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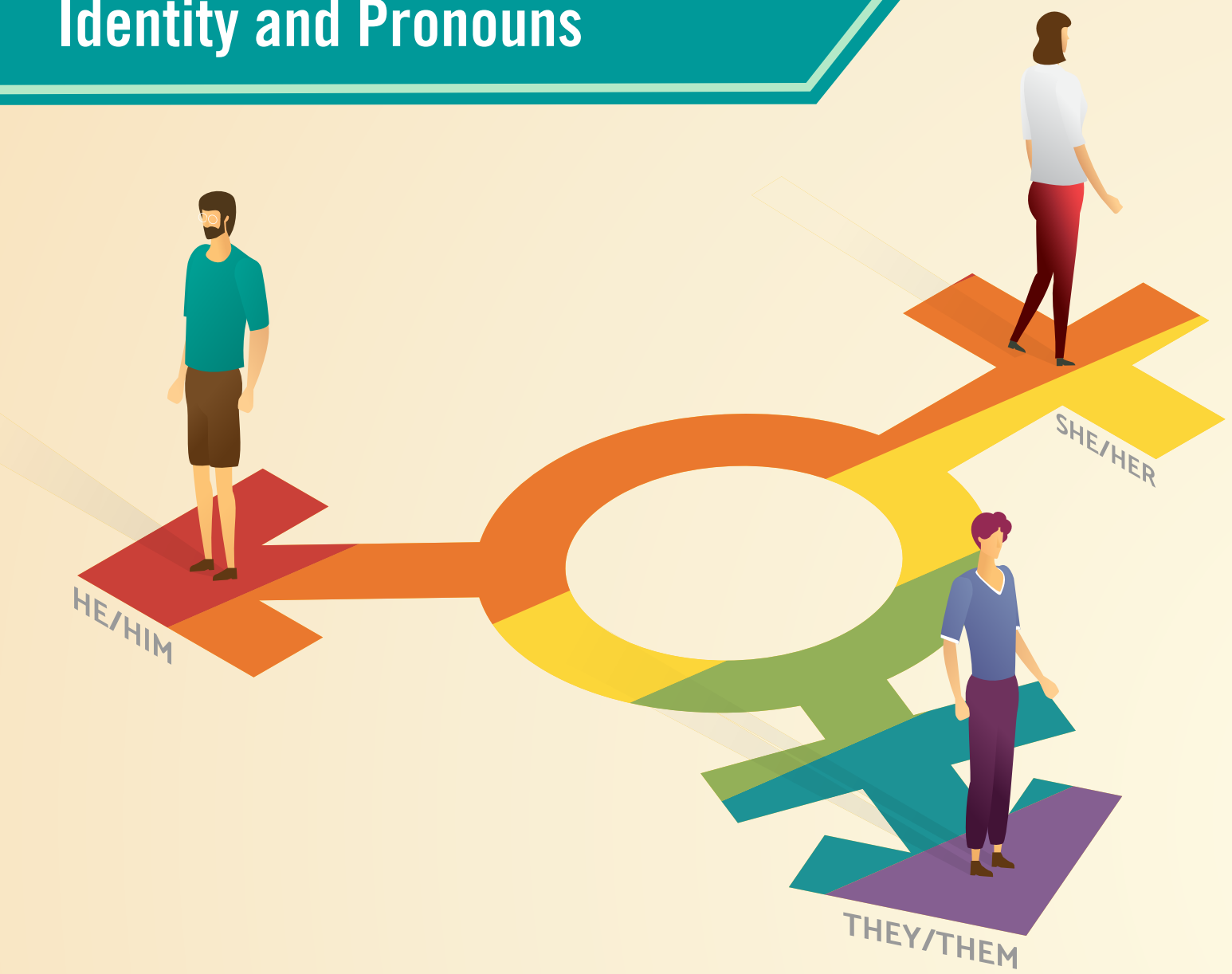
UpFront: Thinking About Gender Identity and Pronouns



September/October 2022

Continuing Education

Features

Original Work

Review Articles

Spotlight

The Journal
of the Pharmacy Society of Wisconsin

The Journal of the Pharmacy Society of Wisconsin is a professional publication for original research, review, experience, and opinion articles that link science with contemporary pharmacy practice to improve patient care. Together we can inspire each other to advance our profession with the single purpose of enhancing the lives of our patients.

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Features

UpFront: Thinking About Gender Identity and Pronouns

by Anna Marceau (they/them/theirs), Amrita Geddam (she/her/hers), Ellina Seckel (she/her/hers)

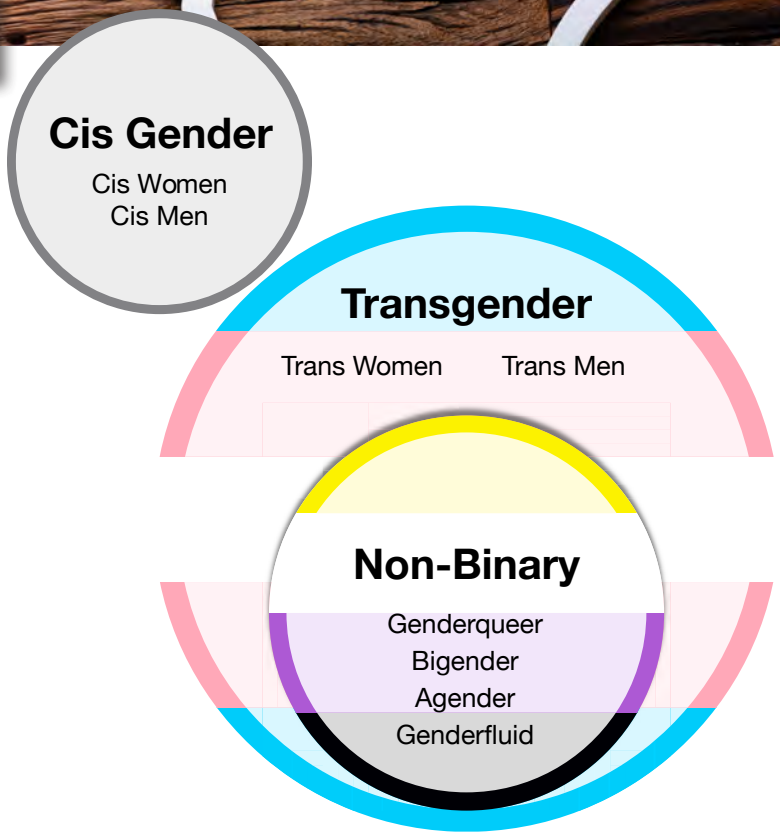
As part of PSW's commitment to diversity, equity, and inclusion, we want to share some guidance and collective understanding about gender identity, pronouns, and other related terms.

In a recent NPR story, Mary Emily O'Hara, a communications officer at GLAAD, explained, "Pronouns are basically how we identify ourselves apart from our name. It's how someone refers to you in conversation. And when you're speaking to people, it's a really simple way to affirm their identity. It's really just about letting someone know that you accept their identity. And it's as simple as that."

Here are some current, accepted definitions of gender-related terms:

- **Gender:** Set of social, physical, psychological, and emotional traits, often influenced by societal expectations, that classify an individual as feminine, masculine, androgynous or other
- **Gender identity:** One's innermost concept of self from the perspective of one's gender
- **Gender expression:** Outward manner in which an individual expresses or displays their gender
- **Sex:** The biology a person is born with, including genetic, hormonal, anatomic, and physiological characteristics; related terms include "sex assigned at birth," "natal sex," "biologic sex," or "birth sex." DFAB/AFAB stands for "designated/assigned female at birth." DMAB/AMAB stands for "designated/assigned male at birth."
- **Transgender:** An umbrella term, sometimes shortened to "trans" or "trans,*" that refers to a person whose gender identity differs from their sex assigned at birth
- **Cisgender:** Refers to a person whose gender identity aligns with their sex assigned at birth
- **Non-binary:** Having a gender that is in between or beyond the two categories "man" and "woman," or fluctuating between man and woman as having no gender, either permanently or some of the time
- **Social titles:** Not legally part of a name, used for identity purposes and as a matter of courtesy (e.g., Mr., Ms., Miss, Mrs., Mx.)

Pronouns are used to refer to someone in the third person. Examples include she/her/hers, he/him/his, they/them/theirs, and ze/hir/hirs.



While you might hear discourse about whether using "they" to refer to a single person is grammatically correct, it is important to remember that this is not merely a matter of linguistics, but an integral part of a person's identity and expression thereof. A person's sense of self should not be used as a stage for a debate. To support this, in recent years, major style guides like the Associated Press Stylebook have updated their guidance to include provisions for using "they" and "them" when referring to an individual.

What does it mean if a person uses the pronouns "he/they" or "she/they"?

In the NPR story, Rodrigo Heng-Lehtinen, deputy executive director of the National Center for Transgender Equality, says, "That means that the person uses both pronouns, and you can alternate between those when referring to them. So either pronoun would be fine — and ideally mix it up, use both. It just means that they use both pronouns that they're listing."

GLAAD's associate director of transgender representation, Alex Schmider, says it depends on the person. "For some people, they don't mind those pronouns being interchanged for them. And for some people, they are using one specific pronoun in one context and another set of pronouns in another, dependent on maybe safety or comfortability." The best approach, Schmider says, is to listen to how people refer to themselves.

When should you provide your pronouns?

- All introductions
- Start of meetings
- Email signature
- Zoom names/other platforms
- Pronoun pin
- Social media bios
- Recruitment materials
- Surveys that gather demographic information
- Presentations

PSW Diversity, Equity and Inclusion Statement

One voice, one vision for all. PSW supports diversity in our membership, equity in our opportunities, and inclusiveness in our organization. We embrace our differences, unifying efforts to enhance patient care while advancing our profession. Our patients are diverse, and so are we. Click here to view the PSW DEI Organization Recommendations.

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FOR MORE INFORMATION & RESOURCES:

- https://www.mypronouns.org/resources
- https://www.npr.org/2021/06/02/996319297/gender-identity-pronouns-expression-guide-lgbtq
- https://owl.purdue.edu/owl/general_writing/grammar/pronouns/gendered_pronouns_and_singular_they.html

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Pharmacy Society of Wisconsin

DIVERSITY, EQUITY, AND INCLUSION

Organization Recommendations

PSW will support diversity in our membership, equity in opportunities, and inclusiveness in our organization, empowering pharmacists, technicians, and student pharmacists to address systemic racism, and have broader cultural humility in the care of patients.

PHARMACIST CE:

A Review of Pathophysiology and Treatment of Polycystic Ovary Syndrome (PCOS)

by Amy N. Bowman, 2023 PharmD Candidate, Taylor A. Shufelt, 2023 PharmD Candidate, Amy M. Wolff, 2024 PharmD Candidate, Dolyn Salm, 2024 PharmD Candidate, Joyce Hu, 2024 PharmD Candidate, Marina L. Maes, PharmD, BCPS, BCACP

Polycystic ovary syndrome, or PCOS, is a condition characterized by hormonal imbalances in people of reproductive age with ovaries. This condition is characterized by irregular or extended menstruation, high levels of androgens, and/or cysts in the ovaries that prevent regular function. Specifically, the most salient clinical feature of PCOS is the impact on menstruation, including oligomenorrhea, amenorrhea, and menorrhagia.[1] Additionally, infertility is a hallmark characteristic of the condition, related to the presence of cysts or enlarged ovaries that may preclude proper ovulation. Other clinical characteristics of PCOS include skin disorders, including hirsutism, acne, and, in a smaller proportion of people, androgenic alopecia. Insulin resistance is present in many people with PCOS, which is also associated with metabolic syndrome and obesity. While PCOS has traditionally been described as a condition that impacts women, it is important to note that PCOS can impact cisgender women, transgender men, and nonbinary individuals. Therefore, we will use the phrase "individuals with PCOS" or "patients with PCOS" throughout the article. It is estimated that 6-20% of people of reproductive age are affected by PCOS.[2] PCOS is an endocrine disorder with androgenic, menstrual, fertility-related, and metabolic effects on the human body. While PCOS is a condition that impacts many people, pharmacists may lack adequate knowledge of how to support treatment decisions for patients with PCOS, given the wide range of clinical symptoms and treatment options. This review will assess available information regarding treatment of PCOS and compile it into one resource for pharmacists to use when caring for patients with PCOS.

CE FOR **PHARMACISTS**

COMPLETE ARTICLE AND CE EXAM AVAILABLE ONLINE: **WWW.PSWI.ORG**

Learning Objectives

- Recognize the most common characteristics and presentation of PCOS.
- Describe the hormonal imbalances involved in the pathophysiology of PCOS.
- Define commonly used terms that relate to ovulatory and menstrual dysfunction in patients with PCOS.
- Compare and contrast the most common manifestations of hyperandrogenism, oligomenorrhea, metabolic disorders, and fertility challenges in PCOS.
- Identify preferred treatment options for PCOS in relation to hyperandrogenism, oligomenorrhea, metabolic changes, and fertility.

Pathophysiology

There are several hypotheses that may explain the pathophysiology leading to PCOS, including functional ovarian hyperandrogenism (FOH), the luteinizing hormone (LH) hypothesis, and the insulin theory. The FOH theory points to the ovary as the source of dysregulation, which is independent of cysts in the ovaries or an elevation in LH. In patients with PCOS, FOH occurs on a cellular level in the thecal cells of the ovary, where the activity level of certain oxidative enzymes is higher, resulting in the increased production of androgens in the ovary. Most of the time, hyperandrogenism is a result of ovary androgen production; however, in some cases, adrenal androgen production can also cause this to occur. Regardless of the source of hyperandrogenism, androgen excess is present in 60-80% of patients with PCOS. Additionally, elevated testosterone, LH, and LH-to-FSH (follicle stimulating hormone) ratio are present in many people with PCOS, which has led some researchers to hypothesize that an increased amount of circulating luteinizing hormone is responsible for PCOS.[3] Hyperinsulinemia, resulting from insulin resistance, can reduce the amount of sex hormone binding globulin and increase testosterone in circulation. Insulin along with excess LH work together to increase the production of androgens. Ultimately, ovarian follicle development is interrupted as result of hyperinsulinemia and hyperandrogenism, resulting in an anovulatory state.[4] Based on the pathophysiology, there are 3 main diagnostic criteria: evidence of

TABLE 1. Acronyms

BMI	Body mass index
COC	Combined oral contraceptive
FOH	Functional ovarian hyperandrogenism
FSH	Follicle stimulating hormone
GLP-1	Glucagon-like peptide 1
LH	Luteinizing hormone
OSA	Obstructive sleep apnea
PCOS	Polycystic ovary syndrome
T2DM	Type 2 diabetes mellitus

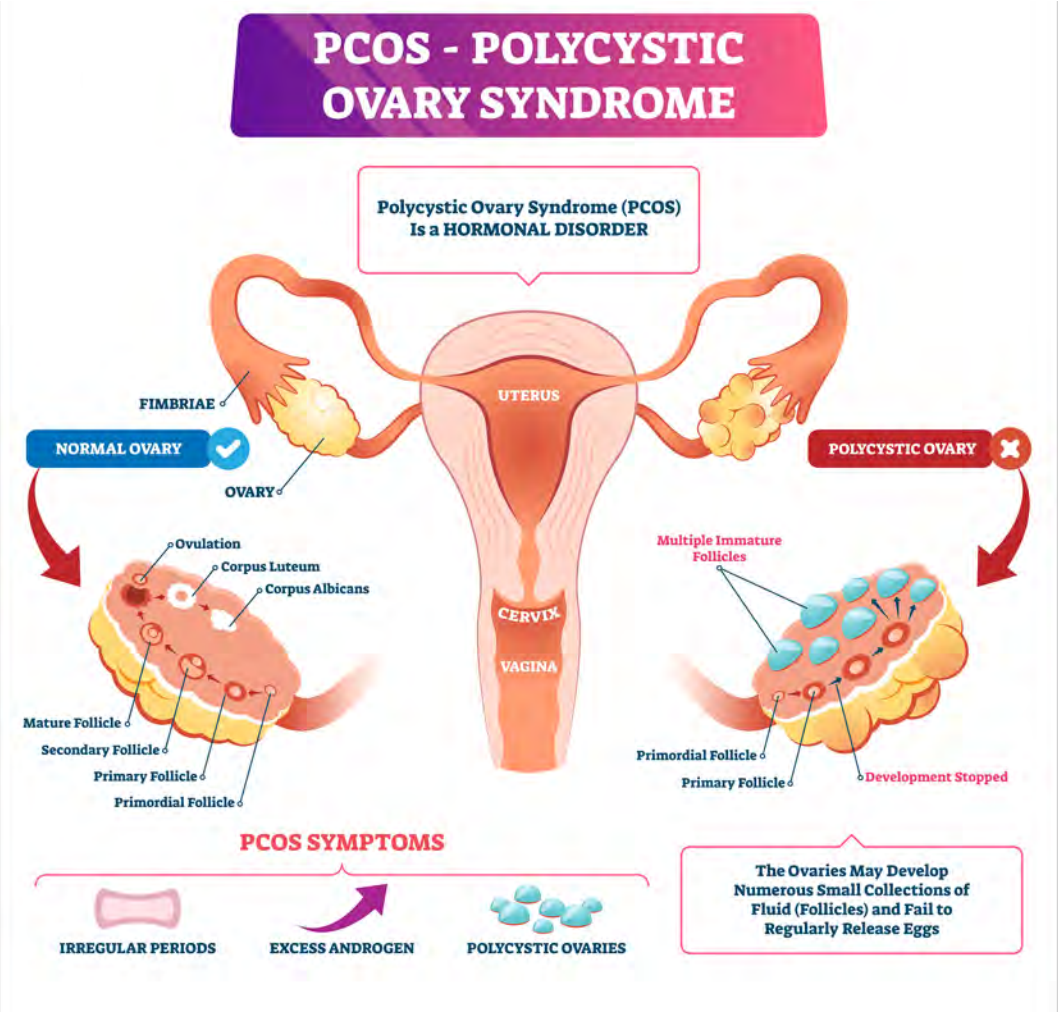
hyperandrogenism, ovulatory dysfunction, and polycystic ovaries. A diagnosis of PCOS is typically made when at least 2 of these are present and other related disorders are excluded. The pharmacotherapy treatment for this condition is centered around targeting the clinical manifestations that result from these hormonal imbalances.

Clinical Presentation

Metabolic

PCOS can present through a multitude of signs and symptoms, one of which is the presence of metabolic changes that could progress to metabolic syndrome. Metabolic syndrome is a cluster of characteristics that increases a patient's risk of developing cardiovascular disease, type 2 diabetes mellitus (T2DM), and stroke.[5] Characteristics may include waist circumference of 102 cm or more in men or 88 cm in women, triglyceride levels of 150 mg/dL or greater, high density lipoprotein cholesterol levels less than 40 mg/dL in men or 50 mg/dL in women, blood pressure of 130/85 mm Hg or more, and fasting glucose of 100 mg/dL or more.[5] Patients with PCOS are at a twofold increased risk of coronary heart disease or stroke compared to those without PCOS.[6] In addition, they are also at a fourfold increased risk of developing T2DM. The number of women presenting with metabolic syndrome was significantly higher among those with PCOS compared to those without PCOS.[6] Therefore, guidelines recommend that individuals with PCOS are screened for these metabolic changes.[7] Metabolic differences are more prevalent in patients who are overweight and obese but have also been identified in nearly 40% of nonobese patients with PCOS.[8] Obesity is not a diagnostic factor in PCOS but may affect the severity of metabolic and reproductive features of this disease state.[9]

A defining feature of metabolic syndrome in PCOS is insulin resistance, which can lead to T2DM. In patients who have T2DM without PCOS, this typically presents with impaired fasting glucose and is a result of insulin-mediated hepatic glucose production. In contrast, the hyperglycemia tends to be postprandial in PCOS due to impaired peripheral insulin-mediated glucose uptake. Therefore, this is more likely to present as impaired glucose tolerance rather than impaired fasting glucose.[9] A 2018 study found that patients with PCOS had a 25% prevalence of impaired glucose tolerance while patients in the control group had 9.2% prevalence.[10] Insulin resistance in individuals with PCOS predisposes them to long-term health conditions such as T2DM.[11] A meta-analysis found higher rates of diabetes mellitus in patients with PCOS.[12]



Given the metabolic changes that occur with PCOS, these individuals are also at an increased risk of cardiovascular disease. A 2020 meta-analysis found increased rates of hypertension and total cholesterol, no difference in low density lipoprotein and triglycerides, and decreased high density lipoprotein in those with PCOS compared to those without PCOS.[12] For non-fatal cardiovascular events, no difference was identified in coronary events, but a higher rate of cerebrovascular events was found in patients with PCOS. No difference was identified for fatal cardiovascular events.[12] The increased risk of cerebrovascular events, hypertension, and dyslipidemia in PCOS patients prompts screening and identification for these concomitant disease states to ensure appropriate treatment.

In addition to T2DM and cardiovascular disease, patients with PCOS represent a population at higher risk for sleep disordered breathing and hepatic steatosis. Obstructive sleep apnea (OSA) as well as PCOS is commonly associated with hypertension, diabetes mellitus, and coronary artery disease.[10] Patients with PCOS have a prevalence of OSA of 32% compared to 2% to 5% of adults with a uterus without PCOS.[9] Hepatic steatosis—more specifically nonalcoholic fatty liver disease—has a prevalence of 25% in the general population, while in PCOS patients its prevalence is 67%.[13]

Ovulatory and Menstrual Dysfunction

PCOS is often diagnosed using 3 different diagnostic criteria, one of which is ovulatory dysfunction.[14] Ovulatory dysfunction is commonly accompanied by menstrual dysfunction, including oligomenorrhea, amenorrhea, and menorrhagia. Oligomenorrhea refers to

a menstrual cycle that lasts more than 35 days in length, correlating to 10 or fewer cycles per year. However, some prefer to use a more rigorous definition of fewer than 8 cycles per year (cycle lasting more than 45 days). Amenorrhea, on the other hand, refers to the absence of monthly menstrual bleeding.[15] Menorrhagia is defined as menstrual bleeding lasting longer than 7 days, often involving a very heavy flow.[16]

Menstrual dysfunction is a very common feature of PCOS, with 75% to 85% of patients experiencing menstrual dysfunction in some capacity.[17] Despite menstrual dysfunction commonly occurring with ovulatory dysfunction, ovulatory dysfunction can present without menstrual dysfunction. It is important to note that when using ovulatory dysfunction as a diagnostic criterion for PCOS, it is not appropriate to assess until at least 1 year after menarche, or longer.[18] Prior to this point in time, irregular menstrual cycles are a normal part of the transition in puberty.

With all of this in mind, it is important to recognize the relevant health implications of menstrual and ovulatory dysfunction in PCOS, including an increased risk of developing endometrial hyperplasia and carcinoma as well as fertility challenges.[14,19] Endometrial hyperplasia is caused by unopposed and prolonged estrogen exposure on the endometrium, which is ultimately due to anovulation.[20] Thus, an increased malignancy risk is found in patients with PCOS. Additionally, ovulatory dysfunction may lead to anovulatory infertility, resulting in difficulties with conception.[14] Infertility caused by PCOS accounts for 27% of all cases of infertility globally.[7] This may even be the first sign that an individual has PCOS. For those who wish to conceive naturally, this may be viewed as a despairing consequence of the condition. Of note, reproductive challenges seem to be limited to difficulties in conception; once conception is achieved, individuals with PCOS have not been found to have any significant increased risk of miscarriages or early pregnancy loss.[14] However, pregnant individuals with PCOS have been found to be at an increased risk of developing obstetric complications, including preeclampsia, gestational diabetes, and macrosomia.

Androgenic

An additional characteristic of PCOS includes hypersecretion of androgens, or hyperandrogenism.[21] Physiologic manifestations of high testosterone levels commonly include hirsutism, acne, and occasionally male-patterned balding. Hirsutism can be measured using tools such as the Ferriman-Gallwey score. The Ferriman-Gallwey scoring tool ranks the degree of hair growth in nine body areas prone to hair growth upon androgen exposure. The ranking is on a scale of 0 to 4 in each area, where 0 represents no or minimal hair. A total sum of eight or more qualifies as generalized hirsutism among black and white women in the United States and United Kingdom.[7] Of note, Ferriman-Gallwey scores must be considered within the context of patient ethnicity since hair growth differs across ethnic backgrounds and cut-off points can differ (≥ 9 to 10 in Mediterranean, Hispanic, and Middle Eastern Women; ≥ 6 in South American women; range for Asian women from ≥ 2 to for Han Chinese women to ≥ 7 for Southern Chinese women).[22]

Psychological

One study found that patients with PCOS had a 26-38% and 20-39% increased incidence of depression and anxiety, respectively, when compared to two different sets of controls.[23] Additionally, this study found a 37-54% increased incidence of eating disorders in patients with PCOS compared to matched controls.[23] There is likely an array of contributing factors, but the psychological stress that comes with the physiological and societal impacts of PCOS, such as hirsutism, obesity, and infertility, is a major consideration. Therefore, screening for depression and anxiety among patients with PCOS should be strongly considered.

Treatment

Metabolic

American College of Obstetricians and Gynecologists Practice Bulletin Guideline recommendations relating to metabolic syndromes associated with PCOS are divided into level A and level B.[1] Level A recommendations are consistent and evidence based, while level B recommendations are based on limited or inconsistent evidence. The guidelines recommend increasing exercise combined with dietary changes to reduce the risk of diabetes, and the use of insulin-sensitizing agents for improved glucose tolerance (Level A). They also recommend screening women with a PCOS diagnosis for impaired glucose tolerance and cardiovascular risk (Level B). Lifestyle management of PCOS includes dietary changes, physical activity, and behavioral strategies to reduce weight. These strategies decrease the risk of insulin resistance, therefore preventing progression to diabetes mellitus and reducing the risk of cardiovascular disease.

When lifestyle modifications alone are not beneficial, the addition of insulin-sensitizing agents may be considered. The most commonly used insulin-sensitizing agent is metformin, a member of the biguanide drug class. Metformin's mechanism of action is to inhibit hepatic glucose production, increase glucose uptake, and therefore increase insulin sensitivity. The 2018 International Evidence-Based Guideline for the Assessment and Management of PCOS recommends the use of metformin in addition to lifestyle changes for management of weight and metabolic outcomes.[7] Side effects of metformin include nausea, vomiting, diarrhea, and abdominal bloating. Pharmacists can help patients with PCOS manage these symptoms through education and slow titration of the dosage.

Glucagon-like peptide 1 (GLP-1) receptor agonists have also shown benefit in patients with PCOS. A 2019 meta-analysis found patients who take GLP-1 receptor agonists to have improved insulin sensitivity, reduced body mass index (BMI), and decreased abdominal girth when compared to patients taking metformin. GLP-1 receptor agonists did not have an effect on triglycerides, total cholesterol, or blood pressure.[24] In addition, patients reported higher rates of nausea and headache when taking GLP-1 receptor agonists compared to metformin. This class of medications may be a good option in patients with PCOS who are obese and also have insulin resistance. However, data is still fairly limited in evaluating the effects of GLP-1 agonists in patients with PCOS.

Pioglitazone, which is a thiazolidinedione, may be beneficial in PCOS by reducing fasting serum glucose. This class of medications works by increasing peripheral glucose uptake

and regulating insulin action. When compared to metformin, pioglitazone as monotherapy resulted in increased BMI and increased triglycerides.[11] A 2021 meta-analysis found a combination of metformin and thiazolidinediones to be more efficacious to lower fasting glucose than metformin alone.[13] Furthermore, they found gastrointestinal side effects and peripheral edema to be more frequent in thiazolidinediones compared to metformin. Notably, the use of metformin with thiazolidinediones was more efficacious than metformin alone to reduce triglycerides and total cholesterol.[13] When selecting a drug to target insulin resistance, the impact on weight, glucose, and lipids should be considered.

Due to dyslipidemia being a strong predictor of cardiovascular risk, patients with PCOS may benefit from use of a statin. Statins, with atorvastatin being the primary medication studied, showed reduced insulin resistance and inflammatory markers in patients with PCOS compared to placebo.[11] A diagnosis of PCOS alone does not necessarily warrant statin treatment, as it is not currently known whether statin initiation in young individuals with PCOS prevents cardiovascular events in the long-term.

The clinical use of orlistat, a lipase inhibitor used for weight loss, remains controversial. Although it has been associated with improvements in lipid profiles, weight, BMI, and waist circumference, it comes with significant side effects, including diarrhea, abdominal pain, flatulence, and fatty stool. Bariatric surgery as a method to decrease metabolic abnormalities may be indicated in obese patients with a BMI of 40 kg/m^2 or more or BMI greater than 35 kg/m^2 with comorbidities.[11]

Ovulatory and Menstrual Dysfunction

For the treatment of menstrual dysfunction in patients with PCOS who are not looking to become pregnant, combined oral contraceptives are recommended as first-line therapy.[20] Oral contraceptives work by helping to regulate the menstrual cycle and can also help to reduce the risk of endometrial hyperplasia in PCOS, thereby reducing the risk of endometrial cancer. For those who do not tolerate combined oral contraceptives, there are a few other options to be considered, including non-oral combined hormonal contraceptives or progestin-only contraceptives.[14] Based on use in the general population, it is plausible to consider use of a contraceptive patch or vaginal ring in those who are unable to tolerate oral contraceptives.[25] Before selecting a patch, it is important to note that its effectiveness for pregnancy prevention may be decreased in patients who weigh more than 198 pounds.[26] Progestin-only contraceptives may be considered in patients where estrogen is contraindicated.[25] Options for progestin-only contraceptives include long-acting injectables like depot medroxyprogesterone, an etonogestrel-containing implant, or an intrauterine device. Progestin-only options prevent pregnancy and reduce risk of endometrial hyperplasia, but there is less data supporting their usefulness and effectiveness specifically in individuals with PCOS compared to combined oral contraceptives.

For any of the previously listed treatment options, it is important to first screen whether a patient has any contraindications to using hormonal contraception. Then, careful evaluation of the side effects and how these may impact other clinical features associated with PCOS should be considered.[25] For example, the depot medroxyprogesterone acetate (DMPA) injection is known to cause weight gain and insulin resistance, and the etonogestrel-containing implant is associated with more irregular bleeding. Through shared decision-making, the provider and patient can work to find the most suitable regimen.

For patients who wish to conceive children naturally, treatment of the subfertility/infertility caused by PCOS may be pursued. This may be done by ovulation induction through lifestyle modification and various possible pharmacological and non-pharmacological methods. Obesity is a common concomitant condition in patients with PCOS and can independently impact fertility. For patients with obesity and PCOS, the first intervention to be made in treating infertility is body weight reduction through lifestyle modifications in diet and exercise. Weight loss can aid in regulating ovulation and thus increasing the likelihood of conception.[1,7,21]

Pharmacologic options for ovulation induction include letrozole, clomiphene citrate, and clomiphene citrate plus metformin. Letrozole is an aromatase inhibitor, which promotes the secretion of FSH and has the resulting effect of facilitating the process of ovulation. Clomiphene citrate is a selective estrogen receptor modulator, which is used to stimulate final maturation of follicles and increases the probability of ovulation. Metformin works in conjunction with clomiphene citrate to further promote ovulation.

While clomiphene citrate has traditionally been used first-line, recent randomized controlled trials and meta-analyses actually suggest that letrozole is more effective for ovulation induction and live birth rates.[27] In a Cochrane Review, among 2954 patients in 13 studies, live birth rates were significantly higher among those who used letrozole compared to clomiphene citrate with or without adjuncts (OR 1.68, 95% CI 1.42 to 1.99).[27] Clomiphene citrate may still be used first line over letrozole if cost is a concern as clomiphene is less expensive. Combination of clomiphene citrate plus metformin can be considered if patients do not have success

TABLE 2. Clinical Guidelines for PCOS

Organization	*Year Published*	*Title*
American College of Obstetricians and Gynecologists[1]	2018	Polycystic Ovary Syndrome: ACOG Practice Bulletin, Number 194
American Society for Reproductive Medicine[7]	2018	Recommendations from the international evidence-based guideline for the assessment and management of polycystic ovary syndrome
The Endocrine Society[21]	2013	Diagnosis and Treatment of Polycystic Ovary Syndrome: An Endocrine Society Clinical Practice Guideline

TABLE 3. Summary of medications used for PCOS

Drug	Considerations when initiating and monitoring treatment	Weight Loss	Insulin Resistance	Endometrial Protection	Menstrual Dysfunction	Infertility	Hirsutism/ Acne
Metformin	May cause gastrointestinal side effects; start at low dose and titrate slowly		✓			✓	
Pioglitazone	May increase weight due to peripheral edema		✓				
GLP-1 agonist	May cause gastrointestinal side effects; start at low dose and titrate slowly	✓	✓				
Orlistat	May help with weight loss but associated with many side effects	✓					
Combined oral contraceptive	Consider selecting COC containing drospirenone or norgestimate when being used for hirsutism/acne. Use caution or avoid COC with higher levels of ethinyl estradiol (35 mcg) due to increased risk for thromboembolism.			✓	✓		✓
Non-oral combined contraceptive (patch, ring)	Avoid patch in patients who weigh more than 198 lbs due to decreased efficacy.			✓	✓		
Progestin-only contraceptives	May be considered but less studied for purposes of menstrual cycle regulation in patients with PCOS.			✓	✓		
Letrozole	Important to educate patient on timing of initiation in relation to menses or progestin-induced bleed					✓	
Clomiphene citrate	Important to educate patient on timing of initiation in relation to menses or progestin-induced bleed					✓	
Spironolactone	Teratogenic; some form of contraception recommended in patients at risk of pregnancy						✓
Eflornithine	Hair removal techniques should be continued, and cream can be applied after at least 5 minutes after hair removal						✓

with clomiphene citrate alone. Of note, pharmacists can play an essential role in providing education to patients about how to take these oral medications for ovulation induction. The timing of dosing these medications is important in relation to the patient's menses or progestin-induced bleed. Additionally, intercourse should be timed for when it is expected that ovulation will occur, which can be estimated based on when the medication was taken.

Second-line treatments for anovulatory infertility are low-dose follicle-stimulating hormone stimulation and the non-pharmacological procedures of ovarian electrocautery.[1] Low-dose FSH stimulation may be indicated in patients who fail first-line treatments; however, it is not preferred due to the possible need to turn to in-vitro fertilization, a very costly process with mediocre success rates, later on in the treatment. Ovarian electrocautery is not fully understood and has the risk of physical injury, but some evidence points towards its effectiveness in decreasing testosterone levels and in patients who are resistant to clomiphene citrate.

Androgenic

Use of combined oral contraceptives can be used to target cutaneous symptoms such as hirsutism and acne. Oral contraceptives are a first-line recommendation for patients who are not planning to become pregnant and desire management of aforementioned PCOS symptoms. When selecting a COC, special consideration should be taken in the progestin component. Progestins with no androgenic activity (drospirenone) or low androgenic activity (norgestimate) may be preferred given the pathophysiology of acne and hirsutism in patients with PCOS. If the response to COC is inadequate, use of an antiandrogen such as spironolactone can be initiated as monotherapy or in combination with a COC. If used as monotherapy, it is important to note that spironolactone is teratogenic and other methods to prevent pregnancy should be recommended. Before initiating a COC, patients should be screened for risk factors that may increase their risk of venous thromboembolism.[28]

Non-pharmacologic options such as waxing, electrolysis, or shaving could

also be considered to manage hirsutism. Plucking, or epilation, should be avoided as it can cause scarring and tissue damage, especially to those with more pigmented skin. While many methods are advertised as "permanent," these follicles may experience regrowth due to continued stimulation via the patient's androgens. Suppression of androgens through pharmacologic means may be helpful in these situations. Finally, topical agents such as eflornithine cream can be used to facilitate more rapid and sustained hair loss in combination with laser hair removal. Eflornithine is a hair growth inhibitor and will not remove existing hair if used as monotherapy.[22]

Psychological

There are currently no specific recommendations regarding pharmacotherapy for treatment of mental health disorders specifically in patients with PCOS. Patients with PCOS should be screened for depression, anxiety, and other mental health conditions as necessary and then treated according to guidelines for the general population.[29]

Role of the Pharmacist

Pharmacists are the most accessible healthcare providers in the community setting. As such, patients commonly ask pharmacists for assistance in treating a wide array of symptoms and ailments. When pharmacists are approached by a patient complaining of excessive hair growth, oily skin, balding, acne, or menstrual abnormalities, for example, pharmacists can make an impact by assisting patients in the next steps for managing these symptoms. This could include referring to physicians for further workup, recommending non-pharmacologic options to treat their symptoms, or recommending appropriate prescription treatment to their provider.

Pharmacists are important practitioners in ensuring patients are adequately educated about the correct use and expected outcomes of pharmacotherapy for PCOS. Pharmacists are well trained to elicit information from patients to guide their counseling through the use of frameworks like the Three Prime Question approach developed by the Indian Health Service.[30] First, pharmacists can identify individuals with PCOS during medication consultation by using the first prime question: "What are you using this medication for?" It is important for pharmacists to recognize that certain medications, such as metformin or pioglitazone, may be prescribed for PCOS, not for diabetes mellitus. When conducting patient education, including key components—such as time to benefit, realistic goal setting, and establishing expectations—is crucial for pharmacists, to help ensure optimized treatment for patients with PCOS. Pharmacists can help to recognize potential gaps in treatment, as there are many different clinical features of PCOS and subsequent long-term consequences. Pharmacists should then be able to recommend treatment for specific manifestations of PCOS, like hyperandrogenism, metabolic changes, oligomenorrhea, or infertility. Lastly, community pharmacists are uniquely positioned in the community to monitor for efficacy, safety, and tolerability of pharmacotherapy when patients pick up refills of medications. A list of the most recent guidelines can be found in table 2, and a summary of which treatment options can be used for which clinical manifestations can be found in Table 3.

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Assessment Questions

1. Which of the following are common conditions or characteristics that people with PCOS present with?
   a. Irregular menstruation
   b. Cysts in the ovaries
   c. Changes in fertility
   d. Excess hair growth
   e. All of the above

2. Which of the following is found in excess in a majority of people with PCOS?
   a. Serotonin
   b. Androgens
   c. Angiotensin
   d. Histamine

3. Menstrual dysfunction in PCOS may present as oligomenorrhea, often defined as a menstrual cycle lasting longer than ____ days in length.
   a. 15
   b. 25
   c. 30
   d. 35

4. Which of the following is first-line therapy in the treatment of menstrual dysfunction in patients with PCOS?
   a. Progestin-only contraceptives
   b. Metformin
   c. Clomiphene citrate
   d. Combined oral contraceptive

5. Which of the following metabolic conditions are people with PCOS at an increased risk of developing?
   a. Type 2 Diabetes
   b. Cardiovascular Disease
   d. Arthritis
   d. Chronic Kidney Disease
   e. Both A and B

6. What is the best option for insulin resistance in a patient with PCOS, obesity, and history of pancreatitis?
   a. Pioglitazone
   b. Metformin
   c. Liraglutide
   d. Insulin

7. Which of the following is the most commonly used scoring system used to analyze hirsutism in patients with PCOS?
   a. Ferriman-Gallwey tool
   b. Rotterdam criteria
   c. PCOSQ scale
   d. Stein-Leventhal

8. Which of the following would be the best option for inducing ovulation in patients with PCOS?
   a. Metformin alone
   b. Clomiphene citrate plus letrozole
   c. Clomiphene citrate plus metformin
   d. Letrozole plus metformin

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

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

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

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

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

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

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

15. Were the authors free from bias?
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   b. No

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Exploring the Use of Opioid-Related Best Practice Alerts Across Wisconsin

by Martha Maurer, PhD, MSSW, MPH, Erica Martin, MHA, Sarah Pagenkopf, PharmD, BCPS

Key Points

- Seventy respondents holding various pharmacy roles and representing a variety of practice settings responded to the survey completed in May to June 2022.
- Forty-three (61%) respondents reported that their sites were currently implementing an opioid-related best practice alert (BPA); twenty-six (37%) respondents indicated they did not have (or were not aware of) an existing opioid-related BPA within the electronic health record/pharmacy software at their setting.
- More than three-quarters of respondents who did not currently have an opioid-related BPA in their workplace setting were interested in implementing an opioid-related BPA but acknowledged a need for additional support to facilitate implementation.

In Wisconsin, little is known about the extent to which clinical decision support best practice alerts (BPAs) are being used or even whether they exist within electronic health record (EHR) systems or community pharmacy software or other technology. BPAs have been shown to optimize opioid prescribing and dispensing.[1-3] BPAs are defined as clinician decision support tools available in the EHR, community pharmacy software, or state prescription drug monitoring programs that direct clinician attention to patients who meet criteria for being at risk of negative health outcomes. BPAs leverage the power of technology to identify gaps in care that can be addressed for patients or customers and do so without requiring the clinician to search the patient chart for this information. Emerging findings in the literature suggest that pharmacists play a critical role in initiating and implementing these types of alerts and that they are effective at optimizing opioid prescribing practices consistent with evidence-based clinical guidelines (e.g., Centers for Disease Control Guidelines for Prescribing Opioids for Chronic Pain). Therefore, it is important to examine the current pharmacy practice in this area as well as the level of interest in implementing this type of alert in pharmacy practice into the future as part of opioid stewardship practices. Aggregate data from this survey will be used to inform future research and programmatic decisions related to addressing the opioid crisis in Wisconsin.

In response to this need for more information and data, the Pharmacy Society of Wisconsin (PSW) partnered with the University of Wisconsin-Madison School of Pharmacy (UW SoP) Sonderegger Research Center for Improved Medication Outcomes to develop and administer a survey to Wisconsin pharmacy personnel. The purpose of the survey was to gain an understanding of pharmacists' experiences with, and perceptions of, BPAs in relation to optimizing opioid prescribing and dispensing. Specifically, the research team wanted to better understand the current status of, and opportunities for, using BPAs to optimize opioid prescribing and dispensing. Additionally, the team aimed to capture the extent to which pharmacy practices are interested in implementing this type of alert as part of opioid stewardship practices in their work setting.

Data Collection

A team from PSW and UW SoP collaboratively developed a short survey and subsequently built it in the University of Wisconsin Institute for Clinical and Translational Research's Research and Electronic Data Capture (REDCap) survey tool.[4-5] In late May 2022, an invitation to complete the survey was distributed to

TABLE 1. Respondent Characteristics (n=70)

Workplace Setting	Frequency (%)
In-patient pharmacy	19 (27%)
Clinic pharmacy	10 (14%)
Community-Chain pharmacy	5 (7%)
Community-Health System Outpatient pharmacy	18 (26%)
Community-Independent pharmacy	13 (19%)
Other (managed care organization, PBM)	5 (7%)
Role in Workplace Setting	**Frequency (%)**
Manager/Director/ Supervisor	17 (24%)
Clinical Pharmacist	45 (64%)
Informatics Pharmacist	1 (1%)
Technician	5 (7%)
Pharmacy Intern (PharmD Student)	0 (0%)
Other	2 (3%)

TABLE 2. Software Usage in Respondent's Workplace (n=70)

Inpatient Electronic Health Record (EHR) Vendor Software Used in Setting	Frequency (%)
Epic	45 (64%)
Cerner	1 (1%)
Not Applicable	14 (20%)
Other	10 (14%)
Outpatient / Community Pharmacy Software Used in Setting	**Frequency (%)**
Pioneer Rx	12 (17%)
QS1	7 (10%)
Rx30	5 (7%)
Enterprise Rx	7 (10%)
Epic Willow	18 (26%)
Not applicable	14 (20%)
Other	7 (10%)

PSW's membership via the PSW regular, weekly e-newsletter, *FastFacts*. The survey was also distributed via a PSW and UW SoP partner, PearlRx, which is a UW SoP-administered research network, through a regular e-newsletter. Four additional invitation reminders were included in subsequent e-newsletters through the survey closure at the end of June 2022.

The survey was divided into three sections. All respondents were instructed to complete Section 1 to share information about role, practice setting, and type of health-record software used. Respondents were directed to respond to follow-up questions related to current alerts (Section 2) if they confirmed an opioid-related BPA was currently active or being implemented at their practice site. Respondents who indicated that they did not currently use an opioid BPA in their setting were directed to respond to a series of questions in Section 3, which asked respondents to summarize barriers and challenges they noted preventing them from implementing a BPA. In follow up, respondents in Section 3 of the survey were also asked to share their level of interest in implementing a BPA in the future.

Survey Results

Respondent Characteristics

A total of 70 pharmacy personnel responded to the survey. Respondents represented a variety of workplace settings. The most common sites included in-patient pharmacy (27%), community-health system outpatient pharmacy (26%), community-independent pharmacy (19%), and clinic pharmacy (14%) (Table 1). Over half (64%) of respondents reported practicing in the role of clinical pharmacist and about a quarter (24%) indicated they practiced in a manager, director, or supervisor role in their work setting.

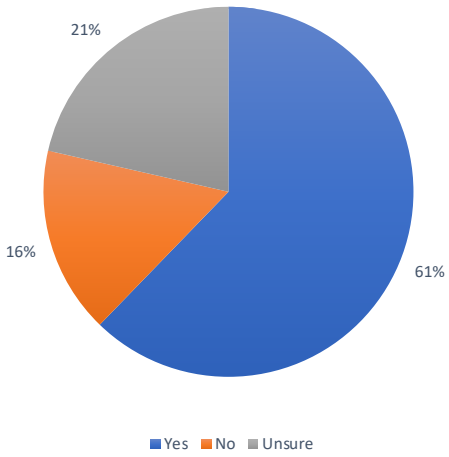
Software Used

The largest percentage of respondents working in inpatient settings (64%) reported using the Epic health-record software, and one respondent reported using Cerner health-record software as their inpatient EHR (Table 2). Other inpatient software used included Meditech, MTM Exchange, Centric, LTC Rx, and CPRS. Epic Willow and PioneerRx were the most frequently reported outpatient/community pharmacy software systems used in the community workplace setting, followed by an equal number of pharmacists who reported use of QS1 and Enterprise Rx.

Current Status of Opioid-Related BPA Implementation in Setting

Respondents were asked if any opioid-related BPAs were currently being used to support clinical decision-making in their setting. Forty-three (61%) respondents reported that their sites were implementing or had implemented an opioid-related BPA and 11 (16%) reported that they did not currently use an opioid-related BPA. An additional 15 (21%) respondents reported that they were unsure whether an opioid-related BPA was being used or implemented at their practice site. One respondent did not submit an answer to this question (Figure 1).

FIGURE 1. Currently Implementing 1 or More Opioid-Related Best Practice Alerts



Part I. Characteristics of Existing Opioid-Related BPAs

If respondents indicated that their site currently was using or implementing a BPA (61%), they were directed to follow-up questions about the use of those alerts (Part I). Respondents indicating no active use of any opioid BPAs in their practice setting currently were directed to respond to an alternate series of questions focusing on the barriers and challenges perceived by respondents preventing implementation of a BPA. Additional questions asked the respondent to indicate level of interest in implementing a BPA in the future (Part II). The following data represents the responses for Part I.

The 43 respondents who reported their clinical pharmacy practice sites were using or implementing an opioid-related BPA reported the following topics were being addressed by the BPA (Table 3).

The survey allowed respondents to select more than one topic, as the research team understood that some practice sites may use multiple BPAs to address different evidence-based opioid risk areas to better serve patients. Opioid-related clinical alerting addressed by BPAs in the other category, included: reminders to check the prescription drug monitoring program (PDMP); alerting that the specific patient had high risk for adverse events; alerts to the clinical team to check and confirm usual and customary doses for opioid naive patients; opioid naive patient flag alerting clinicians the patient has not previously used opioid medications routinely; cash-paying patient warning; alerts noting that the patient had arrived too early to refill their prescription; a recommendation to the clinical team for the need for a urine drug screen (guideline-based care); PDMP check documentation missing (Wisconsin regulation); alerting to the clinical team that the patient is at risk for co-prescribing of multiple central nervous system depressants (including gabapentin, multiple opioids, benzodiazepines, etc.); and alerting that the

TABLE 3. Frequency of Opioid Topics Addressed by the Currently Implemented Best Practice Alerts (BPAs) (n=43)

Topic	*Frequency (%)*
Prescribing or discussing naloxone	32 (74%)
High-dose morphine milligram equivalent (MME)	33 (77%)
Opioid treatment agreements	22 (51%)
Opioid and Benzodiazepine co-prescribing	25 (58%)
Other	7 (16%)

prescription/order exceeded quantity limits on discharge prescriptions according to the indication (i.e. number of tablets).

About half (47%) of respondents indicated that Centers for Disease Control and Prevention guidelines had informed their opioid-related BPA(s) and about a fifth (21%) indicated the US Food and Drug Administration had informed them (Table 4). Similar numbers of pharmacists reported BPAs were developed to align with US Health and Human Services, Veterans Health Administration, or Wisconsin Medical Examining Board criteria.

About three-quarters of respondents reported that existing and active BPAs in their workplace settings were created to assist and aid prescribers (77%) and to a greater extent to aid and support pharmacists (84%).

Respondents were also asked what the data captured by the opioid-related BPAs was used to evaluate at their practice setting. Table 5 shows that collected BPA activation/firing data were used for quality improvement, to improve patient care, and to inform compliance with regulatory requirements. Some respondents were not aware of, or involved in, the data capture/review process and another respondent's practice site was just implementing the BPA, and data had not yet been collected.

Part II. No Existing BPA Being Implemented

Eleven (16%) respondents indicated that their site did not have any opioid-related BPAs and 15 (21%) responded they were unsure whether their site had one (Figure 1). These respondents were directed to a series of questions about barriers to implementing a BPA and whether they had any interest in pursuing an alert in the future. The following data represent the responses from these 26 respondents (i.e. Part II).

Nearly 70% of respondents who reported their practice site did not have an opioid-related BPA or were unsure whether the practice site had one indicated that implementing an opioid-related BPA in their setting would be valuable or very valuable (Table 6).

Respondents were asked to rank, from most to least important, four opioid prescribing best practice topics that would be affected by use of a BPA in their

TABLE 4. Opioid Prescribing Guidelines that Informed Best Practice Alerts Currently Implemented in Practice Setting (n=43)

Prescribing Guideline	*Frequency (%)*
US Centers for Disease Control and Prevention	20 (47%)
US Food and Drug Administration	9 (21%)
US Health and Human Services	6 (14%)
US Surgeon General	3 (7%)
Veterans Health Administration	5 (12%)
Wisconsin Medical Examining Board	5 (12%)
Unsure	16 (37%)
Other	1 (2%)

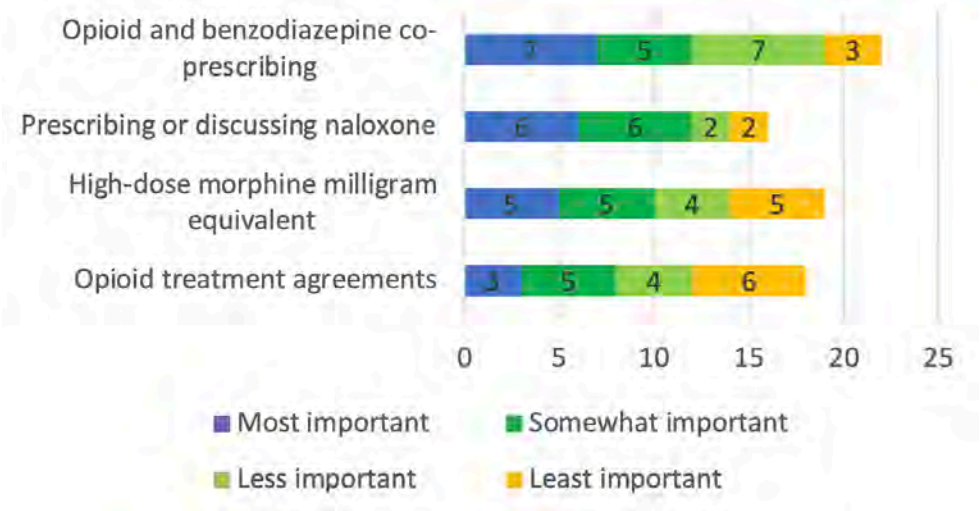
TABLE 5. How Data Captured by the Opioid-Related Best Practice Alerts is Used in the Practice Setting (n=43)

Use for Data	*Frequency (%)*
Reviewed and analyzed to measure quality outcomes	22 (51%)
Reviewed and discussed to inform patient care improvements	22 (51%)
Reported to site leadership to inform compliance with regulatory requirements	19 (44%)
Other	6 (14%)

TABLE 6. How Valuable Implementing an Opioid-Related Best Practice Alert Would be at Workplace Setting (n=26)

Prescribing Guideline	*Frequency (%)*
Very valuable	12 (47%)
Valuable	7 (21%)
Neutral	5 (14%)
Not valuable	2 (7%)

FIGURE 2. Number of Pharmacists Indicating Importance for Each Best Practice Alert Topic



workplace setting. Figure 2 displays the number of pharmacists who assigned a level of importance for each BPA topic. Opioid and benzodiazepine co-prescribing was identified as the most important topic by the highest number of respondents (7), followed by prescribing or dispensing naloxone (6). Opioid treatment agreements was identified as the least important BPA topic by the most respondents (6), followed by high dose morphine milligram equivalent (5).

Respondents were asked to identify barriers to implementing an opioid-related BPA at their practice site. The two most frequently identified barriers were provider alert fatigue (62%) and lack of resources to support the technology infrastructure and staffing needed to implement a BPA (42%) (Table 7). Barriers like a site's prioritization of improving opioid prescribing, EHR functionality, and leadership support were identified only by a few respondents each. Other barriers mentioned included: initial setup and training to implement a BPA; lack of time; and negative experiences with BPAs in past that disrupted workflow or did not require a thoughtful response.

TABLE 7. Number of Respondents that Selected Each Barrier (n=26)

Barriers to implementing Best Practice Alert at Site	*Frequency (%)*
Improving opioid prescribing is not a high priority at site	1 (4%)
Leadership is not supportive	2 (8%)
Lack of resources to support the technology infrastructure and staffing needed to implement a BPA	11 (42%)
Current EHR vendor/package does not provide functionality option for opioid-BPAs	1 (4%)
Prescribers are resistant to introducing another BPA-"alert fatigue"	16 (62%)
Other	3 (12%)

TABLE 8. Level of Confidence in Being Able to Overcome Barriers to Implementing an Opioid-Related Best Practice Alert (n=22)

	Frequency (%)
Very confident	5 (23%)
Confident	4 (18%)
Neutral	9 (41%)
Not confident	4 (18%)

TABLE 9. Level of Interest in Implementing an Opioid-Related Best Practice Alert (n=26)

	Frequency (%)
Very interested	10 (38%)
Somewhat interested	10 (38%)
Neutral	4 (15%)
Not interested	2 (8%)

Part III. Opportunities and Interest in Implementing an Opioid-Related BPA

The respondents in this subset (n=22), 9 (41%) felt confident or very confident that barriers to implementing an opioid-related BPA could be addressed in their practice site with additional support from external experts and tools, and 18% were not confident (Table 8).

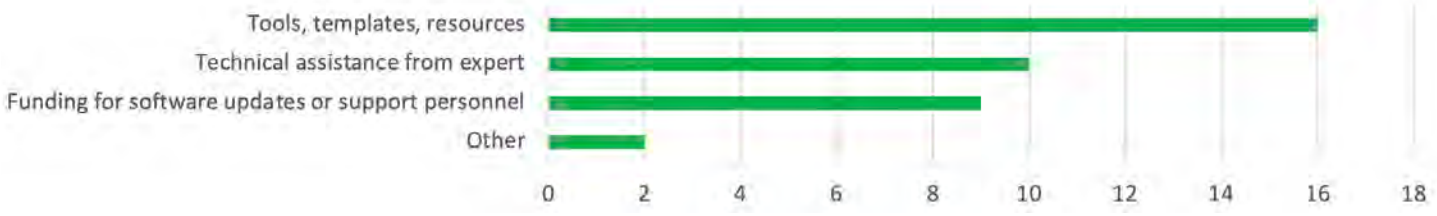
Respondents were asked to select all resources they deemed necessary to facilitate the implementation of a BPA at their practice. The most frequently identified resource was tools, templates, and resources to be used independently (n=16), followed by technical assistance from an external expert (n=10), and funding for software updates or support personnel (n=9) (Figure 3). Other resources identified by respondents included leadership buy-in and ensuring that the stakeholders who can most directly impact change are the focus of the BPA.

Finally, of the 26 respondents who reported their practice site did not have an opioid-related BPA or were unsure if the practice site had one, 20 (77%) indicated that they were very or somewhat interested in implementing an opioid-related BPA, while the remaining respondents were either neutral or not interested (Table 9).

Conclusions

Data gathered from this survey provides Wisconsin-specific information about the extent and nature of clinical decision support BPAs, as defined by pharmacy personnel, which are embedded in electronic health record systems, community pharmacy software, or other technology to aid pharmacists in optimization of opioid prescribing and dispensing. The survey data additionally characterizes the respondents' knowledge, experience, and attitudes about the use of best practice alerts. The data provides insights on how respondents perceive the use of BPAs can optimize opioid prescribing and dispensing, and the barriers that prevent BPAs from being implemented and used at their practice sites. As it relates to future work and methods to improve patient care and reduce risk associated with opioids, the survey captured the extent to which respondents were interested in implementing this type of clinical decision support alert as part of

FIGURE 3. Number of Respondents Selecting Resources to Implement a Best Practice Alert



patient-focused opioid stewardship practices in their practices and communities.

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Original Work

Evaluation of Blood Pressure Control and Quality Measure Performance Following Pharmacist Hypertension Management in the Primary Care Setting

by Jordyn T. Kettner, 2022 PharmD Candidate, Laura I. Belmonte, PharmD, Katherine J. Hartkopf, PharmD, BCACP, April J. Weaver, PharmD, BCACP, Kristina M. Heimerl, PharmD, BCACP

Abstract

Objective: The impact of primary care pharmacists practicing under a hypertension management protocol at a health system is captured by the state quality measure benchmark of blood pressure measurement less than 140/90 mmHg. However, this measure does not manage factors that may result in inaccurate reporting of patient hypertension control. This quality improvement project was designed to evaluate why prior pharmacist-managed patients had recent in-clinic blood pressure measurements above goal, and to identify opportunities for improvement.

Methods: A report was generated to identify family medicine patients with a most recent blood pressure measurement above goal following participation in the pharmacist hypertension management program. A retrospective chart review was conducted, and reasons for above goal in-clinic blood pressure measurements were categorized. Additional factors were collected for all patients and analyzed for patients categorized as unknown to identify trends.

Results: Of the 141 patients evaluated, the most common reason for above goal in-clinic blood pressure was white coat hypertension (38%). Of the patients without an identifiable cause for elevated blood pressure (9%), almost half had a history of non-adherence to medications.

Conclusions: For patients with hypertension, there are reasons for above goal in-clinic blood pressures deemed not controlled with the state quality measure. Opportunity exists to capture hypertension control more accurately within health systems with use of home readings, as well as to re-evaluate blood pressure management strategies and adherence for patients without an identifiable reason for uncontrolled hypertension.

Nearly 47% of adults in the United States have hypertension or are taking an antihypertensive medication.[1,2] Hypertension, or high blood pressure, is a significant cause of morbidity and mortality in the United States. In 2019, more than 500,000 deaths in the United States had hypertension as a primary or contributing cause of mortality.[3] Hypertension often has no signs or symptoms, but significantly increases the risk of heart disease and stroke, two of the top five leading causes of death in the United States.[4] While high blood pressure is a leading risk factor for stroke, congestive heart failure, coronary heart disease, and renal disease, adequate blood pressure control can minimize the risk of and help prevent these conditions.[5] Several factors contribute to uncontrolled blood pressure, including competing comorbidities, lack of understanding of hypertension, stress, suboptimal medication adherence due to financial or transportation barriers, and poor diet and sedentary lifestyle.[6] In Wisconsin, about 33% of adults have hypertension, and of those, almost half do not have their hypertension adequately controlled.[4,7] Additionally, in Wisconsin, about 25% of adult patients diagnosed with high blood pressure do not take their blood pressure medications as prescribed, highlighting the need for improved medication adherence and education to optimize hypertension management and treatment.[8]

The incorporation of pharmacists into primary care teams for chronic disease state management, to optimize medication selection and treatment, has been described.[9,10] Pharmacist and physician team-based, collaborative models have been shown to improve patient care for chronic medical conditions including hypertension. Previous literature has shown positive impact with the incorporation of pharmacist-driven hypertension management into patient care teams for monitoring blood pressure, improving medication adherence, and optimizing antihypertensive medications.[11] Several other evaluations have found significant, positive impacts on patient blood pressure control, among patients with hypertension, through the use of pharmacist and physician collaborative management. Through these team-based interventions,

pharmacists closely monitor patients and adjust antihypertensive regimens as needed. Previous studies have found the percentage of patients with hypertension and well-controlled blood pressure control to range from 43% to 89% when managed through interventions that leverage pharmacists.[12-16] Therefore, pharmacists are well positioned to improve hypertension quality measures as previously demonstrated for other chronic disease states such as diabetes.[17]

This quality improvement initiative took place at a health system where primary care pharmacists practice under an expanded hypertension management protocol that gives pharmacists the authority to modify antihypertensive medications and counsel on lifestyle management strategies. This protocol gives clinic-based pharmacists the authority to initiate, titrate, and discontinue antihypertensive medications, and the ability to enter orders for labs to monitor therapy for adult patients ages 18 and older with a diagnosis of hypertension who meet protocol criteria. Specific antihypertensive medications and labs are outlined in the protocol, which allows primary care pharmacists to provide hypertension management to patients to optimize blood pressure control. The effectiveness of pharmacist work is captured by the state hypertension quality measure benchmark of proportion of patients with a blood pressure less than 140/90 mmHg, developed by the Wisconsin Collaborative for Healthcare Quality (WCHQ).[18]

The WCHQ reports a variety of health care performance measures for ambulatory and hospital care in the state of Wisconsin, with the purpose of improving health and increasing the value of health care.[5] The WCHQ currently reports one heart care measure pertaining to controlling high blood pressure. This blood pressure control measure assesses the percentage of patients ages 18 to 85 who have a diagnosis of essential hypertension and whose blood pressure is adequately controlled based on the Eighth Report of the Joint National Committee treatment goals of less than 140/90 mmHg for all patients. The WCHQ measure includes only in-clinic blood pressures and does not control for factors that may result in inaccurate reporting of patient blood pressure control. Therefore, it may not capture the full impact of a pharmacist-driven hypertension management program. Unfortunately, many health care quality measures are imperfect and lack standards that ensure accuracy.[19] Additionally, inaccurate or incomplete documentation of diagnoses and chart data often affect the credibility of electronic health record (EHR) data.[20] Factors found in the literature that may contribute to inaccurate reporting of patient blood pressure control include white coat or masked hypertension.[21,22] White coat hypertension is defined as when an individual who has elevated office blood pressure readings of greater than or equal to 140/90 mmHg also has a 24-hour blood pressure average less than 130/80 mmHg, with ambulatory blood pressure monitoring or home blood pressure readings.[23-25] White coat hypertension occurs in 15% to 30% of patients with an elevated in-clinic blood pressure reading and is more common in women, older adults, non-smokers, pregnant women, patients without evidence of target organ damage, and patients recently diagnosed with hypertension with a limited number of office blood pressure readings.[23] With this in mind, an opportunity exists to capture more accurately the controlled blood pressure of patients with white coat hypertension, within WCHQ hypertension quality control measures.

The objectives of this quality improvement evaluation were to (1) identify reasons that patients who have previously participated in the pharmacist hypertension management program have recent in-clinic blood pressure measurements above goal and (2) identify opportunities for improvement in internal data capture for WCHQ quality measures within a health system.

TABLE 1. Definitions of Categories for Above Goal In-Clinic Blood Pressure Measurement

Categorization	*Definitions*
White Coat Hypertension	Elevated clinic blood pressure readings, and below goal home readings
Home Blood Pressure Monitoring	Below goal home blood pressure readings and no clinic readings in the past twelve months
Specialty Clinic Visit	Most recent blood pressure reading above goal at a specialty clinic visit (e.g. cardiology, nephrology, neurology)
Isolated Hypertension	Above goal blood pressure reading on one occasion, or on multiple occasions with an identifiable cause (e.g. pain)
Unknown	Above goal blood pressure reading without an identifiable cause and requires additional blood pressure follow-up

Methods

This retrospective quality improvement project reviewed patients in the family medicine department who were enrolled in the pharmacist-led hypertension management program between January 1, 2019, and February 29, 2020. A report was generated from the EHR to identify patients with a most recent in-clinic blood pressure measurement above goal following participation in the program. Patients were included in this quality improvement evaluation if they were previous participants of the pharmacist hypertension management program; received care from the family medicine department; and had a most recent blood pressure of greater than 140/90 mmHg documented in the EHR. Patients were excluded if they were unengaged with the pharmacist program (by never returning phone calls or letters to follow up on their blood pressure), lost to follow-up as the patient had an initial visit but never followed through on getting their blood pressure to goal, or had hypertension management transitioned from the pharmacist-led program to a primary care or specialty provider.

Based on internal multidisciplinary hypertension workgroup findings for opportunities for improved blood pressure control, reasons for above goal blood pressure were identified and denoted by the following categories: white coat hypertension, home blood pressure monitoring, specialty clinic visit, isolated hypertension, or unknown. Definitions for these designations are included in Table 1. The multidisciplinary hypertension workgroup previously identified that white coat hypertension was not captured

routinely on the patient problem list. Additionally, home blood pressure monitoring was not routinely entered in designated EHR flowsheets, leading to missed WCHQ achievement metrics. Specialty clinic staff were not trained to routinely check a second blood pressure reading if a patient's initial clinic reading was elevated. Therefore, these categories were reviewed for further analysis. Patients with above goal readings on multiple occasions without an identifiable reason for a most recent elevated blood pressure reading were assigned to the unknown category. These patients had blood pressure readings indicative of uncontrolled hypertension, which was likely due to factors such as medication non-adherence or weight gain, and required additional blood pressure follow-up to identify contributing factors. A need to re-establish hypertension-focused care was identified for patients in the unknown category.

Additional patient-specific factors were collected for all patients, including: number of antihypertensive medications; documented medication non-adherence; recorded resistance to medication change; and no-show rates. These factors were assessed for all patients at each hypertension visit with the pharmacist. For the subset of patients with an unknown reason for elevated blood pressure, these factors were analyzed to identify potential trends. A sub-analysis based on comorbidity was also performed for these patients. Comorbidities evaluated included obstructive sleep apnea, hypothyroidism, diabetes, obesity, coronary artery disease, chronic kidney disease, anxiety, depression, and dementia. The pharmacist assessed adherence to continuous positive airway pressure (CPAP), routine lab, and disease state monitoring at hypertension visits. If these comorbidities were identified as sub-optimally managed, they might have impacted blood pressure control or medication adherence.[2] Institutional Review Board approval was deemed not necessary for this quality improvement initiative.

Results

A total of 431 patients were managed by the pharmacist-led hypertension management program during the project period. Of the 431 patients, we identified 141 patients who had a most recent in-clinic blood pressure measurement above goal following participation in the pharmacist hypertension management program.

White coat hypertension was identified as the most common reason for an above goal blood pressure reading. Of the 53 patients (38%) with white coat hypertension, only 19 of those patients (36%) had white coat hypertension documented on their problem list in the EHR (Table 2). After white coat hypertension, isolated hypertension was the second most common reason identified for most recent in-clinic blood pressure measurements above goal. Isolated hypertension was present in 39 patients (28%). Additional reasons for most recent above goal blood pressure readings in patients who received prior hypertension management from primary care pharmacists were specialty clinic visit (24, 17%) and home blood pressure monitoring (11, 8%). The remaining 13 patients (9%) were identified as having an unknown cause for the above goal blood pressure reading. Of those 13, six patients (46%) had a history of non-adherence to antihypertensive medications. The sub-analysis based on comorbidity revealed that eight of the 13 patients in the unknown subgroup had at least one comorbidity (62%). Comorbidities included diabetes, obesity, and sleep apnea. Of the patients with comorbidities, three patients (37.5%) had one comorbidity, four patients (50%) had two comorbidities, and one patient (12.5%) had three or more comorbidities.

TABLE 2. Reasons for Above Goal In-Clinic Blood Pressure Measurement (n=141)

Patients per Category of Elevated Blood Pressure, n (%)	
White Coat Hypertension	53 (38)
Home Blood Pressure Monitoring	11 (8)
Specialty Clinic Visit	24 (17)
Isolated Hypertension	39 (28)
Unknown	13 (9)
Sub-Analysis of Comorbidities for Unknown Category (n=13)	
History of Non-Adherence to Antihypertensive Medications	6 (46)
Patients with Comorbidity of Interest	8 (62)
≥3 Comorbidities	1 (8)
2 Comorbidities	4 (31)
1 Comorbidity	3 (23)

Discussion

Multiple reasons for above goal in-clinic blood pressures were identified and are not accounted for within the WCHQ hypertension control quality measure, including home blood pressure monitoring, specialty clinic visit, isolated hypertension, white coat hypertension, and unknown causes.

Regarded as a standard of care for hypertension management by major international hypertension societies, home blood pressure monitoring (HBPM) is an important method for evaluating a patient's ambulatory blood pressures.[26-28] Home blood pressure monitoring provides multiple blood pressure measurements from the patient's typical environment and allows for the detection of white coat and masked hypertension. Additionally, compared to in-clinic blood pressure measurements, HBPM has been shown to have superior prognostic value. While HBPM is an important tool for evaluating a patient's blood pressure control, it can lead to inaccurate pressures when patients have suboptimal technique or if the home monitoring device is not validated.[27,28] Therefore, it is important to educate patients on proper HBPM technique. Pharmacists are well positioned to provide education on HBPM.

As noted, HBPM can be a useful tool for accurately capturing a patient's blood pressure when proper technique is followed. At the time of this quality improvement evaluation, HBPM was not a validated method for data collection for the WCHQ hypertension quality control measure. Our evaluation indicates a need for revisions to the WCHQ hypertension quality measure to control for factors that may lead to inaccurate reporting of patient hypertension control. Since the time of completion of this evaluation, WCHQ now accepts home blood pressure measurements for patients.

Specialty clinic blood pressure readings were another reason for above goal in-clinic blood pressures identified. Previous

literature has demonstrated that blood pressure readings taken at specialty clinic appointments are less likely to demonstrate hypertension control compared to primary care visits. One cohort study demonstrated that for 86,512 patients, patients with their most recent blood pressure measurement taken in a specialty care setting (n=43,364) were significantly less likely to have hypertension control compared to patients with most recent measurement taken in primary care (n=43,148, 63% vs. 68%).[29] This variation in blood pressure measurements can be attributed to differences in blood pressure reading technique used. Additionally, when a patient is found to have high blood pressure, it is rarely addressed in specialty clinics. A previous study demonstrated that blood pressure was not discussed or documented in two-thirds of rheumatology visits when a blood pressure greater than or equal to 160/100 mmHg was taken, and only one in 10 patients received advice regarding follow-up for their elevated blood pressure reading.[30] With this in mind, documented specialty clinic blood pressure readings may not accurately reflect a patient's hypertension control. Within the health system where this evaluation was performed, many specialty clinics check a blood pressure reading but do not check a second blood pressure reading when the first one is elevated, decreasing accuracy. Additionally, when patients are seen by specialty clinics, other factors often exist that may contribute to their blood pressure being above goal. For example, patients seen by a rheumatology clinic may be experiencing pain, and patients seen by oncology clinic may be anxious, which can increase blood pressure. Therefore, specialty clinic blood pressure readings may not accurately reflect a patient's hypertension control. This presents an opportunity for enhanced organizational communication and for improved quality of blood pressure readings taken at specialty clinic visits.

Additionally, patients following up in primary care may have an isolated hypertensive reading. This often occurs when a patient is acutely ill or in pain. For these patients, returning to clinic for a blood pressure check may be inconvenient or unnecessary if blood pressure was previously well-controlled. Home blood pressure monitoring is a way to follow-up on isolated hypertensive readings to ensure blood pressure control.

A primary reason for elevated clinic blood pressure readings is white coat hypertension, which accounted for 37% of patients with elevated blood pressure readings in-clinic for this project. White coat hypertension contributes to above goal in-clinic blood pressure readings, leading to the inaccurate reporting of patient blood pressure control for quality metrics.[31] For patients with suspected or diagnosed white coat hypertension, ambulatory blood pressure measurement is critical for diagnosis, assessment, and monitoring.[32] For these patients, in-clinic blood pressure readings are not an accurate reflection of hypertension control and HBPM is preferred. When HBPM was not included in the WCHQ hypertension control quality measure, the measure did not adequately reflect patient blood pressure control for patients with white coat hypertension. Therefore, it did not reflect the full impact of this pharmacist-driven hypertension management program.

Lastly, for patients without an identified reason for uncontrolled hypertension, it is important to evaluate other patient-specific factors that may contribute to above goal blood pressure readings, including non-adherence, inappropriate antihypertensive medication classes, drug interactions, and resistance to medication changes.[6] Pharmacists are able to assess and resolve barriers to medication adherence and select evidence-based antihypertensive medications.[11]

This quality improvement evaluation is not without limitations. One limitation of this evaluation is the small sample size, with data collection from a limited number of patients within one health system. This limits the generalizability of this project to other institutions. Second, data was collected via retrospective chart reviews, requiring interpretation due to ambiguous or incomplete documentation in the EHR.

This evaluation showcases the potential for pharmacists to improve organizational quality measures within health systems. Specifically, for the WCHQ hypertension quality control measure, there is an opportunity to improve the capture of controlled blood pressure for patients with white coat hypertension within this health system. Our results also show a need to improve the accuracy of measurement collections in this health system. Future directions include developing internal protocols to ensure patients with white coat hypertension are appropriately diagnosed and documented in the EHR throughout the health system. Additionally, health system adaptations should be proposed to ensure home blood pressure readings are consistently and accurately collected, reported, and documented, and to improve the accuracy of blood pressure values collected at specialty clinic visits.

Conclusion

For patients who have previously participated in the pharmacist hypertension management program, white coat hypertension was the most common cause for most recent in-clinic blood pressure elevations followed by isolated hypertension. Of the patients with white coat hypertension, only about one-third had it documented on their problem list in the EHR. This presents the possibility for improvement in the accuracy of capturing hypertension control within health systems, especially for those who have white coat hypertension.

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Original Work

Optimization of Automated Dispensing Unit Inventory and the Impact on Department Waste and Inventory Control

by Jennifer Vogel, PharmD, Erica Timm, PharmD

Abstract

Purpose: To determine if application of a standard inventory formula from literature and manufacturer recommendations will improve automated dispensing cabinet (ADC) inventories by increasing vend:fill ratios, decreasing stock out rates, and improving the percentage of doses from ADCs.

Methods: Seventeen profiled ADCs were optimized over two months. The optimization process included removing medications that had not been dispensed in over 180 days, adding medications that had been repeatedly loaded to the ADC and dispensed from pharmacy, and adjusting the desired par levels for medications within the ADC. The inventory levels were adjusted using a standard inventory formula. The primary outcome was the vend:fill ratio, and secondary outcomes included percentage of stockouts, total number of medications in a machine, percentage of medication doses from the ADC, and number of outdated transactions.

Results: In total, 1,995 medication par values were adjusted in the seventeen machines over a one-month optimization period. The mean vend:fill ratio increased from 8.34 to 9.27. Prior to optimization, 78,684 (86.1%) doses were dispensed from ADCs. Post-optimization, the number of medication doses from ADCs increased to 80,663 (92.4%).

Conclusion: This study confirms that ADC optimization via a standard inventory formula improves vend:fill ratios, stockout percentages, and percentage of doses from ADC.

Automated dispensing cabinets (ADCs) were first used in hospitals in the late 1980s.[1] ADCs are decentralized, computerized medication dispensing systems that enable the storage of medications within hospital units, while also assisting with inventory control, order entry, medication administration, and documentation.[2] They are a gold standard for medication administration. ADCs have been found to enhance workflow efficiency, reduce medication errors, and improve medication administration by increasing access to medications.[1,2] Research has shown ADCs led to lower rates of dispensing errors compared to traditional unit-dose cassettes, fewer errors in drug administration, and fewer missing doses.[1]

Par levels, or the inventory levels of medications stored in an ADC, are commonly listed as maximum and minimum values. Most commonly in pharmacy, inventory levels are estimated by calculating average usage over time. In ADCs, quantities are commonly expressed as a minimum of a 2- or 3-day supply and a maximum of up to a 7-day supply. This approximation comes with issues: amounts for minimum and maximum day supplies can be subjective, usage can fluctuate with prescriber preferences and drug shortages, and quantities may not be updated as usage changes.

There are few published articles about the optimization of ADCs. Mark and Mehta used a days-supply approach to improve ADCs within their hospital to achieve a vend:fill ratio of >11, which is recommended for a tertiary medical center.[3] They did not achieve a vend:fill ratio of greater than 11, but they did increase their ratio from 6.5 to 9.4.[3] Lupi and colleagues evaluated a pharmacist-led ADC optimization program.[4] This group noted lower medication dispenses from central pharmacy and lower stockout rates after optimization.[4] O'Neil and colleagues compared a days-supply method to a standardized formula to improve inventories.[5] They found the formula method improved inventory metrics, including vend:fill ratio and led to a cost savings of $44,981 for the pharmacy department.[5] Literature is lacking in identifying a standard approach to optimizing ADC inventory. This study was designed to replicate the outcomes of a standardized formula found to be beneficial by O'Neil and colleagues.

This study was completed at a not-for-profit, 188-bed tertiary care center with 90 ADCs in Milwaukee, Wisconsin. The tertiary care center uses a cartless medication distribution model that dispenses the majority of medication doses from ADCs, with patient-specific medications stored in ancillary units of the ADC and ordered medications being loaded to ADCs as needed.

For this study, ADC optimization was defined as the modification of inventory and inventory levels within an ADC to improve the medication-use process and increase departmental efficiency. The optimization process was adapted from O'Neil: (1) removing stock of unused medications,

(2) adding medications as standard stock if repeatedly loaded, (3) adjusting desired on-hand inventory levels to decrease refills and "stockouts," and (4) rearranging stock to better suit new quantities.[5] The authors of this study hypothesized that the use of a standardized formula from O'Neil would reduce the number of refills by pharmacy between dose removals by nursing staff, increase the percentage of medications from ADC, and reduce waste of outdated medications.

Methods

Seventeen profiled ADCs (Pyxis, BD, Franklin Lakes, NJ) located within the emergency department, intensive care units, and medical-surgical units were optimized and studied from October 2021 until March 2022. The optimization of each machine required 4 hours to complete and was performed by a pharmacy resident to maintain consistency. It took one month to complete all 17 machines. Data, including vend:fill ratios, stockout percentages, machine inventories, and outdated medications, were collected through BD's integrated analytic Web portal (Knowledge Portal for Pyxis, BD) for a three-month period before optimization occurred and for a two month period after optimization. This study was determined to be exempt by the institutional review board.

Optimization of each machine was based on three-month usage reports generated 24 hours prior to assessing each cabinet. Medications were removed if not dispensed in 180 days and not considered to be an emergent medication. Emergent medications for the ADCs assessed are listed in Table 1. The removal of medications occurred first to free up space in each machine and to decrease the number of expiring, unused medications. Next, medications loaded four or more times were reviewed and added to each machine.

Prior to October 2021, the electronic health record at this facility did not communicate effectively with the ADC software; it did not identify when other medication strengths in ADC inventories could be used for dosing, or what medications were stored in nearby machines. Often, this led to more doses coming from central pharmacy and more medications being pulled for cartfill. In November 2021, a new electronic health record was introduced that had improved interfacing with the ADCs. The new electronic health record provided a reference of medications within each ADC for pharmacists and would link to an ADC that could provide an ordered dose before dispensing a medication from central pharmacy.

For this study, the par level calculations were adapted from standard inventory formulas by O'Neil and colleagues. The minimum par value (Min), or the quantity at which the pharmacy would be alerted to refill the medication, was calculated as the quantity of safety stock (SS) plus the mean average quantity dispensed between deliveries over 24 hours (qLT): Min = qLT + SS.5 The SS value is defined previously by O'Neil and colleagues and the formula is as follows:[5]

The maximum par value (Max) was calculated as the Min value plus a reorder

$$SS = (z)(\sigma qLT)\sqrt{\frac{1}{14}}$$

quantity (ROQ): Max = Min + ROQ.[5] The reorder quantity was also defined previously by O'Neil and colleagues, with the formula as follows:[5]

Medications were refilled on delivery runs completed by pharmacy staff based

$$ROQ = \sqrt{\frac{(qLT)(52)}{2}}$$

on generated reports listing medications at or below minimum par levels. Minimum par values were set to a quantity of at least 2. Items considered bulk, such as topical agents, and electrolyte infusions were excluded from par value assessment since their par values already reflected maximum amount of drug for pocket size.

Study Endpoints

Endpoints of the study included vend:fill ratio, percentage of doses from ADCs, number of outdated medications in each machine, stockout percentages, and overall inventory quantities of each machine. Vend:fill ratio was selected as the primary endpoint. The goal vend:fill ratio was determined to be 11, as noted previously by Mark and colleagues.[3] An improvement in this ratio would mean increasing the amount of times nursing staff pulls a medication while decreasing the amount of times the pharmacy department refills the medication. Vend:fill ratio, number of outdated medications, stockout percentages, and inventory quantities were calculated using the ADC analytic website. Lower stockout rates and lower numbers of outdated medications were considered to represent more appropriate inventory quantities.

TABLE 1. Emergent Medications

Emergent Medications
Adenosine 6 mg/2 mL Vial
Atropine 1 mg/10 mL Syringe
Calcium Chloride 1 g/10 mL Vial
Calcium Gluconate 1 g/10 mL Vial
Dextrose 50% 50 mL Syringe
Diphenhydramine 50 mg/1 mL Vial
Dobutamine 500 mg/250 mL Infusion
Dopamine 400 mg/250 mL Infusion
Epinephrine 1 mg/ 1 mL Vias
Epinephrine 1 mg/10 mL Syringe
Glucose Gel
Glucagon 1 mg/10 mL Kit
Labetalol 20 mg/4 mL Syringe
Nicardipine 40 mg/200 mL Infusion
Nitroglycerin 50 mg/250 mL Infusion
Rapid Sequence Intubation Kit
Sodium Bicarbonate 8.4% 50 mL Syringe
Tranexamic Acid 1000 mg/100 mL Infusion

Results

A total of 1,995 medication par values were adjusted, 50 medications were added, and 138 medications were removed. The mean vend:fill ratio prior to any inventory updates was 8.34, with the ED machines having a ratio of 4.70, the ICUs having a ratio of 7.95, and the Med-Surg units having a ratio of 10.13 (Table 2). After optimization, the average vend:fill ratio increased to 9.27 overall, with the EDs, ICUs, and Med-Surg units increasing to 5.45, 8.43, and 11.34, respectively. Before any inventory changes, approximately

78,684 (86.1%) medications were dispensed from the ADCs each month. After the updates were completed, 80,663 (92.4%) medications were dispensed from the ADCs each month. The number of doses dispensed from each ADC increased. The number of outdated medications increased from 15.8 to 19.5 medications per station. Stockout rates improved from 1.22% overall to 0.91%. The average number of medications in each ADC decreased from 387 to 342 medications. The total number of medications in each of the seventeen stations was reduced.

TABLE 2. Pre- and Post-Optimization Automated Dispensing Cabinets Characteristics

Metric	Pre-Optimization	Post-Optimization	Change
Vend:Fill Ratio, overall	***8.34 ± 2.34***	***9.27 ± 2.56***	***0.93***
Emergency Department	4.70 ± 1.09	5.45 ± 0.86	0.75
Intensive Care Units	7.95 ± 0.25	8.43 ± 0.78	0.48
Medical-Surgical Units	10.1 ± 0.45	11.3 ± 0.66	1.2
Doses from ADC, overall percentage	***85.6%***	***92.0%***	***6.40%***
Emergency Department	75.4%	82.4%	7.00%
Intensive Care Units	77.6%	92.0%	14.4%
Medical-Surgical Units	90.2%	93.9%	3.70%
Outdated Drugs per Station, overall	***15.8***	***19.5***	***3.7***
Emergency Department	10.8	10.8	0
Intensive Care Units	20.3	23.0	2.7
Medical-Surgical Units	16.0	18.0	2
Stockout Rates, overall percentage	***1.22% ± 1.08***	***0.91% ± 0.58***	***- 0.31%***
Emergency Department	2.80% ± 1.23	1.51% ± 0.58	- 1.30%
Intensive Care Units	1.13% ± 0.10	1.19% ± 0.46	0.10%
Medical-Surgical Units	0.56% ± 0.15	0.48% ± 0.26	- 0.10%
Number of Medications per Station, overall	***387***	***342***	***- 45***
Emergency Department	217	208	- 9
Intensive Care Units	421	379	- 42
Medical-Surgical Units	447	385	- 62

Discussion

The optimization of ADC inventory by adaptation of standard inventory formula was successful in improving inventory control with ADCs and efficiency within the hospital. Additionally, this study included more than double the number of ADCs as the original findings by O'Neil and colleagues.[5] This study also confirms that a pharmacist-led optimization program, similar to Lupi's study, can decrease stockouts and dispenses from central pharmacy.[4] However, this investigation had several limitations. During the optimization process, the hospital adopted a new electronic health record that had a better interface with the ADC software. The increased number doses from ADC could have been influenced by both the study and the new EHR. Another limitation is the ability of pharmacy staff to adjust par levels at any time throughout the study. Therefore, adjustments could have been changed within days of implementation. However, changing inventories within ADC machines is an ongoing practice and did not appear to substantially influence the improvement in inventory metrics. The number of outdated medications did increase, but it was noted that March 2022 had a high rate of outdated medications. March is considered to be an outlier and following months have had outdated medication quantities similar to February 2022. Trending outdated medications over a longer period of time is predicted to show an overall decrease in outdated medications. More studies completed over a longer period of time are needed to confirm that the formula method of ADC optimization is a valid form of inventory management.

Conclusion

This study has confirmed that using a standard inventory formula to optimize ADCs has a positive impact on vend:fill ratios and stockout percentages. The results of this study correlate with other literature that a formula-driven inventory optimization process does improve inventory metrics.

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Original Work

Incorporating Interprofessional Education Into a Graduate Nurse Practitioner Pharmacotherapeutics Course with a Pharmacist Educator

by Emma Stoflet, PharmD, BCPS, Robin Beeman, PhD, RN, Richard L. Berg, MS, Kathrine Barnes, MS, MPH, CPH, Sara Griesbach, PharmD, BCPS, BCACP, James Lokken, PharmD, MS, MEd, Jennifer Grimm, PharmD, BCPS

Abstract

Background: Limited literature exists on the value of a pharmacist co-educator in Doctor of Nursing Practice (DNP) didactic education.

Purpose: Incorporate a pharmacist co-educator into a DNP pharmacotherapeutics course to improve the education of DNP students.

Method: A pharmacist and nurse practitioner co-taught a DNP pharmacotherapeutics course. At course completion, students received an evaluation form. Mean scores on the final evaluations from the previous three years were combined and compared with the mean score for each response item post-implementation of the pharmacist co-educator. Thematic analysis was conducted on open-comment responses in the evaluation.

Discussion: AThematic analysis of course evaluations indicated a positive shift in DNP student perception of the course and their view of interprofessional collaboration with pharmacists. Mean final evaluation scores demonstrated slight improvement, though not statistically significant.

Conclusions: Implementation of interprofessional education (IPE) in a DNP pharmacotherapeutics course may enhance learning and promote collaboration among early-career DNPs and pharmacists.

Incorporating interprofessional education (IPE) into the training curricula of health care professionals is of increasing relevance for today's health care environment because of the need for professionals to work collaboratively in team-based medicine. National centers focused on the guidance and accreditation of training programs and health care systems are increasingly calling for novel education programs that prepare students for patient care, with the ultimate goal of making a positive impact on health outcomes; even the World Health Organization released a statement in support of IPE.[1]

In 2015, the American College of Clinical Pharmacology (ACCP) released a policy statement regarding the need to improve and expand clinical pharmacology education in medical and nursing schools to ensure learners have a solid background in clinical pharmacology and therapeutics prior to applying these concepts in practice.[2] In the same year, the American Association of Colleges of Nursing also released a position statement entitled "Interdisciplinary Education and Practice" that provided recommendations for nursing schools to develop curricula with opportunities for students to interact with other disciplines, collaborate with other disciplines to implement IPE, and conduct research to evaluate outcomes of incorporating IPE into nursing curricula.[3] One potential avenue of incorporating ACCP and AACN's recommendations into curriculum could be to include other disciplines, such as pharmacists, as educators in the didactic education of nurse practitioner students. However, currently there is limited literature available directly related to involving pharmacists as educators in a doctor of nurse practitioner (DNP) pharmacotherapeutics course.

Preliminary evidence suggests a benefit from incorporating pharmacist educators into other healthcare professional curricula, as demonstrated by the following studies. A study by Mcguire et al. used objective structured clinical examinations (OSCEs) facilitated by clinical pharmacists to help medical students review commonly reported prescribing errors and evaluated the

ABBREVIATIONS

ACCP - American College of Clinical Pharmacology

DNP - Doctor of Nursing Practice

IPE - interprofessional education

OSCEs - objective structured clinical examinations

students' self-reported learning.[4] Analysis of student reviews demonstrated that pharmacist involvement was beneficial and helped improve prescribing knowledge. Another study by Tittle et al. evaluated the impact of a pharmacist-taught course in practical prescribing to medical students completing their final-year clinical placements.[5] The course consisted of a 2-hour, pharmacist-led teaching session each week for 4 weeks at 5 different hospitals. Teaching methods in these sessions included small group tutorials, practice prescribing questions, shadowing of pharmacists, etc. Focus group discussions conducted at the end of each course demonstrated that students had increased confidence in prescribing and viewed pharmacists as knowledgeable and approachable resources. Though neither of these studies incorporated a pharmacist into formal didactic learning, both demonstrated promising results from pharmacists' involvement in the education of other health care professionals.[4,5]

In an effort to improve the learning experience of DNP students and better prepare them for their experiential education and future medication prescribing as nurse practitioners, we incorporated IPE in their pharmacotherapy didactic course. By integrating pharmacists into a pharmacotherapy course for DNPs, our aim was to improve the prescribing knowledge base of future DNPs and promote collaborative practice skills and competencies between DNPs and pharmacists.

Materials and Methods

Background

This project was conducted through an established DNP program in Wisconsin. In the fall of 2018, the director of the DNP graduate program requested pharmacist involvement in their Spring 2019 Pharmacotherapeutics for Advanced Clinical Practice course with the goal of promoting IPE among early-career nurse practitioners and pharmacists. The aims of the project were two-fold: enhance the course for students in the second semester of their DNP program curriculum, and enhance student learning of the materials. The primary coordinator of the project was a licensed pharmacist in a first-year pharmacy residency program at a rural, tertiary care health system.

TABLE 1. Course Topics

Topic	Pharmacist or Nurse Practitioner Led	Online or In-Person
Introduction to Pharmacotherapeutics	Pharmacist	In-person
Infectious Disease (antibacterial, antifungals)	Nurse Practitioner	Online
Infectious Disease (antivirals, vaccines, HIV/AIDS); Lab/Diagnostics	Nurse Practitioner	In-person
Head, Eyes, Ears, Nose, Throat	Pharmacist	Online
Cardiovascular (dyslipidemia, hypertension)	Nurse Practitioner	In-person
Cardiovascular (arrhythmia, heart failure, ischemic heart disease, acute coronary syndromes)	Nurse Practitioner	Online
Respiratory	Nurse Practitioner	In-person
Gastrointestinal/Liver	Pharmacist	In-person
Renal/Genital/Urologic	Pharmacist	Online
Musculoskeletal	Pharmacist	In-person
Pain/Neuromuscular Disorders	Nurse Practitioner	Online
Neurologic/Mental Health	Pharmacist	In-person
Endocrine/Immunity/Skin	Pharmacist	In-person
Endocrine	Pharmacist	Online

Project Design/Activity Description

Prior to the Spring 2019 semester, the department chair, graduate programs director, course coordinator, and other key stakeholders met to determine course needs and how to best structure pharmacist educator involvement. The group decided a pharmacist would co-teach the course with the existing nurse practitioner instructor from the past several years. The lectures were then divided between the nurse practitioner and pharmacist based on designated instructor credit load, expertise in the material, and scheduling coordination. This course was designed to be a combination of in-person and online lectures, with topics coordinated with the other DNP course topics. The nurse practitioner taught six lectures (three online, three in-person) and the pharmacist taught eight (three online, five in-person; Table 1). The entire course consisted of 14 lectures (six online and eight in-person), five online reading quizzes, five online discussion posts, and four in-class exams. The pharmacist had access to all previous presentation materials and revised the materials for the pharmacist-led online and in-person lectures (n=8) based on preferred teaching style, content, and required updates to course lectures. To ensure consistency in content between educators, course updates focused on the following elements: learning objectives; brief background on disease state; relevant treatment guidelines; non-pharmacologic treatment; and dosing, mechanism of action (MOA), adverse effects, contraindications, and precautions for each medication. "Knowledge Check" questions, designed to reinforce key concepts covered in the lectures, were added throughout the lectures as participation aides. Students would anonymously answer these questions using an online polling function. The pharmacist co-educator also developed discussion questions, reading quizzes, and exam questions to match the updates to the materials. Materials were peer-reviewed by other pharmacists at Marshfield Clinic Health System to ensure content accuracy.

Objectives

The primary objectives of this project were to identify changes in student satisfaction scores and thematic content of student-provided feedback as a proxy

measure of enhanced student learning. Evaluation of student feedback was chosen as the primary objective rather than knowledge/exam performance due to differences in exam structure and questions in each year limiting the capability for direct comparison.

Evaluation

Student course evaluations from the Spring 2019 semester were compared to student course evaluations of the same course from the previous 3 years (Spring 2016, Spring 2017, and Spring 2018). All evaluations from students enrolled in those 4 years were included in the analysis. Prior to Spring 2016, differences in course design limited the applicability of course evaluation assessment for the impact of pharmacist-led IPE on student learning; therefore, these evaluations were not included in the analysis. Information on past course evaluations was acquired retrospectively from the course records of previous years. All evaluations were obtained anonymously by a third party and were not linked to the students who completed them. This project was classified as exempt by the health system's Institutional Review Board (IRB) and the DNP program's IRB.

Following the final exam, students in the Spring 2019 course were given the same course evaluation that was used in previous years (Table 2). These evaluations included eight response items, each on a 4-point Likert rating scale in which students were instructed to rate each item as strongly disagree (1), disagree (2), agree (3), or strongly agree (4), as well as two open-comment response items. The students also completed a separate evaluation with both Likert rating scale questions and open-response questions specifically assessing the value of pharmacist involvement in the course (Table 2).

TABLE 2. Course Evaluation Response Items

	Rate strongly agree to strongly disagree (Likert rating scale)	*Open comment response items*
Standard response items	1. The objectives of the course were clear and understandable. 2. I was able to achieve the course objectives. 3. The organization of the course helped me to learn. 4. Course content supported achievement of the course objectives. 5. Readings were helpful in achieving course objectives. 6. Other supporting course materials were helpful in achieving course objectives. 7. I was encouraged to be an active participant in my learning. 8. Evaluation in the course was fair and measured my learning.	1. Identify specific components of the course you found most helpful and why. 2. Identify suggestions for improvement.
Response items specific for pharmacist involvement	1. Having a pharmacist co-teach this course helped me to learn. 2. I will be more likely to consult a pharmacist when prescribing medications in my future practice after this course.	1. Identify the benefits of having a pharmacist involved in teaching this course. 2. Identify concerns or suggestions for improving pharmacist involvement in this course.

Data analysis

Evaluation response items were summarized with descriptive statistics, and the Kruskal-Wallis test was used to compare results for each response item by time period using SAS software (SAS Institute, Cary, NC, USA). The scale from 2018 had a neutral category for students to choose, while the other 3 years did not, so 2018 was excluded from the comparison. Results were deemed statistically significant at the 5% level ($p < 0.05$) without adjustment for multiple comparisons. To conduct the thematic analysis of the open-comment response items, the primary investigator (pharmacist instructor) identified similar comments across student course evaluations to identify codes. Codes were further organized into larger overarching themes. Evaluations from Spring 2016–2018 were then compared to the Spring 2019 course evaluations. At each point, the codes and potential themes were reviewed by a pharmacy mentor and a researcher professionally trained in qualitative data analysis. A similar thematic analysis was also conducted on evaluation response items specific to pharmacist involvement (Table 2) to determine how students responded to having a pharmacist co-teach the pharmacotherapeutics course.

Results

Quantitative Analysis

Overall, 42 course evaluations were used in the statistical analysis (19 from Spring 2019, and 23 from Spring 2016 (n=11) and 2017 (n=12) combined), with scores from Spring 2018 only reported in Figure 1 (not included in pooled statistical analysis). Figure 1 shows the trends in mean scores by year over the eight evaluation response items. The only scores that were slightly higher in 2016–2018 than in 2019 were the two response items related to course objectives in 2016 and the response item related to readings in 2017. The 2019 scores were somewhat higher than those in 2018 for all eight response items.

In 2019 when a pharmacist co-taught the course, the mean scores were slightly higher than the means for the previous years combined (Table 3), though none of the response items had a statistically significant positive change ($p<0.05$) in the semester with IPE compared to the combined results from 2016 through 2017. This may in part be due to a reduced sample size since 2018 was not included in the pooled analysis.

For each of the eight evaluation response items, the 2019 semester had a smaller percentage of students choosing the "Strongly Disagree" category than previous years (data not shown). The response items assessing students' perceptions of pharmacist involvement in the course scored 3.5 and 3.6 on a 4-point scale with a score of 4 indicating that the student strongly agreed with the statements (Table 4).

Qualitative analysis

A number of codes were identified from the open comment response items from Spring 2016 to Spring 2019. Responses from Spring 2016, Spring 2017, and Spring 2018 were analyzed together (Table 5). Spring 2019 course evaluations were analyzed (Table 6) and then compared to codes and themes identified from previous years. Finally, responses to the pharmacist-specific evaluation response items from Spring 2019 were analyzed (Table 7).

Responses from previous years identified several areas for improvement including the need to update material for new and emerging information, to create greater concordance across course materials, and to streamline presentation and organization of the material to maximize retention. In contrast, responses from Spring 2019 instruction did not include references to these deficiencies. Students referred to the expanded knowledge base provided by pharmacist instruction, though paired this strength with a request to highlight medications more commonly used in general practice. The breadth of material covered in each exam continued to be a critique from previous years. Several changes suggested by students, such as reorganizing material to increase user-friendliness, could easily be incorporated in future iterations of the course.

TABLE 3. Mean and Median Scores for Course Evaluation Response Items before (Combined 2016–2017) and after Including a Pharmacist Co-Educator

	2016 - 2017		*2019*		*P-value*
	Mean	*Median*	*Mean*	*Median*	*P-value*
The course objectives were clear and understandable.	2.9	3	2.9	3	0.927
I was able to achieve the course objectives.	2.7	3	2.8	3	0.822
The organization of the course helped me to learn.	2	1	2.4	2	0.175
Course content supported achievement of the course objectives.	2.3	2	2.8	3	0.117
Readings were manageable and helpful in achieving objectives.	2.5	3	2.6	3	0.746
Other supporting course materials were helpful in achieving course objectives.	2.5	3	2.8	3	0.308
I was encouraged to be an active participant in my learning.	2.8	3	3	3	0.563
Evaluation in the course was fair and measured my learning.	2.3	2	2.9	3	0.071

For each response item, the student was asked to circle strongly agree, agree, disagree, or strongly disagree. For the purposes of analyzing the data, strongly agree was interpreted as a 4, agree as a 3, disagree as a 2, and strongly disagree as a 1.

TABLE 4. Average Scores for Pharmacist Involvement Course Evaluation Response Items

	Score
Having a pharmacist co-teach this course helped me to learn.	3.5
I will be more likely to consult a pharmacist when prescribing medication in my future practice after this course.	3.6

**For each response item, the student was asked to circle strongly agree, agree, disagree, or strongly disagree. For the purposes of analyzing the data, strongly agree was interpreted as a 4, agree as a 3, disagree as a 2, and strongly disagree as a 1.*

TABLE 5. Themes and Codes in Standard Open Comment Response Items - 2016 through 2018

Response Item	*Theme*	*Codes and Example Comments*
Identify specific components of the course you found most helpful and why	**Good Organization**	Instructor was well organized and approachable • "Content was appropriate for class." • "Instructors were approachable."
	Course Materials Beneficial	**Assignments helpful** • "The discussions were helpful to utilize our knowledge from our book." • "In class quizzes were helpful when the questions were straightforward." • "The discussions helped me remember things in more detail." **Powerpoints helped explain content** • "Powerpoints were super helpful in review for exams verses going through 19 chapters for one exam." • "Voice over one notes were extremely helpful for learning the material." • "Voice over PowerPoints were helpful." **Readings/textbook helpful** • "The readings helped me learn the most." • "The textbook was organized well and easy to read, very informative." • "Readings were also helpful."

TABLE 5 CONT. Themes and Codes in Standard Open Comment Response Items - 2016 through 2018

Response Item	*Theme*	*Codes and Example Comments*
Identify suggestions for improvement	**Course Materials Not Beneficial**	**PowerPoints and readings not useful** • "The powerpoints and handouts were not helpful and made it difficult to focus during studying for exams." • "Please teach content on exams in PowerPoints, I feel as if the content is important to test, should be taught in PowerPoint/in class lecture." • "Powerpoint were not helpful and most were a waste of time to go through." **Outdated powerpoints/materials** • "Content was often incorrect or did not agree with the book/literature. PowerPoints were hard to follow and often did not contain pertinent information." • "Assure that materials are up to date instead of just reusing from previous years." • "UPDATE YOUR POWERPOINTS – a lot of information is outdated." • "The PowerPoints had conflicting points, mis-spelled words, unknown abbreviations, and the organization was difficult to follow." **Assignments not beneficial** • "Sometimes in class quizzes covered obscure content or had multiple correct answers – this did not really enhance my learning." • "Some D2L scenarios did not incite very animated student discussion." **Exams poorly written/not reflective of materials.** • "The exams had many questions that went against what the textbook said." • "Ensure that exams are reflective of the information presented and the information in the readings." • "Exams were not reflective of any book or lectures." **Lectures not beneficial** • "Need better prepared lectures. Information sometimes wasn't clear, contradictory, or incorrect." • "I personally did not find class lectures very helpful… did not help me prioritize class content and did not help me understand concepts any better." • "In class meetings did not assist me in learning the content."
	Content too Broad/ Extensive	**Too much content per exam** • "There are not enough exams – there is far too much content to effectively learn the material. We were cramming rather than learning." • "18 chapters for one exam is to much content, one does not learn when info is crammed, it was a struggle just to read all the chapters and notes." • "Having 15+ chapters to cover on one test was difficult." **Content not focused enough** • "Focus lectures on important pieces of the powerpoint we need to know." • "PowerPoints must address need to know pharmacology – it was too focused on the pathophysiology and had very little need to know info on pharmacotherapy that instructors expect students to know." • "This class needs to be teaching medications not patho." **Need learning objectives** • "Goals need to match the teaching, and goals for learning were not made clear." • "Objectives need to be identified for each test." • "Have clearer objectives for each lecture to guide studying."
	Need Better Course Organization	**Better/more timely feedback and instructor engagement** • "Also feedback from the instructors would be helpful. Course questions were never answered timely on [the distance learning platform] and sometimes not at all." • "Instructors did not always give timely feedback on these discussions which made them even less helpful." **Timely posting of materials** • "Have course material ready at beginning of course." • "Please inform students in a timely manner when audio is up or if no audio will be up." • Consistency in course • "Information needs to be in one place and one place only." • "If multiple instructors are teaching, please coordinate to ensure that the scope of exam questions reflects the general approach to the course." **Need better overall organization** • "The organization of information made this course confusing." • "Overall the design of this course I feel did not facilitate learning." • "Content is disorganized."

TABLE 6. Themes and Codes in Standard Open Comment Response Items - Spring 2019

Response Item	*Theme*	*Codes and Example Comments*
Identify specific components of the course you found most helpful and why	**Course Materials Beneficial**	**Readings/textbook helpful** • "Content and readings were appropriate." • "I actually liked the textbook." • "The supplemental guidelines were helpful tools/aids from ADA/AHA, etc. to summarize major concepts." **Objectives were helpful** • "It was helpful that the Pharm D told us what was just for our information and what was important for us to remember." • "When objectives were put on the powerpoints that was helpful." • "Learning objectives helpful when studying for exams." **Assignments were beneficial** • "Discussion very time consuming but beneficial." • "The quizzes before class helped me prepare for the subject matter we would be learning about." • "Quizzes were helpful in identifying what might be considered key points of the concept." **PowerPoints were helpful** • "Good thorough lectures." • "PowerPoints helpful." • "Meds for disease conditions were emphasized."
	Instructors were Helpful	**Enjoyed having a pharmacist co-teach** • "Having a Phar[m]D instructor was most helpful for lectures and an excellent resource to have in class answering questions." • "I really enjoyed having a pharmacist co-teach the course." • "I appreciate the way she explained background and mechanisms of each action so clearly."
Identify suggestions for improvement	**Content too Broad/ Extensive**	**Too much content per exam** • "A lot of content in short time periods made it difficult to absorb/memorize material in a meaningful way." • "There are so many chapters/ppts to prepare and read before each exam…it's too much." • "Possibly more frequent exams/quizzes to reduce the amount of info on each." **Content not focused enough** • "Focus more on meds that we as family practice providers will actually be prescribing." • "Readings were hard to say if they were beneficial because the book was overwhelming how in depth it went." • "Reduce reading to relevant info, not just 'good to know'." **Need learning objectives** • "Objectives to be put on every powerpoint would be helpful." • "Post clear learning objectives for each section." • "Learning objectives need to be highlighted and provided prior to presentation of topics."
	Course Materials Not Beneficial	**Quizzes/discussions not beneficial** • "I didn't find the discussions helpful because I was restating a lot of what was in the book." • "Don't think quizzes on material not taught yet should be graded." • "Discussions and posts online should not be included."
	Need Better Course Organization	**Need timely posting of materials** • "PowerPoints should be posted a week ahead of time or at least 24 hrs prior to start of class." • "Having powerpoints out early would be helpful in focusing areas of study." • "Make sure all material is given to use in a timely manner." **Better/more timely feedback** • "Grading of discussions was inconsistent and feedback was unclear on what could be improved upon, what was missing, and why points were deducted." • "Discussion feedback on lacking areas would be helpful instead of just highlighting the category." **Need better overall organization** • "Voiceovers were long, preferred in person content to ask questions/clarify." • "Need clearer instructions for what is expected of us in the discussions." • "Organization needs much improvement."

TABLE 7. Themes and Codes in Pharmacist-Specific Open Comment Response Items

Response Item	*Theme*	*Codes and Example Comments*
Identify the benefits of having a pharmacist involved in teaching this course	**Positive Interdisciplinary Cooperation**	**Helpful to have pharmacist because they are the experts on medications** • "Has depth of knowledge of medications and felt as though having an expert in that area was beneficial." • "Extensive knowledge beyond what a Nurse Practitioner would know." • "More knowledge of adverse effects of meds and insurance info." **Good to have a different perspective** • "Fresh interdisciplinary perspective. Supplemented nursing and medical approaches." • "Interesting broad insight." • "Able to give a pharmacist's perspective."
	Pharmacist was a Helpful Resource	**Pharmacist had good interaction with students** • "Strongly encourage keeping the instructor because of positive interaction with students." • "Having a pharmacist was amazing." • "Good to have a Pharm." **Pharmacist was knowledgeable** • "Answered questions on the spot." • "Very knowledgeable." • "Having a pharmacist teach was most beneficial for up to date information." **Gave tips/supplemental information** • "Explains mechanics of action in an easy manner, gives real life examples." • "Helpful hints of what to write on Rx, etc." • "Able to point out prescriptive concerns." **Provided helpful resources for future practice** • "Having a pharmacist teach was most beneficial for…bringing attention to what resources are available." • "She guided us to use pharmacists as resources." • "Aware of resources for future practice."
Identify concerns or suggestions for improving pharmacist involvement in this course	**Need Better Course Coordination**	**Need more timely posting of materials** • "Have voiceover powerpoitns [powerpoints] and powerpoints for notes for lecture ready the Friday before." • "Post powerpoints/study materials in a timely manner." • "Having readings and lectures post more timely." **Slide voice-over needs to be improved** • "Voice overs could be put together so we don't have to play each slide separately." **Need better accessibility to pharmacist while off campus** • "Accessibility with not being on campus was difficult."
	More Pharmacist Experience	**May be helpful to include Acute Care pharmacist/pharmacist with more experience** • "Alternating an Acute Care vs Primary Care Pharm D would be ideal." • "Perhaps someone with a little more practical experience in the field." **Worried may lose nursing/prescriber view of medications** • "Don't lose the nursing/provider side to managing medications."

Discussion

Summary of Findings

Overall, DNP students responded positively to pharmacist instruction on pharmacotherapeutics. Many deficiencies identified from previous years' evaluations seemed to have been resolved with the addition of a new instructor, and thematic analysis of the pharmacist-specific evaluation questions indicated that students appreciated pharmacist involvement in the course. New deficiencies could be easily remedied in future iterations of the course, such as organization of material on the distance learning platform, greater inclusion of common medications prescribed in general practice, and increasing concordance between instructors' feedback before returning comments to students. Incorporating feedback, such as reducing the amount of material covered in an exam, may take a more concerted effort, but this remained a common critique across years. Interestingly, students sometimes gave conflicting opinions, possibly because of varying preferences and learning styles, which may contribute to the results of the study. For example, some students enjoyed the assignments and textbook, while other students (even in the same year) did not find the same readings and assignments beneficial. Future studies could further refine data quality by asking students to rate their opinion on different aspects of the course and how much each aspect impacted their learning.

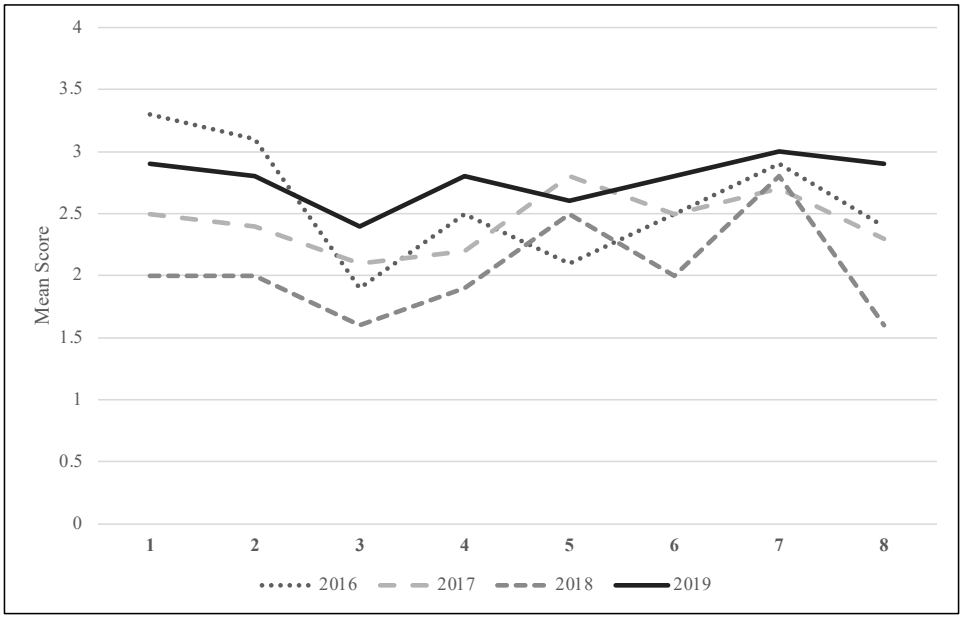
One major thematic change noticed between previous years and the 2019 semester was in the helpfulness of course materials. In the Spring 2016, 2017, and 2018 semesters, the most common theme mentioned was that the course materials were not beneficial; however, in the Spring 2019 evaluations, one of the most mentioned themes was that the course

materials were beneficial. This may be in part due to the pharmacist updating the materials and directing students to the most important information, indicating interdisciplinary cooperation with a pharmacist taking the lead in medication teaching may be beneficial for student learning. Teaching methods that the pharmacist incorporated into the course (e.g. knowledge check questions, updated discussion and reading quiz questions) may also have impacted the improved perception of benefit of course materials.

One of the most mentioned suggestions for improvement in the 2019 course evaluations was the timeliness of posting material, in that students would have appreciated the materials being available to view earlier. However, the overall feedback from students regarding pharmacist involvement in the course appeared to be positive. An example comment from one of the students highlights the positive reaction students had to a pharmacist educator: "Strongly encourage keeping the instructor because of positive interaction with students."

When asked to identify the benefits of having a pharmacist involved in teaching this course, students identified that having a pharmacist involved was helpful for interprofessional collaboration. Students also identified that the pharmacist developed positive interactions with the students and was a good resource for providing additional information outside of what was typically taught. The students suggested improving course organization similar to what was mentioned in the standard course evaluation response items. There were two comments on ensuring the pharmacist had practical experience in the field to provide the best resource for students in their learning environment. These types of comments highlight the importance of IPE in teaching healthcare professionals, as both the pharmacist and nurse practitioner educator have different perspectives to share with students. The identified themes in students' evaluations indicating students enjoyed the positive interdisciplinary cooperation and acknowledging pharmacists as a helpful resource for future practice highlights the benefit of IPE on student perception of benefit of interprofessional practice. This finding is supported by Vinluan and colleagues who evaluated both pharmacy and nurse practitioner students' perceptions of IPE, and found that students' perceptions and attitudes towards IPE were positive after involvement in an interprofessional activity.[6]

FIGURE 1. Response Item Mean Scores by Year



1. The objectives of the course were clear and understandable. 2. I was able to achieve the course objectives. 3. The organization of the course helped me to learn. 4. Course content supported achievement of the course objectives. 5. Readings were helpful in achieving course objectives. 6. Other supporting course materials were helpful in achieving course objectives. 7. I was encouraged to be an active participant in my learning. 8. Evaluation in the course was fair and measured my learning.

Limitations

It was determined that course evaluations, prospectively collected for the 2019 year and retrospectively available from the 3 previous years, would be the primary method used to analyze the impact of including a pharmacist in a DNP course. Course evaluation review, rather than analysis of exam scores, was selected because of potential confounding factors. Different exam questions from each year would make it difficult to compare content knowledge instead of varying question difficulty. Additionally, some sections of the course content are inherently more difficult than others, so comparing different exam scores may not provide a clear picture of whether pharmacist involvement made a difference.

Students expressed wide variability in perceptions of what was beneficial and what was not. We attempted to minimize this limitation by including 3 years of previous data, but a larger sample size may be required to fully evaluate the potential variability across student cohorts. Additionally, analysis was limited to feedback students chose to self-report. Student fatigue may have limited the breadth of feedback a student was willing to provide. Another potential factor that may have impacted our analysis was that the improvement in course evaluations could be solely because there was a new instructor, regardless of whether the individual was a pharmacist or not. Improvement in evaluations may also have been seen based on the methods the pharmacist used to teach the content, rather than general pharmacist expertise. We attempted to explore this possibility by assessing student evaluation of pharmacist involvement, but future studies of larger data with more than one classroom may help further explore this question. Lastly, course evaluations did not differentiate between the sections taught by the pharmacist and the ones taught by the nurse practitioner.

Future Directions

These results merit replication in an additional course with different instructors. One potential way to continue improving interprofessional practice and education of nurse practitioner students is by including pharmacists from specific specialties to lecture. As mentioned previously, the impact of IPE on DNP student outcomes could further support co-instruction by a pharmacist on a regular basis. Since nurse practitioners seemed to appreciate IPE with a pharmacist, future projects could

look at the impact of incorporating a pharmacist into other prescribers' education and visa-versa, including bringing a nurse practitioner educator into pharmacy school courses. Another potential area of research would be studying the long-term impact of IPE education on board pass rates for nurse practitioners and other health care professionals.

Conclusion

Collaboration with pharmacists and the field of pharmacy in general may enhance graduate nurse practitioner education and clinical practice in pharmacotherapeutics. By using IPE as a framework to incorporate a pharmacist into a DNP curriculum through a co-teaching model, students appear to both learn from and observe cross-disciplinary collaboration in action. Future projects are needed to evaluate the impact of such interprofessional/co-teaching models on student outcomes.

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ROSALIND FRANKLIN UNIVERSITY OF MEDICINE & SCIENCE COLLEGE OF PHARMACY STUDENT WRITING CLUB:

Novel Antihyperglycemics and their Uses in Type 2 Diabetes Mellitus and Beyond

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Abstract

While United States guidelines for the treatment of type 2 diabetes mellitus (T2DM) have not undergone a major change in the most recent update, the number of treatments and the amount of research into novel approaches are in constant flux. Currently, there are 11 antihyperglycemic classes used in the treatment of T2DM. The newer SGLT-2 inhibitors (SGLT2is) and glucagon-like peptide-1 receptor agonists (GLP-1 RAs), adjunct to lifestyle modifications, help reduce hemoglobin A1c and maintain glycemic control; however, recent investigations for their use beyond T2DM have earned them a place in the treatment of heart failure, chronic kidney disease, and obesity management.

Type 2 diabetes mellitus (T2DM) is a complex metabolic disorder associated with a wide range of long-term complications. The primary pathophysiology responsible for a T2DM diagnosis is insulin resistance, although its manifestation can vary from one person to another, with potential implications for damaging many organs, including the eyes, heart, vasculature, and kidneys.[1] Macrovascular complications from untreated or subtherapeutic treatment can include atherosclerotic cardiovascular diseases (ASCVD) such as stroke or myocardial infarction.[2] Potential microvascular complications include retinopathy, neuropathy, and nephropathy.[2,3] Resulting chronic kidney disease (CKD) and heart failure from these complications can be seen in patients with T2DM. Comorbid conditions in T2DM, such as dyslipidemia, hypertension, and obesity, further aggravate these complications.[4] In turn, the treatment protocol for each patient with T2DM must include the mitigation and close monitoring of these potential complications.

Certain antihyperglycemic agents have shown efficacy in lowering the risk of some of these diabetes-related complications in addition to improving glycemic control. Sodium-glucose cotransporter-2 inhibitors (SGLT2is) and glucagon-like peptide-1 receptor agonists (GLP-1 RAs) are two such antihyperglycemic classes. When compared to placebo, GLP-1 RAs provide A1c reduction ranging from 0.78 to 1.9% while SGLT2is provide A1c reduction ranging from 0.4 to 1.1%. [5-7] In addition to glycemic control, SGLT2is in general have shown a significant reduction in major cardiovascular (CV) events including CV deaths; worsening heart failure and heart failure-related hospitalizations; and worsening of kidney disease or progression to end-stage renal disease (ESRD).[8] Additionally, GLP-1 RAs have shown reductions in major CV events, including CV deaths and worsening of kidney disease. Specific GLP-1 RAs, such as semaglutide and liraglutide, both at higher doses, are also approved for the chronic management of obesity. Table 1 summarizes these agents and their additional indications; however, the rest of the article elaborates on the evidence supporting these additional indications.

Sodium-Glucose Cotransporter-2 Inhibitors

Currently, in the United States, there are four SGLT2is approved for use by the Food and Drug Administration (FDA). The generic and brand names of the agents in this drug class are canagliflozin (Invokana®), dapagliflozin (Farxiga®), empagliflozin (Jardiance®), and ertugliflozin (Steglatro®). These agents inhibit the reabsorption of sodium and glucose from the renal tubule, resulting in increased arteriole dilation and decreased glomerular pressure.[9] They decrease the glucose excretion threshold in the kidneys, allowing increased elimination of glucose in the urine. The natriuresis process aids in the decrease of systolic blood pressure, thereby improving a significant risk factor for CV events. They are generally taken as a once-daily regimen and require renal dose adjustments based on patients' estimated glomerular filtration rates (eGFR) values. The most common adverse events reported with this class are diuresis, urinary tract infection including mycologic infections, and hyperkalemia.[10,11] The rare but serious adverse events reported with this class are hypoglycemia, lower limb amputation and bone fractures, and necrotizing fasciitis.[12-14]

Canagliflozin (Invokana®) gained its first FDA approval in 2013 for the treatment of T2DM, but in recent years, with new research, new indications have been added, which include risk reduction of major adverse CV events (MACE) in adults with T2DM and established ASCVD; and risk reduction of ESRD, increase of serum creatinine, CV death, and hospitalization from of heart failure in adults with T2DM and diabetic nephropathy with microalbuminuria.[15] When used as an add-on therapy, canagliflozin has been shown to result in fewer hypoglycemic incidents, reduced postprandial glucose levels, statistically significant weight reduction, and reduction in systolic blood pressure.[16] The CREDENCE trial has shown that a dose

TABLE 1. Therapeutic Agents for T2DM with Additional FDA Indications

	SGLT2i			GLP-1 RA		
	CANAGLIFLOZIN	DAPAGLIFLOZIN	EMPAGLIFLOZIN	LIRAGLUTIDE	SEMAGLUTIDE	DULAGLUTIDE
BRAND NAME	Invokana®	Farxiga®	Jardiance®	Victoza® Saxenda®	Ozempic® Rybelsus® Wegovy®	Trulicity®
FDA INDICATIONS*	Cardiovascular (CV) disorders prophylaxis	Risk of CKD progression, CV disorders, Heart Failure (HFrEF)	CV disorders prophylaxis, HFrEF	CV disorders prophylaxis, chronic weight management	CV disorders prophylaxis, chronic weight management	CV disorders prophylaxis
HF BENEFITS	✗	✓	✓	✗	✗	✗
RENAL BENEFITS	✗	✓	✓	✓	✓	✗
ASCVD BENEFITS	✓	✓	✓	✓	✓	✓

*INDICATED FOR TYPE 2 DIABETES MELLITUS

ASCVD = atherosclerotic cardiovascular disease; CKD = chronic kidney disease; CV = cardiovascular; FDA = US Food and Drug Administration; GLP-1 RA = glucagon-like peptide-1 receptor agonist; HFrEF = heart failure with reduced ejection fraction; SGLT2i = sodium-glucose cotransporter-2 inhibitor; T2DM = type 2 diabetes mellitus

of canagliflozin 100 mg daily reduces the risk of ESRD and death from CV disease compared to a placebo (HR 0.70; 95% CI [0.59-0.82]).[8]

Dapagliflozin (Farxiga®) was FDA approved for improving glycemic control in adults with T2DM in 2014. Its positive impact on renal and CV outcomes includes lowering the risk of kidney failure and major CV events in patients with T2DM with concurrent renal and CV diseases.[17] In particular, renal outcomes show improvements in eGFR, and CV outcomes include decreased CV death in patients with heart failure and reduced ejection fraction (HFrEF) or hypertensive heart failure.[18] These outcomes have been consistently achieved in patients with T2DM, both with and without comorbidities impacting renal or cardiac function.[19,20] While diminishing renal function is a common complication of T2DM, delaying its progression in patients with or without diabetes has been assisted by dapagliflozin in patients with eGFR ranging from 25 to 75 mL/min/1.73 m^2.[21] In the DAPA-CKD trial, the composite risk of a sustained decline in eGFR of 50%, onset of ESRD, and death from renal or CV causes was found to be significantly lower with the use of dapagliflozin compared to placebo (HR 0.61; 95% CI [0.51 - 0.72]). These findings were consistent among patients both with and without diabetes mellitus present, showing a potential for the use of SGLT2is outside of glycemic control. Despite these findings, dapagliflozin is not recommended for patients with T2DM when eGFR is below 45 mL/min/1.73 m^2. Additionally, the analysis following the DAPA-CKD trial concluded that not only did dapagliflozin reduce the risk for major adverse kidney events including eGFR decline, but dapagliflozin also reduced the risk of major adverse CV events and death.

Dapagliflozin has been shown to mitigate risk factors for major adverse CV events in patients with T2DM and ASCVD risk factors. In the DECLARE-TIMI trial, 17,160 patients with T2DM were double blinded to either 10 mg of dapagliflozin once daily or placebo to analyze the drug's CV safety and efficacy.[23] Patients had either established ASCVD or risk factors for ASCVD. The primary safety outcomes in the trial included 3 point MACE: time to first event of CV death, myocardial infarction, or ischemic stroke. Participants were followed for a median of 4.2 years. The trial found that dapagliflozin did not result in a lower rate of MACE (HR 0.93; 95% CI [0.84 - 1.03]), but did allow for a lower rate of CV death or hospitalization for heart failure (HR 0.83; 95% CI [0.73 - 0.95]), which also reflected a lower rate of hospitalization for heart failure (HR 0.73; 95% CI [0.61- 0.88]). In the DAPA-HF study, dapagliflozin was found to be most effective to prolong life and minimize hospitalizations in patients with HFrEF (HR 0.70; 95% CI[0.59 to 0.83]).[24] Patients included in the study had heart failure in New York Heart Association functional class II or greater, a left ventricular ejection fraction ≤ 40%, and an elevated N-terminal pro-B-type natriuretic peptide concentration, while receiving standard heart failure treatment.[25] A total of 4,744 patients were randomized;

42% had known diabetes and 3% had undiagnosed diabetes. Among those without T2DM, 67% had pre-diabetes and 33% had a normal A1c. Dapagliflozin increased glycemic control with a low intrinsic propensity for causing hypoglycemia, glucosuria induced body weight reduction, and reduced levels of serum uric acid, lipids, and blood pressure.[26]

Empagliflozin (Jardiance®) was approved in 2014 by the FDA for the improvement of glycemic control in adults with T2DM. As further data became available, the indications for reducing CV death risk, established ASCVD, and reducing heart failure-related hospitalizations were added. Dosing for each indication is slightly different: 10 mg daily for heart failure while 10 mg daily as a starting dose with the potential to increase to 25 mg daily for T2DM treatment.[27] Renal dose adjustment is required for patients with T2DM or HFrEF that fall below a specific eGFR level.

The Empagliflozin Outcome Trial in Patients with Chronic Heart Failure and a Reduced Ejection Fraction (EMPEROR-Reduced) randomized 3,730 patients with HFrEF class II-IV to receive empagliflozin 10 mg once daily or placebo in addition to recommended therapy to test the primary outcome of CV death or hospitalization for worsening heart failure.[28] The study found that the primary outcome occurred significantly less in the treatment group compared to the placebo group regardless of the presence or absence of diabetes (HR 0.75; 95% CI [0.65- 0.86]). This study showed that the decrease in annual rate in eGFR was slower in the treatment group versus the placebo group (–0.55 vs. –2.28 mL/min/1.73 m^2 per year, P<0.001).[29]

Moreover, a meta-analysis of the DAPA-HF trial and EMPEROR-Reduced trial showed an improvement in combined clinical outcomes for CV death or first hospitalization for heart failure, composite of heart failure recurrent hospitalizations or CV death, and risk for the first hospitalization for heart failure in patients with HFrEF with or without T2DM.[30] Also, it showed that there were no significant differences in clinical outcomes between these two trials.

The most recent trial, completed in October 2021, was the Empagliflozin Outcome Trial in Patients with Chronic Heart Failure with Preserved Ejection Fraction (EMPEROR-Preserved), which showed significant clinical outcomes for patients with heart failure with a preserved ejection fraction (HFpEF).[31] It randomized 5,988 patients with class II-IV heart failure and an ejection fraction of more than 40% to receive empagliflozin 10 mg once daily or placebo in addition to usual therapy to test the primary outcome of a composite of CV death or hospitalization for heart failure. The study found that the primary outcome occurred significantly less in the treatment group compared to the placebo group regardless of the presence or absence of diabetes (HR 0.79; 95% CI [0.69 - 0.90]). Also, the study found that the total number of hospitalizations for heart failure was lower in the treatment group compared to the placebo group (HR 0.73; 95% CI [0.61-0.88]). The study found that empagliflozin compared to the placebo showed a slower progression in the rate of decline in eGFR.

Ertugliflozin (Steglatro®) is an SGLT2i approved for T2DM management. The Evaluation of Ertugliflozin Efficacy and Safety Cardiovascular Outcomes Trial (VERTIS CV) randomized 8,246 patients with T2DM who were 40 years old or older and had established ASCVD to test the primary outcome of composite of death from CV causes, nonfatal myocardial infarction, or nonfatal stroke.[32] The trial showed that the deaths from CV causes or heart failure hospitalizations did not differ significantly in the ertugliflozin group compared to the placebo group (HR 0.88; 95% CI [0.75-1.03], P=0.11 for superiority). One of the secondary outcomes tested the renal composite outcomes of

ertugliflozin, which included death from renal causes, renal replacement therapy, or doubling of the serum creatinine level. That outcome showed no significant benefit (HR 0.81; 95% CI [0.63-1.04]).

Glucagon-like Peptide-1 Receptor Agonists

The GLP-1 RAs are increasingly being used for other indications besides T2DM management, such as obesity, renal, and CV risk reduction, by improving cardiometabolic parameters. Most of these agents are available in the injection form with the exception of semaglutide, for which an oral tablet formulation is available. Depending on the agent, the dosing frequency varies; however, most follow a gradual titration to help tolerate gastrointestinal (GI) side effects.[33-35] They exert their main effects by increasing glucose-dependent insulin secretion, slowing gastric emptying, and acting in some areas of the brain that are involved in regulation of appetite. Some common adverse events are GI-related, such as nausea, diarrhea, and vomiting, but these have been shown to subside after the first few weeks of treatment. The rare but severe adverse effects include acute pancreatitis, pancreatic cancer, and malignant thyroid C cell tumor. Overall, GLP-1 RAs are still a favorable option for treatment of T2DM because they are effective at lowering A1c while presenting a low risk of hypoglycemia and offering the aforementioned additional benefits.

There have been multiple trials that showcase the benefit of adding a GLP-1 RA to a patient's regimen to reduce the risk of having a CV event. In the LEADER trial, researchers evaluated liraglutide (Victoza®) and its long-term effects on CV outcomes.[36] They randomized 9,430 patients to either receive liraglutide or placebo to test the primary outcome of first occurrence of death from CV causes, nonfatal myocardial infarction, or nonfatal stroke in a time to event analysis. The study found that the number of primary events occurred in significantly fewer participants that received liraglutide compared to placebo (HR 0.87; 95% CI [0.78 - 0.97]; P<0.001 for noninferiority; P=0.01 for superiority). Significantly fewer patients also died from CV causes in the liraglutide group compared to placebo (HR 0.78; 95% CI [0.66 - 0.93]).

Semaglutide subcutaneous injection (Ozempic®) is FDA approved for risk reduction of major CV events in those with established T2DM and CV disease.[34] Semaglutide shows benefit in glucose, weight, and blood pressure lowering similarly to liraglutide; however, it is only dosed once weekly compared to daily injections for liraglutide. The SUSTAIN-6 study randomized about 3,000 participants to either subcutaneous semaglutide or placebo to assess the primary outcome of first occurrence of CV death, nonfatal stroke or myocardial infarction.[37] In the study, they found that the rate of the primary outcome was significantly lower in the semaglutide group compared to the placebo (HR 0.74; 95% CI [0.58 - 0.95]; P=0.02.

Dulaglutide (Trulicity®) is a once-weekly injectable GLP-1 RA that is FDA approved for reducing major adverse CV events for those with T2DM with ASCVD or major ASCVD risk factors.[35] The REWIND trial evaluated CV benefits of dulaglutide.[38] In this study, the authors assessed the effect of dulaglutide for the primary endpoint which was the first occurrence of non-fatal myocardial infarction, non-fatal stroke, or death from CV causes including unknown causes. In 9,900 participants who underwent randomization, they found that those in the dulaglutide group experienced significantly lower rates of first occurrence compared to the placebo group (HR 0.88; 95% CI [0.79–0.99]). The study establishes the use of dulaglutide to reduce the risk of CV events for those not only with CV disease but those who have risk factors for developing CV disease as well.

In addition to ASCVD risk reduction, the secondary outcomes of the cardiovascular outcomes trials (CVOT) evaluated the effects of GLP-1 RA on renal outcomes.[36,37] Within the LEADER and SUSTAIN-6 trials, the authors evaluated that liraglutide and semaglutide both reduced the risk of new or worsening nephropathy. Although these trials did not select the patient population to specifically reflect those with CKD, a large number of the population included people with stage 3a kidney disease. The proof of benefit with renal outcomes with semaglutide is ongoing and will be evaluated in the FLOW trial; however, these findings of potential benefit are still reflected in the guidelines and GLP-1 RAs are recommended after a failed use of a SGLT2is in patients with established CKD.[8]

It has been shown that obesity management has a strong correlation with delaying the progression of prediabetes and treatment of diabetes.[39] Weight loss is known to improve glycemic control and ultimately reduce A1c. Although diet and physical activity will remain as a first-line recommendation for weight loss, GLP-1 RAs can be incorporated into an individual's therapy for additional weight loss. Based on study findings discussed later, subcutaneous higher dose semaglutide (Wegovy®) and higher dose liraglutide (Saxenda®) are also FDA-approved for the chronic management of obesity in people without T2DM.

The STEP 1 trial examined the use of semaglutide 2.4 mg once weekly subcutaneous injection in adults with obesity, with or without diabetes.[40] The study demonstrated that semaglutide 2.4 mg once weekly resulted in sustained and clinically relevant weight reduction in individuals with overweight or obesity compared to placebo (P<0.001). In the SCALE trial, the authors examined the use of liraglutide 3.0 mg once daily in patients with established obesity (BMI ≥30) or those with a BMI of 27 with dyslipidemia or hypertension for weight management.[41] They found that liraglutide had a mean loss of 8.4±7.3 kg compared to 2.8±6.5 kg difference in placebo (P<0.001) and that 63.2% of patients had lost 5% of their total body weight. This trial concluded that liraglutide provided weight loss benefits along with improved metabolic control.

In the AWARD-11 trial, the safety and efficacy of dulaglutide at higher doses (3.0 mg or 4.5 mg) in patients with T2DM and a BMI of 25 or greater were compared to normal doses (1.5 mg).[42] The authors found that an escalation of dose to 3.0 mg or 4.5 mg resulted in further reductions in weight and A1c (P <0.001). It should also be noted that at all treatment doses, dulaglutide was able to lower A1c by –1.54% for 1.5 mg, –1.64% for 3.0 mg, and –1.77% for 4.5 mg. This study included patients with T2DM; currently, dulaglutide does not have an FDA approval for the management of chronic obesity in patients without diabetes.

Guideline Recommendations

The American Diabetes Association has updated its current recommendations for first-line treatment.[8] This allows healthcare providers to take an individualized approach and initiate an SGLT2i or a GLP-1 RA based on the patient's specific factors, such as obesity, CKD, and CV disease. Metformin has been the first-line treatment for an extended period, and with this change, providers are able to make appropriate changes earlier on and initiate a treatment that has proven benefit in those specific comorbidities. The American Heart Association (AHA) and Kidney Disease: Improving Global Outcomes (KDIGO) organizations have also updated their guidelines based on the findings mentioned. It is now recommended that patients with T2DM and either established ASCVD or at high ASCVD risk should use an SGLT2i to prevent hospitalizations for HF. In the AHA guidelines, SGLT2is and GLP-1 RAs are also strongly recommended for patients with T2DM and established ASCVD or high risk for ASCVD.[43] The KDIGO guidelines recommend early initiation of an SGLT2i in a patient with T2DM and CKD across all albuminuria levels and eGFR stages to maximize potential renal benefits.[44]

Future Developments

The SGLT2is inhibit the reabsorption of sodium and glucose from the renal tubule, resulting in increased arteriole dilation and decreased glomerular pressure.[45] With this discovery of the SGLT2i mechanism of action, there has been a foray into research concerning additional disease state benefits with canagliflozin. It reduces renal oxygen consumption, leading to the hypothesis that canagliflozin can effectively increase erythropoietin production. This oxygen consumption hypothesis was applied further to begin research on how canagliflozin could be used in cancer treatment. In a 2016 study to determine what this mechanism could be, canagliflozin was shown to activate adenosine monophosphate activated protein kinase (AMPK) by reducing mitochondrial respiration in human kidney cells and mice liver cells.[46,47] Canagliflozin inhibited the proliferation and survival of cell clones from prostate, breast, and lung cancer cells as both monotherapy and an add-on to radiation therapy. There are currently two National Cancer Institute-supported clinical trials in progress regarding canagliflozin use in preventing hyperglycemia in patients with metastatic breast cancer; and canagliflozin use with the solid tumor cancer drug, serabelisib.[48] According to the United States National Library of Medicine, there are a total of 23 clinical trials in the United States that are ongoing to learn more about the use and mechanisms of benefit from canagliflozin.[49] These disease states of interest include polycystic ovary syndrome, T2DM in patients with Human Immunodeficiency Virus (HIV), decreased left ventricular function in patients without T2DM, and use in acute COVID-19 treatment.

Conclusion

Given the presence of microvascular and macrovascular complications during the course of T2DM, it is important to address them while achieving glycemic control. The SGLT2is and GLP-1 RAs offer such benefits. They can provide varying levels of cardioprotective benefits, delayed kidney damage progression, and positive metabolic effects. With further research and clinical trials, there are more insights gained into how their pharmacology is applicable beyond T2DM.

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ROSALIND FRANKLIN UNIVERSITY OF MEDICINE & SCIENCE COLLEGE OF PHARMACY STUDENT WRITING CLUB:

A Review of Overactive Bladder Treatment

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Abstract

The sudden urge to urinate and the uncontrolled feeling of having to go frequently describes the life of an individual with an overactive bladder. As many as 30 percent of men and 40 percent of women in the United States live with an overactive bladder.[1] Many people feel embarrassed, don't ask for help, don't know how to talk with their health care provider about their symptoms, or think there are not treatments that can help. Symptoms can severely impact the physical and social life of an individual with an overactive bladder. In this article, we will explore the disease state and investigate the role of novel vibegron and of a combination of mirabegron/solifenacin in patients with overactive bladder.

Overactive bladder (OAB) is a syndrome classified by the compelling desire to pass urine, which presents with or without urinary incontinence and nocturia. OAB affects a significant proportion of the U.S. population, with an overall prevalence of 23.3%. Nearly twice as many women as men have OAB (30% of women and 16.4% of men).[2] Relative to race, 45.9% of Black, 43.4% of White, 42% of Hispanic, and 26.6% of Asian women have OAB, while for men the percentages are 33.3%, 28.0%, 27.0%, and 26.6%, respectively.

In healthy patients, normal bladder function is defined as a bladder free of bacterial infections or tremors and having the ability to store urine without discomfort.[3] Conversely, the pathophysiology of OAB has either neurogenic factors or non-neurogenic factors, which encompass myogenic and urotheliogenic factors.[4] Neurogenic factors include damage to the central inhibitory pathways of the brain or spinal cord, or sensitization of peripheral afferent terminals, leading to OAB. Non-neurogenic, myogenic factors involve unstable increases in the intravesical pressure leading to damage of the bladder wall, and secondary changes to the smooth wall muscles of the bladder. Meanwhile, urotheliogenic factors include damage to the urothelium that leads to an increase in urinary frequency and a decrease in storage of urine. The etiology of OAB consists of a multitude of factors, including weak pelvic muscles, nerve damage, urinary tract infection, excess weight, menopause, and intake of alcohol or caffeine.[5] The significant risk factors for OAB are increasing age, current smoking, hyperlipidemia, cardiovascular disease, and renal disease.[6]

Typical clinical presentations of OAB involve a sudden urge to urinate that is difficult to control, urinary urgency incontinence, urinating frequently (eight or more times in 24 hours), or waking up one to two times in the night due to urination.[6] Diagnosis of OAB includes an initial assessment of symptom history and fluid intake, and a urinalysis to rule out infection or hematuria. However, if a patient reports bothersome symptoms of urgency with or without urinary incontinence, and absence of a urinary tract infection, an OAB diagnosis may be made.[7] After a diagnosis is made, there are many healthcare professionals involved in the care of patients with OAB, including family practice physicians, urologists, nephrologists, gynecologists, and pharmacists, who optimize the care for these patients.

Treatment Modalities and Approach

The American Urological Association (AUA) and the Society of Urodynamic, Female Pelvic Medicine and Urogenital Reconstruction (SUFU) are the two organizations that co-publish the treatment guidelines for OAB.[8,9] The "Diagnosis and Treatment of Non-Neurogenic Overactive Bladder in Adults: an AUA/SUFU Guideline" outlines non-pharmacological and pharmacological treatment options for OAB.

Non-pharmacological treatments are considered first-line treatment options.[8,9] They include education and the implementation of behavioral therapies. Some key points to emphasize during patient education are: the benefits versus risks of treatment options; that multiple treatment options may be needed; and that not all symptoms may be resolved. Behavioral therapies include bladder training, pelvic floor training, and fluid management.[8] Bladder training allows patients to train their bladders to urinate on a fixed schedule in order to increase the amount of urine held in the bladder by urinating first thing in the morning, then urinating again after a set interval, such as 15 minutes. Over time, the patient should be able to increase their interval time in order to decrease urinary incontinence.[10] Pelvic floor muscle training, also known as Kegels, involves contracting and then relaxing the pelvic floor muscles, typically repeated in several sets throughout the day. This training provides patients with the ability to strengthen the muscles that control urination. Lastly, fluid management can be implemented as a behavioral therapy to manage urinary incontinence. Educating the patient on drinking smaller amounts of liquid throughout the day, drinking more fluids earlier in the day, or skipping the fluids that increase urine production, such as alcohol and caffeine, are methods that can help manage fluid for those with OAB.[11] The main goals of the education and behavioral therapies for OAB are to change voiding habits and improve the control of

TABLE 1. Clinical Trials of Blood Pressure Lowering Strategies in Patients with Diabetes

Generic/Brand	*Dosing & Modifications*	*Important Drug Interactions*	*Patient Education*
Antimuscarinic Antagonists[30-35] Mechanism of Action: competitively antagonizes the muscarinic receptor on urinary bladder smooth muscle, resulting in reduced contractions Class Adverse Drug Reactions: dry mouth, constipation, diarrhea, headache, somnolence, and dizziness Class Contraindications: urinary retention, gastric retention, uncontrolled narrow angle glaucoma			
Oxybutynin/Ditropan XL® [30]	Dosing: 5 mg, 10 mg or 15 mg extended-release tablets by mouth daily Modifications: • Adults: Start with 5 mg or 10 mg, once daily. Dose should not exceed 30 mg per day • Pediatric patients (6 years of age or older): Start with 5 mg, once daily. Dose should not exceed 20 mg per day	• Potent CYP3A4 inhibitors • Other anticholinergic drugs	• Take at approximately the same time each day. Should be swallowed whole with the aid of liquids. Patients should not chew, divide, or crush tablets. • May produce angioedema.
Tolterodine/Detrol® LA[31]	Dosing: 2 mg or 4 mg extended-release capsule by mouth daily Modifications: • Mild to moderate hepatic impairment, Creatinine Clearance 10-30 mL/min, and drugs that are potent CYP3A4 inhibitors: 2 mg by mouth daily • Severe renal and hepatic Impairment: Not recommended	• Potent CYP3A4 inhibitors • Other anticholinergic drugs	• Take with or without food and at the same time each day.
Trospium/Sanctura®[32]	Dosing: 20 mg tablets by mouth twice daily Modifications: • Creatinine clearance less than 30 mL/min): 20 mg once daily at bedtime • Geriatric patients greater than or equal to 75 years of age, dose may be titrated down to 20 mg once daily based upon tolerability	• Drugs elimination by active tubular secretion • Metformin immediate release tablets • Other anticholinergic drugs	• Should be taken with water on an empty stomach at least one hour before a meal.
Darifenacin/Enablex®[33]	Dosing: Extended-release tablets 7.5 mg or 15 mg by mouth daily Modifications: • Patients with moderate hepatic impairment and patients taking potent CYP3A4 inhibitors: daily dose should not exceed 7.5 mg daily • Severe hepatic impairment: Not recommended	• CYP3A4 inhibitors • CYP2D6 substrates • Other anticholinergic drugs	• May be taken with or without food. The tablet should be swallowed whole with water and not chewed, divided or crushed.
Solifenacin/Vesicare®[34]	Dosing: 5 mg or 10 mg tablets by mouth daily Modifications: • CrCl <30 ml/min, moderate hepatic impairment, concomitant use of potent CYP3A4 inhibitors: do not exceed 5 mg tablet once daily	• Inhibitors and inducers of CYP3A4 enzyme • Other anticholinergic drugs	• Take with water and swallow the tablet whole, can take with or without food.
Beta-3 Adrenoreceptor Agonist[35,36] Mechanism of Action: activates beta-3 receptors resulting in relaxation of the detrusor smooth muscle Class Adverse Drug Reaction: hypertension (Mirbegron only), nasopharyngitis, urinary tract infection and headache Class Contraindications: Hypersensitivity reaction			
Mirabegron/Myrbetriq®[35]	Dosing: 25 mg or 50 mg extended-release tablets by mouth daily Modifications: • Severe renal impairment or patients with moderate hepatic impairment: maximum dose of 25 mg once daily • End Stage Renal Disease and severe hepatic impairment: Not recommended	• Mirabegron is CYP2D6 inhibitor; appropriate monitoring and possible dose adjustment of those CYP2D6 substrate drugs may be necessary • Digoxin: prescribe the lowest dose of digoxin when concomitant use of mirabegron	Swallow whole with water, do not chew, divide or crush tablets
Virbegron/GEMTESA®[36]	Dosing: 75 mg tablet once daily Modifications: • End-stage Renal Disease with or without Hemodialysis: Not recommended. • Severe Hepatic Impairment: Not recommended	• Digoxin	• May be taken with out without food but must be swallow whole with water • May be crushed and mixed into applesauce

urge suppressions.

Per the AUA/SUFU guidelines, pharmacological treatments options are considered as second-line therapies, which are to be added if behavior therapies alone are not sufficient to treat the symptoms.[8] Antimuscarinics such as oxybutynin, tolterodine, trospium, darifenacin, and solifenacin are commonly used drug agents to treat OAB. Guidelines suggest that the extended-release form of the antimuscarinics should be used due to fewer side effects, specifically dry mouth.[8,12,13] In addition to antimuscarinics, beta-3 adrenoreceptor agonists, such as mirabegron, are commonly used for overactive bladders, with vibegron being the most recently approved drug agent in this class.[13] Table 1 describes available agents in detail. These medications can be used as monotherapy, or in a combination of the two different drug classes if the disease state becomes refractory, in order to achieve better clinical outcomes.[8]

Third- and fourth-line OAB therapies include the use of surgical and non-surgical procedures.[8] Intradetrusor onabotulinumtoxinA (100U) can be administered in order to cause bladder muscle contraction.[14] Peripheral tibial nerve stimulation is a non-surgical procedure in which a needle is placed near the tibial nerve. When stimulated, electrical impulses block the nerve signals that cause unwanted muscle spasms.[15] Sacral neuromodulation simulation is a surgical procedure that sends electrical impulses directly to the sacral nerve to alter the bladder function.[16] In rare cases, patients may undergo bladder augmentation cystoplasty, in order to enlarge the bladder, or may undergo urinary diversion, in order to create a new pathway for voiding.[17] These procedures are reserved for patients categorized with OAB refractory to previous therapies, patients not candidates for second-line therapies, and those who are willing to undergo surgery.

Novel Pharmacologic Approaches

Gemtesa® - vibegron

In December of 2020, a new beta-3 adrenergic agonist, Gemtases®, emerged to treat overactive bladder with symptoms of urinary incontinence, urgency, and urinary frequency in adults. Gemtases® is also known by its generic name, vibegron, and was approved by the Food and Drug Administration (FDA). The drug comes in a 75 mg tablet and is generally administered once daily. Vibegron's common adverse reactions include headache, urinary tract infection, nausea and diarrhea; and it is contraindicated for those who have hypersensitivity to the drug. Also, vibegron has a potential to interact with digoxin by increasing the blood levels of digoxin. The approval was based on a randomized, double-blind, placebo and active controlled phase III trial called the EMPOWUR trial.[18] This trial assessed the efficacy and safety of vibegron in OAB "wet" (urinary urgency with urge incontinence) and "dry" patients (urinary urgency without urge incontinence). It followed 1,518 eligible participants who were randomized to receive 75 mg vibegron or matching placebo or tolterodine for 12 weeks.

The trial primarily investigated the change in the average number of daily urge urinary incontinence (UUI) episodes in patients with one or more episodes per day, and the change in daily urinary micturitions.[18] The average change of UUI episodes was statistically significant in the vibegron group by -2.0 episodes per day vs. -1.4 episodes for placebo ($p < 0.0001$) and -1.8 episodes for tolterodine with a p-value of 0.0123. The mean change of urinary micturitions at week 12 was statistically significant by -1.8 episodes per day for vibegron vs. -1.3 for placebo ($p < 0.001$) and -1.6 for tolterodine with a p-value of 0.0020. Vibegron exhibited a statistically significant improvement in the key secondary outcome measures, such as number of urgency episodes, volume per micturition, and proportion of incontinent patients with a ≥75% reduction in urge incontinence episodes ($p < 0.01$).

In the vibegron group, the incidence of adverse events that were observed 2% or more than in the placebo group were headache (4%), nasopharyngitis (2.8%), and diarrhea and nausea (2.2%).[18] Furthermore, other adverse events were consistent with cystitis and urinary tract infection. Safety measures also included vital signs assessments. The proportion of patients at week 12 that had an increase in blood pressure was 0.7% for vibegron, 0.9% for placebo, and 1.9% for tolterodine. The proportion of patients who experienced tachycardia in both the placebo and tolterodine groups was 0.2% while there was no tachycardia reported in the vibegron group.These results were not statistically significant. Furthermore, based on the adverse effects observed during the study, vibegron was less associated with adverse events such as dry mouth and cognitive decline, which are commonly observed with anticholinergics agents used in the treatment of OAB. In conclusion, vibegron provided a significant improvement in OAB symptoms with a better safety profile.

Similar to the antimuscarinics, all beta-3 adrenergic agonists are second-line agents after trialing first-line therapy of behavioral therapies.[19] Vibegron's place in therapy falls as second-line among the other beta-3 adrenergic agonists.[20] Further, as vibegron is a relatively newer agent, it is unavailable in the generic formulation. This is the reason behind its limited insurance coverage and high cost.[21]

Combined Use of Mirabegron and Solifenacin

Mirabegron, a beta-3 adrenergic agonist, and solifenacin succinate, a muscarinic receptor antagonist, are two drugs approved by the FDA in 2012 and 2004 respectively as monotherapies for treatment of OAB.[22,23] More recently in 2018, the FDA approved the use of mirabegron in combination with solifenacin for treatment of OAB with evidence of increased efficacy over use as monotherapy.[23]

Mirabegron (Myrbetriq®) eases symptoms of OAB such as urinary urgency, urinary frequency, and urinary incontinence. It is a beta-3 adrenergic agonist that works by relaxing the bladder muscles to prevent symptoms of OAB. Mirabegron comes as an extended-release tablet with an initial dosage of 25 mg orally once daily and may be titrated up to 50 mg once daily after 4 to 8 weeks as necessary.[23] Mirabegron for OAB is recommended to be taken with food in children ages 8-18, and can be taken with or without food in adults. A max dose of 25 mg daily is recommended in patients with renal or hepatic impairment. This medication is also indicated in children ages 3 and older as a suspension in treatment for neurogenic detrusor overactivity (NDO), a bladder control condition caused by brain, spinal cord, or nerve problems. Mirabegron is a moderate CYP2D6 inhibitor and should be monitored in patients also taking medications such as digoxin and warfarin. Patients initiating treatment with digoxin and mirabegron should consider the lowest

digoxin dose initially and monitor serum digoxin concentrations when titrating up. While effects of mirabegron on multiple doses of warfarin have not fully been investigated and no effect was seen in the pharmacodynamic endpoints of a single dose of warfarin, prothrombin time should be monitored with concurrent use of both agents. The most common adverse effects reported with monotherapy include hypertension, nasopharyngitis, urinary tract infection, angioedema, and headache. Blood pressure should be monitored periodically, especially in patients with hypertension. Worsening of pre-existing hypertension has been reported infrequently with mirabegron in clinical trials and is not recommended for use in patients with severe uncontrolled hypertension (>180/110 mmHg). Mirabegron reportedly has lower incidences of dry mouth and constipation compared to antimuscarinic counterparts.[29]

Solifenacin succinate (Vesicare®) is a muscarinic receptor antagonist, selective for the M3 receptor to relax and reduce spasms of bladder muscles.[22] Solifenacin, similar to mirabegron, is indicated for OAB and NDO in children ages 2 and older. The oral tablet is initially dosed at 5 mg daily and can be titrated up to 10 mg daily. A max dose of 5 mg is recommended in patients with severe renal impairment or moderate hepatic impairment. It is not recommended for use in patients with severe hepatic impairment. Solifenacin is metabolized by CYP3A4 and should be used with caution in concurrent administration of CYP3A4 inhibitors. Grapefruit juice and St. John's Wort should be avoided, and a maximum dose of 5 mg should be used with concomitant use of ketoconazole, an azole antifungal. Solifenacin should not be used in pregnant or breastfeeding women. It is contraindicated in patients with narrow-angle glaucoma, gastric retention, and urinary retention. Furthermore, anticholinergic CNS effects have been reported with monotherapy, including headache, confusion, somnolence, and hallucinations. Patients should be monitored for anticholinergic CNS effects, especially at initiation or dose titration, and be advised not to operate heavy machinery until they know how solifenacin affects them. Solifenacin should be discontinued or reduced in dose for patients who experience such CNS effects.

Combination therapy with these two agents have been shown to improve OAB symptoms compared to monotherapy with either agent. Most effects of combination therapy were seen by week 4 in clinical trials with effect sizes consistent with an additive effect and without any significant effect in the safety profile.[24] Dual therapy improved number of incontinence episodes, number of micturition, and volume voided per micturition.[24-26,28] Long-term data shows these results were maintained over the course of one year. The most current 2019 AUA/SUFU guidelines for diagnosis and treatment of OAB suggest combination therapy as a second-line treatment, refractory to monotherapy.[8] Guidelines were based on four major trials that compared combination mirabegron (25 to 50 mg) plus solifenacin (5 mg) with monotherapies and placebos over a period either 12 or 52 weeks.[24-26,28] While these trials showed overall significant increased efficacy with combination therapy, there were increased reports of adverse effects.[29] Patient-assessed symptoms were measured in all four trials using the Patient Perception of Bladder Condition questionnaire (PPBC) and the OAB-q Symptom Bother score. Based on the SYNERGY and SYMPHONY trials showing significant reduction in OAB symptoms including urinary urgency, urinary frequency, and urinary incontinence, the combination therapy doses are mirabegron 50 mg and solifenacin 5 mg daily.[24,28] Adverse effects seen in clinical trials were additive for dual therapy with increased rates of dry mouth, constipation, and dyspepsia compared to monotherapy. Additionally, more incidents of urinary retention were reported with the combination of mirabegron and solifenacin.[24,25] Combination therapy is still a new concept with lack of robust data, and is currently considered secondary to monotherapy.

Conclusion

OAB is a chronic condition with varying symptoms among patients that requires a treatment plan tailored to each patient's needs. While a cure for this condition is rare, management of OAB through non-pharmacologic and pharmacologic options greatly improves symptoms and increases patient satisfaction. Non-pharmacologic treatments are first-line, and are intended to help develop strategies to manage urge and urge incontinence. These options include bladder training, pelvic floor training, and fluid intake management. Patients should be educated on OAB and the consistency needed for non-pharmacologic options to see long-term improvements. Pharmacologic treatments are intended to be used as additional management if non-pharmacologic options are not enough.

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UNIVERSITY OF WISCONSIN-MADISON SCHOOL OF PHARMACY STUDENT WRITING CLUB:

Business Member Spotlight: The Medicine Shoppe in Two Rivers

by Amy M. Wolff, 2024 PharmD Candidate, Judy Zheng, 2024 PharmD Candidate

Marvin Moore, PharmD, is the owner of The Medicine Shoppe Pharmacy in Two Rivers, Wisconsin, where he also serves as a full-time pharmacist. As the owner of The Medicine Shoppe, Moore has become dedicated to providing exceptional care tailored to his patients' and community's needs. Moore's interest in community pharmacy practice began during an Advanced Pharmacy Practice Experience (APPE) rotation at Marshland Pharmacy in Horicon and Mayville, Wis. It was here that Moore describes having a "lightbulb" moment in which he realized how valuable forming meaningful relationships with patients is to him. Creating these relationships has continued to be a fundamental pillar of Moore's practice as a community pharmacist. Moore graduated with a PharmD degree from the University of Wisconsin-Madison in 2002, and subsequently completed a community pharmacy residency through the University of Iowa. Following this, Moore decided to move back to Wisconsin, where he came into contact with Brian Jensen of The Medicine Shoppe. Upon meeting the Two Rivers community and the staff at The Medicine Shoppe, Moore knew this was the right place for him. Shortly thereafter, he entered into a junior partnership with Jensen for roughly five years and, in 2011, Moore assumed ownership of the pharmacy. Since then, he has worked to expand the services that the pharmacy offers, such as enhancing the immunization services available to patients, implementing a medication synchronization program, and expanding the multi-dose packaging services offered.

Daily Practice & Community Ties

The Medicine Shoppe remains the only independent pharmacy located in Two Rivers, Wis. The pharmacy offers a wide range of services, including traditional dispensing, multi-dose packaging, delivery, blood pressure monitoring, medication synchronization, auto-refill, diabetic shoe fittings, medication therapy management (MTM), and immunizations. These services are made possible by the three pharmacists and 15 support staff members who work to provide quality care to the Two Rivers community.

Two Rivers, Wis. is a small town with a population of 11,000. That small size makes it easy for community members to know each other. Hence, word of mouth is a major method for potential customers to entrust their medication needs to

Below: *(left) Owner of The Medicine Shoppe, Marv Moore. (right) The Medicine Shoppe in Two Rivers, WI.*

Above: *The Medicine Shoppe Staff in Two Rivers, WI.*

The Medicine Shoppe. Other means of advertisement include the pharmacy's website and Facebook page.

Moore describes his typical day as similar to that of other community pharmacists throughout Wisconsin, primarily focused on the services listed previously. His day to day activities are largely centered around providing the best possible care to his patients, which he does by tailoring the services offered at The Medicine Shoppe to his community's needs. In fact, The Medicine Shoppe is highly invested in the well-being of the community, which has allowed for deep ties to be formed. Many staff members are committed to supporting and sponsoring local events. Moore has been a member of the Kiwanis Club (an organization consisting of volunteers dedicated to serving their communities) for the past 18 years, acting as the president for the past three years. He also serves on the board of directors for the Chamber of Manitowoc County and has served on the board of directors and as president of Two Rivers Main Street.

Additionally, The Medicine Shoppe is willing and eager to foster the learning of future pharmacists. The pharmacy is both an Introductory Pharmacy Practice Experience (IPPE) site and an APPE site for pharmacy students. Moore encourages current pharmacy students to gain as many experiences in IPPEs and APPEs as possible and find a practice that will ignite their inner passion. Local high school students are also encouraged to shadow in the pharmacy, if interested. Moore is actively involved in the Pharmacy Society of Wisconsin (PSW), where he serves on the Community Pharmacy Advisory Committee. He makes it a point to promote PSW to any student that completes a rotation at The Medicine Shoppe. In addition, his wife, Joylyn Moore, PharmD, serves on the PSW Board of Directors. Through these roles, the Moores have continued to foster growth and advancement in the practice of pharmacy in the state of Wisconsin.

Pursuit of Excellence

At The Medicine Shoppe, Moore makes great effort to implement best practices whenever possible. The pharmacy has been a part of the Community Pharmacy Enhanced Services Networks (CPESN) and Flip the Pharmacy, both programs aimed at advancing pharmacy services and delivering a higher level of care to patients. Moore claims that the key to success is "knowing our patients really well and making sure we are meeting their needs." He acknowledges that each patient's needs are unique and ensures the staff at The Medicine Shoppe are trained to tailor their services to the individual.

Similar to other independent pharmacies, staff, often without a background in pharmacy, receive on-the-job training. Employees develop skills through day-to-day experience and patient interactions to become an asset to the Two Rivers community. Moore strives to hire the right person and find the right role for the individual; he places emphasis on the applicant's attitude as opposed to aptitude. The Medicine Shoppe has experienced continued success largely due to the pharmacy team's dedication to place patients first and having the best intentions for them. The staff focuses on treating people the way they want to be treated and a willingness to work alongside patients to resolve a problem regardless of its magnitude.

Since taking on the ownership of The Medicine Shoppe, Moore has made "small successes every day" from figuring out how to take care of patients to empowering patients to become actively engaged in the management of their health. The work done by the pharmacy staff does not go unnoticed by the Two Rivers community. These residents know that they can safely place their medication needs in the hands of the Medicine Shoppe pharmacy team and trust that they will be taken care of.

Overcoming Obstacles

The Medicine Shoppe has been serving patients for the past 30 years, but that accomplishment has not come without

challenges. One major challenge The Medicine Shoppe currently faces is the decline in reimbursement for traditional pharmacy dispensing services. While The Medicine Shoppe is proud to offer a wide range of other services, traditional dispensing still remains the pharmacy's primary source of revenue. This creates a conflict when trying to expand new services that may not yet have the ability to generate much revenue, but are needed in the community. To tackle this issue, The Medicine Shoppe has learned to complete traditional dispensing tasks as efficiently as possible, leaving time for new initiatives.

Another notable challenge that The Medicine Shoppe has recently experienced centers on the COVID-19 pandemic. Once the vaccine rollout began, Moore was motivated by his desire to protect the Two Rivers community and immediately jumped on board. The Medicine Shoppe, similar to other pharmacies, would not know the amount of vaccines they would receive on any given Monday until the Wednesday of the week prior. This meant that no appointments could be scheduled until that Wednesday, leaving only a few days to fill the spots for the following week. In addition, to accommodate all patients, The Medicine Shoppe opted to keep the COVID-19 vaccine scheduling process manual. This meant that no app or website was used; rather, appointments were scheduled over the phone by staff at The Medicine Shoppe. This required a great deal of additional staff time, but the effort was greatly appreciated by the Two Rivers community, especially older adults without internet access. Despite the many challenges faced as a result of COVID-19 vaccinations, Moore is thankful that The Medicine Shoppe had the opportunity to be a part of the solution to an ongoing pandemic.

The Medicine Shoppe was among a select group of pharmacies to receive the William Penn Foundation (WPF) grant to advance racial equity and racial justice for COVID-19 vaccine distribution. The fund helped to offset initial costs and minimize financial barriers that impede the pharmacy's ability to vaccinate the community. As a result, Moore and his team were able to target a wider range of individuals, especially those who encountered barriers to access the vaccines. It further enabled the pharmacy staff to focus on individual patients and ensure their needs were met despite the ongoing pandemic. Moore expresses that the WPF grant allowed The Medicine Shoppe staff to truly gain a sense of urgency and reinforce their commitment to the Two Rivers community.

While Moore knows that implementing any new service will always have its challenges, he firmly believes that one of the most important things to consider first is whether or not there is a need in the community. If there is truly a need, Moore is determined to do everything possible to make that service accessible for his patients. Moore acknowledges that he rarely fears new opportunities or challenges, and instead remains optimistic and ready for the benefits that something new may bring to the pharmacy.

Plans to Expand

At the present time, The Medicine Shoppe has no major plans for growth. The pharmacy's primary objective is to continue its current services and focus on keeping the doors open amid ongoing challenges. However, Moore has plans to shift the pharmacy team's task dynamic in order to better accommodate patient needs and to continue to provide them with exceptional care. He expects to implement changes that will ultimately expand pharmacy technician roles to free up pharmacists' time. This will enable pharmacists to maximize their expertise in medications, permitting them to focus on providing MTM, counseling, and building rapport with patients.

Advice for Independent Pharmacy Ownership

To pharmacies looking to implement practice advancement initiatives, Moore emphasizes the importance of doing your homework to thoroughly understand market needs. Like a true entrepreneur, he understands the large initial investment of time and resources required to implement any new services. As a business owner and community member, Moore is always ready and willing to step up when a need arises that is not filled or not properly filled.

To those considering independent pharmacy ownership, Moore stresses the significance of honing the ability to communicate with people of various backgrounds. At the pharmacy, the staff interacts with patients, other health care providers (HCPs) and staff members, and students on a daily basis. He makes it a point that strong communication is the key to getting to know people and their needs. Each patient is unique in that their skill sets and understanding of medications are different and their interests in how the medications will impact their body or other aspects of their lives. Having strong communication ensures the staff at The Medicine Shoppe can uniquely tailor their services to any individual patient needs. Thus, for anyone, student and practicing professional alike, there is always room to improve your communication skills.

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MEDICAL COLLEGE OF WISCONSIN SCHOOL OF PHARMACY STUDENT WRITING CLUB:

Member Spotlight: Lindsey Ladell, PharmD, BCPS

by Tracy Zook, PharmD

Lindsey Ladell, PharmD, BCPS is the high reliability organization program manager at the Clement J. Zablocki Veterans Hospital (Milwaukee VA) in Milwaukee, Wisconsin. After graduating in 2011 from the UW-Madison School of Pharmacy, she went on to complete her postgraduate year one (PGY1) and year two (PGY2) training at the Milwaukee VA. In addition to her PGY2, she also completed the Chief Resident in Quality and Safety (CRQS) program alongside physician and nursing colleagues.

Ladell was the first resident to complete the PGY2 residency program in Medication Use Safety, and the first pharmacist in the nation to complete the CRQS program. She jokes, "I was born and raised at the Milwaukee VA." Following the completion of her PGY2 program, Ladell was hired by the Milwaukee VA as a clinical pharmacy specialist, patient safety manager. She currently serves as the facility's high reliability organization program manager.

Raising the Bar

Throughout her 11-year career at the VA, Ladell has been passionate about expanding the reach of pharmacy into roles that have not traditionally been held by pharmacists, demonstrating value and opening doors for others. She was the first graduate of the PGY2 Medication Use Safety residency and CRQS programs. Upon graduation, she became the first pharmacist to serve in the patient safety manager role at the Milwaukee VA, where she oversaw the their patient safety reporting system and a wide –variety of organization-wide improvement efforts. When Ladell took the patient safety manager role, there were only a handful of VA medical centers across the country that had pharmacists in these types of roles; since then, at least four other sites in Veterans Integrated Service Network (VISN) 12, Milwaukee's region of care, have added pharmacists in those roles. There's been another pharmacist added to the patient safety manager team at the Milwaukee VA, too. "Process-based thinking and patient safety comes second nature to pharmacists; it is our superpower. It just makes sense that we belong in roles where the responsibilities include dissecting processes to look for patient safety improvements," Ladell says.

Her strengths with shaping and developing new ideas, as well as being comfortable paving her own way, were instrumental in launching a new high reliability organization (HRO) program in December of 2019, launching the Milwaukee VA on its journey toward zero patient or employee harm. High reliability is a concept taken from other industries, such as nuclear power or the airline industry, that

Left: *Lindsey Ladell, PharmD, BCPS*

Below: *Clement Zablocki VA Medical Center, Milwaukee WI*

operate in complex, high-risk environments but have very low catastrophic error rates. Many organizations, including the Veterans Health Administration, have begun to translate the lessons from these industries into healthcare. In this role, Ladell works with the executive leadership team on shaping purposeful leadership, cultural and improvement efforts across the organization.

In 2021, Ladell was promoted into a new leadership role, high reliability organization program manager, adding both a social worker and a nurse to her team. In this role, she also serves alongside Todd Burner, MD, who is a hospitalist and rheumatologist at the Milwaukee VA. "My time as a trainee taught me the value of working closely with an interprofessional team which I continue to value today," says Ladell. "Despite us all working towards the same cause, each of us have different perspectives that are incredibly valuable."

Bumps in the Road

Just when the high reliability program was launching in March 2020, Ladell was asked to serve on the Milwaukee VA's Covid-19 incident command team. Like other areas in healthcare, day-to-day practice became less defined and more responsive. "At first we needed to identify how to provide safety for both our employees and our patients," says Ladell. This was accomplished by creating and implementing screening tools and additional safety measures to slow the spread of virus. Ladell's ability to thrive in new environments and with interprofessional teams allowed her to use her skills to support the medical center during an uncertain time with ever-changing needs. She had a hand in everything from standing up a drive-thru Covid-19 testing site to pulling together a walk-in, weekend vaccination clinic that vaccinated hundreds of Veterans in less than 24 hours.

In 2021, Ladell was asked to take on a leadership role serving as the planning section chief of the incident command team for the Milwaukee VA. During this this time, her team stood up unvaccinated employee testing operations for the Milwaukee VA. Going where the organization needed her required her to pause some lanes of effort for her high reliability program. But she had the opportunity to bake high reliability concepts into the work that she did with incident command, in leadership, communication, and the prioritization of patient and employee safety.

Moving Forward

With some slowing of the pandemic and a return to a day-to-day practice, Ladell has a lot of excitement about how the high reliability program can serve both the employees and patients at the Milwaukee VA Medical Center. During this new normal, the high reliability team has been focusing efforts on employee safety, which is a unique twist on high reliability in healthcare, where the focus is often on patient safety. "If our employees are not safe, we cannot expect them to keep our Veterans safe," says Ladell. Current and future efforts include a focus on reducing employee burnout and the prevention of workplace violence. Additionally, her team will also be working to embed high reliability behaviors into teams across the Milwaukee VA through the launch of a clinical team training program, which is modeled after the airline industry's crew resource management program that supported that industry's journey towards high reliability. When asked about when she will consider her program a success, Ladell says, "When I do new employee orientation, I ask our new employees to raise their hands if they themselves or a family member has been impacted by a medical error. Every time that question is asked, over half of the packed room raises their hand. My hope is that someday I ask, and no one raises their hand. Until then, I will keep at this important work."

At the time of this interview Tracy Zook was a Doctor of Pharmacy Student on APPE rotation with the Medical College of Wisconsin School of Pharmacy in Milwaukee, WI.

Member Spotlights: Cali Felix, PharmD of Advanced Care Pharmacy of Omro and Melanie Engels, PharmD, MBA of Froedtert Pharmacy

by Camille Ortiz Rivera, PharmD, MBA, Tyler Wolosek, PharmD

Pharmacies and Long-Term Care Facilities Collaborate to Vaccinate against COVID-19 and Influenza

Pharmacists and pharmacy technicians helped protect Wisconsinites during the COVID-19 pandemic by administering COVID-19 vaccinations, collecting specimens for point-of-care testing, and managing COVID-19 therapeutics. Pharmacy personnel had to navigate the logistics of creating, implementing, monitoring, and improving these new services in addition to providing their usual services and managing the staffing and burnout challenges created or exacerbated by the pandemic. These challenges led to many pharmacy personnel working more hours than pre-pandemic, volunteering their personal time, and collaborating with new organizations and institutions. All of these actions speak to pharmacists' and pharmacy technicians' dedication to their patients and their communities.

In fall 2021, the Wisconsin Department of Health Services turned to the Pharmacy Society of Wisconsin (PSW) with the request to engage pharmacies to organize and lead COVID-19 booster and influenza vaccination clinics at long-term care facilities (LTCFs) that did not have a vaccinator. Many pharmacists, pharmacy technicians, and pharmacies responded quickly, taking on the extra responsibilities of hosting a clinic. These responsibilities included ordering vaccine supply, transporting the supply to the LTCFs, administering the vaccinations, completing the necessary documentation, and billing.

To facilitate the process, PSW connected LTCFs that requested assistance finding a vaccinator with a pharmacy that was willing to facilitate the vaccination clinic. Once introduced by PSW, the pharmacy and the LTCF coordinated the vaccination clinic date and number of doses requested. PSW would like to recognize two outstanding pharmacists and their team members for their successful organization and conduction of LTCF vaccination clinics: Cali Felix, PharmD of Advanced Care Pharmacy of Omro, and Melanie Engels, PharmD, MBA of Froedtert Pharmacy. Below, the authors asked them about their experiences, the challenges they faced, their takeaways, and their advice for others who are considering organizing a vaccination clinic.

What prompted you to step-up to the challenge of organizing a vaccination clinic at a long-term care facility/ facilities?

Cali Felix: I recently obtained my board certification in geriatrics because I love working with the older population. Interacting with our patients is one of my favorite parts of being a pharmacist. I knew I would genuinely enjoy this experience, but once PSW started to reach out saying there were so many people unable to find vaccinators, I really felt a duty to do as much as I could to help.

Melanie Engels: There was an unmet need in our community to provide preventative care with immunizations in a high-risk population…This action ties directly back to our mission of advancing the health of the people of the diverse communities we serve.

Did you or your pharmacy have prior experience organizing vaccination clinics for long-term care facilities?

CF: Yes, as an LTC pharmacy, Advanced Care Pharmacy of Omro regularly provides vaccination clinics to our facility residents, mainly for influenza.

ME: At the previous organization that I worked for, my [roles] included manager of long-term care pharmacy. We provided vaccination clinics for skilled nursing facilities, assisted living facilities, adult foster cares, group homes and the like.

What challenges did you face?

CF: My biggest challenge was the toll it took on my body giving so many shots in one day. You don't think much of it while giving shots, but when I work with this special population, it isn't a simple "Come sit in front of me, and I'll lean over to give this to you." Secondly, the amount of time needed was difficult. Luckily, I

Below: *Cali Felix, PharmD (left), and Melanie Engels, PharmD, MBA (right)*

have an amazing team that really stepped up while I was out of the pharmacy 2-3 days a week. Many new facilities I went to could not find a local partner, so I sometimes needed to drive 2+ hours one way and tried to combine 2-3 facilities per day to be more efficient. Lastly, of course, all of the paperwork! Consents, vaccine documentation, WIR data entry, [and] billing are all time-consuming tasks that you need to be prepared for.

ME: The most efficient LTC vaccine clinics occurred when residents had designated time slots assigned. This creates a smooth workflow and pace. In other cases, residents showing up at the same time created some complexity with immunizer workflow and maintaining proper social distancing.

What role did PSW play in assisting you with any challenges you experienced?

CF: [PSW] did an outstanding job connecting me with facilities in need, making it a very simple email meet-and-greet, then we could take it from there.

ME: PSW facilitated the initial electronic connection between Froedtert Pharmacy and the long-term care facility. This assisted in ensuring both parties had contact information for each other.

What advice would you give other pharmacists who are considering organizing vaccination clinics for the first time or at a new site?

CF: I take it upon myself to keep the residents comfortable, so that means a lot of kneeling, bending, and hunching. Helping remove layers of clothes, working around walkers [and] wheelchairs, [and] going to the rooms of the bed-bound are all different things you have to be prepared for versus a vaccine clinic for the general public.

ME: Develop a standard tracking tool to use for each facility you are organizing a clinic for; this will help to make sure each step is being tracked and avoid a last minute rush to complete a task. When working with multiple facilities to plan clinics during the same timeframe, it is easy to mix up or forget what each of the facility needs are. Having this centralized tracking tool provides the information clearly and succinctly.

Did any technicians assist with administering vaccines?

ME: We do have pharmacy technicians administering vaccines that have participated in our on-site vaccine clinics.

What are some of your takeaways from your experience?

CF: The gratefulness of the residents and staff for having someone come to them is always the most rewarding.

ME: Advanced planning and strategizing was key to running a smooth clinic. Not all facilities operate under a one-size-fits-all model, so it was important to understand the needs of each individual facility and the clinic model that would best serve their residents and staff. Providing any paperwork ahead of time to allow the facility staff to collect prior to the clinic date keeps the immunizer focused on the resident and providing care and counseling and reduces administrative burden.

Is there anything else you would like to share with us about COVID-19, vaccinations, or the pharmacist's role during the pandemic?

CF: I am glad pharmacists were able to play such a vital role during the pandemic. I know many people, including myself, were incredibly overwhelmed with the workload, but I know doing LTC clinics, and my fellow Omro Pharmacy pharmacists doing numerous vaccination clinics, [we] gained an overwhelming satisfaction in providing care for our community, and in return we got so much support and thank yous from our community.

ME: All of the immunizers were critical to the success of these clinics. A huge thank you to the pharmacists who worked with me on meeting facility schedule needs, arriving to the pharmacy early to collect the supplies for the clinics, transporting the items to the clinics, providing outstanding patient care in administration of the vaccines and education for the staff and residents, and traveling back to the pharmacy at the clinic conclusion to drop off any unused items and file the paperwork.

Our pharmacy team has been absolutely magnificent throughout the pandemic. The team's resiliency to show up ready to take care of patients every day is truly admirable and I am grateful to work with such a marvelous group of individuals. Navigating uncharted territories and moving forward despite the unknown has allowed us to provide COVID-19 vaccines, COVID-19 self-test kits, and COVID-19 oral antivirals.

Conclusion

The stories of Advanced Care Pharmacy of Omro and Froedtert Pharmacy during the pandemic show us how pharmacy personnel can have a significant impact in our communities. Being prepared, having a plan, preparing for setbacks, and leveraging your team are key to the success of vaccination clinics. Both Cali Felix and Melanie Engels demonstrated incredible leadership skills and fulfilled their duty to serve this high-risk population by collaborating with the LTCFs. They demonstrated selflessness and dedication when battling the pandemic by serving a high-risk population and sharing their stories to improve the outcomes of future vaccine clinics for LTCFs.

Camille Ortiz Rivera, PharmD, MBA is a pharmacist at CVS in San Juan, Puerto Rico. Tyler Wolosek, PharmD is a PGY1 pharmacy resident at Mayo Clinic Hospital of Arizona in Phoenix, AZ.

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