmacy in Kansas in May 2016.

“The long-term and personal interaction with patients of independent pharmacies captured my attention and emotion the most. In a town of 2500, one gets to know folks pretty quickly,” she said.

Peterson recently purchased the pharmacy and plans to finish out her working years serving the Clearwater community. She finds that helping patients with overwhelming tasks, such as Medicare open enrollment, is essential. The pharmacy’s staff members make appointments with patients and sit down with them and their caregivers to explain the options available.

“It is alarming how many seniors simply don’t understand how many options they have and the effects, by not exploring those options, it can have,” Peterson said.

It is the little things that make the most impact, she continued. “We make it a point to greet every patient as they walk in, by name if possible. We also strive to communicate any issues, such as a third-party rejection, no refill situation, or the need to order medication promptly via phone or text,” Peterson said. “We also try to find manufacturer coupons for expensive meds.”

In addition to caring for patients, the most charming and unique aspect of Clearwater Pharmacy is that it is home to Rosie the Rabbiter,
a 15-pound Flemish Giant certified therapy rabbit. The breed is known for its calm nature and is often used in therapy. Rosie has been on site during business hours since she was about 3 months old.

“The community has fallen in love with her,” Peterson said.

On her and Rosie’s days off, to the pharmacy posts a sign on the door with Rosie’s “hours” to prevent countless inquiries from patients looking for their furry friend.

“Young and old alike come to the store to pet and talk to Rosie. She loves the attention and the occasional treats,” Peterson said, adding that the bunny is “very laid back and welcoming.”

A brilliant marketer, Peterson has even given Rosie her own Facebook page (Rosie the Rabbiter) and Instagram account (@RosieRabbiter), and a personal website is in the works. Peterson has started the process of forming a nonprofit organization centered around Rosie and her offspring “so that we will be able to continue to spread her joy and comfort to as many folks in the area as we can. We plan to call it ‘Rosie’s Snuggle Bunnies,’” she said.

Like most pharmacy staff members, Rosie does not have much downtime. In addition to her “shifts” at the pharmacy, she regularly visits the hospice and Transitional Living Center units at the Robert J. Dole VA Medical Center as well as the Wesley Children’s Hospital, both in Wichita, Kansas. Rosie also sometimes visits a local home for teenage girls and nearby assisted-living and long-term-care facilities.

“We have designed little trading cards with Rosie’s picture and information about her to hand to patients and families that she visits,” Peterson said.

Despite Rosie’s popularity, Peterson is also proud of her human employees. “My staff have become family members to me. I am so fortunate to have amazing [technicians], interns, and delivery staff,” she said. “I certainly could not do the things that I do without their help and support.”

In her spare time, Peterson, who got married in January 2020, enjoys spending time with her husband, a Bronze Star retired veteran.

“My husband never thought he would be a ‘bunny dad’ but has fully embraced the situation,” she pointed out.

Peterson says their blended family is a “true Brady Bunch,” as she has 3 daughters, he has 3 sons, and they have 2 grandchildren. She and her husband also enjoy traveling.

“We love to visit the local establishments that are off the beaten path when traveling,” Peterson said. “Our Christian faith is the center of our lives, and we strive to serve in whatever aspect that we can.”

A recent week-long mission trip to Kingston, Jamaica, ignited a fire in the couple to continue to serve outside the United States, and they hope to travel to Tanzania and Hungary soon.
Pharmacists Are Needed to Provide Birth Control
A Contraception Toolkit Helps Them Improve Women’s Reproductive Health
By ASHLEY WALSH, PHARMD

IN THE UNITED STATES, ALMOST half of pregnancies are unintended.1 Globally, maternal mortality has declined steadily over the past 3 decades,2 but tragically, the number of American women dying during childbirth continues to climb.1

Accessible, affordable birth control could decrease unintended pregnancies and maternal mortality by 30%.1 Family planning allows women to obtain college educations, pursue advanced professional degrees, and join the nation’s workforce.1 The American Gynecological and Obstetrical Society advocates for full unrestricted access to contraception,2 and pharmacists are poised to help.

CURRENT SITUATION
Forty-nine states have awarded some form of prescriptive authority to pharmacists with variable prescriber oversight and restrictions.3 Pharmacists address antimicrobial stewardship, chronic conditions, immunization, and the opioid crisis (eg, naloxone) every day.4

Oral contraception’s safety is well established.5 Although combined oral contraception creates a venous thromboembolism risk, it is small compared with the risk during pregnancy and post partum.2 Studies show that women can self-screen and nonphysicians can safely assess contraindications to using oral contraception.5 Pharmacists can refer patients who need to use other methods.6

Fifteen states already allow pharmacists to prescribe birth control without collaborative practice agreements, and that number is increasing (TABLE 1).7 Successful pharmacist prescribing initiatives demonstrate its potential. Already, 46% of Oregon’s pharmacies prescribe contraception.8

All states require training and patient visit documentation.9 Typically, training involves certification or continuing education (CE) modules. Most locations use statewide protocols that identify when physician referral is required.5,9 Patient questionnaires address health history and pregnancy status, identify patient preferences, require blood pressure measurement, and screen for eligibility and interacting medications.2,10

TOOLS
The CDC has great contraception-prescribing resources. The evidence-based US Medical Eligibility Criteria (US MEC) for Contraceptive Use and the Selected Practice Recommendations for Contraceptive Use guide contraception choice based on medical conditions and help with managing challenges. The US MEC is updated at least every 5 years, and its components are available as mobile apps and include an easy-to-use summary chart.11 The CDC offers CE on the US MEC’s clinical application (https://www.cdc.gov/reproductivehealth/contraception/unintendedpregnancy/training.htm).12

Women hesitant to start birth control are most concerned with potential adverse effects. Pharmacists can guide patient decisions and discuss alternatives that may alleviate undesired effects.13 Birth control is a journey for women, and TABLE 2 lists factors that influence their selection of methods.14

BREAKING DOWN BARRIERS
Barriers affecting all health care curb access to contraception. Limited appointment availability and having to miss work cause patients to avoid

» Continued on page 40
office visits. Expanding pharmacy services is the very definition of health care convenience. Patients may also prefer pharmacies because of the availability of multilingual staff, pharmacy hours, and the facility’s proximity to their home.

Might access at the pharmacy decrease regular physician visits? On the contrary, pharmacist-patient interaction could encourage regular physician visits. Contraindications to prescription birth control require physician referral, and states often require pharmacists to inform the patient about the importance of regular exams.

Cost remains a barrier for 11.7% of women of reproductive age who are uninsured or underinsured. Without insurance, contraception’s average out-of-pocket cost is $240 to $900 yearly including secondary expenses (eg, lost wages and transportation).

**REIMBURSEMENT**

Pharmacist participation varies across states, and reimbursement influences participation. Paying pharmacists reasonable fees for patient assessment and prescribing or referral is critical.

States often delay developing payment policies for contraception prescribing, so pharmacists may consider temporarily increasing dispensing fees for the additional services. For example, in 2014, Illinois established a $35 dispensing fee.

**CONCLUSION**

Pharmacists ready to exercise prescriptive authority have the education and tools to successfully provide birth control to women.
A REGULAR PATIENT VISITS A COMMUNITY PHARMACY with a new prescription for buprenorphine/naloxone (Suboxone). The patient has been getting oxycodone for years and regularly talks with the pharmacy technician about everything from grandchildren to the weather. This time, however, the patient appears uncomfortable and does not talk much.

Technicians are at the forefront of drug distribution in community pharmacies across the United States and are often the first point of contact in the pharmacy for patients who have been prescribed a controlled substance. The responsibilities of accepting, processing, and assisting in the distribution of these prescriptions often falls to technicians. Therefore they play a vital role in preventing drug diversion, providing care for patients, and upholding the law. In addition, technicians handle prescriptions for drugs that treat opioid use disorder (OUD), such as buprenorphine, which are critical in fighting the continuing opioid epidemic in the United States.

CONTROLLED SUBSTANCES ACT
The Drug Enforcement Administration (DEA) regulates controlled substances under the Controlled Substances Act (CSA) of 1971. Drugs, certain chemicals used to make drugs, and substances are classified under 5 different schedules. Schedule I drugs, those with no accepted medical use in the United States, are not sold in pharmacies and have the highest level of regulation. Schedule V drugs have the fewest number of restrictions, as they are shown to have the lowest potential for abuse and addiction.

All hard copy prescriptions for controlled substances require the following, regardless of their schedule:
- Patient’s full name and address
- Drug name, strength, dose form, and quantity prescribed
- Adequate directions for use
- Prescriber’s signature and the date of issue
- Name, address, and DEA number of prescriber

Buprenorphine prescriptions have the same requirements as other controlled prescriptions, with the addition of a prescriber’s narcotic addiction DEA number (NADEAN), also known as a DATA 2000 waiver identification number (X-number). A technician should check that these prescriptions have a NADEAN in addition to the prescriber’s DEA to ensure they are for a valid medical purpose.

The CSA also details record-keeping requirements for controlled substance prescriptions. In 2018, the Substance Use-Disorder Prevention that Promotes Opioid Recovery and Treatment for Patients and Communities Act mandated the electronic prescribing of II, III, IV, or V controlled substances under Medicare Part D. However, exceptions do apply, so it is still important for technicians to understand the requirements for both electronic and hard copy prescriptions.

» Continued on page 45
PREVENTING DIVERSION
Pharmacists have a corresponding responsibility to ensure that prescriptions are for a legitimate medical purpose. Technicians serve as a first-line defense against drug diversion by identifying common red flags on forged or fraudulent prescriptions. Red flags may include an out-of-town prescriber, different handwriting or ink colors, directions that do not use acceptable standard abbreviations, handwriting that is too legible, or prescription paper that appears to be photocopied. Alerting the pharmacist when a prescription appears altered or false is a vital way that technicians can help prevent drug diversion.

OPIOID CRISIS
In 2019, 71,000 people died from drug overdose, with more than 70% of those deaths involving opioids. These can include dangerous synthetics, heroin, or prescription opioids. Although OUD is a pervasive issue in the United States, stigmas exist regarding patients with the condition. Technicians who are compassionate and empathetic toward patients create an environment that focuses on helping them get better. A regular patient, such as the man who was recently prescribed buprenorphine/naloxone, may be standoffish because of the stigma associated with OUD. Seeking treatment can be difficult for these patients. Individuals in treatment for OUD may be prescribed medication-assisted therapy, such as buprenorphine products, which can often be more highly stigmatized than other opioids. By upholding their compassion and sensitivity, technicians can play an important part in ending the opioid epidemic by empowering patients with OUD to continue their treatments.

CONCLUSION
Technicians already play a vital role in processing controlled prescriptions in community pharmacies but they can also care for patients affected by OUD. Additionally, by understanding the different regulatory requirements of controlled prescriptions and watching for red flags when accepting controlled prescriptions, they can prevent drug diversion. Further, patients often interact with technicians during their pharmacy visits, giving technicians the opportunity to reduce the stigma around OUD and the prescription drugs used to treat it. Appropriate handling of controlled substance prescriptions is the responsibility of all technicians, and gives them the potential to improve the lives of many patients.

REFERENCES
Children, Youth With T1D Register Better Glucose Control During Lockdown

INVESTIGATORS IN THE UNITED KINGDOM saw improved blood glucose levels among children and teens with type 1 diabetes (T1D) during the first 12 weeks of the COVID-19 lockdown, according to the results of a study published by the Endocrine Society.

Aspects of normal life outside the pandemic could create difficulties for children with T1D, according to the study authors. Without these challenges, the investigators said that children might be able to better manage their diabetes.

Hospitals in the United Kingdom implemented many changes for individuals with diabetes and other chronic diseases during the pandemic. According to the investigators, the hospitals wanted to know whether these changes were detrimental to the care of children and adolescents with T1D.

They noted that some clinicians and families were concerned that remote consultations could result in poorer care. However, the study results showed a significant improvement in blood glucose measurements in the 12 weeks after lockdown. Average and long-term blood glucose measurements had dropped, and readings showed less variability and a greater time in the target range of glucose (70-180 mg/dL) than the investigators had asked patients to aim for.—Aislinn Antrim

Evidence Exists of Disparities in Contraception Use

NEW RESEARCH FROM BOSTON UNIVERSITY suggests that women with diabetes are less likely to use contraception after receiving their diagnosis. The finding could have significant implications for fetal and maternal risks during pregnancy.

Uncontrolled diabetes poses significant risks to both fetal and maternal health during pregnancy, according to the study authors. Because of these risks, the American Diabetes Association (ADA) recommends that physicians discuss family planning with patients and that effective contraception be available to women of reproductive age with diabetes.

The study findings indicate that receiving a diagnosis of diabetes does not make patients more likely to use effective contraception. Further, it may actually lead to a drop in use of certain types of effective contraception, especially short-acting hormonal methods such as pills or injections, according to the authors.

Women with diabetes have the same contraception options and recommendations as those without diabetes, according to the ADA, and the risks of an unplanned pregnancy in this population outweigh the risks of most contraception options.—Aislinn Antrim

Study: Drug May Be a New Weapon Against HIV

INVESTIGATORS AT THE UNIVERSITY OF NORTH CAROLINA (UNC) School of Medicine discovered that when HIV infects immune cells known as CD4 T cells, it helps fuel its own replication by boosting a key process in the cells’ production of chemical energy. Additionally, they found that the diabetes drug metformin inhibits the same process, thereby suppressing HIV replication in these cells, in both cell-culture and mouse experiments.

The investigators also examined a prior study of patients with HIV receiving antiretroviral therapy (ART), whose results showed that after 6 months of treatment, patients who had type 2 diabetes had, on average, 33% lower levels of HIV in the blood than those who did not have diabetes. The patients with diabetes also had higher baseline CD4 cell levels and a quicker recovery of these levels with ART.

The investigators plan to continue preclinical studies of metformin’s potential as an anti-HIV treatment. They also intend to investigate its potential as a therapy that reduces the need for toxic antiretrovirals and that patients could receive earlier to reduce HIV reservoir formation.—Jill Murphy
The Role of the Pharmacist During the COVID-19 Pandemic With the Emergence of New Vaccines

TO ADDRESS THE extensive COVID-19–related deaths and infections that have occurred throughout the world, there has been a global effort to develop vaccines that can prevent the spread of the virus. In a program titled Advancements in Emerging COVID-19 Vaccines: Identifying the Barriers to Widespread Administration and the Role of the Pharmacist presented at the 11th annual spring CE conference, Directions in Pharmacy®, James Lewis, PharmD, FIDSA, discussed recent developments with the COVID-19 vaccines and strategies that community pharmacists can use to communicate information about the vaccine and address patient fears or questions.

Dr Lewis provided a background about the COVID-19 pandemic both on a global and a national level, where the number of deaths in the United States has exceeded 500,000 and is continuing to grow daily. Fortunately, there has been a huge ramp up in the number of vaccinations administered with the number of Americans being fully vaccinated rising significantly since early 2021. He then took note of trends in vaccination rates in various groups and barriers to receiving vaccination, emphasizing the importance of designing appropriate messaging to overcome these barriers and targeting these individuals for education regarding the benefits of the vaccine.

He then discussed the COVID-19 vaccines currently available and in development, offering information regarding unique aspects of each vaccine and discussing available efficacy and safety data. Dr Lewis highlighted vaccines with emergency use authorizations, including Pfizer-BioNTech, Moderna, and Janssen, a company of Johnson & Johnson. The first two are mRNA vaccines with the third being an adenovirus vector vaccine. The vaccines have been studied rigorously and have efficacy rates of approximately 90%. The vaccines are currently authorized for use in patients aged 12-18 years depending on the particular vaccine.

Safety was discussed with local reactions such as injection-site reactions commonly seen. A topic of interest was the thrombotic events associated with the Janssen vaccine. There are many more vaccines in various stages of development, but also covered were those developed by Oxford/Astra Zeneca and Novavax. Despite this progress, Dr Lewis noted, widespread vaccination of the United States and the globe continues to present several challenges, including logistical considerations such as transportation and storage of the vaccine as well as hesitancy among patients.

Dr Lewis completed his presentation by emphasizing the important role of the pharmacist in becoming educated about the available vaccines to help overcome these barriers and encourage all eligible patients to receive the vaccine. It is essential for patients to understand how to manage adverse effects and the importance of returning for a second dose if applicable. He also noted that pharmacists must be properly licensed and trained in vaccine delivery, dosing, distribution, and storage and handling. Additionally, it is critical that pharmacists assuage fears or answer questions that patients may have regarding the vaccine. Ultimately, the ACIP encourages patients to receive the earliest vaccine available to them. Dr Lewis concluded that the pharmacist takes on a significant role as a frontline responder and resource for patients, especially in the changing landscape of health care during the COVID-19 pandemic.

“These authorized COVID-19 vaccines do an outstanding job at preventing severe disease and keeping people out of the hospital. Once patients are fully vaccinated, the efficacy rates are high.”
—James Lewis, PharmD, FIDSA

TO VIEW THE ON-DEMAND CE SESSION, PLEASE VISIT WWW.PHARMACYTIMES.ORG/GO/DIP-2021-COVID. THE ACTIVITY IS AVAILABLE THROUGH JUNE 15, 2022.
Influenza is a contagious respiratory illness spread via respiratory droplets that continues to pose a significant burden annually. Rupal Mansukhani, PharmD, CTTS, FAPhA, recently provided an update on the critical role of influenza vaccinations in the current climate at the Directions in Pharmacy® conference in an activity titled Reducing and Preventing Influenza-Related Morbidity and Mortality Through Vaccinations: Educating Patients During the COVID-19 Pandemic. Select risk factors for influenza include age younger than 2 years; age 65 years or older; body mass index greater than or equal to 40 kg/m^2; and heart, blood, kidney, lung, liver, neurologic, endocrine, immune, or metabolic disorders. Pregnant and 2-week postpartum women as well as certain racial or ethnic minority groups and those residing in nursing homes or long-term care facilities are also at risk.

Two new influenza vaccines were licensed of late: high-dose inactivated influenza vaccine quadrivalent (HD-IIV4, Fluzone High-Dose Quadrivalent) in November 2019 for persons aged 65 years or older and adjuvanted inactivated influenza vaccine quadrivalent (aIIV4, Fluad Quadrivalent) with adjuvant MF59 in February 2020. HD-IIV4 is expected to replace the previously available trivalent formulation, HD-IIV3. The ACIP recommendation for adults is a single influenza vaccine dose annually every influenza season. High-dose quadrivalent vaccines contain 4 times the antigen, with the intention to give older people a better immune response. An adjuvant is an ingredient used in some vaccines that helps create a stronger immune response and improve efficacy in persons receiving the vaccine.

In a study of influenza vaccines among the US elderly population from 2018 to 2019, researchers have concluded that consistent with prior studies, egg-based adjuvanted and high-dose vaccines were slightly more effective than the egg-based quadrivalent vaccines. In 2016-2017, adults aged 65 years or older residing in nursing homes were randomized to aIIV3 or IIV3 to evaluate relative vaccine effectiveness for hospitalization due to all causes, respiratory causes, or pneumonia and influenza. Rates of all 3 aforementioned outcomes were lower for recipients of the adjuvanted vaccine compared with IIV3 recipients. Similarly, nursing home residents 65 years or older were randomized to high-dose IIV3 or IIV3 during the 2013-2014 season to study hospital admissions related to pulmonary and influenza-like illness. Pulmonary-related hospital admissions were significantly lower in facilities where residents received the high-dose vaccine.

In light of recent events, Dr Mansukhani highlighted the need to improve influenza vaccination rates during the COVID-19 pandemic as symptoms of both viral infections predominantly overlap. There is also a list of overlapping underlying medical conditions that may increase the risk of influenza and COVID-19. Health care personnel should administer influenza vaccines to all eligible persons, including essential workers and persons at risk for severe influenza or COVID-19. Dr Mansukhani reviewed strategies for safe delivery of the influenza vaccine such as screening for COVID-19 before vaccination and minimizing chances for exposures by adhering to infection control measures. However, influenza vaccine should be deferred for symptomatic persons with suspected or confirmed COVID-19 until criteria have been met for them to discontinue isolation, which may be for at least 10 days from their positive test result and symptom onset. It is especially important for pharmacists to help bring awareness regarding the importance of obtaining the annual influenza vaccine during these challenging times.

“Pharmacists play a role in identifying patients who are high risk, assessing barriers and raising awareness regarding the importance of obtaining an annual influenza vaccine, especially during the COVID-19 pandemic. For patients who are 65 years or older, a focus should be put on vaccinating with the adjuvanted or high-dose vaccine, which both help boost immunity.”

—Rupal Mansukhani, PharmD, CTTS, FAPhA
Influenza can result in worldwide outbreaks and epidemics that impose a high burden, including hospitalization, loss of productivity, and even mortality. Symptoms may lead to complications, which increase the likelihood of hospitalization or death. It is important to identify and prevent influenza early. This has been made more difficult yet essential during the COVID-19 pandemic, as this coronavirus presents many similar symptoms as the influenza virus. In a recent activity titled *Initiating Antivirals for the Prevention and Treatment of the Influenza Virus: Highlights of the Latest Safety and Efficacy Data for Pharmacists*, Rupal Mansukhani, PharmD, CTTS, FAPhA, discussed the role of health systems and community pharmacists in minimizing the burden of influenza at the Directions in Pharmacy® conference.

Dr Mansukhani covered how to detect influenza and differentiate these symptoms from COVID-19 symptoms. There are various treatment options available for influenza, including the neuraminidase inhibitors (NAIs) oseltamivir, zanamivir, and peramivir, as well as a cap-dependent endonuclease inhibitor, baloxavir marboxil, which was approved as an oral, single-dose formulation. Patients treated with antivirals for influenza were associated with significant reductions in complications, health care resource utilization, and overall costs.

There is growing evidence regarding the use of baloxavir, the most recently approved antiviral. It is the only medication approved specifically for individuals at high risk of developing influenza-related complications. Baloxavir has demonstrated a large decrease in viral shedding in multiple studies with either adult or pediatric patients including CAPSTONE-1, CAPSTONE-2, and mini-STONE 2. There have been many published studies, and now there are real-world evidence and posters. For example, there was a reduction in costs with baloxavir versus oseltamivir, which helps us understand that this medication may help health care as a whole by decreasing costs.

Chemoprophylaxis may be considered to prevent influenza in select situations after exposure to a person with influenza. The real-world burden of influenza transmissions is clear, as a significant number of secondary cases of influenza was identified among families with primary cases and may represent a large burden on the health care system. Results from the BLOCKSTONE study recently led to a postexposure prophylaxis indication for baloxavir. Oseltamivir and zanamivir can also be used for prophylaxis.

There are additional studies of baloxavir including CENTERSTONE, which is evaluating the reduction of direct transmission of influenza in otherwise healthy patients to household contacts. FLAGSTONE studied the potential of combining baloxavir with standard-of-care NAIs in patients hospitalized with severe influenza. This combination with baloxavir resulted in more rapid reduction of viral titers versus an NAI alone.

Dr Mansukhani then provided an overview of guidelines from the CDC, Infectious Diseases Society of America, and American Academy of Pediatrics regarding antiviral recommendations for managing influenza. She emphasized the importance of pharmacists in treating and preventing influenza and engaging patients in counseling on treatment options. Pharmacists should educate patients about the proper use of antivirals, as a heightened awareness of the infectious nature of respiratory diseases will likely drive more patients to seek care and treatment. Dr Mansukhani affirmed that pharmacists take on a significant responsibility in treating influenza early on, a role that is only made more prevalent due to the evolving state of the COVID-19 pandemic.

“It is important to ensure early initiation of antiviral therapy for treatment or chemoprophylaxis as recommended. It is essential to educate all patients, especially if they’re high risk and they’re having influenza symptoms, that they need to seek medical attention immediately.”

—Rupal Mansukhani, PharmD, CTTS, FAPhA

NEUMOCOCCAL DISEASE IS a widespread vaccine-preventable bacterial infection that transmits person-to-person via respiratory droplets. Carrie Koenigsfeld, PharmD, FAPhA, recently provided an update on pneumococcal vaccinations at the Directions in Pharmacy® conference at a session titled Current Pneumococcal Immunization Recommendations in Adults and the Role of the Pharmacist. The persons most vulnerable to severe pneumococcal disease are adults older than 65 years, children younger than 2 years, and individuals with immunocompromising conditions (cerebrospinal fluid leaks or cochlear implants, sickle cell disease, asplenia, HIV, chronic renal failure or nephrotic syndrome, malignancies, and medically immunosuppressed) and some chronic conditions (heart disease, lung disease, liver disease, diabetes, alcoholism, and cigarette smoking).

Current Advisory Committee on Immunization Practices (ACIP) recommendations include 2 approved vaccines, pneumococcal conjugate vaccine 13 (PCV13) and pneumococcal polysaccharide vaccine 23 (PPSV23). The PCV13 is 75% effective against invasive pneumococcal disease in patients older than 65 years. PPSV23 contains 23 serotypes and is 60% to 70% effective in preventing invasive pneumococcal disease; approximately 40% of invasive pneumococcal disease among adults aged 65 years or older is caused by serotypes unique to PPSV23. Both PCV13 and PPSV23 are single 0.5-mL injections typically administered intramuscularly; PPSV23 can be administered subcutaneously as well.

ACIP recommends adults aged 19 to 64 years with chronic medical conditions should receive 1 dose of PPSV23 followed by another dose of PPSV23 at least 5 years after the previous dose at age 65 years or older. Immunocompromised adults aged 19 to 64 years should receive 1 dose of PCV13 followed by 1 dose of PPSV23 at least 8 weeks after, then an additional PPSV23 at least 5 years after the previous dose for select patients. Dr Koenigsfeld said that once a dose of PPSV23 is given at age 65 years or older, no additional doses of PPSV23 should be administered, regardless of medical conditions.

“All eligible adults aged 19 to 64 years with chronic medical conditions should get 1 dose of PPSV23. Immunocompromised adults should get both PCV13 and PPSV23. For those 65 years or older, PPSV23 is recommended. Shared clinical decision making is recommended for immunocompetent adults for receipt of PCV13. It is important for pharmacists to understand and continue to stay abreast of ACIP recommendations.”

—Carrie Koenigsfeld, PharmD, FAPhA

As of November 2019, the ACIP no longer recommended routine administration of PCV13 to immunocompetent adults aged 65 years or older; instead, the provider and patient should make a shared clinical decision on whether to administer PCV13 before PPSV23. Patients who may be at increased risk for PCV13 serotype exposure may benefit from a PCV13 dose. When a decision to administer PCV13 is made, PCV13 should be given first, followed by 1 dose of PPSV23 1 year later. When a decision not to administer PCV13 is made, administer 1 dose of PPSV23 (at least 5 years after any previous PPSV23 dose). Dr Koenigsfeld also highlighted new conjugate pneumococcal vaccines in development as well.

Strategies to identify opportunities for vaccination are for pharmacists to screen adults with chronic medical or immunocompromising conditions when a patient is in the pharmacy for another vaccination, waiting for a prescription, or at discharge during transitions of care. Decreasing the burden of pneumococcal disease by addressing barriers and encouraging vaccination can decrease related morbidity and mortality, resulting in reduced hospitalizations and allowing frontline workers to focus on managing patients during the COVID-19 pandemic.

TO VIEW THE ON-DEMAND CE SESSION, PLEASE VISIT WWW.PHARMACYTIMES.ORG/GO/DIP-2021-PNEUMO.
**With mortality rates** once again on the rise, cardiovascular disease (CVD) is one of the leading causes of death both in the world and the United States. Because of this, CVD poses a significant burden to the US economy. By 2035, the projected total cost of CVD will approach $1.1 trillion. The main risk factors for developing atherosclerotic CVD (ASCVD) are high blood pressure, high serum cholesterol, and smoking, but by reducing LDL cholesterol (LDL-C) through lifestyle interventions or statins, these risks may be reduced. However, statin therapy presents many challenges due to patient intolerance, ineffectiveness, or noncompliance.

In an activity titled *Current and Emerging Treatment Options to Lower LDL-C in Patients With Statin Intolerance*, Joseph Saseen, PharmD, BCPS, BCACP, at the Directions in Pharmacy® conference examined nonstatin medications for patients who may benefit from reductions in their LDL-C.

Dr Saseen reviewed the 2018 AHA/ACC/Multisociety Cholesterol Guidelines and illustrated the importance of LDL-C lowering in patients with or at risk of developing ASCVD. High levels of LDL-C are directly associated with an increased risk of developing CVD, and evidence shows that lowering LDL-C levels can reduce this risk. Often, patients are not able to reach their LDL-C goals through statin therapy alone, and therefore nonstatin therapy may be necessary.

Dr Saseen discussed several nonstatin medications that can be used in addition to statin therapy to further decrease LDL-C levels. The medications he reviewed included ezetimibe, bile acid sequestrants, PCSK9 inhibitors, and bempedoic acid, which was FDA approved in February 2020. Dr Saseen highlighted the development of bempedoic acid, a citrate lyase inhibitor, as an oral LDL-C-lowering medication. The FDA also approved a fixed-dose combination of bempedoic acid with ezetimibe that provides a reduction in LDL-C comparable to a moderate-intensity statin. Evinacumab-dgnb was approved in 2021 as an adjunct to other LDL-C-lowering therapies for homozygous familial hypercholesterolemia. In addition, Dr Saseen covered inclisiran, an emerging small-interfering RNA therapy that selectively blocks PCSK9 protein production.

Dr Saseen emphasized the integral role of the pharmacist in identifying patients who may require further LDL-C lowering. This can be achieved by recognizing patient nonadherence to their statin or assessing their individual CVD risk. Pharmacists should remain educated on all current LDL-C-lowering options in order to provide individualized recommendations to health care providers or patients and promote adherence and proper medication use. Interventions should be focused on improving adherence to prescribed therapy, including reminders, integrated multidisciplinary educational activities, and pharmacist-led interventions, such as simplification of the drug regimen to once-daily dosing. Dr Saseen concluded that the pharmacist plays an influential role in improving outcomes in the management of hypercholesterolemia through explaining the benefits of LDL-C-lowering medications and including evidence-based nonstatin options into shared clinical decision making.

—Joseph Saseen, PharmD, BCPS, BCACP

*TO VIEW THE ON-DEMAND CE SESSION, PLEASE VISIT [WWW.PHARMACYTIMES.ORG/GO/DIP-2021-LDL-C](http://www.pharmacytimes.org/ce/go/dip-2021-LDL-c)*

*THE ACTIVITY IS AVAILABLE THROUGH JUNE 15, 2022.*
Expanding the Treatment Armamentarium for Patients With Heart Failure

The annual Directions in Pharmacy® conference had a variety of topics, and of particular interest was the session on heart failure (HF) presented by Robert J. DiDomenico, PharmD, BCPS-AQ Cardiology, FCCP, FHFS, ACC. In a program titled *Heart Failure With Reduced and Preserved Ejection Fraction: Optimizing Management and the Pharmacist’s Role in Patient Care*, Dr DiDomenico began by illustrating the growing burden of HF, with an estimated prevalence of over 8 million individuals in the United States by 2030. Management of HF is complicated by the presence of comorbidities and necessitates complex medication regimens.

Current management of HFpEF includes renin-angiotensin-aldosterone system inhibitors, β-blockers, nitrates/hydralazine, ivabradine, diuretics, and digoxin. Guideline-directed medical therapy of patients with HFpEF includes consideration of the stage and NYHA class of a patient with therapies added as needed. Pharmacists play a vital role in the management of these patients, offering guidance with medication selection and dose titration, monitoring symptoms and renal function as needed, providing patient education and assisting with transitions in care.

Despite these therapeutic options, there are remaining gaps in the optimal management of patients. Dr DiDomenico shared promising developments with the evolving landscape for patients with HFpEF and discussed clinical trial information. He began with sodium glucose co-transporter 2 (SGLT2) inhibitors, which have shown potential in patients with and without diabetes. An SGLT2 inhibitor studied includes empagliflozin in the EMPEROR-Reduced trial. The DAPA-HF trial for dapagliflozin led to the approval of this medication for HFpEF. Both of these SGLT2 inhibitors significantly lower the risk of HF hospitalization or cardiovascular (CV) death.

Vericiguat was approved in January 2021 and belongs to a novel class of medications known as soluble guanylate cyclase (sGC) activators which impact nitric oxide, vascular tone, and myocyte functioning. Vericiguat was shown to be a safe and well-tolerated option for patients with HFpEF in the VICTORIA trial, significantly reducing the risk of first HF hospitalization or CV death.

Omecamtiv mecarbil is a novel, cardiac myosin activator that improves cardiac muscle contractility by increasing the rate and magnitude of contraction without increasing oxygen demand. Studied in the GALACTIC-HF trial, omecamtiv mecarbil modestly lowered the risk of having an HF event or CV death.

The presentation then shifted to the discussion of HFpEF, where there are even fewer potential treatment options for patients, which makes management challenging. Treatment options under investigation have included medications that are studied or used in HFpEF including sacubitril/valsartan, vericiguat, and SGLT2 inhibitors.

It is important for pharmacists to remain current on the advancements in emerging therapies in the treatment of HF and to have a thorough understanding of the advantages and differences among medications. Pharmacists will play an important role in identifying patients that may benefit from new therapies and managing the complexity of regimens based on their risks and comorbidities as these new options are initiated and real-world experience provides additional evidence for their use.

“Outcomes in patients with HF are still poor, but we have several new therapies that have been shown to reduce outcomes in these patients. These emerging therapies include SGLT2 inhibitors, and also vericiguat and omecamtiv mecarbil, which may have a role in decreasing hospitalizations and mortality in these patients.”

—Robert J. DiDomenico, PharmD, BCPS-AQ Cardiology, FCCP, FHFS, ACC

PTCE WOULD LIKE TO ACKNOWLEDGE MERCK SHARP & DOHME CORPORATION FOR THEIR GENEROUS SUPPORT OF PHARMACIST EDUCATION.

To view the on-demand CE session, please visit www.pharmacytimes.org/go/dip-2021-heart-failure. The activity is available through June 15, 2022.
Importance of Contraceptive Use and the Role of the Pharmacist in Preventing Unintended Pregnancy

Unintended pregnancy is a serious public health concern in the United States, with rates of approximately 50%, partly due to incorrect or inconsistent contraceptive use. Planning and preparing for pregnancy is associated with socioeconomic benefits, but also decreased maternal and child morbidity and mortality. In a presentation at the Directions in Pharmacy® conference titled Current and New Contraception Methods: Key Considerations for Pharmacists to Individualize Options for Women, Brooke L. Griffin, PharmD, BCACP, reviewed current short-acting reversible contraception (SARC) methods, as well as the pharmacist’s role in helping female patients with selection and counseling.

Dr. Griffin reviewed different types of contraception and their efficacy, demonstrating that many options exist for those who do not intend to become pregnant. Dr. Griffin provided an overview of both long-acting reversible contraception (LARC) and SARC, with an emphasis on recently available short-acting products. LARC methods include intrauterine devices and an implant, which do not require self-administration to ensure efficacy. SARC methods, used more commonly, include combined hormonal contraceptives (CHCs) such as oral contraceptive pills, patches, and vaginal rings, as well as injections and a vaginal gel.

Of particular interest was discussion of how recently approved products are similar or differ from previously available contraceptive agents. Drospirenone/estetrol (Nextstellis) is a CHC that was approved in April 2021. It is the first approved contraceptive product containing estetrol, a naturally occurring estrogen derived from a plant source. The levonorgestrel/ethinyl estradiol transdermal patch (Twirla) is a new patch designed with additional layers to help maintain adhesion. Similar to the other available patch, individuals wear 1 patch for 1 week, then replace it with a new patch on the same day every week, with the fourth week being patch-free. Segesterone acetate/ethinyl estradiol vaginal ring (Annovera) is reusable for 1 year and is not refrigerated. Once inserted, the ring remains in place for 3 weeks, then is removed for 1 week. Drospirenone tablets (Slynd) offers another option for a progestin-only pill. It has a longer half-life allowing for a 24-hour intake window for missed pills. The lactic acid, citric acid, and potassium bitartrate vaginal gel (Phexxi) is hormone-free and is used only when needed. It works by maintaining an acidic environment.

Despite the various contraceptive options available to patients, a failure to choose the most optimal method and a lack of proper use can lead to unintended pregnancies. A useful tool is the CDC Medical Eligibility Criteria for Contraceptive Use. Dr. Griffin urges pharmacists to educate health care providers and patients about the effectiveness of LARC and SARC methods. Pharmacists must then inform patients about how to correctly use their selected contraceptive method, especially if it requires self-administration. Pharmacists should educate patients about potential adverse effects (AEs) and how to manage them, as well as signs of serious AEs.

Dr. Griffin also noted the role of pharmacists in improving access to contraceptive care with new state laws allowing pharmacists to expand their scope of practice by prescribing select hormonal contraceptives. It is necessary that when prescribing contraceptives, the pharmacist provides individualized drug therapy. This can prevent unintended pregnancy by ensuring that patients use the most effective method for their personal needs and increasing likelihood of adherence. Proper contraceptive use may increase the prospect of healthier pregnancies and allow women to engage in family planning, as well as other health benefits.

“Pharmacists should stay abreast of new and recently available contraceptives and the pharmacist’s role and responsibilities in contraceptive care. It is important to understand the nuances of all the products because there are many unique characteristics, which is a benefit to our patients.”

—Brooke L. Griffin, PharmD, BCACP

TO VIEW THE ON-DEMAND CE SESSION, PLEASE VISIT WWW.PHARMACYTIMES.ORG/GO/DIP-2021-CONTRACEPTIVES. THE ACTIVITY IS AVAILABLE THROUGH JUNE 15, 2022.
Continuing the Conversation:
Optimizing the Role of the Pharmacist in Diabetes Management With CGM

**Educational Objectives**

*At the completion of this activity, the participant will be able to:*

- Classify the limitations of self-monitoring of blood glucose and the evolving role of continuous glucose monitoring (CGM) devices in the management of diabetes
- Examine the FDA-approved CGM devices including features, proper use, and accuracy
- Determine the clinical benefits associated with CGM devices and impact that data have on diabetes management
- Identify the role of the pharmacist in recognizing patients who may benefit from CGM devices and providing necessary counseling to improve diabetes management

**Target Audience:** Pharmacists

**Activity Type:** Application

**Release Date:** May 27, 2021

**Expiration Date:** June 15, 2022

**Estimated Time to Complete Activity:** 2.0 hours

**Fee:** This lesson is offered for free at www.pharmacytimes.org.

**Introduction: Understanding the Clinical Burden of Diabetes**

According to the Centers for Disease Control and Prevention (CDC), an estimated 10.5% of the US population had diabetes in 2018. Diabetes is associated with many complications and comorbidities, including hypertension, kidney disease, obesity, dyslipidemia, mental health disorders, and stroke. There is significant financial cost with diabetes, and the American Diabetes Association (ADA) notes an increase in economic burden by 26% from 2012 to 2017. The cost of diabetes care and medications has continued to increase, and quality care has been linked to social determinants of health (SDOH). Environmental, social, political, and economic factors strongly influence health outcomes, especially related to diabetes.

Glycemic control is assessed by monitoring glucose and hemoglobin A1c (HbA1c). Patients can monitor glucose with glucometers or with continuous glucose monitoring (CGM) devices. Traditionally, self-monitoring blood glucose (SMBG) has been measured via fingerstick with lancets, test strips, and glucometers. Though these measurements are clinically useful, there are many limitations. Fingerstick SMBG does not always correlate with HbA1c, as the readings provide only a snapshot of a person’s blood glucose (BG) at a certain point in time, and HbA1c is a measure of average glycemia over 3 months. An HbA1c of 7% correlates with an estimated average glucose of 154 mg/dL; however, HbA1c does not provide data on hypoglycemia or variability in glucose, and mean glucose may actually range from 123 to 185 mg/dL. Adherence to fingerstick SMBG is a concern and is influenced by social, psychological, and financial concerns, including fear of needles, social stigma, and cost of testing materials.
Usage of CGM in Diabetes Management

CGM is another option for monitoring glucose. CGM devices use interstitial fluid to measure glucose as opposed to the traditional capillary blood glucose with SMBG. The interstitial fluid measurements are transmitted to a receiver that can show glucose readings, trends, and fluctuations over 24 hours, allowing measurements of glucose at times when SMBG is inconvenient (eg, while sleeping). The available information with the use of CGM is vast, and these devices can provide more than just a snapshot in time, which allows for targeted medication adjustments. In the age of technology, real-time information not only provides valuable information but also may be associated with greater satisfaction.

Utilizing CGM has the potential to improve overall glycemic control and decrease hypoglycemic episodes in many persons with diabetes. To ensure the best outcomes when employed, effort must be put in to individualizing CGM use, along with adequate initial and periodic training, education, and support for providers, persons with diabetes, and their caregivers. Data supporting the use of CGM are more robust for individuals with type 1 diabetes (T1D), including youths and adolescents, and during pregnancy than for persons with type 2 diabetes (T2D), though use is still supported in T2D. The ADA recommends the use of personal real-time CGM (rtCGM, patient-placed, automatically transmitted) or intermittently scanned CGM (isCGM, patient-placed, requires scanning for data transmission) when multiple daily injections (MDIs) or continuous subcutaneous insulin infusion (CSII) delivery devices are being used, noting that the frequency of use should be high (at least daily for rtCGM and scanned at least every 8 hours for isCGM) to provide the greatest impact. Additionally, professional CGM (clinic-based device placed by provider) with or without other types of CGM may be beneficial in finding and correcting hyper- or hypoglycemia in persons with diabetes on basal insulin or noninsulin therapies. The American Association of Clinical Endocrinologists (AACE) and American College of Endocrinology (ACE) recommend utilizing CGM over SMBG in the majority of persons with diabetes due to CGM affording the ability for more rapid medication adjustments, increased availability of data to assist in glucose management, the potential for improved patient understanding, and improvements in glycemic control. CGM may be useful for persons with diabetes who are concerned or at risk for hypoglycemia, those with hypoglycemia unawareness, and those with severe hyperglycemia.

Interpretation of CGM Data

An ambulatory glucose profile (AGP) is the main reporting mechanism for interpretation of CGM. AGPs provide essential information to assist in the management of glucose, such as time in range (TIR), time below range (TBR), time above range (TAR), and glucose management indicator (GMI). TIR provides information on the time a patient’s glucose is within target ranges, and the ADA suggests it...
can be used as a method for assessing glycemic control. TIR should be patient specific, but typically is recorded as time between 70 and 180 mg/dL. TBR is broken down into time between 54 and 69 mg/dL and time below 54 mg/dL; TAR is delineated as 181 to 250 mg/dL and time above 250 mg/dL. Each aspect has a percent acceptable cutoff, which is listed in the FIGURE. Interpreting an AGP can be challenging, but considering TBR and TAR, among other reported parameters, can assist in specializing care for persons with diabetes. GMI represents estimated HbA1c, in this case the 10- to 14-day average glucose but has not been the focus of CGM interpretation due to misinterpretation and confusion. Though the calculation can be cumbersome, GMI alongside other CGM data gives more real-time glucose data to assist in medication adjustments. See SIDEBAR for questions to think about.

Additionally, data are available that suggest the percent TIR correlates well with HbA1c. TIR may be used, possibly in addition to or in place of HbA1c, as a clinical trial outcome measure, an assessment of glycemic control, and an assessment of the potential for complications related to diabetes. One study evaluated 18 articles with percent TIR and HbA1c pairings using linear regression and Pearson correlation coefficient. The authors concluded that for every 10% change in TIR, a 0.8% change in HbA1c could be anticipated. Additionally, correlations between percent HbA1c and percent TIR were deduced and are presented in TABLE 1. More robust data are needed to verify this correlation and confirm that percent TIR relates to improved long-term outcomes, but the potential for additional sources of data to assist in glucose management is an exciting prospect.

Data Supporting Use of CGM
Several meta-analyses have been conducted in persons with both T1D and T2D assessing the comparative impact of CGM use versus SMBG on HbA1c, TIR, TBR, TAR, and glucose variability (reported as coefficient of variance). A systematic review of 15 open-label, randomized controlled trials (RCTs) consisted of a variety of patient populations (T1D, T2D, children, pregnancy) using MDI or CSII therapy and CGM (rtCGM, isCGM, or sensor-augmented pump [SAP]) versus SMBG, CGM sensor off, or CSII alone (comparator groups). Outcomes were reported as weighted mean difference (WMD) and included co-primary outcomes of change in HbA1c and TIR (minutes). Secondary outcomes included TBR, TAR, and glucose variability as coefficient of variation (CV). Additionally, a prespecified subgroup analysis was completed regarding different CGM types, type of diabetes, insulin delivery device, and reasoning for CGM use. The authors demonstrated that the use of CGM versus comparator groups provided a “modest” reduction in HbA1c (WMD –0.17% [–0.29 to –0.06]; \( P = .003, I^2 = 96.2\%\)), more TIR (WMD 70.74 minutes [46.73-94.76]; \( P <.001, I^2 = 66.38\%\)), and less TBR, TAR, and CV. When rtCGM and isCGM were evaluated separately, rtCGM resulted in a significantly lower HbA1c and improved TIR, TBR, and TAR, whereas isCGM demonstrated better impact on TIR, TBR, and level 2 TAR (>250 mg/dL). SAP showed significantly better outcomes for TIR and level 2 TBR (<54 mg/dL). A significant HbA1c reduction was also noted for patients with T1D, but this was not found for patients with T2D. Though there were several limitations to this meta-analysis, including high heterogeneity of the RCTs included for many of the assessments, this adds to the plethora of data supporting the use of CGM in appropriate patient populations to assist in improving glycemic outcomes. This trial, in addition to previously published literature, supports the role of CGM in improving glycemic parameters in persons with T1D and T2D.

### TABLE 1. HbA1c AND TIR CORRELATION

<table>
<thead>
<tr>
<th>TIR (%)</th>
<th>HbA1c (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>100</td>
<td>4.3</td>
</tr>
<tr>
<td>90</td>
<td>5.1</td>
</tr>
<tr>
<td>80</td>
<td>5.9</td>
</tr>
<tr>
<td>70</td>
<td>6.7</td>
</tr>
<tr>
<td>60</td>
<td>7.5</td>
</tr>
<tr>
<td>50</td>
<td>8.3</td>
</tr>
<tr>
<td>40</td>
<td>9.0</td>
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<td>30</td>
<td>9.8</td>
</tr>
<tr>
<td>20</td>
<td>10.6</td>
</tr>
<tr>
<td>10</td>
<td>11.4</td>
</tr>
<tr>
<td>0</td>
<td>12.1</td>
</tr>
</tbody>
</table>

HbA1c, hemoglobin A1c; TIR, time in range.

Appropriate Patient Selection and the Evolving Landscape of CGM
Data supporting the use of CGM in a variety of patient populations are available. Many studies have been described previously in the literature, so this review will focus on special populations.
**STAR**

What impact has COVID-19 had on the use of CGM in persons with diabetes?

*S = Stop; T = Think; A = Assess; R = Review

**Coronavirus-19 (COVID-19)**

With the onset of the COVID-19 pandemic, new strategies were needed to combat a highly infectious virus, lack of personal protective equipment (PPE), and critically ill patients with variable BG. Traditional inpatient BG monitoring is performed with point-of-care devices using multiple daily samples of capillary blood. In response to the public emergency, the Food and Drug Administration (FDA) issued a policy expanding the use of remote, noninvasive monitoring technology in hospitalized patients, which included the use of CGM. 21

Persons with diabetes appear to be at higher risk of contracting COVID-19 as well as developing complications and severe illness related to the virus. 22,23 Maintaining glycemic control is an important factor in preventing severe illness, and individuals with diabetes may need more frequent glucose monitoring, adjustment in medications, or education on proper sick day management. 23

There are many considerations for implementation of CGM in the inpatient setting during the COVID-19 era, as well as several clinical recommendations to help conserve PPE and improve clinical staff ratios. 24 Patients with moderate to severe hyperglycemia (BG ≥200 mg/dL) who require more intensive insulin regimens or those who are prone to hypoglycemia, frailty, and falls may benefit from the frequent monitoring provided by CGM devices. The authors of one review stressed the importance of training staff, choosing appropriate patients for CGM, using the device/sensor correctly, documenting information in the medical record, removing sensors when delicate procedures are performed, and downloading/reviewing data when implementing CGM. 24

A pilot study was conducted that used CGM in critically ill patients with COVID-19. 25 The study included patients with COVID-19 and diabetes or hyperglycemia (BG >300 mg/dL) who received intravenous (IV) or subcutaneous (SC) insulin. Eleven patients were monitored with Medtronic Guardian Connect or Dexcom G6 CGM device, and readings were correlated with fingerstick capillary BG. The authors concluded that the use of CGM in this patient population was beneficial in achieving glycemic control, reducing staff exposure to the virus, and conserving valuable PPE. 25

The acute need for CGM in the inpatient setting has brought to light the potential impact of CGM for patients who are hospitalized. Benefits have been seen with reduction of PPE and reduced high-risk patient exposure for hospital staff; however, there are some limitations with its use, including patients undergoing magnetic resonance imaging, computed tomography, and diathermy. 14,15,24-26

In the setting of the COVID-19 pandemic, CGM was also helpful in the ambulatory setting. Efforts to decrease in-person visits enhanced the need for remote monitoring. CGM assisted in productive telehealth visits, allowing for easily transmittable glucose data and medication adjustment. 27

**Children and Adolescents**

Reductions in hypoglycemic episodes have been seen in children and adolescents with T1D when rtCGM is used. Adolescents may also see an improvement in HbA1c. Though rtCGM is approved for glucose monitoring in children aged 2 years and older and isCGM is approved for those aged 4 years and older, the ideal TIR has not been established. Data for the use of CGM in this age group with T2D are lacking. 2

In a survey of primary caregivers for children aged 1 year to less than 8 years with T1D, parents and caregivers discussed the benefits and barriers of using CGM. 28 Noted benefits included continuous access to the child’s glucose levels even while separated from the child, decreased worry, increased confidence in secondary caregivers, and ability to manage glycemic excursions. Caregivers discussed barriers of physical issues (pain on insertion), overwhelming amounts of information, and technical issues (frequency of alerts, inaccurate information). 28 Evidence supporting CGM use in children and adolescents has been discussed elsewhere. 8

**Pregnancy**

Glycemic targets are stricter in persons with T1D during pregnancy to assist in positive outcomes. Though not approved in the United States for patients who are pregnant, CGM has demonstrated the potential to improve HbA1c without increasing hypoglycemia and has been associated with decreased fetal outcomes, such as large birth weight, length of stay, and neonatal hypoglycemia, in clinical trials. 2

An open-label, randomized, controlled trial conducted in 7 countries, including the United States, evaluated 325 pregnant women or women who were planning to become pregnant with T1D on CSII or MDI therapy. 29 Participants were aged between 18 and 40 years (average 32 years), had T1D for at least a year with an HbA1c of 6.5% to 10% if pregnant or...
7.0% to 10.0% if planning on becoming pregnant, and could not have used CGM regularly prior to the trial. Randomization was 1:1, CGM (with SMBG) versus control (SMBG), stratified by insulin delivery device and baseline HbA1c. In participants who were pregnant, the difference in HbA1c at 34 weeks was the primary outcome. In those planning to become pregnant, the primary outcome was change in HbA1c at 24 weeks from randomization or to conception. Secondary outcomes included TIR, TAR, and TBR; hypoglycemia; and, for pregnant women, gestational complications, fetal outcomes, and length of hospital stay. Most participants were of European descent and had T1D for approximately 17 years, with an average HbA1c of 7.6%, though participants who were pregnant had lower baseline HbA1c (7.4% vs 7.9%). Change in HbA1c from baseline to 34 weeks’ gestation was significantly greater in the CGM versus SMBG group (−0.19%; CI, −0.34 to −0.03; \( P = .0207 \)). Pregnant women in the CGM group also spent more TIR (\( P = .0034 \)), and infants were less likely to be considered large for gestational age (\( P = .021 \)), less likely to require dextrose for neonatal hypoglycemia (\( P = .025 \)), and had shorter length of hospital stay (\( P = .0091 \)). No significant reductions were seen in other secondary outcomes, such as loss of pregnancy, preterm births, or maternal complications, and no significant change in HbA1c within the group of patients planning to become pregnant was observed. Additionally, no significant differences were noted in hypoglycemia in either of the CGM groups compared with their respective SMBG group. A significant increase in clinic visits in pregnant participants using CGM was seen (7.2 vs 6.8; \( P = .0171 \)), and overall, more adverse effects were reported in those wearing a CGM (RR, 1.4; CI, 1.0–1.8; \( P = .041 \)), of which the most common issue reported was skin reaction, though no difference in serious events was seen. Of note, both groups (CGM and SMBG) were requested to complete SMBG at least 7 times daily, which may not be generalizable to clinical practice.29 Suggested targets for CGM use in pregnancy are provided in TABLE 2.2

### Older Adults
The use of CGM in persons with T1D aged older than 60 years may help mitigate hypoglycemia.2 The Wireless Innovation for Seniors with Diabetes Mellitus (WISDM) study group evaluated the impact of CGM versus SMBGs on hypoglycemia incidence in persons with T1D who were older than 60 years, used CSII or MDI therapy, had not used CGM in the past 3 months, and whose HbA1c was 10% or lower. Two hundred and three people from 22 endocrine clinics within the United States were included. The primary outcome was the pooled percent of time glucose was below 70 mg/dL within the 7 days prior to several follow-up visits (weeks 8, 16, and 26). Several secondary outcomes were assessed, including percent of time glucose was less than 54 mg/dL, percent of time above 180 and 250 mg/dL, and mean change in HbA1c. Significantly less time was spent below 70 mg/dL in the CGM group versus the SMBG group (−1.9% [−2.8 to −1.1]; \( P < .001 \)). Additionally, people using CGM had significantly less time below 54 mg/dL (−1% [−1.4 to −0.5]; \( P < .001 \)), time above 180 mg/dL (−5.8% [−8.8 to −2.8]; \( P < .001 \)), and time above 250 mg/dL (−3.6% [−5.2 to −2.2]; \( P < .001 \)), and they had a significantly lower HbA1c at 26 weeks (−0.3% [−0.4 to −0.1]; \( P < .001 \)). These data suggest that hypoglycemia may be minimized with the use of CGM in older adults with T1D and may provide overall better glucose control as well.30

### Currently Available Integrated CGM Devices
Integrated CGM (iCGM) devices function to assist in the management of diabetes or a related disorder and have the ability to connect to multiple digital devices to transmit glucose readings frequently and accurately.31 FDA approval must be granted to be considered an iCGM. Currently, 2 devices have achieved this designation (G6 and FreeStyle Libre 2), though completion of a recent clinical trial suggests an additional device may become available (FreeStyle Libre 3).32 Criteria that must be met include demonstrating glucose readings within 15% of lab glucose 70% of the time if the

### TABLE 2. TARGETS FOR CGM USE IN PREGNANCY AND ADULTS

<table>
<thead>
<tr>
<th>Goals</th>
<th>Targets for CGM Use in Adults</th>
</tr>
</thead>
<tbody>
<tr>
<td>TIR (70-180 mg/dL)</td>
<td>&gt;70%</td>
</tr>
<tr>
<td>TBR &lt;70 mg/dL</td>
<td>&lt;4%</td>
</tr>
<tr>
<td>TBR &lt;54 mg/dL</td>
<td>&lt;1%</td>
</tr>
<tr>
<td>TAR &gt;180 mg/dL</td>
<td>&lt;25%</td>
</tr>
<tr>
<td>TAR &gt;250 mg/dL</td>
<td>&lt;5%</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Goals</th>
<th>Targets for CGM Use in Pregnancy</th>
</tr>
</thead>
<tbody>
<tr>
<td>TIR (63-140 mg/dL)</td>
<td>&gt;70%</td>
</tr>
<tr>
<td>TBR &lt;63 mg/dL</td>
<td>&lt;4%</td>
</tr>
<tr>
<td>TBR &lt;54 mg/dL</td>
<td>&lt;1%</td>
</tr>
<tr>
<td>TAR ≥140 mg/dL</td>
<td>&lt;25%</td>
</tr>
</tbody>
</table>

CGM, continuous glucose monitoring; TAR, time above range; TBR, time below range; TIR, time in range.
reading is between 70 and 180 mg/dL and 80% of the time if lab glucose is greater than 180 mg/dL. Additionally, if the device glucose is less than 70 mg/dL, lab glucose must be within 15 mg/dL 85% of the time.

Other available CGM devices, though not integrated, include Medtronic Guardian Connect and Guardian Connect 2 and Senseonics Eversense.

Dexcom G6
The G6 was the first iCGM approved in the United States (in 2018) and has 3 main components: a sensor, transmitter, and reader. The transmitter is reusable for up to 3 months, and the sensor is a one-time use piece that can be worn for up to 10 days. Readings are available every 5 minutes and wearers are alerted to high, low, and urgent low readings. High and low alerts may be set by the wearer and can be set for between 120 and 300 mg/dL and between 60 and 90 mg/dL, respectively. The urgent low alert is not adjustable and sounds if glucose is at or below 55 mg/dL. The G6 device is compatible with smartphone applications, pump systems, and an InPen device, and readings are transmitted directly to the device reader.

Abbott FreeStyle Libre 2
The Libre 2 was approved in the summer of 2020 as an iCGM and has 2 components: a sensor and a reader. The sensor may be worn for up to 14 days, and readings are available every minute. High and low reading alerts are customizable for ranges between 120 and 400 mg/dL and between 60 and 100 mg/dL, respectively. The Libre 2 has a smartphone application but is not currently compatible with pumps or automated pen delivery devices. Acetaminophen and other common substances that interfere with accuracy of glucose readings in other CGM devices do not affect the Libre 2 accuracy, but ascorbic acid in high doses (>500 mg/day) may make glucose appear higher and lead to missed hypoglycemia.

Rate and Direction of Change
Rate and direction of change are additional important concepts to review. Each CGM provides arrows indicating trends to assist with interpretation and management. Wearing CGMs are able to identify if glucose is increasing, decreasing, or remaining stable, as well as how quickly those changes are occurring. Definitions of arrows provided by each FDA-approved iCGM device and their associated meaning are denoted in TABLE 5.

The Role of the Pharmacist
Optimizing the Use of CGM and Interpreting Data
Pharmacists can play a critical role in the optimization and interpretation of CGM data and are uniquely positioned to educate persons with diabetes about CGM. As such, pharmacists should know some of the limitations of SMBG and be able to discuss the use of newer technologies with patients. When dispensing CGM devices, pharmacists should educate patients on how to correctly place the sensor; how to connect

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**TABLE 3. SUMMARY OF G6 FEATURES**

<table>
<thead>
<tr>
<th>Feature</th>
<th>Details</th>
</tr>
</thead>
<tbody>
<tr>
<td>Approved age group (years)</td>
<td>≥2</td>
</tr>
<tr>
<td>Sensor wear time (days)</td>
<td>10 (extender available, but if used may not meet iCGM requirements)</td>
</tr>
<tr>
<td>Calibration</td>
<td>No</td>
</tr>
<tr>
<td>Warm-up period (hours)</td>
<td>2</td>
</tr>
<tr>
<td>Frequency of glucose reading (times per hour)</td>
<td>12</td>
</tr>
<tr>
<td>Alarms/alerts</td>
<td>Yes (high and low, adjustable; urgent low, not adjustable)</td>
</tr>
<tr>
<td>Device compatibility</td>
<td>Yes</td>
</tr>
<tr>
<td>Pump, automated delivery device compatibility</td>
<td>Yes</td>
</tr>
</tbody>
</table>

**TABLE 4. SUMMARY OF FREESTYLE LIBRE 2 FEATURES**

<table>
<thead>
<tr>
<th>Feature</th>
<th>Details</th>
</tr>
</thead>
<tbody>
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<tr>
<td>Sensor wear time (days)</td>
<td>14</td>
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<tr>
<td>Calibration</td>
<td>No</td>
</tr>
<tr>
<td>Warm-up period (hours)</td>
<td>1</td>
</tr>
<tr>
<td>Frequency of glucose reading (times per hour)</td>
<td>60</td>
</tr>
<tr>
<td>Alarms/alerts</td>
<td>Yes (high and low, adjustable)</td>
</tr>
<tr>
<td>Device compatibility</td>
<td>Yes</td>
</tr>
<tr>
<td>Pump, automated delivery device compatibility</td>
<td>No</td>
</tr>
</tbody>
</table>

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**STAR**
What role do pharmacists play in the use of CGM for the management of diabetes?
Facilitating Access to CGM

The advent of new technology for diabetes is an exciting potential addition to treatment regimens, but the cost associated with CGM devices may be of concern for some people. Pharmacists are able to assist persons with diabetes by choosing the correct or covered CGM device. Medicare

the sensor, transmitter, and receiver; and how to use the information available. With proper education, pharmacists can ease patient concerns regarding technology and help enhance the utility of the device. Additionally, pharmacists can counsel on potential drug interactions that may affect the CGM, including acetaminophen and vitamin C.14,15 Additional counseling pearls and questions that may be asked by patients are reviewed in the COUNSELING CORNER.

A recent article describes a 5-step acronym (DATAA) for reviewing CGM data with the following steps: (1) Download the data, (2) Assess safety, (3) Time in range, (4) Areas for improvement, and (5) Action plan.37 Pharmacists can follow this process to assess blood glucose data, hypoglycemia risk, potential adjustments in medication, and need for additional patient education.37

The International Diabetes Center developed a 9-step plan to standardize the interpretation of the AGP and its use in practice.38 This plan includes ensuring an adequate number of days of data for decision making; personalizing patient information including doses of insulin, meal times, medication administration, and type of diabetes; allowing the person with diabetes to describe their interpretation of the data; finding patterns of hypo- and hyperglycemia; discussing areas of wide glycemic variability; creating an action plan; and documenting the information both for the patient’s use and documentation in the electronic medical record.38 Persons with diabetes can use the data from the AGP to analyze days when TIR was greater and reflect on diabetes self-management behaviors. The information can help individuals with diabetes see the effects of factors, such as exercise, meals, and medications, on glucose.38

Pharmacist-driven and physician-driven interpretation of CGM profiles in adults with FreeStyle Libre Pro (a professional CGM) have been examined.39 The study evaluated change in HbA1c from baseline to 6 months, as well as pharmacologic and nonpharmacologic interventions made during the study period. Though both pharmacist- and physician-driven interpretation and management resulted in significant reductions in HbA1c from baseline, pharmacist-driven review and management correlated with greater HbA1c reduction and a larger number of pharmacologic interventions.39

<table>
<thead>
<tr>
<th>TABLE 5. CGM TRENDS</th>
<th>FREESTYLE LIBRE 2</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>G6</strong></td>
<td><strong>FREESTYLE LIBRE 2</strong></td>
</tr>
<tr>
<td><strong>Arrow</strong></td>
<td><strong>Arrow</strong></td>
</tr>
<tr>
<td>▶️</td>
<td>▶️</td>
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<td>▶️</td>
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</tbody>
</table>

CGM, continuous glucose monitor.
*Arrows may appear differently. 

COUNSELING CORNER

**EDUCATIONAL PEARLS**

Q “Can I shower or swim with a CGM?”
A The sensor (FreeStyle Libre 2) or sensor/transmitter (G6) is water-resistant. The reader should not be submerged in water.

Q “What should I do if I'm concerned that my CGM readings aren't correct?”
A Apply the sensor to a hairless, dry area. Do not apply to areas with lotion or other oily substances that may affect the adhesive. Additionally, products are available to increase adhesiveness. If sensor falls off, dispose of sensor and use a new one.

Q “What's the range of glucose that my CGM will measure?”
A FreeStyle Libre 2: back of the arm. G6: abdomen. Patients aged 2-17 years can also use buttocks.

Q “What's the range of glucose that my CGM will measure?”
A For both FreeStyle Libre 2 and G6, the displayed range is 40-400 mg/dL.

Q “Where can I place my sensor?”
A Rotate site of insertion every use. Avoid applying to areas with scars or other skin abnormalities.
beneficiaries who meet eligibility requirements can receive coverage for FreeStyle Libre 2 and G6. These requirements include: SMBG 4 or more times per day, 3 or more insulin injections per day or pump therapy, need for frequent insulin adjustments, visit with diabetes provider within last 6 months, and has follow-up appointment at least every 6 months. Commercial insurance payers vary in coverage; however, as these technologies become more common, it is likely that these devices will become a new standard of care. Pharmacists can identify persons with diabetes who might need further financial assistance and help locate coupon cards or vouchers offered through manufacturers.40

Conclusion
The data supporting the use of CGM within the practice of diabetes management continue to expand, including information regarding correlation to HbA1c and overall glucose control. Though data are lacking regarding long-term outcomes with CGM, continued research and usage within practice may assist in expanded use and impact. With the continued evolution of CGM in various populations and enhancement of technology allowing CGMs to be integrated with automated systems and devices, the likelihood of encountering CGMs in practice is heightened. As an easily accessible health care resource, it is vital that pharmacists stay up-to-date on innovations in diabetes management.

ADDITIONAL RESOURCES

American Diabetes Association Standards of Medical Care in Diabetes 2021
care.diabetesjournals.org/content/44/Supplement_1

Association of Diabetes Care and Education Specialists (ADCES)
diabeteseducator.org

American Association of Clinical Endocrinologists (AACE) Diabetes Resource Center
pro.aace.com/disease-state-resources/diabetes

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17. Pickup JC, Freeman SC, Sutton AJ. Glycaemic control in type 1 diabetes during real time continuous glucose monitoring compared with self monitoring of blood glucose: meta-analysis of randomised controlled trials using individual patient data. BMJ. 2011;343:d3805. doi: 10.1136/bmj.d3805


21. FDA. Enforcement policy for non-invasive remote monitoring devices used to support patient monitoring during the coronavirus disease 2019 (COVID-19) public health emergency. Published
31. FDA. Product classification: integrated continuous glucose monitor, factory calibrated.

INSTRUCTIONS FOR EARNING CREDIT:

Begin the activity by reading the content in its entirety.
Go to www.pharmacytimes.org/go/CC-CGM to access the online version of this activity.
Click “Proceed,” then complete the online pretest.
Once completed, click “Next” until reaching the activity posttest.
Complete the online posttest and activity evaluation form.
After successfully completing the posttest and evaluation form, this information will be uploaded to CPE Monitor.
You must complete these steps before the activity expires in order to receive your credit.
You may view your credit within 48 hours at www.mycpemonitor.net.

NOTE: Your CE credit will be automatically uploaded to CPE Monitor. Please ensure that your Pharmacy Times® account is updated with your NABP e-profile ID number and your date of birth. Participation data will not be uploaded into CPE Monitor if you do not have your NABP e-profile ID number and date of birth entered into your profile on www.pharmacytimes.org.

SYSTEM REQUIREMENTS FOR COMPLETION:
Computer or smartphone with internet-access web browser (IE7.0+ or Webkit-/Mozilla-compatible) with JavaScript enabled.

FOR QUESTIONS ABOUT THIS INTERNET CPE ACTIVITY, PLEASE CONTACT: ceinfo@pharmacytimes.com.

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POSTTEST QUESTIONS

1. What is a potential limitation of using a continuous glucose monitor (CGM) in the inpatient setting?
   A. Personal protective equipment conservation
   B. Limiting staff exposure
   C. Lack of FDA policies for use in this setting
   D. Need for removal for procedures

2. Which patient is the best candidate for CGM use?
   A. A 10-year-old patient recently diagnosed with type 2 diabetes (T2D) on metformin
   B. A 32-year-old patient diagnosed with type 2 diabetes (T2D) on metformin and semaglutide
   C. A 45-year-old patient diagnosed 6 years ago with T2D on metformin and multiple dose injection (MDI) therapy who has refilled glucagon multiple times
   D. A 62-year-old patient diagnosed 3 years ago with T2D on metformin and empagliflozin

3. Though not approved for use in the United States in persons who are pregnant, CGMs have been shown to decrease the risk of which maternal/fetal complications?
   A. Large birth weight
   B. Loss of pregnancy
   C. Preterm birth
   D. Maternal hypertension

Please use the following case to answer questions 4 and 5.

A parent of a child with type 1 diabetes (T1D) presents to your pharmacy counter to pick up prescriptions for test strips and lancets. While you are counseling the parent, they inquire about “wearable” glucose monitors they have seen on TV and if their child would be a good candidate. The parent indicates their child is 5 years old, has some issues with hypoglycemia, and is currently using MDI therapy. The parent is concerned with additional “sticks” and would like a device with the longest wearable time.

4. Which is the best device to discuss with the parent?
   A. FreeStyle Libre 2
   B. FreeStyle Libre 3
   C. Dexcom G6
   D. The child is not a good candidate for any CGM device

5. What is the most appropriate education point to discuss with the parent about CGM use in children?
   A. CGM readings are only accessible to the child, not the caregiver.
   B. All integrated CGMs (iCGMs) have low and high glucose alerts to assist with glucose management.
   C. Time-in-range goals are well established for children.
   D. All iCGMs do not require a warm-up period.

6. A patient presents to your community pharmacy while grocery shopping. They picked up their FreeStyle Libre 2 last week and started using it yesterday. The patient indicates they feel fine and their glucose was 118 mg/dL a few minutes ago, but that an arrow pointing slightly downwards (▼) was on the screen also. They wanted to check to see what the arrow meant as they have not seen this before. What is the most appropriate interpretation to provide the patient?
   A. Your glucose is decreasing by 30-90 mg/dL in 30 minutes.
   B. Your glucose is decreasing by >2 mg/dL/min.
   C. Your glucose is decreasing by >90 mg/dL in 30 minutes.
   D. Your glucose is decreasing by 1-2 mg/dL/min.

7. Which option is a potential limitation associated with CGMs identified by caregivers?
   A. Information overload
   B. Decreased worry
   C. Improved confidence addressing glucose
   D. Increased access to glucose readings

8. How frequently (times per hour) does the Dexcom G6 read glucose?
   A. 2
   B. 12
   C. 30
   D. 60
9. A 70-year-old person with T2D presents to your community pharmacy. The person has Medicare coverage, checks their blood glucose 4 times daily, and their medications include metformin, insulin glargine, and insulin aspart TID with meals. The patient is interested in CGM but reports they have not seen their diabetes provider in over a year. What is the best assessment regarding this patient’s Medicare eligibility for CGM?
   A. The patient meets current Medicare eligibility criteria for CGM.
   B. The patient does not check blood glucose enough times per day to qualify.
   C. The patient needs to be seen by their diabetes provider before considering CGM.
   D. The patient needs to be on pump therapy to be eligible.

10. In a person with diabetes using FreeStyle Libre 2 to help manage blood glucose, which of the following medications on a patient’s profile should a pharmacist identify as a potential drug/CGM interaction?
   A. Hydroxyurea
   B. Ascorbic acid
   C. Metformin
   D. Acetaminophen
Exploring the Efficacy and Safety of Short-Acting Reversible Contraception Methods: A Review for Pharmacists

**EDUCATIONAL OBJECTIVES**

At the completion of this activity, the participant will be able to:

- Explore the clinician and patient factors that may influence selection of a contraception method
- Compare hormonal versus nonhormonal formulations of short-acting reversible contraception (SARC) methods
- Investigate the mechanisms of action, dosing, administration, and potential adverse effects associated with current and new SARC options
- Identify the role of the pharmacist in improving patient access to novel SARC formulations and in educating patients about the proper use of these agents

**TARGET AUDIENCE:** Community pharmacists

**ACTIVITY TYPE:** Application

**RELEASE DATE:** June 15, 2021

**EXPIRATION DATE:** June 15, 2022

**ESTIMATED TIME TO COMPLETE ACTIVITY:** 2.0 hours

**FEE:** This lesson is offered for free at www.pharmacytimes.org.

**Introduction**

Pharmacists are an important resource to patients for providing education on contraception and contraceptive methods as well as providing services such as prescribing or administering contraception. As of April 2021, 15 states (including the District of Columbia) have authorized pharmacists to provide hormonal contraception through a statewide protocol or standing order process; these states are Arkansas, California, Colorado, District of Columbia, Hawaii, Idaho, Maryland, Minnesota, New Hampshire, New Mexico, Oregon, Utah, Vermont, Virginia, and West Virginia.¹ Pharmacists can prescribe hormonal contraception through collaboration practice agreements in Tennessee, Michigan, Montana, Nebraska, South Dakota, Washington, and Wisconsin.² They can increase access to contraceptives by actively participating in pharmacist prescribing of contraception where available and encouraging additional state legislatures to adopt similar programs.

The primary indication for use of contraception is preventing unintended pregnancy. Unintended pregnancy is defined by the Centers for Disease Control and Prevention (CDC) as a pregnancy that is either unwanted or mistimed, with most unintended pregnancies occurring due to incorrect, inconsistent, or no use of contraception.³ In the United States, 45% of all pregnancies are unplanned, and 42% of those result in abortion.⁴ More than half of pregnancies that end in abortion (51%) occur in women who report using contraception during the month they became pregnant.⁵ In one study of contraceptive use in the previous 12 months, 24% of women reported changing methods at least once, nearly 25% of women reported...
Data are emerging to help better understand pregnancy intention and use of contraception on the individual level. Disparities exist in the frequency of unintended pregnancy, with the highest rates among women of low income, aged 18 to 24 years, without a high school degree, cohabiting women, and women of color. Improving access, reducing barriers, and subsidizing costs of effective contraception can reduce unintended pregnancy. Pharmacist, as medication therapy experts, can play a valuable role in encouraging the safe and effective use of contraception.

Preventing unintended pregnancy has public health benefits. Women in the United States are more likely to die from childbirth than women living in other countries with well developed health care services. In a thorough review of the literature, authors state that family planning demonstrates lower mother-to-infant transmission of human immunodeficiency virus (HIV), increased birth spacing, lower infant and maternal mortality risk, and reduced number of abortions. In another study, women with unintended pregnancies were more likely to smoke during and post-pregnancy, delay prenatal care, consume inadequate folic acid, and report postpartum depression. The ability to plan and prepare for pregnancy also has significant social and economic benefits for women. Results from a 2011 survey of women found access to contraception was important to take better care of themselves or their families (63%), support themselves financially (56%), complete their education (51%), or get or keep a job (50%). Healthy People 2030, a national effort that sets goals for improving the health and well-being of people in the United States, includes specific objectives to reduce the proportion of unintended pregnancies and increase the use of effective contraceptive methods in women at risk for unintended pregnancy. In addition, the Health Resources and Services Administration (HRSA) supports the Women’s Preventive Services Initiative, which states contraceptive care should include the full range of U.S. Food and Drug Administration (FDA)-approved methods of contraception, effective family planning practices, and sterilization procedures. Pharmacist can play an active role in recommending contraceptives to women at risk for unintended pregnancies. One study demonstrated that use of contraception is lacking in women on teratogenic medications. Another study demonstrated that women of reproductive age with chronic disease, such as diabetes, are more likely to use less effective methods.

There are approximately 72 million women of reproductive age (15-49 years) in the United States. According to the CDC’s National Center for Health Statistics, from 2017 to 2019, 65.3% of all women of reproductive age in the United States were currently using some form of contraception. The most frequently used methods are female sterilization (18.1%), oral contraceptive (OC) pills (14%), long-acting reversible contraception (LARC) (10.4%), male condoms (8.4%), and injection, vaginal ring, or transdermal patches (3.1%). Method usage (but not percentage) correlates with data collected from an international survey of more than 12,000 women, in which the 2 most common methods were OCs (44%) and male condoms (37%). Use of contraceptives increases with age, with women aged 40 to 49 years having the highest rate of use (74.8%) and women aged 15 to 19 years having lower rates of use (38.7%). Education level did not impact contraceptive use; however, racial disparities exist, with 69.2% of non-Hispanic White women using contraception compared with 61.4% of non-Hispanic Black and Hispanic (60.5%) women. The type of method used changes with age, with more women aged 15 to 29 years using OCs and more women aged 40 to 49 years undergoing female sterilization.

Using contraceptives consistently and correctly reduces the risk of unintended pregnancy. Effectiveness rates for contraception are often reported as “perfect use,” meaning consistent and correct use over 1 year. “Typical use” is defined as how effective a contraceptive method is during actual use, which includes factors of consistency and correct administration over 1 year. Typical use failure rates are highest with fertility awareness-based methods, methods that require daily, weekly, or monthly use, and methods that are needed immediately prior to or during intercourse. Approximately 50% of women miss taking at least 1 OC pill per month, and 14% of women miss 2 or more pills per month. Pharmacists can play an important role by providing education related to the optimal use of contraception, as a patient’s knowledge is correlated with adherence. Dispensing more than 1 month’s supply of OCs is associated with lower rates of unintended pregnancies, and pharmacists who prescribed contraception were more likely to dispense a 6-month or greater supply compared with other clinicians. In addition to preventing pregnancy, contraception can offer additional health benefits. All methods offer the ability to plan or space pregnancies to achieve healthier outcomes. It may be beneficial to discuss different types of contraception with patients who are having challenges with adherence.
**STAR**

What are examples of nonhormonal methods of contraception? What are examples of hormonal methods?

*S = Stop; T = Think; A = Assess; R = Review

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### Available Methods of Contraception

A wide variety of contraceptive methods and technologies are available in the United States (FIGURE 1). Methods can be grouped into categories such as hormonal or nonhormonal, prescription or over-the-counter, reversible or permanent, or short-acting or long-acting. Pharmacists have an important role in providing up-to-date information about available options and helping patients find the contraceptive option that meets their needs. In a large international survey of reproductive-aged women, over two-thirds (72%) were aware of at least 4 contraceptive methods, whereas 9% were aware of 1 or 2 methods. Given that there are many more options available, pharmacists can play a large role in increasing this awareness. Pharmacists are well equipped to educate patients and health care providers on the advantages and disadvantages of specific pharmacologic products used for contraception.

Hormonal contraceptives contain a progestin with or without estrogen. The mechanism of action of hormonal contraceptives is preventing ovulation and thickening cervical mucus. Currently, all hormonal methods except levonorgestrel-containing emergency contraception require a prescription.

Contraceptive methods are often categorized by the duration of contraceptive action as short-acting reversible contraception (SARC) or long-acting reversible contraception (LARC). LARC methods include intrauterine devices (IUDs) and the subdermal implant whereas SARC methods include all other contraceptives. Efficacy is measured by the Pearl Index and the life table. The Pearl Index indicates the number of contraceptive failures per 100 woman-years of exposure and the life table indicates the number of contraceptive failures for each month of use. Although the Pearl Index measurement is still required by the FDA for drug approval, it has limitations for data analysis. Failure rate is also defined by the World Health Organization as the number of pregnancies per 100 women in 1 year. There are many factors that can lead to contraception failures, and experts recommend that regulating bodies standardize reporting requirements that more accurately demonstrate imperfect versus perfect use. Aside from abstinence and sterilization, LARC methods are the most efficacious products on the market, offering less than 1% failure rate for typical use. The efficacy rate of SARC methods, such as contraceptive pills, patches, or rings, may not be as high, partly because they are dependent on adherence and timing-related method failures by the patient. LARC methods require a clinician visit for initiation, insertion, and removal, whereas a benefit of SARC methods is that most are self-administered. A review of all available contraceptive methods is outside the scope of this activity, so the following sections will focus on SARC, with an emphasis on novel methods that have recently changed the landscape of contraceptive care by offering new options for women.

### Clinician and Patient Factors Affecting Contraception Selection

Both clinician and patient factors may influence selection
of contraception. The recommendations about contraception that women receive may differ according to their provider.32 Studies have demonstrated that a patient’s selection of a contraceptive is influenced not only by their demographics and prior pregnancies but also their health care provider’s age, gender, and preferences.33 Literature has demonstrated bias in the health care system, and while further research is needed to identify its specific impact on medical encounters, it is essential that pharmacists and other providers are aware of this potential bias and methods to manage it to ensure patient-centered care is provided.34 When it comes to the decision-making process regarding contraception, women have felt that their provider’s preference could outweigh their own desire, and this could undermine the trust between patients and providers.35 An important guiding principle for contraceptive care is voluntary informed choice of a contraceptive method. Important elements to consider for a provider when selecting a method include availability, which can include affordability and accessibility, acceptability, effectiveness, and safety.36 In addition to the typical benefits of contraception in terms of pregnancy prevention, other potential benefits, such as the effect on bleeding and whether it will be increased or decreased or make it more or less predictable, may play a role.

Patient-specific items may also include a similar list of elements. Additional factors that may affect selection of a contraceptive include a patient’s age or life stage and whether there is a desire for return to fertility. Patient preferences may differ in terms of wanting a LARC versus SARC method or a nonhormonal versus hormonal method. For instance, a patient who may want children in the near future may not want a LARC method which has a longer duration of action. One study in a resource-limited setting identified potential reasons for choosing a SARC including decreased cost, privacy, and the ability to stop use of the method without seeing a health care provider (eg, to remove a LARC).36 When choosing a method of contraception, protection from the risk of sexually transmitted infections (STIs) is also a key consideration. Though hormonal contraceptives are highly effective at preventing pregnancy, they do not protect against STIs, such as HIV, so it is essential to educate patients to continue to consistently and correctly use male latex condoms to reduce the risk of STIs.33 Due to the wide variety of elements that can be considered when selecting an optimal method of contraception, it is essential that providers of contraceptive care offer patient counseling that is individualized to assist with the selection of a method that is optimal for the needs and desires of the patient. Additional information regarding selection of contraception will be discussed, but it is important to understand the nuances among available products to assist with the decision-making process.

**STAR**

What characteristics differentiate the new SARC methods?

**SARC Methods**

The SARC methods are mostly self-administered, except for intramuscular depot medroxyprogesterone acetate (DMPA), and vary in their effectiveness, safety, and affordability.37 Several new products have been FDA approved in recent years including segesterone acetate/ethinyl estradiol (EE) vaginal ring (Annovera) in 2018; a progestin-only pill (POP) drospirenone oral tablet (Slynd) in 2019; levonorgestrel/EE transdermal patch (Twirla) in 2020; lactic acid, citric acid, and potassium bitartrate vaginal gel (Phexxi) in 2020; and a combined oral contraceptive (COC) drospirenone and estetrol tablets, with a new estrogen component (Nextstellis) in 2021.36,37-40 Pharmacists can be instrumental in informing clinicians and patients about the efficacy, safety, and features associated with recently approved contraceptives.

**Combined Hormonal Contraceptives (CHCs)**

CHCs encompass all products with both estrogen and progestin hormones, including COCs, transdermal patches, and vaginal rings. The mechanism of action is a decrease in secretion of luteinizing hormone (LH) and follicle-stimulating hormone (FSH), which prevents ovulation. Proges-
terone has the added effect of thickening cervical mucus to prevent or delay sperm movement.41

CHC products are associated with an increased risk of adverse effects (AEs) including venous thromboembolism and stroke at higher estrogen doses.42,43 This risk is increased with older age, surgery, obesity, smoking, hypertension, and family history of thrombosis.42,43 Women taking CHCs should be monitored for warning signs of rare but potentially serious AEs using the acronym ACHES (see FIGURE 2).44

COCs may have many positive outcomes on female reproductive health. COCs decrease the risk of ovarian and endometrial cancer and improve dysmenorrhea as well as premenstrual and menopausal symptoms. Patients on COCs generally experience fewer and lighter days of menstrual bleeding and cramping.45

COC Pills
Aside from female sterilization, COCs are the most widely used contraceptive method.17 With typical use, approximately 9% of women will become pregnant within the first year of use.20 COC pill packs contain active (hormone-containing) tablets, and some pill packs also contain inactive tablets (placebo). Extended-cycle OCs contain more active tablets to be taken consecutively, with fewer or eliminated placebo tablets throughout the cycle. These products are used in women who experience conditions such as endometriosis and premenstrual syndrome.46 The COC regimens may be monophasic, containing identical active pills, or multiphasic, containing varying doses of estrogen and/or progestin in the active tablets throughout each cycle. Data comparing monophasic versus multiphasic regimens are lacking.47 All COCs require daily oral administration and are reversible upon discontinuation.46

The estrogen component in most OC pills is EE, with a small number of pills containing mestranol, which is converted to EE.46 The drospirenone/estetrol tablet is the newest COC approved in 2021. Estetrol is a naturally occurring estrogen derived from a plant source. Unlike EE, it shows receptor agonist activity in the vagina, uterus, and endometrium, and antiestrogenic effects on breast cells.40,48 Authors of a phase 3 trial of estetrol-containing contraceptives state that this formulation offers a predictable bleeding pattern.49 AEs of any combination product include nausea, breast tenderness, and changes in menstrual bleeding. These AEs will often improve as women adjust to the hormone levels.50 Some AEs may persist and will require adjustment of hormone doses, either estrogen or progestin depending on the symptoms. Adjusting the dose sooner than 3 cycles (6 cycles for extended cycle COC) is generally not recommended.50

Vaginal Rings
There are 2 currently available vaginal contraceptive rings that have similar efficacy and tolerability as OCs. Both products are flexible, nonlatex rings that are inserted vaginally. Both products are designed to follow a 28-day cycle, with 21 days of ring insertion followed by 7 days ring-free for withdrawal bleeding. The etonogestrel/EE (Nuvaring) product is a single-use ring that is discarded after 1 cycle of use and a new one is inserted after the 7-day ring-free period. The segesterone acetate/EE product is dispensed as 1 ring per year, as it can be washed and reinserted every cycle. Differences in storage, effects of body weight, and size can be found in TABLE 1.37,51

Advantages to using the ring for contraception over OCs are avoidance of daily oral administration and similar efficacy. A potential disadvantage is that some women may not be as comfortable with the site of drug delivery.

<table>
<thead>
<tr>
<th>TABLE 1. CHARACTERISTICS OF VAGINAL RINGS</th>
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</thead>
<tbody>
<tr>
<td></td>
<td>Etonogestrel/EE</td>
<td>Segesterone acetate/EE</td>
</tr>
<tr>
<td><strong>Hormones/Dose per Day</strong></td>
<td>0.015 mg EE/0.12 mg etonogestrel</td>
<td>0.013 mg EE/0.15 mg segesterone acetate</td>
</tr>
<tr>
<td><strong>Ring Size</strong></td>
<td>2.13” diameter</td>
<td>2.20” diameter</td>
</tr>
<tr>
<td><strong>Displacement</strong></td>
<td>Up to 3 hours; &gt;3 hours use back-up method (7 days)</td>
<td>Up to 2 hours; &gt;2 hours use back-up method (7 days)</td>
</tr>
<tr>
<td><strong>Storage</strong></td>
<td>Fridge prior to dispensing</td>
<td>Room temperature</td>
</tr>
<tr>
<td><strong>Effects of Body Weight</strong></td>
<td>Has not been studied in women with BMI ≥30 kg/m²</td>
<td>Has not been studied in women with BMI &gt;29 kg/m²</td>
</tr>
<tr>
<td><strong>How to Use</strong></td>
<td>Insert vaginally; remains in place x3 weeks, then remove x1 week for menses</td>
<td></td>
</tr>
<tr>
<td><strong>How Supplied</strong></td>
<td>1 ring monthly</td>
<td>1 ring yearly</td>
</tr>
</tbody>
</table>

BMI, body mass index; EE, ethinyl estradiol.
Transdermal Patch

There are 2 currently available transdermal patches that have similar efficacy and tolerability as OCs. Both products are self-administered by applying the patch to a clean and dry area of the body. The patch is worn for 1 week, replaced with a new patch for 3 weeks total, and no patch is worn during the fourth week for menstruation. The norelgestromin/EE (Xulane) patch can be worn on the abdomen, buttock, upper outer arm, or back. The levonorgestrel/EE patch can be worn on the abdomen, buttock, or upper torso. Both patches should be checked daily to ensure adhesion; however, the levonorgestrel/EE patch is designed with additional layers to help maintain adhesion. Differences in dosing and size can be found in Table 2.

Advantages to the patch over OCs include weekly self-administration frequency and similar efficacy, while disadvantages include potential reduced efficacy in overweight and obese women and a potential increased risk of venous thromboembolism. The patch is contraindicated in women with a body mass index 30 kg/m² or greater because of this risk. The levonorgestrel/EE-containing patch offers a lower dose than the norelgestromin/EE-containing patch. As part of levonorgestrel/EE approval, the FDA is requiring a long-term prospective, observational postmarketing study comparing the risks for venous thromboembolism and arterial thromboembolism in new users of levonorgestrel/EE with new users of other CHCs.

Progestin-only Contraceptives

Progestin-only SARC methods contain only a progestin and include POPs and injections. Two LARC methods, the subdermal implant and levonorgestrel-containing IUDs, are also progestin-only.

POPs

Norethindrone (Camila, Errin, Nor-QD, and others) and drospirenone are 2 oral progestin-only formulations available

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**TABLE 2. CHARACTERISTICS OF TRANSDERMAL PATCHES**

<table>
<thead>
<tr>
<th></th>
<th>Norelgestromin/EE</th>
<th>Levonorgestrel/EE</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Hormones</strong></td>
<td>0.035 mg EE/0.15 mg norelgestromin</td>
<td>0.030 mg EE/0.12 mg levonorgestrel</td>
</tr>
<tr>
<td><strong>Description</strong></td>
<td>• Smaller (14 cm²), square, beige</td>
<td>• Larger (28 cm²), round, beige</td>
</tr>
<tr>
<td></td>
<td>• 3-layer matrix design</td>
<td>• 5-layer matrix designed to help maintain adhesion</td>
</tr>
<tr>
<td><strong>Where to Use</strong></td>
<td>Abdomen, buttock, upper outer arm, back</td>
<td>Abdomen, buttock, upper torso</td>
</tr>
<tr>
<td><strong>How to Use</strong></td>
<td>• Wear 1 patch x1 week, then replace with a new patch on the same day every week</td>
<td>• Menses occurs during the 4th week (no patch wear)</td>
</tr>
<tr>
<td></td>
<td>• Menses occurs during the 4th week (no patch wear)</td>
<td>• Avoid frequent/long water exposure and large amounts of body lotion/oil</td>
</tr>
<tr>
<td><strong>Displacement</strong></td>
<td>• If &lt;24 hours, try to reapply the patch. If it does not adhere completely, apply a new patch immediately. No back-up method is needed and the “patch change day” will stay the same.</td>
<td>• If ≥24 hours, apply new patch and use back-up method x7 days.</td>
</tr>
<tr>
<td><strong>Adverse Effects</strong></td>
<td>Similar to COC; skin irritation</td>
<td></td>
</tr>
</tbody>
</table>

COC, combination oral contraceptive; EE, ethinyl estradiol.

**TABLE 3. CHARACTERISTICS OF PROGESTIN-ONLY PILLS**

<table>
<thead>
<tr>
<th></th>
<th>Norethindrone</th>
<th>Drospirenone</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Daily Dosing</strong></td>
<td>0.35 mg daily</td>
<td>4 mg PO daily on a 28-day cycle</td>
</tr>
<tr>
<td><strong>Regimen</strong></td>
<td>1 tablet (0.35 mg) PO daily every day; no breaks</td>
<td>4 mg PO daily for 24 days; inert tablet PO daily for 4 days</td>
</tr>
<tr>
<td><strong>Time Window for Missed Pills</strong></td>
<td>3 hours: If 1 pill is taken &gt;3 hours late, back-up contraception should be used if the patient has sex within 48 hours.</td>
<td>24 hours: If 1 active pill is missed, take the last missed tablet as soon as possible. Back-up contraception should be used if the patient has sex within 7 days after missing ≥2 tablets.</td>
</tr>
<tr>
<td><strong>Adverse Effects</strong></td>
<td>Spotting, irregular bleeding, breast tenderness, weight gain</td>
<td>Unscheduled bleeding (40% after 1 year)</td>
</tr>
<tr>
<td><strong>Contraindications</strong></td>
<td>• Benign or malignant liver tumors</td>
<td>Liver or renal impairment</td>
</tr>
<tr>
<td></td>
<td>• Acute liver disease</td>
<td></td>
</tr>
</tbody>
</table>
in the United States by prescription only. Norethindrone-containing pills have lower efficacy than COCs for typical use, and the short window allowed for missed pills (see TABLE 3\textsuperscript{38,55}) may be a contributing factor.\textsuperscript{20} Drospirenone-containing pills demonstrated similar efficacy to COCs, with 4 of 100 women becoming pregnant during the first year of use.\textsuperscript{38} Both oral pills are administered daily. Norethindrone-containing pills do not have any placebo tablets and the pills must be taken daily continuously, whereas drospirenone-containing pills have 24 active tablets and 4 placebo tablets.\textsuperscript{38,55} The advantages of POPs over CHC methods are no estrogenic AEs, so they can be used in women who have a contraindication or intolerance to estrogen. Another advantage over COCs is postpartum use, as the CDC does not recommend COC use in non-breastfeeding women less than 21 days postpartum (or <42 days with thromboembolic risk factors) and during lactation; the CDC does not recommend COC use in breastfeeding women less than 42 days postpartum.\textsuperscript{56} Disadvantages include irregular and unpredictable menstrual bleeding and timing of administration.\textsuperscript{57} With different time windows for missed pill administration, pharmacists should be aware of the counseling needed if this should occur. TABLE 3\textsuperscript{38,55} contains more information about POPs.

**TABLE 3**

<table>
<thead>
<tr>
<th>Nonhormonal Methods of Contraception</th>
</tr>
</thead>
</table>
| Nonhormonal contraception includes male condoms, female condoms, copper IUD, vaginal gel, diaphragm, cervical cap, sponge, and permanent methods. Abstinence and natural family planning methods are also utilized for contraception. Patients may seek nonhormonal contraception due to concerns about AEs, future fertility, or decreased libido.\textsuperscript{18} Barrier methods (condoms) reduce the risk of STI transmission.\textsuperscript{65} Both the copper IUD and vaginal gel are available by prescription, the copper IUD offers a long duration of action (10 years),\textsuperscript{66} and the vaginal gel is used on-demand with each episode of intercourse.\textsuperscript{26} Male condoms are commonly used for contraception in the United States\textsuperscript{17} and globally,\textsuperscript{18} likely due to their low cost, availability, and lower STI transmission risk.\textsuperscript{67} Male condoms should not be used concurrently with female condoms because it can cause tearing.

**Vaginal Gel**

In 2020, the FDA approved a vaginal gel formulation of lactic acid, citric acid, and potassium bitartrate as the first nonhormonal prescription vaginal gel for the prevention of pregnancy. The mechanism of action is maintaining the vaginal pH within the range of 3.5 to 4.5, representing an acidic environment that is inhospitable to sperm.\textsuperscript{26} A phase 3 trial (AMPOWER) of more than 1300 women of reproductive age demonstrated safety, tolerability, and 86.3\% effectiveness.\textsuperscript{68} As with condoms, this product is used on-demand with each episode of vaginal intercourse. The product is available in a box containing 12 individually wrapped 5-gram applicators. The patient inserts 1 prefilled, single-dose applicator vaginally immediately before (or up to 1 hour before) each episode of vaginal intercourse. If more than 1 episode occurs within 1 hour, an additional dose must be inserted.\textsuperscript{26}

In the AMPOWER trial, this gel demonstrated high user satisfaction and low discontinuation rates due to AEs.\textsuperscript{68} FIGURE 3\textsuperscript{56} shows the 7-cycle cumulative pregnancy rate reported during clinical trials was 13.7\%, excluding cycles with back-up contraception, cycles shorter than 21 days or longer than 35 days, and cycles in which no intercourse was reported.\textsuperscript{68} Fewer than 2\% of women in trials discontinued use due to AEs, which were primarily local in nature. The most common AEs include vulvovaginal burning sensation, vulvovaginal
pruritus, vulvovaginal mycotic infection, urinary tract infection (UTI), vulvovaginal discomfort, bacterial vaginosis, vaginal discharge, genital discomfort, and dysuria. Patients with a history of recurrent UTIs or urinary tract abnormalities should avoid use of this product due to an association with cystitis and pyelonephritis. Post hoc analyses demonstrated that genitourinary AEs decreased substantially over time, and those with existing genitourinary infections had higher rates of symptoms compared with the general study population.

This vaginal gel may be used during any part of the menstrual cycle and can be used concomitantly with hormonal contraceptives, latex, polyurethane or polyisoprene condoms, and vaginal diaphragms. It should not be used with vaginal rings.

Future Directions
Use of a non-contraceptive, investigational vaginal gel, EVO100, has had a positive impact on sexual satisfaction and maintenance of lubrication in the AMPREVENCE study, as well as significant reductions in specific STIs in women at high risk of infection, which may highlight other potential benefits of vaginal gels outside of pregnancy prevention. The vaginal gel will be further investigated in a phase 3 clinical trial (EVOG UARD) for the prevention of urogenital Chlamydia trachomatis and Neisseria gonorrhoeae infection in women; these STIs remain commonly reported despite the advocacy of condom use to prevent their transmission. This product is also being studied for a role in preventing recurrent bacterial vaginosis.

Aside from male condoms and vasectomies, male contraception does not currently exist. Current research includes hormonal and nonhormonal male contraceptive methods that are showing promising results. If safety and efficacy trials are successful, these options may be available for patients by the end of the decade. Another area of research is with new nonhormonal contraception for both men and women. Although many methods of contraception currently exist, there is a market for innovative therapies.

The Role of the Pharmacist in Contraception and Patient Counseling
Selecting a Method of Contraception

Studies have demonstrated that patients are most interested in the following attributes of contraceptives: efficacy, safety, cost, and AEs. In a study of women aged 18 to 29 years, most women identified efficacy and STI/HIV prevention to be the most important attributes of contraception. In a small study (N = 52) of women who were interviewed about their use of contraception in the past 12 months, almost all (n = 48) stated they used more than 1 method. The authors outlined these strategies and captured the intent while stressing the importance of needing to better understand this practice in future research. An international survey found that 49% of women prefer nondaily forms of contraception, and 73% would prefer a method that allows them to stop using the method at the moment they choose.

The selection of a contraceptive method from the array of methods available is a complex process for patients and providers. Pharmacists can play a significant role in this process by providing education and support, helping patients make informed decisions about their contraceptive choices. Through counseling, pharmacists can address patient concerns, discuss side effects and benefits, and assist in choosing a method that aligns with the patient’s lifestyle and personal values.

FIGURE 3. EFFICACY OF LACTIC ACID, CITRIC ACID, AND POTASSIUM BITARTRATE VAGINAL GEL.
options may be influenced by many factors. Routinely assessing reproductive desires and providing contraceptive and preconception care is recommended by the CDC for all clinicians.\(^7\)

The role of the pharmacist is to collect information about the patient’s medical history and use of contraception in the past, assess medical eligibility, educate on the available methods, counsel on how to use the selected methods, and follow up with any patient-related questions or concerns. Choosing a method of contraception is a patient-centered decision. The Desire to Avoid Pregnancy (DAP) scale is a validated evaluation tool that can be used to measure a woman’s pregnancy preferences, and it is available for free in both English and Spanish languages.\(^7\)

For clinicians and pharmacists with more limited time, One Key Question is a tool that was developed to help facilitate this discussion. The question is: “Would you like to become pregnant in the next year?” followed by at least 4 patient response options (“Yes,” “No,” “Unsure,” and “Ok either way”) and then corresponding counseling.\(^8\) The results of using the DAP scale and One Key Question tool were compared in a recent study that demonstrated a correlation of responses from patients.\(^8\)

Once the pharmacist has collected patient-specific information, they can help determine the safety of the available methods utilizing the Contraceptive Guidance for Health Care Providers, which was developed by the CDC and is updated regularly.\(^8\)

This guidance includes the US Medical Use Criteria for Contraceptive Use (MEC), US Selected Practice Recommendations for Contraceptive Use (SPR), Quality Family Planning (QFP), and social media tools.\(^8\) The MEC provides evidence-based recommendations for the selection of reversible contraception based on the patient’s current and past medical history, current medications, and other factors (eg, cigarette use). It can be utilized to assess potential drug interactions with current medications. Review the CASE utilizing the MEC to determine medical eligibility for a patient. The CDC material is free and available both online and in print. The MEC and SPR are also available in smartphone applications that can be downloaded.\(^6,8\)

### Summary Chart of U.S. Medical Eligibility Criteria for Contraceptive Use

<table>
<thead>
<tr>
<th>Condition</th>
<th>Sub-Condition</th>
<th>Cu-IUD</th>
<th>LNG-IUD</th>
<th>Implant</th>
<th>DMPA</th>
<th>POP</th>
<th>CHC</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>&lt;20 yrs:1</td>
<td>I</td>
<td>I</td>
<td>I</td>
<td>I</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>≥20 yrs:1</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Diabetes</td>
<td>a) History of gestational disease</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td>b) Nonvascular disease</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>i) Non-insulin dependent</td>
<td>1</td>
<td>2</td>
<td>2</td>
<td>2</td>
<td>2</td>
<td>2</td>
</tr>
<tr>
<td></td>
<td>ii) Insulin dependent</td>
<td>1</td>
<td>2</td>
<td>2</td>
<td>2</td>
<td>2</td>
<td>2</td>
</tr>
<tr>
<td></td>
<td>c) Nephropathy/retinopathy/neuropathy(^6)</td>
<td>1</td>
<td>2</td>
<td>2</td>
<td>3</td>
<td>2</td>
<td>3/4*</td>
</tr>
<tr>
<td></td>
<td>d) Other vascular disease of &gt;20 years’ duration(^4)</td>
<td>1</td>
<td>2</td>
<td>2</td>
<td>3</td>
<td>2</td>
<td>3/4*</td>
</tr>
</tbody>
</table>

**Key:**

1. No restriction (method can be used)
2. Advantages generally outweigh theoretical or proven risks
3. Theoretical or proven risks usually outweigh the advantages
4. Unacceptable health risk (method not to be used)

**Source:** [https://www.cdc.gov/reproductivehealth/contraception/pdf/summary-chart-us-medical-eligibility-criteria_508tagged.pdf](https://www.cdc.gov/reproductivehealth/contraception/pdf/summary-chart-us-medical-eligibility-criteria_508tagged.pdf)

Kris is a 26-year-old woman who has used OCs in the past, but has trouble remembering to take it each day. She has non-insulin-dependent type 2 diabetes that was diagnosed last year. She denies nephropathy, retinopathy, or neuropathy. She describes her diabetes as being well controlled, and her current medications include metformin and a multivitamin.

**QUESTION:** The first step in helping Kris is determining which products are safe to use. According to the CDC MEC (excerpts included below), for which contraceptive products is she medically eligible?

**ANSWER:** For Kris’s age, all products are options as category 1. For diabetes, all products are options as category 1 or 2.
The MEC applies 4 categories of safety/risk to provide guidance to clinicians in decision making based on different conditions. The categories are as follows:

1 = There is no restriction for the use of the contraceptive method.
2 = The advantages of using the method generally outweigh the theoretical or proven risks.
3 = The theoretical or proven risks usually outweigh the advantages of using the method.
4 = There is an unacceptable health risk if the contraceptive method is used.56

The SPR offers evidence-based guidance for clinicians to help manage common questions about contraception, such as initiation, AEs, missed doses or displaced products, and use of emergency contraception.57 The QFP provides recommendations for family planning services to help patients with birth spacing plans, preconception health, adolescent health, and preventive screenings.

Since 2013, many states have passed legislation for pharmacists to prescribe or furnish selected contraceptive products by either a statewide protocol or standing order. Other states allow this practice via collaborative practice agreement. An updated list of state approvals with specifics about each state, an overview of this movement in pharmacy, implications for pharmacists, the process of prescribing contraceptives in a pharmacy, and other useful tools and factsheets can be found at www.birthcontrolpharmacist.com, naspa.us/resource/contraceptives, and www.powertodecide.org.

States that allow pharmacist-prescribed hormonal contraception have developed screening questionnaires to identify the medical conditions and patient factors that present safety concerns. In addition to the questionnaire, a patient’s blood pressure measurement is considered medically necessary before obtaining a form of contraception.58 A well woman exam, laboratory tests, and a weight measurement are important and should be recommended, but they are not medically necessary before initiating contraception.82

The importance of counseling on contraception has been reviewed in the literature.83 Though clinicians may encourage women to use highly effective methods, patients may not prioritize efficacy over their other concerns. Shared decision making lies in between these areas.83 Experts state that contraceptive education may need more than one visit and utilizing a variety of educational methods is recommended.84 Practicing pharmacists may consider using online tools, such as www.bedsider.org, which highlights an easy-to-use way for patients to learn about the available methods and their features.85

Contraceptive Education

Counseling on a new SARC product should include information about how to start the product and potential AEs. Pharmacists should utilize the CDC documents previously mentioned to help guide this discussion.56,58 Depending on the type of SARC, the patient may need a back-up method of contraception, such as a condom. AE profiles vary depending on the product and dose, but patients can be educated that minor AEs should improve after 3 cycles. Pharmacists should discuss the acronym ACHES (see FIGURE 24) with patients to remember the rare but dangerous AEs associated with estrogen-containing products. Counseling should include how to manage missed, late, or displaced medication. Patients should be educated to use the selected SARC method regularly as directed, regardless of the frequency of intercourse. If the patient should ever question whether she may be pregnant, she should stop using the SARC method, use barrier contraception, or abstain from intercourse until the pregnancy is confirmed. Pharmacists should also strongly encourage patients to reduce, stop, and not start smoking. In addition to assisting and counseling patients, pharmacists can educate other health care providers regarding the effectiveness of SARC methods and the nuances between the recently available formulations as well as identifying patients who may benefit from starting or changing a contraceptive method.

Conclusion

SARC methods offer a variety of safe, effective, reversible, and well tolerated options for women seeking pregnancy prevention. The advantages of the newly approved contraceptive products include a nonhormonal, on-demand formulation (lactic acid, citric acid, and potassium bitartrate vaginal gel), a COC containing a new estrogen with potentially more consistent bleeding patterns (drospirenone and estetrol tablets), stronger transdermal adhesion (levonorgestrel/EE
transdermal patch), increased time window for missed POPs (drospirenone tablets), and increased access with reduced trips to the pharmacy (segesterone acetate/EE vaginal ring). Pharmacists play an important role in providing education about all available products, provision of contraception, and counseling on their use. The future of pharmacy in the field of contraception is exciting, and pharmacists should stay abreast of the changes in legislation in their state.

REFERENCES

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34. Manzer JL, Bell AV. “We’re a little biased”: medicine and the management of bias through the case of contraception. *J Health Soc Behav.* Published online April 12, 2021. doi: 10.1177/00221465211003232


POSTTEST QUESTIONS

1. Which of the following is a benefit of taking combination hormonal contraceptives (CHCs)?
   A. Improvement in menstrual cycle-related problems
   B. Protection against sexually transmitted infections (STIs)
   C. Reduction of migraines
   D. Reduction of blood pressure

2. Which is the best counseling point to educate patients regarding the use of short-acting reversible contraception (SARC) methods?
   A. They all contain hormones and therefore carry a risk of potential adverse effects (AEs) from increased exposure to hormones.
   B. The rates of perfect use versus typical use of SARC methods are generally the same.
   C. One benefit of SARC methods is that most are self-administered.
   D. There are no benefits of SARC methods outside of preventing pregnancy.

3. A 26-year-old woman presents to the pharmacy to ask about contraception. Her past medical history is significant for migraine with aura. According to the CDC Medical Eligibility Criteria (excerpts included below), which contraceptive method is considered category 4 (not recommended)?
   A. CHC
   B. Progestin-only pills (POPs)
   C. Depot medroxyprogesterone acetate (DMPA)
   D. Implant

4. Before a new contraceptive method is initiated, what is medically necessary to obtain?
   A. Urine pregnancy test
   B. Current weight
   C. STI screening
   D. Blood pressure measurement

5. An 18-year-old patient is interested in a contraceptive method that does not contain any hormones. Which approved product is free of hormones?
   A. Vaginal gel
   B. Vaginal ring
   C. Transdermal patch
   D. POP

6. You will be relocating to a state that allows pharmacists to prescribe hormonal contraception. Which question would be most beneficial to ask patients before prescribing hormonal contraception?
   A. How often do you have intercourse?
   B. Have you ever had an STI?
   C. What is your current weight?
   D. Would you like to become pregnant in the next year?

7. Which is a potential risk associated with the use of oral contraceptives?
   A. Heavy menstruation
   B. Venous thromboembolism
   C. Ovarian cancer
   D. Reduced bone mineral density

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<tr>
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<th>Cu-IUD</th>
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<th>DMPA</th>
<th>POP</th>
<th>CHC</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>Menarche to &lt;20 yrs:</td>
<td>I</td>
<td>C</td>
<td>I</td>
<td>C</td>
<td>I</td>
<td>C</td>
</tr>
<tr>
<td></td>
<td>≥20 yrs:</td>
<td>I</td>
<td>C</td>
<td>I</td>
<td>C</td>
<td>I</td>
<td>C</td>
</tr>
<tr>
<td>Headaches</td>
<td>a) Nonmigraine (mild or severe)</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>1*</td>
</tr>
<tr>
<td></td>
<td>b) Migraine</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>i) Without aura (includes menstrual migraine)</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>2*</td>
</tr>
<tr>
<td></td>
<td>ii) With aura</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>4*</td>
</tr>
</tbody>
</table>

8. A 20-year-old patient is seeking your advice regarding a contraceptive option that helps prevent both pregnancy and STIs and can be used on-demand. She wishes to avoid products with hormones. She is currently using male condoms, but she heard about a new product that could be used with condoms. She has no past medical history and no contraindications to the use of hormonal contraception. Which approved product is nonhormonal and can be used with male condoms?
   A. Vaginal gel  
   B. Vaginal ring  
   C. Female condoms  
   D. Injections

9. A patient lives in a very rural area and does not have easy access to a local pharmacy. She is interested in contraception that does not require daily administration. Based on this information, which contraceptive product is the most appropriate to recommend?
   A. Levonorgestrel/ethinyl estradiol (EE) transdermal patch  
   B. Etonogestrel/EE vaginal ring  
   C. Segesterone acetate/EE vaginal ring  
   D. Drospirenone tablets

10. A 24-year-old patient comes to your pharmacy seeking contraception. She used the transdermal patch in the past but had problems with it staying on her skin. Which statement is true regarding the newly approved transdermal patch?
   A. It is double in size to help with drug distribution.  
   B. It was designed with additional layers to help maintain adhesion.  
   C. It is recommended to use with additional adhesive tape to help with adhesion.  
   D. It is suggested to use with lotion to help maintain adhesion.

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Begin the activity by reading the content in its entirety.  
Go to www.pharmacytimes.org/go/SARC to access the online version of this activity.  
Click “Proceed,” then complete the online pretest.  
Once completed, click “Next” until reaching the activity posttest.  
Complete the online posttest and activity evaluation form.  
After successfully completing the posttest and evaluation form, this information will be uploaded to CPE Monitor.  
You must complete these steps before the activity expires in order to receive your credit.  
You may view your credit within 48 hours at www.mycpemonitor.net.

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SYSTEM REQUIREMENTS FOR COMPLETION: Computer or smartphone with internet-access web browser (IE7.0+ or Webkit-/Mozilla-compatible) with JavaScript enabled.

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Addressing Unmet Needs in the Treatment of Schizophrenia: The Role of the Pharmacist

**Overview of Schizophrenia**

Schizophrenia is a chronic severe mental health disorder impacting the thoughts and behaviors of individuals diagnosed with the disorder. The *Diagnostic and Statistical Manual of Mental Disorders* states an individual must have at least 2 of the following symptoms to be diagnosed with schizophrenia—delusions, hallucinations, disorganized speech, disorganized/catatonic behavior, or negative symptoms. However, 1 symptom must include delusions, hallucinations, or disorganized speech. Each symptom must be present predominately for 1 month, unless resolved with treatment, with total duration of symptoms lasting 6 months. The symptoms must cause significant disturbances in one or more major areas of daily life (eg, work, interpersonal relationships, self-care, or academia). Other disorders associated with psychotic symptoms must be ruled out, including substance use and misuse. If the individual has a history of a communication disorder (eg, autism spectrum disorder) a diagnosis may occur if noticeable delusions or hallucinations are included in the disturbances and present for at least 1 month.¹

According to the National Institute of Mental Health, it is estimated that the worldwide incidence of schizophrenia is between 0.33% and 0.75%, with an estimated 3.5 million Americans having a diagnosis of schizophrenia.²,³ Schizophrenia is a leading cause of disability worldwide, ranking 19th, placing this patient population at risk for premature mortality.⁴,⁵ The incidence of schizophrenia between men and women varies in the literature depending on numerous factors including race, ethnicity, country of origin, and geographic origin for immigrants and their children.¹ The emergence of schizophrenia is typically seen in men during late adolescence to early 20s, and early 20s to early 30s in women.¹

While the exact cause is unknown,
genetics and environmental factors appear to play a role in the development of schizophrenia in susceptible individuals.6,7 Studies show individuals with a first-degree or second-degree relative with schizophrenia have a 10% and 3% chance of developing the disorder, respectively.6 If both parents have schizophrenia, the risk of developing it increases to 40%.6 The prevalence in twins is reported to be 40% to 50% in monozygotic twins versus 12% to 14% in dizygotic twins.6,7 Interestingly, when siblings develop schizophrenia, symptoms tend to emerge around the same age.3 Environmental factors increasing the risk of schizophrenia include obstetric complications such as young gestational age (22-32 weeks), preeclampsia, maternal history of stillbirth, low birthweight (under 1500 grams) with relative risks of 3.4, 2.5, 1.7, and 3.0, respectively.8 Childhood trauma, socioeconomic status, living in urban areas, the use of cannabis during adolescence, and the presence of certain medical conditions (eg, head trauma, epilepsy, and autoimmune diseases) have been associated with an increased risk of developing schizophrenia later in life.9 However, future epidemiologic studies are needed to establish a true link to the disorder.

There are 3 hypotheses regarding the pathophysiology of schizophrenia.10 The dopamine hypothesis has been the predominant focus in the literature and postulates that there is an excessive amount of dopamine in the mesolimbic dopamine pathway, specifically at the D2 receptor. This leads to the presence of the positive symptoms associated with schizophrenia (ie, hallucinations and delusions).10 This hypothesis also proposes hypoactivity in the prefrontal cortex, or mesocortical pathway, resulting in the negative symptoms associated with schizophrenia (ie, poverty of speech, lack of motivation, inability to feel pleasure).11 The glutamate hypothesis of psychosis has emerged in more recent years suggesting hypoactivity at N-methyl-D-aspartate (NMDA) glutamate receptors on gamma-aminobutyric acid (GABA) interneurons in the prefrontal cortex, leading to excitation of downstream glutamate signaling pathways. This then stimulates the mesolimbic dopamine pathway, leading to excessive dopamine and, subsequently, positive symptoms. The role of serotonin is slightly less clear. However, the serotonin hypothesis of psychosis proposes hyperactivity at serotonin 5-HT2A receptors. The hyperactivity or overstimulation of these receptors is linked to downstream dopamine networks (ie, excessive serotonin stimulates the glutamate receptors, which then stimulates the mesolimbic dopamine pathway, causing psychosis).10

The effects of schizophrenia carry significant health, societal, and economic burdens. Schizophrenia has been among the leading causes of disability worldwide for decades, currently ranking in the top 25 for persons aged 25 to 49 years.12 Patients with schizophrenia are more likely to die 10 to 25 years sooner than the general population in part due to comorbidities and are more likely to develop cardiovascular disease and metabolic syndrome (ie, obesity, hypertension, hyperlipidemia, and diabetes).3 Numbers of comorbid substance use disorders in patients with schizophrenia are also high, with estimates being over 40% of patients.3 Suicide is also greater among those with schizophrenia, with an estimated 10% lifetime rate of suicide with the rate of attempts ranging from 18% to 55%.13 Factors contributing to increased risk of suicide include younger age (<45 years), male gender, being unmarried, living alone, being unemployed, well-educated, higher intelligence, having high personal expectations, recent (significant) life events, poor work functioning, access to means, and poor adherence to treatment.13,15

Additionally, the economic burden of schizophrenia is immense. In 2013, the estimated annual cost for patients with schizophrenia in the United States was over $155 billion. Most of these costs were attributed to indirect costs, accounting for 76% of total costs. This included unemployment, productivity loss, cost of caregivers, and premature mortality or suicide.16

Treatment Challenges
In addition to the comorbidities associated with schizophrenia, high nonadherence rates, relapse, and rehospitalization, combined with early mortality, further compound the challenges associated with treatment. Approximately 50% of patients receiving pharmacotherapy treatment for schizophrenia are nonadherent to their regimen.17 One factor contributing to nonadherence is adverse effects (AEs). Up to 80% of patients report at least one bothersome AE with antipsychotic treatment.18 Other factors contributing to nonadherence include lack of patient-provider rapport, lack of insight, substance use and misuse, unsecure housing, younger age of onset, stigma, newly started treatment, and residual symptoms of the disorder.17,19,20 Nonadherence is a major predictor of relapse in patients with schizophrenia. Seventy-seven percent of patients will relapse within a year of stopping pharmacotherapy with 90% relapsing within 2 years.17 While maintenance therapy can help prevent relapse, it is estimated that roughly 20% to 30% of patients on maintenance therapy will relapse.17 This could be due, in part, to treatment resistance, defined as failing at least 2 trials of antipsychotics that are appropriate in dose and duration.6,21 For patients on successful treatment regimens, lower hospitalization rates and better outcomes were reported.20
An additional treatment challenge includes medical comorbidities complicated by antipsychotic use. As stated previously, patients with schizophrenia are more likely to develop cardiovascular disease and metabolic syndrome.3 However, antipsychotic use can further exacerbate, or initially cause, these disorders. One meta-analysis looking at weight change, body mass index (BMI) change, clinical relevant weight gain (>7%), and weight reduction (>7%) found that nearly all studied antipsychotics cause a change in weight, BMI, and proportional weight increase with increased duration of use.22 This analysis also concluded that there may be limited benefit, in terms of weight mitigation, when switching to a less weight gain offending agent.22 These AEs may further impact treatment via adherence. One study reported an odds ratio (OR) of 0.64 for adherence in patients who experienced metabolic changes associated with antipsychotic treatment ($P = .0079$).18

Health Care Disparities

Literature has shown that health care disparities exist among patients with severe mental illness, including schizophrenia, impacting the care these patients receive. As previously stated, patients with schizophrenia have an increased morbidity and mortality. This can be attributed to the rate of diabetes, cardiovascular disease, substance use disorder, and respiratory disease.23 Race and ethnicity have been shown to impact the rate of diagnosis in some populations. One study reported that Latino and Black patients have a lifetime prevalence of being diagnosed with psychosis of 13.6% and 15.3%, respectively, when compared with White (9.7%) and Asian (9.6%) patients.24 The diagnosis of schizophrenia contributes to additional disparities. Patients often have difficulties in major areas of life including lower rates of education, unemployment, and secure housing.23 Thus, it is important to consider disparities among patients when referring patients for further care. A study evaluating antipsychotic management during and subsequent hospitalizations after outpatient visits in patients diagnosed with schizophrenia found that race-ethnicity may play a role with these parameters. The study found that patients included in the non-Hispanic Black race-ethnicity group had an increased chance of antipsychotic management and hospitalization versus the reference group (OR of 1.01-2.72 and 1.06-11.35, respectively). Additionally, the study found that uninsured patients were found to be hospitalized less than those with private insurance (OR ≤.001).25

Patients with schizophrenia have been vulnerable to social isolation amid the COVID-19 pandemic. In the presence of the stigma associated with severe mental illness, poorer health outcomes, lower household incomes, and small social networks, the sanctions associated with the pandemic may further put this patient population at risk for negative psychological outcomes. The pandemic has led to changes in the delivery of “normal health care” (ie, disruptions to laboratory testing centers, in-person appointments, etc). This has presented numerous challenges for health care providers in providing optimal patient care.26 It is essential for health care providers to recognize these challenges and offer extra support to this vulnerable patient population, especially during a pandemic.

Current Pharmacologic Treatment Landscape in Schizophrenia

Goals of Treatment

The goals for treating schizophrenia should be individualized for each patient but, overall, will include symptom improvement or resolution of symptoms, relapse prevention, adherence to treatment regimens, and improved overall functioning while maximizing quality of life (QOL). Elements that are imperative to address while developing specific treatment plans would include social support systems, personal relationships, housing status, occupational status, financial considerations including insurance, and any legal issues in addition to response to therapies from both a safety and efficacy standpoint.21

Nonpharmacologic and pharmacologic treatment should be considered while developing treatment goals for the patient. Nonpharmacologic treatment includes psychotherapy, cognitive behavioral therapy, group therapy or group education, occupational therapy, and support groups. Pharmacologic treatment is approached from an acute and maintenance phase. The goal of acute therapy is to reduce any current symptoms and lessen agitation or hostility that may be present. Once the acute phase is treated, the patient will move into the maintenance phase of treatment. This phase should involve the continuation of antipsychotic therapy, either with an oral or long-acting injectable antipsychotic (LAIA). The goal of maintenance treatment is to maintain the baseline level of functioning of the patient, minimize AEs from treatment, improve overall QOL, and to prevent relapse and rehospitalization.21,27 Approximately two-thirds of
patients will respond to antipsychotic treatment. However, the remaining one-third will continue to have residual symptoms.

Treatment Guidelines

Several guidelines influence the management of schizophrenia. Among them, and perhaps the most robust in nature, are the American Psychiatric Association (APA) guidelines, updated in 2020. The goal of the APA guidelines is to improve the overall QOL in patients with schizophrenia while improving treatment outcomes. In recent years, there have been numerous studies on the pharmacologic and nonpharmacologic management of schizophrenia added to the literature. The 2020 guidelines were developed to enhance clinicians’ ability to optimize care for patients with schizophrenia, reducing mortality and morbidity in addition to significant psychosocial and health consequences.

With specific regard to pharmacologic treatment, guidelines agree that patients with schizophrenia be treated with antipsychotic medication while being monitored for clinical effectiveness and AEs. If symptom improvement is noted, the general guideline consensus recommends to continue treatment with the same antipsychotic medication used to achieve symptom improvement. Guidelines also agree that patients with treatment-resistant schizophrenia be treated with clozapine. Additionally, the APA recommends that clozapine be used to treat patients with persistent suicidal ideation or at risk for suicide attempts or aggressive behavior. Lastly, guidelines recommend that LAIAs be used in patients with a preference for LAIAs or with an affinity for poor adherence.

Antipsychotics are divided into 2 classes: first-generation antipsychotics (FGAs) and second-generation antipsychotics (SGAs). There is not a specific algorithm of FGA versus SGA use due to differences in study design and lack of head-to-head trials. Therefore, patient preferences, past response, tolerability, the medication AE profile, general medical conditions, formulations and drug–drug interactions (DDIs), receptor-binding affinities, and pharmacokinetic considerations must be taken into account when selecting a medication regimen. Discussions with the patient should occur to understand their personal aspirations, goals of treatment, and treatment preferences.

When deciding between the 2 classes of antipsychotics, risks versus benefits should be considered for each class. The FGAs have a higher incidence of hyperprolactinemia, extrapyramidal symptoms (EPS), and QTc prolongation while the SGAs have a higher incidence of metabolic syndrome. The degree to which each of these AEs will affect treatment will need to be individualized according to patient-specific factors (eg, comorbid medical conditions). Additionally, combination antipsychotic treatment is not well defined in the literature. However, the use of dual antipsychotic treatment is reserved for patients who do not respond adequately to antipsychotic monotherapy.

Nonadherence is prevalent in this patient population and reported to be between approximately 40% and 75%. Poor adherence has been shown to lead to poor outcomes, including increased risk for relapse and rehospitalization, increased suicidal ideation and agitation, and mortality. Adherence should be evaluated prior to the implementation of a treatment regimen to help identify potential barriers. While many factors can contribute to nonadherence, some may be directly related to the prescribed product. For instance, patients may have difficulty remembering to take medication, especially if it involves a complex dosing regimen, have difficulty swallowing medication, or experience AEs. If patients cannot remember to take their medication, a discussion about LAIA formulations may be beneficial. Patients with difficulty swallowing tablets/capsules may find other formulations to be more beneficial (eg, oral deconsecrating tablets, patches, injectables, and oral solutions). Patients who experience bothersome AEs (eg, sedation) may benefit from an agent with less incidence of that same AE.

LAIAs

While head-to-head trials comparing LAIAs with oral antipsychotics have not shown overwhelming evidence in favor of one formulation with regard to adherence, cohort studies and “mirror image” studies, where the patient serves as their own control with the addition of medication serving as the intervention, have shown a decreased risk of mortality, reduced hospitalization, and decreased rate of discontinuation due to efficacy. LAIAs have been shown to decrease relapse when compared with oral medications (RR, 0.7). Another study found that the initiation of LAIAs reduced hospitalization by over 27%, shortened duration of stay, and decreased the overall cost of stay.

Clinician perceptions of LAIAs, including perceived patient refusal and preference for oral medications, may impede the use of LAIAs. One study found that only 36% of patients report being informed about LAIA treatment. However, 64% of patients receiving LAIAs report preference of LAIAs over oral medications. One real barrier to receiving LAIAs includes accessibility to injection administration. Currently 44 states allow pharmacies to administer LAIAs. Patients receiving their LAIA at a community pharmacy for more than 6 months are
4.5-fold more likely to be adherent to their medication regimen. This enhances access to care for the patient because pharmacists are more easily accessible for some patients. Additionally, pharmacies offer extended and weekend hours. This can be helpful for patients who live in underserved areas and face additional transportation challenges. Nearly 90% of Americans live within 5 miles of a pharmacy. Administration of LAIAs can also help to normalize the process of receiving LAIA therapy, helping to reduce stigma.37

**STAR** When comparing LAIAs, what advantages does each agent offer?

### New Therapies

**Asenapine Transdermal System**

While asenapine has been available in oral formulation since 2009, the asenapine transdermal patch is the first transdermal delivery system approved for the treatment of schizophrenia. It offers an alternative treatment option for patients who may be nonadherent or otherwise unable to tolerate other formulations. It is available in 3 doses: 3.8 mg/24 hours, 5.7 mg/24 hours, and 7.6 mg/24 hours, to be applied once daily. It was approved partially based on the oral formulation of asenapine. Additionally, a 6-week, fixed-dose, randomized, double-blind, and placebo-controlled trial consisting of adult patients diagnosed with schizophrenia was evaluated. The primary end point of the trial was the Positive and Negative Syndrome Scale (PANSS) total score, and the Clinical Global Impressions-Severity (CGI-S) rating scale was the secondary end point. The decrease in the PANSS total score was –22.1, –20.4, and –15.5 in the 3.8 mg/24 hours, 7.6 mg/24 hours, and placebo, respectively. The decrease in the CGI-S scale was –1.3, –1.2, and –0.9 for the 3.8 mg/24 hours, 7.6 mg/24 hours, and placebo, respectively. Both end points were statistically significant.38,39

### Emerging Therapies

While dopamine and 5-HT2A antagonism play an integral role in the treatment of schizophrenia, additional agents are needed to target different/additional receptor types to help alleviate residual symptoms and mitigate common AEs of current agents.

**KarXT**

The role the muscarinic cholinergic system plays in schizophrenia has been of interest for many years. KarXT is composed of xanomeline and trospium. Xanomeline is a muscarinic M1/M4 receptor-preferring agonist. It has demonstrated improvement in positive and negative symptoms of schizophrenia in early trials. It is thought that M1 agonism in the prefrontal cortex improves cognition and negative symptoms with M4 agonism in the subcortical areas maintaining normal dopamine levels.43 Trospium, a peripheral muscarinic antagonist that does not cross the blood-brain barrier, is used to prevent the common AEs of xanomeline (eg, vomiting,
nausea, diarrhea, excessive sweating, and salivation). The double-blind, placebo-controlled, 5-week inpatient EMERGENT-1 phase 2 trial showed improvement in the total PANSS score of 11.6 over placebo. The discontinuation rate of KarXT was similar compared to placebo with 20% and 21%, respectively.\textsuperscript{45,46}

Olanzapine/Samidorphan

Olanzapine/samidorphan is a fixed-dose combination medication consisting of a μ-opioid receptor antagonist, samidorphan, and atypical antipsychotic, olanzapine. Samidorphan has been shown to reduce the amount of weight gain in patients receiving olanzapine. In a phase 2, international, multicenter, randomized trial, patients were randomized to a 1:1:1:1 ratio to receive olanzapine plus placebo, olanzapine plus 5, 10, or 20 mg of samidorphan. The primary end point was to confirm antipsychotic efficacy and to assess the effect of samidorphan on olanzapine-induced weight gain. Efficacy was established and weight gain was less in the samidorphan groups, with statistical significance in all but the 20 mg group.\textsuperscript{47} The ENLIGHTEN-1 trial was a 4-week phase 3, randomized, double-blind, placebo- and olanzapine-controlled trial examining the change in the PANSS and CGI-S scores from baseline. Patients were randomized to a 1:1 ratio to olanzapine and samidorphan, olanzapine monotherapy, and placebo. A total of 401 patients were included in the study. The combination group showed significant improvements in the PANSS and CGI-S scores, −6.4 (P = .004) and −0.38 (P < .002) compared with placebo. Results were similar in the olanzapine monotherapy group, demonstrating efficacy and clinical use.\textsuperscript{48} The ENLIGHTEN-2 trial was a 24-week, double-blind trial; patients (N = 561) were randomized to receive olanzapine/samidorphan or olanzapine alone. The primary/co-primary end point was percent change in body weight and the proportion of patients with greater than or equal to 10% weight gain. The secondary end point was the proportion of patients with greater than or equal to 7% weight gain. The least squares mean change in percent body weight was 4.21% and 6.59% in the olanzapine/samidorphan and olanzapine groups, respectively. In the olanzapine/samidorphan group, 17.8% of patients experienced greater than or equal to 10% weight gain compared with 29.8% in the olanzapine group (number needed to treat [NNT] = 7.29). For the secondary end point, 27.5% of patients experienced greater than or equal to 7% weight gain in the olanzapine/samidorphan group compared with 42.7% in the olanzapine group (NNT = 6.29). These studies demonstrate the potential for the combination of olanzapine and samidorphan to offset weight gain in patients taking olanzapine.\textsuperscript{49}

Paliperidone

There is currently a 1-month and a 3-month intramuscular (IM) injectable formulation of paliperidone palmitate available. The 3-month IM injection has shown an adherence rate of 87% to 90% for receiving the third injection.\textsuperscript{50} With non-adherence being as high as 50% in patients with schizophrenia, the development of a 6-month injection would theoretically further increase adherence rates.\textsuperscript{17} A randomized, double-blind, non-inferiority phase 3 study compared time to relapse between the 6-month and 3-month paliperidone IM injection formulations.\textsuperscript{51} The data showed non-inferiority between the 2 formulations after 12 months. The safety profile of the 6-month injection was similar to other formulations of paliperidone LAIAs (1-month and 3-month formulations).\textsuperscript{52} The study was completed in May 2020. Full details of the study are not yet available.

Risperidone (LYN-005)

An extended-release oral formulation of risperidone is being studied to reduce the frequency of dosing. A phase 2, multi-dosed, randomized, parallel group, placebo-controlled study looked at the safety, tolerability, and pharmacokinetic profile of extended-release risperidone in 32 participants. The study concluded in January 2021. Results are not yet available.\textsuperscript{53}

Risperidone ISM

Risperidone ISM is a novel antipsychotic that uses ISM technology to deliver risperidone via a monthly injection. ISM technology relies on in situ formation of biodegradable matrices after the administration of an injection. This delivery method allows for therapeutic levels to be obtained quicker after administration, eliminating the need for oral overlap of medication, booster, or loading dose injections. Theoretically, this mode of administration can help to increase adherence.\textsuperscript{54}

A phase 2 trial looked at the pharmacokinetics, safety, and tolerability of risperidone ISM. The study examined the 75 mg monthly injection in the gluteal and deltoid muscles. Sixty-seven patients received at least 1 dose and C\textsubscript{max} was achieved within 24 to 48 hours regardless of the injection site. The active moiety achieved therapeutic levels 2 hours after the injection; levels were maintained for the 4-week duration. Hyperprolac-tinemia was reported in over 57% of patients.\textsuperscript{55} The PRISMA-3 study was a 12-week, multicenter, randomized, double-blind, placebo-controlled phase 3 study conducted to determine the
efficacy and safety of risperidone ISM 75 mg, 100 mg, or placebo. The primary end point was the PANSS total score at the end of 12 weeks. Both the 75 mg and 100 mg doses proved to be statistically significant in reducing the PANSS total scores when compared with placebo. An open-label 12-month extension phase was conducted; AEs were similar to other risperidone/paliperidone formulations with the most prominent being increased prolactin and hyperprolactinemia (7.8% and 5%, respectively), headache (7.3%), and weight gain (4.8%).

Roluperidone (MIN-101)
The successful treatment of negative and cognitive symptoms of schizophrenia continues to be a challenge in this patient population. It is postulated that these symptoms may be due to excessive glutamate activity and dopaminergic in the mesolimbic dopamine pathway. Roluperidone is a novel, first-in-class compound with sigma-2, 5-HT2A, and α1-adrenergic antagonism. It has a low affinity for dopaminergic, muscarinic, cholinergic, and histaminergic receptors. A 12-week phase 2b study showed that doses of roluperidone 32 mg and 64 mg were statistically significant for the reduction in the PANSS negative symptoms scale when compared with placebo (P ≤.028, d = 0.34 and P ≤.009, d = 0.41, respectively). These are promising results for an area of schizophrenia lacking in treatment options. A multi-center, randomized, double-blind, parallel-group, placebo-controlled, 12-week phase 3 trial was conducted to determine the efficacy and safety of roluperidone as monotherapy. While the full study has not been reported, preliminary results reported using mITT population which indicates that roluperidone 64 mg reduces Marder Negative Symptoms Factor scores at week 4, 8, and 12. Further, Personal and Social Performance total scores were shown to increase at these same time points.

SEP-363856
SEP-363856 is a trace amine-associated receptor 1 (TAAR-1) and 5-HT1A receptor agonist. TAAR-1 is a G-protein-coupled receptor found throughout the brain, though primarily acts in the limbic system. It is a modulator of neurotransmission and appears to be localized in the dopaminergic and serotonergic regions of the brain. TAAR1 is thought to reduce the amount of dopamine and serotonin neurons firing in the limbic system, reducing dopamine in the mesolimbic pathway, thereby reducing psychosis.

A phase 2, randomized, controlled trial was performed to evaluate the safety and efficacy of SEP-363856 in adult patients with schizophrenia. Patients were randomized in a 1:1 ratio to receive either SEP-363856 (50 mg or 75 mg) or placebo for 4 weeks. The primary end point was the change in the PANSS total score. The secondary end points included the change in CGI-S Scale and Brief Negative Symptom Scale scores. A total of 225 patients were enrolled in the study with 120 being assigned to the SEP treatment group. The change in the PANSS total was −17.2 and −9.7 in the treatment versus placebo groups (P = .001). The secondary end points trended in the same direction but were not statistically significant. A 6-month extension trial was then performed to examine the incidence of AEs, AEs leading to discontinuation, and serious AEs. Secondary outcomes included weight, laboratory values, electrocardiogram, EPS, suicidality, and sleep quality. Over 56.4% of the 156 patients enrolled in the study experienced one AE, with the most common being symptoms of psychosis, headache, insomnia, and anxiety (12.2%, 11.5%, 8.3%, and 5.1%, respectively). Overall, SEP-363856 was well tolerated with minimal effects on weight and metabolic parameters, prolactin, and EPS measures. The changes in the PANSS score were reported to be −22 and sustained throughout the duration of the study. There are 4 phase 3 studies in progress for SEP-363856, the DIAMOND 1-4. They are expected to conclude in November 2022.

TAK-831
D-serine is needed to open the NMDA receptor (NMDAR) channel, along with glutamate. However, enzyme D-amino acid oxidase metabolizes D-serine to inactivate it. TAK-831 is a selective and potent D-amino acid oxidase inhibitor, prolonging D-serine as an NMDAR agonist. With increased levels of glutamate combined with this mechanism, the activity of the NMDAR is increased, which is thought to improve the negative symptoms associated with schizophrenia. A phase 2 trial examining the efficacy, tolerability, pharmacodynamics, and pharmacokinetics of TAK-831 concluded in December 2020. Results are not yet available.

STAR
How would new and emerging treatments in schizophrenia help bridge the gap in treating patients with the disorder?

Role of the Psychiatric and Clinical Pharmacist in Integrating New Therapies Into Practice
Benefit of Pharmacist on the Interdisciplinary Team
The involvement of a pharmacist as part of the multidisciplinary team improves patient outcomes and adherence to therapy, particularly in patients with schizophrenia.
plinary team has the potential to improve patient outcomes. A systematic review looking at 64 publications showed that pharmacist involvement in patient care increased patient-centered outcomes, such as medication adherence, disease state control, and avoidance of hospitalization. One study looking at pharmacist involvement in the care for patients with schizophrenia receiving antipsychotic polypharmacy treatment was helpful. In this study, pharmacists discussed the use of polypharmacy and/or excessive antipsychotic doses, suggested gradual tapers in patients being discontinued on antipsychotic therapy, suggested the addition or discontinuation of concurrent medications and, where needed, suggested therapeutic monitoring. The study found that there was an overall decrease in the total dosage and number of antipsychotics prescribed per patient. Another study looked at the cognitive function in patients with schizophrenia in pharmacist intervention groups versus care as usual. Pharmacists reviewed patient medication regimens and made suggestions when drug-related problems were identified. The primary end point was the Wisconsin Card Sorting Test. Patients in the pharmacist intervention group improved significantly from baseline and drug-related problems were reduced by 85% versus approximately 10% in the care as usual group. A third study found that pharmacist-led education sessions improved overall QOL and adherence in patients with schizophrenia. This small study looked at 23 patients, randomizing them to the treatment group (pharmacist education) or usual care group (prescriber education). Patients were assessed for adherence and QOL 3 times over the course of the study. Patients receiving education from a pharmacist had better rates of adherence and scored higher on the QOL assessments.

**Individualizing Therapy**

There is no direct algorithm for the treatment of schizophrenia. As stated previously, the goals of a treatment plan are to promote and maintain recovery, maximize QOL and functioning, and reduce or eliminate symptoms. To achieve this, patient-specific factors will need to be considered. Including patients and, where possible, their loved ones in this discussion is a great way to include shared decision making, develop a person-centered treatment plan, and promote adherence. Patients should be asked about their previous experiences with medication, response from previous or current treatment, and preferences for specific formulations or agents. Discussions with loved ones can help identify additional barriers to treatment and help to develop a plan that will overcome said barriers.

When individualizing a treatment plan, a review of medication formulations, AE profiles (class-wide and medication specific), and DDIs should be discussed with the patient. Discussing the availability of alternative formulations to oral medications (eg, transdermal delivery system and long-acting injectables) can be beneficial in addressing the ability to eliminate oral medication. DDIs should also be considered. When multiple medications are prescribed, the risk for a pharmacodynamic or pharmacokinetic DDI increases. From a pharmacodynamic standpoint, common AEs among psychotropic medications include increased sedation, QTc prolongation, and additive anticholinergic effects. Pharmacokinetic DDIs include the metabolic enzymes (ie, cytochrome P450 enzymes). Medications influencing the CYP pathway need to be evaluated on a regular basis, making medication regimen adjustments when necessary. A common substance of use in the psychiatric patient population is cigarettes. Cigarette smoke has the potential to decrease levels of antipsychotics such as clozapine and olanzapine. The initiation or cessation of smoking will greatly affect these levels, necessitating a change in dosage. This will be particularly important for patients admitted to smoke-free facilities receiving CYP1A2 substrate medications. For patients receiving multiple medications, pharmacists should perform a DDI check and address any clinically significant interactions that may be present. Pharmacokinetic profiles of each medication should also be reviewed. Agents with short half-lives may benefit from twice-daily dosing. Conversely, agents with longer half-lives may be consolidated to once-daily dosing, helping to eliminate a barrier to treatment. Absorption parameters should also be considered with each medication (ie, ziprasidone and lurasidone should be taken with food to maximize absorption).

AEs should be discussed with the patient prior to initiation of a medication as these can greatly influence antipsychotic selection. Nearly 80% of patients on antipsychotic medications report at least 1 bothersome AE, contributing to approximately 50% of patients to be nonadherent. Some AEs are dose-dependent and may resolve with a dose reduction while others dissipate once tolerance is established. Pharmacist interventions regarding dose titration (or tapering) is also important in mitigating dose-dependent AEs. Other interventions may include medication management of AEs or alternative medication recommendations.

Guidelines state that antipsychotic treatment should be continued if a patient is responding favorably. However, up to 30% of patients will not respond adequately to treatment. According to the APA, patients whose treatment of 2 adequate
trials of antipsychotics failed are candidates for clozapine treatment.21 However, the United States has one of the lowest rates of clozapine usage at 2% to 4% of eligible patients. Additionally, in patients prescribed clozapine, initiation is often delayed.72 Clozapine has shown efficacy in treatment-resistant schizophrenia and has anti-suicidal and anti-aggressive properties.72 Clozapine has an extensive AE profile that includes agranulocytosis, which led to the development of the risk evaluation and mitigation strategy (REMS) program for clozapine. Other serious AEs include cardiomyopathy, seizures, orthostatic hypotension, metabolic syndrome, sedation, drooling, and more. Clinical pharmacists in the psychiatric setting are in a unique

TABLE 1. ANTIPSYCHOTIC TREATMENT21

<table>
<thead>
<tr>
<th>Medication</th>
<th>Brand name</th>
<th>Initial oral dose (mg/day) (typical dosing range)</th>
<th>Common and serious adverse effects</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>First-generation antipsychotics</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Chlorpromazine</td>
<td>Thorazine</td>
<td>25-100 (200-800)</td>
<td>Tardive dyskinesia, anticholinergic, sedation, orthostasis, QTc prolongation</td>
</tr>
<tr>
<td>Fluphenazine</td>
<td>Prolixin</td>
<td>2.5-10 (6-20)</td>
<td>EPS, hyperprolactinemia</td>
</tr>
<tr>
<td>Haloperidol</td>
<td>Haldol</td>
<td>1-15 (5-20)</td>
<td>EPS, hyperprolactinemia</td>
</tr>
<tr>
<td>Loxapine*</td>
<td>Loxitane</td>
<td>20 (60-100)</td>
<td>EPS, hyperprolactinemia, orthostasis, QTc prolongation</td>
</tr>
<tr>
<td>Perphenazine*</td>
<td>Trilafon</td>
<td>8-16 (8-32)</td>
<td>EPS, hyperprolactinemia, anticholinergic, QTc prolongation, weight gain</td>
</tr>
<tr>
<td>Pimozide</td>
<td>Orap</td>
<td>0.5-2 (2-4)</td>
<td>EPS, hyperprolactinemia, seizures, QTc prolongation</td>
</tr>
<tr>
<td>Thioridazine</td>
<td>Mellaril</td>
<td>150-300 (300-800)</td>
<td>Anticholinergic, sedation, orthostasis, QTc prolongation, sexual dysfunction</td>
</tr>
<tr>
<td>Thiothixene</td>
<td>Navane</td>
<td>6-10 (15-30)</td>
<td>EPS, hyperprolactinemia, seizures</td>
</tr>
<tr>
<td>Trifluoperazine*</td>
<td>Stelazine</td>
<td>4-10 (15-20)</td>
<td>EPS, hyperprolactinemia, anticholinergic, QTc prolongation, weight gain</td>
</tr>
<tr>
<td><strong>Second-generation antipsychotics</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Aripiprazole*</td>
<td>Abilify</td>
<td>10-15 (10-15)</td>
<td>Akathisia</td>
</tr>
<tr>
<td>Asenapine*</td>
<td>Saphris</td>
<td>10 (20)</td>
<td>EPS, sedation, orthostasis, QTc prolongation, weight gain, hyperlipidemia</td>
</tr>
<tr>
<td>Brexpiprazole*</td>
<td>Rexulti</td>
<td>1 (2-4)</td>
<td>Akathisia, sedation, QTc prolongation, hyperlipidemia</td>
</tr>
<tr>
<td>Cariprazine*</td>
<td>Vraylar</td>
<td>1.5 (1.5-6)</td>
<td>Akathisia, anticholinergic, sedation, QTc prolongation, weight gain</td>
</tr>
<tr>
<td>Clozapine</td>
<td>Clozaril</td>
<td>12.5-25 (300-450)</td>
<td>Anticholinergic, sedation, weight gain, orthostasis, hyperlipidemia, glucose abnormalities, hypersalivation, sexual dysfunction, constipation, myocarditis, cardiomyopathy, seizures, and neutropenia</td>
</tr>
<tr>
<td>Iloperidone</td>
<td>Fanapt</td>
<td>2 (12-24)</td>
<td>Orthostasis, QTc prolongation</td>
</tr>
<tr>
<td>Lurasidone*</td>
<td>Latuda</td>
<td>40 (40-120)</td>
<td>EPS, sedation, hyperlipidemia, glucose abnormalities</td>
</tr>
<tr>
<td>Olanzapine</td>
<td>Zyprexa</td>
<td>5-10 (10-20)</td>
<td>Anticholinergic, sedation, weight gain, hyperlipidemia, glucose abnormalities</td>
</tr>
<tr>
<td>Paliperidone</td>
<td>Invega</td>
<td>6 (3-12)</td>
<td>Hyperprolactinemia</td>
</tr>
<tr>
<td>Quetiapine</td>
<td>Seroquel/Seroquel XR</td>
<td>50 IR and 300 XR (400-800)</td>
<td>Sedation, hyperlipidemia</td>
</tr>
<tr>
<td>Risperidone</td>
<td>Risperdal</td>
<td>2 (2-8)</td>
<td>Hyperprolactinemia</td>
</tr>
<tr>
<td>Ziprasidone</td>
<td>Geodon</td>
<td>40 (80-160)</td>
<td>QTc prolongation</td>
</tr>
</tbody>
</table>

*EPS, extrapyramidal symptoms.

* The occurrence of these adverse effects is less but are most prevalent for these agents.
position to help facilitate the enrollment of patients into the REMS program, provide patient education, evaluate and manage AEs, and make dosing recommendations and lab referrals.\textsuperscript{21}

**Dosing and Administration**

The goal of acute exacerbations is symptom resolution. Therefore, when initiating an antipsychotic medication, upward titration can be done fairly quickly based on patient tolerability, with the exception of clozapine. The initial dose of specific antipsychotic will vary depending on the formulation, and patient-specific characteristic.\textsuperscript{21} Initial antipsychotic dosing may be found in TABLE 1.\textsuperscript{21} Clozapine has an extensive AE profile, including dose-dependent seizures and orthostatic hypotension. Titration must occur in increments of 25 to 50 mg per day, until the target dose is reached because of this. This typically takes 2 weeks.\textsuperscript{73} While serum concentrations of antipsychotics are not routine, it may be helpful in the case of clozapine therapy. While efficacy of clozapine levels is not definitive in the literature, examining the ratio of clozapine to norclozapine may be useful. Clozapine to norclozapine ratios less than 2 may be associated with greater toxicities.\textsuperscript{24} Elderly patients may benefit from a slower antipsychotic titration rate due to a change in pharmacokinetic properties, making them more susceptible to certain AEs (ie, central nervous system effects).\textsuperscript{21} Younger patients generally tend to be more susceptible to metabolic effects of medication (eg, weight gain), which can occur early in antipsychotic treatment.\textsuperscript{75} Patients experiencing first break psychosis tend to respond more rapidly to treatment and may only need a smaller dose for symptom resolution.\textsuperscript{76}

Response rate of antipsychotics may vary depending on the course of the illness. However, when initiating treatment, it is important for the patient to understand that they may not see the initial effects of the medication for 2 to 4 weeks, and longer for the full effect. In the interim, if the dose has been escalated quickly, this may cause the false impression that a higher dose is needed to maintain response or resolution of symptoms. It is also important to note that if a patient has not seen a response to the antipsychotic in the first few weeks, defined as 20% reduction in symptoms, they are unlikely to reach full remission at 4 to 6 weeks.\textsuperscript{77} In this situation, it is appropriate to consider a change in therapy.

In addition to traditional oral formulations, LAIAs are also available. These agents may offer an option for patients who cannot remember to take a daily medication, or simply prefer an LAIA. However, there are several considerations when administering these agents. For the FGA LAIAs, administration technique is important. Fluphenazine decanoate and haloperidol decanoate are oil based.\textsuperscript{78,79} When administering these medications, the Z-track method should be used to reduce medication leakage at the injection site.\textsuperscript{80} Dosing intervals for fluphenazine is every 2 to 4 weeks, while haloperidol is every 4 weeks.\textsuperscript{21} A complete list of FGA LAIAs can be found in TABLE 2.\textsuperscript{21}

Second-generation LAIAs include aripiprazole and aripiprazole lauroxil, olanzapine pamoate, paliperidone palmitate (1-month, 3-month), and risperidone formulations (IM, subcutaneous [SC]). There are a few caveats to note between these agents. For instance, risperidone has an IM and SC formulation. These agents should only be administered via their approved route of administration. The dosing interval for these 2 agents differ between the IM and SC injection being every 2 and 4 weeks, respectively.\textsuperscript{21} Aripiprazole comes in 3 formulations, aripiprazole, aripiprazole lauroxil, and aripiprazole with nanocrystal technology. Aripiprazole is intended to be given via IM injection every 4 weeks with an initial 2-week oral overlap, whereas aripiprazole lauroxil can be administered via IM injection every 4, 6, or 8 weeks depending on the stabilizing oral dose. Aripiprazole lauroxil administered by itself requires a 3-week oral overlap. Aripiprazole lauroxil with nanocrystal technology is taken with a one-time oral dose of a 30 mg tablet. The nanocrystals are smaller in size, producing faster dissolution, and achieving therapeutic concentration to be reached in 4 days. The maintenance dose of aripiprazole lauroxil is then administered within 10 days. The use of the nanocrystal technology acts as a loading dose, eliminating the need for an oral overlap.\textsuperscript{80-82} Lastly, olanzapine palmitate has a REMS program associated with its use and due to severe sedation and delirium that may occur post injection. Thus, a 3-hour observation period after administration is required. This should not be administered in a community pharmacy setting.\textsuperscript{81,83} A complete list of SGA LAIAs can be found in TABLE 2.\textsuperscript{21}

**Education and Counseling**

Pharmacists are in a unique position to serve the public due to their accessibility in the outpatient setting. One study found that approximately 92% of study participants perceived the community pharmacists to significantly impact their willingness to participate in medication therapy management and medication optimization.\textsuperscript{84} Pharmacists are in a position to educate, advocate for, and assist in managing monitoring parameters and AEs. The World Health Organization (WHO) recommends that smoking cessation, weight management, substance use disorders, cardiovascular disease and cardiovascular risk, diabetes mellitus, and HIV/AIDS be managed.
among people with severe mental illness (eg, schizophrenia), with a focus on decreasing morbidity and premature mortality. Pharmacists are equipped to manage these comorbidities, helping to bridge the gap in patient care.

Patients often begin medication treatment without having a full understanding of the medication they are taking, what to expect regarding AEs, efficacy, and course of the illness. Pharmacists may help bridge this gap by discussing each of these parameters with the patient. Assessing patients’ attitudes toward medication can be helpful to maximize adherence. One study showed that positive attitudes toward medication resulted in better adherence, while negative attitudes contribute to nonadherence. Factors contributing to attitudes include coordination of care, AEs, social support, insight, stigma, rapport with providers, and presence of paranoia. Engaging loved ones and caregivers can further help assess barriers to treatment that may exist for the patient, identifying obstacles for complete adherence, such as complex regimens, AEs, lack of insight, pill burden, cost of treatment, etc. The inclusion of caregivers and family members may also help to increase the social support for the patient by including those close to them. Pharmacists are able to promote patient adherence by educating the patient about the benefits of treatment, setting expectations for efficacy and safety, and addressing AEs when they arise. Pharmacists are able to educate on the various agents and aid in the selection of an agent that will be best suited to fit the patient’s needs. In addition to education, pharmacists may allow for easier access to injection administration, increasing adherence. Patients receiving LAIAs at their community pharmacy are 4.5-fold more likely to adhere to treatment than when receiving the injection at an alternative injection site (ie, provider’s office).

To increase access to LAIAs, the National Alliance of State Pharmacy Associations has partnered with the College of Psychiatric and Neurologic Pharmacists to assemble a group of stakeholders to advocate for the development of state-level medication administration policies with a focus on LAIAs. As stated previously, 44 states allow for pharmacists to administer LAIA therapy.

Pharmacists should be intentional in counseling on safety considerations with antipsychotic therapy, which includes AEs and monitoring. Antipsychotics vary greatly in their AE profile as shown in Table 1. Given the prevalence of AEs with antipsychotic therapy, it is important to inquire about them with each patient interaction. Some AEs begin with initiation of antipsychotics but dissipate with time while some appear at higher doses. Pharmacists can provide guidance to the patient regarding these AEs. For instance, the pharmacist can recommend that the

<p>| TABLE 2. LONG-ACTING ANTIPSYCHOTIC INJECTABLES (LAIAs)²⁰ |
|-----------------------------------|-----------------|-----------------|-----------------|</p>
<table>
<thead>
<tr>
<th>Medication</th>
<th>Brand name</th>
<th>Frequency of administration</th>
<th>Oral overlap requirement</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>First-generation antipsychotics</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Fluphenazine decanoate</td>
<td>Prolixin</td>
<td>2-4 weeks</td>
<td>Reduce oral by 50% with 1st injection; stop after 2nd injection</td>
</tr>
<tr>
<td>Haloperidol decanoate</td>
<td>Haldol Decanoate</td>
<td>4 weeks</td>
<td>Taper and stop after 2nd or 3rd injection</td>
</tr>
<tr>
<td><strong>Second-generation antipsychotics</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Aripiprazole extended release</td>
<td>Abilify Maintena</td>
<td>4 weeks</td>
<td>2 weeks</td>
</tr>
<tr>
<td>Aripiprazole lauroxil extended release</td>
<td>Aristada</td>
<td>4, 6, or 8 weeks (dose dependent)</td>
<td>3 weeks; however, if administered with Aristada Initio, none needed</td>
</tr>
<tr>
<td>Aripiprazole lauroxil nanocrystal extended release</td>
<td>Aristada Initio</td>
<td>One-time administration</td>
<td>One-time administration with 30 mg aripiprazole tablet</td>
</tr>
<tr>
<td>Olanzapine pamoate</td>
<td>Zyprexa Relprev</td>
<td>2-4 weeks</td>
<td>None</td>
</tr>
<tr>
<td>Paliperidone palmitate extended release</td>
<td>Invega Sustenna</td>
<td>4 weeks</td>
<td>None</td>
</tr>
<tr>
<td>Paliperidone palmitate extended release</td>
<td>Invega Trinza</td>
<td>12 weeks</td>
<td>None</td>
</tr>
<tr>
<td>Risperidone long-acting injection</td>
<td>Risperdal Consta</td>
<td>2 weeks</td>
<td>3 weeks</td>
</tr>
<tr>
<td>Risperidone extended release (SC)</td>
<td>Perseris</td>
<td>4 weeks</td>
<td>None</td>
</tr>
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²⁰ | TABLE 2. LONG-ACTING ANTIPSYCHOTIC INJECTABLES (LAIAs)²⁰ | Medication | Brand name | Frequency of administration | Oral overlap requirement |
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</table>
patient document their reaction to the medication. Some AEs may resolve simply by taking with food or taking at a different time of day (ie, in the case of sedating effects).

Metabolic AEs commonly occur with antipsychotic treatment, especially with SGAs. Pharmacists can provide education regarding their prevalence and recommend monitoring and interventions to minimize these effects. SGAs have been shown to increase fasting glucose levels, elevate serum cholesterol levels, and cause weight gain. These effects place the patient at a higher risk for developing metabolic syndrome. It is estimated that 42% of patients receiving an SGA will develop metabolic syndrome.88 In response to this stark statistic, the American Diabetes Association and APA recommend that weight, waist circumference, blood pressure, fasting glucose, and fasting lipid panels be monitored in patients receiving SGAs.89 Pharmacists in psychiatric settings are in a great position to monitor for metabolic AEs. Electronic interventions may be helpful to identify patients at risk for developing metabolic AEs or syndrome, allowing for early interventions. One study demonstrated that relying on pop-up alerts within an electronic medical system does not increase the incidence of metabolic monitoring.90 Conversely, a systematic review with 10 studies examining the involvement of pharmacists in metabolic monitoring found that pharmacist involvement increased the number of patients identified as having metabolic syndrome, increased referrals for follow-up, and strengthened communication with providers.91

Addressing Health Care Disparities

Literature shows that health care disparities in the treatment of schizophrenia exist. Higher mortality rates occur in patients with severe mental illness, with comorbidities including cardiovascular disease, metabolic syndromes, and respiratory disease.23 Pharmacists are in a position to address the needs of these patients. The COVID-19 pandemic has the potential to increase poor outcomes in patients with schizophrenia, interrupting typical patient care activities. Pharmacists are in a position to reach patients in a multitude of ways, including delivery of patient education and suggesting treatment change recommendations. Pharmacists have been shown to deliver consultation services to the level of direct patient care through telemedicine, helping to ensure patients receive education during social distancing mandates.92 Telemedicine has ensured that patients are able to receive care during the pandemic and should be used where possible. However, there are barriers for the use of telemedicine, economic challenges/access to internet services, technological difficulties, and developing patient-provider rapport.26 In situations where patients are having difficulties obtaining medication or proper monitoring, pharmacists can work with the patient to find alternative means. For instance, mail order pharmacy and curbside deliveries may be available for patients. Pharmacists can suggest these services and help patients with the initial enrollment process. Medications that require monitoring (ie, clozapine) will likely require pharmacist assistance for continuity of care. The clozapine REMS program has temporarily allowed for provider discretion regarding monitoring. Pharmacists are in unique positions to form positive patient relationships, thus they can work closely with the patient’s provider to help evaluate the risks versus benefits of continued or delayed monitoring. However, delaying clozapine monitoring should only be reserved for patients with compelling reasons or risks that would prevent them from obtaining laboratory work.

Conclusion

Schizophrenia is a disorder causing major disturbances in the lives of patients. Current pharmacotherapy is able to offer successful treatment to as much as 80% of patients with schizophrenia.17 The remaining 20% of patients are unable to obtain full remission due to a variety of possibilities including nonadherence and treatment resistance. The new and emerging treatments for schizophrenia offer an opportunity to reach this subset of patients. Pharmacists may further help patients to achieve remission and prevent relapse through developing meaningful relationships with the patients, ensuring continuity of care, providing patient education, and collaboration with providers to deliver health care services.

### ADDITIONAL RESOURCES

<table>
<thead>
<tr>
<th>Resource</th>
<th>Website</th>
</tr>
</thead>
<tbody>
<tr>
<td>National Alliance on Mental Illness (NAMI)</td>
<td>nami.org/Home</td>
</tr>
<tr>
<td>Clozapine REMS Program</td>
<td><a href="http://www.clozapinerems.com/CpmgClozapineUI/home.u">www.clozapinerems.com/CpmgClozapineUI/home.u</a></td>
</tr>
<tr>
<td>NIH: RAISE Resources through the National Institute of Mental Health</td>
<td><a href="http://www.nimh.nih.gov/health/topics/schizophrenia/raise/resources-for-patients-and-families.shtml">www.nimh.nih.gov/health/topics/schizophrenia/raise/resources-for-patients-and-families.shtml</a></td>
</tr>
</tbody>
</table>

### REFERENCES


65. Xu L, DeMartins N, Wu J, et al. Safety, pharmacokinetics (PK) and pharmacody-
POSTTEST QUESTIONS

1. Which of the following factors has been shown to increase the risk for developing schizophrenia?
   A. Autoimmune disorders
   B. First-degree relatives with schizophrenia
   C. Caucasian race
   D. Normal gestation

PK was diagnosed with schizophrenia approximately 6 months ago. He was initiated on quetiapine and responded well. PK has been maintained on quetiapine, with periodic increases in the dosage as symptoms emerged. PK is currently at 300 mg nightly but has been experiencing extreme sedation. He would like to speak with the pharmacist regarding treatment options that may be less sedating.

2. Which of the following agents would be helpful in reducing sedation for PK?
   A. Clozapine
   B. Chlorpromazine
   C. Olanzapine
   D. Ziprasidone

3. Research has shown which of the following as a benefit of having pharmacists as part of the patient care team?
   A. Diagnosing schizophrenia
   B. Providing psychotherapy for patients
   C. Reduction of drug-related problems
   D. Decreasing the need for monitoring

AR has been diagnosed with schizophrenia for 3 years. While AR has shown response to paliperidone 9 mg daily, she frequently stops taking medication due to difficulties with remembering. This has led to multiple relapses over the years. AR is currently being managed by her outpatient primary care provider as she has had difficulty forming a positive rapport with a psychiatric provider. The primary care provider called inquiring about possible ways to enhance AR's adherence.

4. What strategy may help increase adherence in patients with schizophrenia?
   A. Discuss transitioning to paliperidone palmitate 1-month injection
   B. Transition to quetiapine twice daily due to frequent relapses
   C. Continue with paliperidone daily since AR has experienced a response
   D. Increase paliperidone to 12 mg daily to increase AR's response

5. Food increases the absorption of which of the following medications?
   A. Aripiprazole
   B. Loxapine
   C. Ziprasidone
   D. Brexpiprazole

6. According to the American Psychiatric Association (APA) guidelines, when should clozapine treatment be considered?
   A. As first-line therapy
   B. After 1 treatment failure
   C. For treatment-resistant schizophrenia
   D. In combination with a first-generation antipsychotic

A 29-year-old patient with a 3-year history of schizophrenia presents for a follow-up appointment to discuss a potential change in antipsychotic treatment. The patient is 5’9” and weighs 195 lb. The medical history indicates that the patient has hypertension, gastroesophageal reflux disease (GERD) leading to recent dysphagia, and acne. Current medications include lurasidone 60 mg daily, lisinopril 20 mg daily, and esomeprazole 40 mg daily. No other trials of antipsychotics have been tried. The patient states that they have been having difficulties taking medication lately due to GERD.

7. Which of the following antipsychotic medications may be helpful for the patient at this time?
   A. Paliperidone 3-month long-acting injectable antipsychotic (LAIA)
   B. Olanzapine orally disintegrating tablet
   C. Asenapine transdermal patch
   D. Clozapine orally disintegrating tablet

8. According to the APA guidelines, which of the following is an acceptable reason to use LAIAs?
   A. LAIAs are not recommended
   B. Patient preference
   C. To reduce aggression
   D. To reduce suicidal ideation

9. Which of the following emerging therapies for schizophrenia shows promising results for mitigating antipsychotic-induced weight gain?
   A. Trace amine-associated receptor 1 agonist
   B. Roluperidone
   C. Risperidone ISM
   D. Olanzapine/samidorphan
POSTTEST QUESTIONS (continued)

10. Nearly 50% of patients with schizophrenia are nonadherent to their medication; which of the following factors can contribute to medication nonadherence?
   A. Positive provider relationships
   B. Remission of illness
   C. Adverse drug reactions
   D. Stable housing

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Once completed, click “Next” until reaching the activity posttest.
Complete the online posttest and activity evaluation form.
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Manufactured by Braintree Laboratories

For patients seeking a more convenient choice for bowel preparation before a colonoscopy, Sutab offers a tablet-based regimen. The tablets have no sodium phosphate and have been confirmed to be safe and effective. Each dose consists of 12 tablets and 16 oz of water, and 92% of patients in 2 pivotal trials achieved successful bowel cleansing with the regimen. Furthermore, 91% of patients in 1 pivotal trial rated it as “tolerable” to “very easy” to consume, and 78% said they would request Sutab again for a future colonoscopy.

FOR MORE INFORMATION: sutab.com

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Manufactured by L’Oreal

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FOR MORE INFORMATION: cerave.com

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FOR MORE INFORMATION: naturemade.com

SEE OUR AD ON PAGE 25
SEE OUR AD ON PAGE 5
SEE OUR AD ON PAGE 43-44