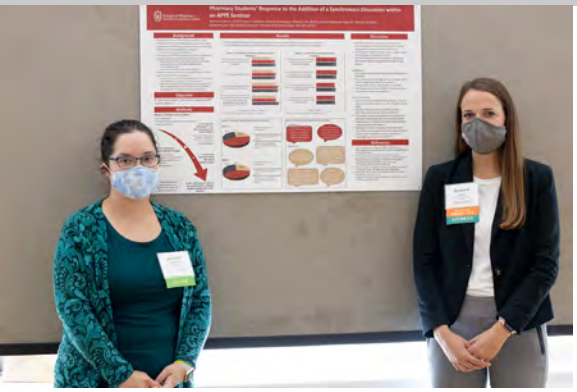
Volume 24 • Issue 6 www.pswi.org

November/December 2021

The Journal

of the Pharmacy Society of Wisconsin



2021 PSW Annual Meeting Recap

Men's and Women's Health

TOMORROW. IMAGINE THAT.

WHY PHARMACISTS MUTUAL?

For more than a century, Pharmacists Mutual has been providing specialized insurance solutions backed by solid industry insight.

- ✓ We stand with integrity beside you, our member, during your most challenging circumstances.
- ✓ Our full range of professional, business, and personal policies deliver an unmatched level of quality, choice, and protection.
- ✓ Pharmacists Mutual is your single resource for reliable, comprehensive insurance protection.

pharmacists mutual™

TOMORROW. IMAGINE THAT.

LEARN MORE AT:
phmic.com

Professional | Commercial | Personal | Life & Disability

phmic.com

Life and disability insurance are written through PMC Advantage Insurance Services, Inc., a wholly-owned subsidiary of Pharmacists Mutual Insurance Company.

November/December 2021

Continuing Education

Features

Original Work

Review Articles

Writing Club

Meeting Recap

PSW News

Spotlight

The Journal
of the Pharmacy Society of Wisconsin

Pharmacist Editor
AMANDA MARGOLIS, PharmD, MS, BCACP

Managing Editor & Creative Content Director
MEGAN GRANT, mgrant@pswi.org

Copy Editor
JENNIFER PITTERLE

CE Coordinator
PATRICIA THORNEWELL, PharmD

Peer Review Coordinators
MARISA GONINEN, PharmD, BCACP
MICHAEL NAGY, PharmD
KHYATI PATEL, PharmD
SARAH PEPPARD, PharmD, BCPS, BCCCP

ID Corner Series Coordinator
LYNNE FEHRENBACHER, PharmD, BCPS-AQ ID

Precepting Series Coordinator
MELISSA THEESFELD, PharmD

Open Access Coordinator
BRIANNA GROEN, 3rd Year PharmD Candidate

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.

Send correspondence to:
Megan Grant, Pharmacy Society of Wisconsin
701 Heartland Trail, Madison, WI 53717, phone: 608-827-9200,
fax: 608-827-9292, thejournal@pswi.org

Authors are encouraged to submit manuscripts to be considered for publication in *The Journal*. For Author Guidelines, see www.jpswi.org

Advertising inquiries:
Megan Grant, Pharmacy Society of Wisconsin, 701 Heartland Trail, Madison, WI 53717, phone: 608-827-9200, fax: 608-827-9292, mgrant@pswi.org

The Journal of the Pharmacy Society of Wisconsin is the official publication of the Pharmacy Society of Wisconsin. Subscription included in membership dues. Published bimonthly by the Pharmacy Society of Wisconsin, 701 Heartland Trail, Madison, WI 53717. Opinions expressed by contributors do not necessarily reflect those of PSW.

Up Front: Supporting our Emerging Writers

by Amanda Margolis, PharmD, MS, BCACP

One of the goals for *JPSW* has always been to foster the growth and professional development of new writers. To that end, the *JPSW* Editorial Advisory Committee (EAC) has two new exciting initiatives to announce:.

- The *JPSW* Emerging Writers Lunch & Learn Series
- Opportunities for increased communication between authors and readers

Based on a survey conducted by Dr. Mike Nagy (peer review coordinator and EAC member) the EAC determined that a structured and centralized writing program to better support *The Journal*'s student writing clubs was warranted. The EAC decided to expand this concept beyond the student writing clubs, to include any pharmacy student, resident, or interested writer. Under the direction of Dr. Cassie Sedgwick (EAC member), the *JPSW* Emerging Writers Lunch & Learn series is intended to cover foundational writing topics for students, residents, and others interested in publishing. This series is comprised of 20- to 30-minute teleconferences that are presented over the lunch hour every two weeks. The goal of this series is to help authors develop the tools needed to successfully write articles for publication.

The first three presentations have already been posted for those interested: 1) Publication Process, Authorship, and Peer Review; 2) PubMed Searching; and 3) Appropriate Paraphrasing and Use of Figures. The presentations can be found at www.pswi.org/Emerging-Writers-Course and a list of upcoming presentations can be found in Table 1.

The *JPSW* EAC's second initiative to support new writers is to create increased opportunities for connection between authors and readers. First, *The Journal* will offer corresponding authors the option to include their email addresses in their work. If readers then have additional questions or want to offer feedback, they can use this preferred contact information. Many national journals include corresponding authors' contact information; however, given the prevalence of spam email, *JPSW* will make this optional.

Next, we're introducing a new article type: a letter to the editor. The letter to the editor is intended to be used as commentary and to promote discussion of other published works in *JPSW*. (Other reflections or persuasive essays that are not editorial takes on previously published articles should continue to use the pharmacist reflection article type; you can check out our guide here for details on manuscript types.

Whether you're an emerging or expert author, I encourage you to review the 2022 and 2023 editorial plans. If you see a topic that interests you, , I encourage you to submit a manuscript to *JPSW*. (This could be a CE, a narrative review, or even a pharmacist reflection.) As you can see, even in this issue, not all articles need to follow the issue theme; so please don't feel confined by the editorial plans. Lastly, as you write, don't forget to take advantage of the resources in the *JPSW* Emerging Writers Lunch & Learn series.

- Amanda Margolis, PharmD, MS, BCACP
Pharmacist Editor, *Journal of the Pharmacy Society of Wisconsin*

TABLE 1. Emerging Writers Course Schedule

Date	Topic	Presenter	Meeting Link
11/2/21 12:30-1pm	Structuring an Introduction/ Conclusion	Cassie Sedgwick	Join Zoom Meeting https://uwmadison.zoom.us/j/96280955543?pwd=bjhWd0JnTWVXY1NLQnpsZzFhU01CZz09
11/16/21 12:30-1pm	Structuring a Paragraph	Michael Nagy	Join Zoom Meeting https://mcw-edu.zoom.us/j/91265068672?pwd=WGdRZ2YrSEpMcmI2VC8zOCs1d3NRdz09
11/30/21 12:30-1pm	Common Grammatical Errors	Jen Pitterle	Join Zoom Meeting https://uwmadison.zoom.us/j/97258147317?pwd=Q05DZ2t2QktBa1pxMWZKUkNJNE9EZz09

2022 *JPSW* Editorial Plan

Journal Issue	Issue Theme	Submission Deadline
January / February	Theme: Year in Review Series: ID Corner / Precepting Tips	Submission Deadline: October 1, 2021
March / April	Theme: Regulation & Accreditation Series: ID Corner / Precepting Tips	Submission Deadline: Dec 1, 2021
May / June	Theme: Health Disparities / Global Health Series: ID Corner / Precepting Tips	Submission Deadline: Feb 1, 2022
July / August	Theme: Cardiology Series: ID Corner / Precepting Tips	Submission Deadline: April 1, 2022
September / October	Theme: Immunizations and Emergency Preparedness Series: ID Corner / Precepting Tips	Submission Deadline: June 1, 2022
November / December	Theme: Specialty Medicine (including oncology, rheumatology, GI, etc) Series ID Corner / Precepting Tips	Submission Deadline: Aug 1, 2022

2023 *JPSW* Editorial Plan

Journal Issue	Issue Theme	Submission Deadline
January / February	Theme: A year in Review	Submission Deadline: October 1, 2022
March / April	Theme: Telehealth Series: ID Corner / Precepting Tips	Submission Deadline: Dec 1, 2022
May / June	Theme: Endocrine / Diabetes Series: ID Corner / Precepting Tips	Submission Deadline: Feb 1, 2023
July / August	Theme: Innovations in patient care Series: ID Corner / Precepting Tips	Submission Deadline: April 1, 2023
September / October	Theme: Immunizations and preventative care Series: ID Corner / Precepting Tips	Submission Deadline: June 1, 2023
November / December	Theme: Mental health / neurology Series ID Corner / Precepting Tips	Submission Deadline: Aug 1, 2023

PHARMACIST CE:

Osteoporosis: A Pathophysiology and Pharmacotherapy Review Highlighting the Parathyroid Hormone Analogues and their Place in Therapy

by Alyssa M. Schaller 2021 PharmD Candidate, Austin T. Mondloch, 2021 PharmD Candidate, Analeah N. Schwind, 2024 PharmD Candidate, Emily A. Mauer, 2022 PharmD Candidate, Sarah Ray, PharmD, BCPS, FAPhA

CE FOR **PHARMACISTS**

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

Learning Objectives

- Explain the homeostatic functions of calcium, phosphorous, and parathyroid hormone (PTH) in the body.
- Differentiate the pathophysiology behind primary and secondary osteoporosis.
- List three risk factors for the development of osteoporosis.
- Identify two nonpharmacologic treatment options for osteoporosis management.
- Compare and contrast the treatment algorithms for osteoporosis according to the National Osteoporosis Foundation (NOF) and American Association of Clinical Endocrinology (AACE) guidelines.
- Describe the place in therapy of parathyroid hormone analogues for the treatment of osteoporosis.
- Design a treatment regimen for a patient who has severe or refractory osteoporosis.

While commonly perceived as a static organ system, the bones that make up the skeletal system are as dynamic as any other organ that comprises the human body. Bones are constantly growing, restructuring, and adapting to lifestyle and environmental changes.[1] Bones remain dynamic through two cell types, osteoclasts and osteoblasts. Osteoclasts cause the demineralization of bones and help "chew" up old bone so new bone can replace it.[1] Osteoblasts cause the mineralization of bones and help build new bone in place of old bone.[1] Osteoblasts and osteoclasts remain in a dynamic equilibrium with one another, constantly replacing old bone with new bone, releasing calcium and inorganic phosphate into the bloodstream when needed, and replacing those same minerals so bones do not become too brittle.[1] When the equilibrium between these two cells is disrupted, pathologic conditions such as osteoporosis occur.

Bones serve as a mineral reservoir for the body, storing 99% and 80% of the body's supply of calcium and inorganic phosphate, respectively.[2] Calcium and inorganic phosphate are stored in bones as a crystalline complex called hydroxyapatite ($Ca_{10}(PO_4)_6(OH)_2$). Crystalline hydroxyapatite is the inorganic component of bone and accounts for about 60% of bone's composition. The remaining 40% is composed of about 10% water, and about 30% organic matter, such as proteins.[1] Bones have an array of functions, such as providing structural support and protecting vital organs. Bones also play a crucial role in maintaining mineral homeostasis.

Mineral homeostasis is maintained through the regulation of calcium resorption and deposition in the bones. Calcium is a crucial mineral in the body that carries out many physiologic and structural functions. It is regulated by parathyroid hormone (PTH), vitamin D, and calcitonin.[2] When serum calcium levels are low, PTH is released from the parathyroid gland. Parathyroid hormone inhibits osteoblast activity and activates

Abbreviations

AACE – American Association of Clinical Endocrinologists
BMD – Bone mineral density
BTM – Bone turnover markers
CCE – American College of Clinical Endocrinology
CKD – Chronic kidney disease
cAMP – Cyclic adenosine monophosphate
DM – Diabetes mellitus
DXA – Dual-energy X-ray absorptiometry
FDA – Food and Drug Administration
FRAX – Fracture Risk Assessment Tool
Fx(s) – Fracture(s)
IV – Intravenous
LS – Lumbar spine
MS – Multiple sclerosis
NOF – National Osteoporosis Foundation
NVFx(s) – Nonvertebral fracture(s)
PPI – Proton pump inhibitor
PTH – Parathyroid hormone
RA – Rheumatoid arthritis
RANKL – Receptor activator of the nuclear factor kappa-B ligand
RCT – Randomized controlled trial
RR – Risk ratio
SSRI – Selective serotonin reuptake inhibitor
SERM – Selective estrogen receptor modulator
SQ – Subcutaneous
VFx(s) – Vertebral fracture(s)
VFFx(s) – Vertebral fragility fracture(s)
WHO – World Health Organizatio

osteoclast activity, which results in increased bone resorption and release of calcium into the bloodstream.[2] Similarly, vitamin D aids in the intestinal absorption of calcium from the diet; increases in vitamin D result in decreased release of PTH, leading to an increase in serum calcium levels.[2] Calcitonin is secreted by the parafollicular cells of the thyroid gland and opposes the action of PTH.[2] When serum calcium levels are high, calcitonin is released from the thyroid gland to decrease intestinal absorption of calcium and prevent bone resorption.[2] This is achieved through inhibition of osteoclasts and activation of osteoblasts, which ultimately decreases serum calcium levels.

The interplay between PTH, vitamin D, calcium, and calcitonin, as well as the balance between osteoblast and osteoclast activity, is essential to healthy bone homeostasis. When these processes are disrupted, bone disease results and can lead to complications and decreased quality of life for patients. Osteoporosis is caused by increased osteoclast activity and decreased osteoblast activity, which leads to excessive bone demineralization.[1] The result of this osteoclast/osteoblast imbalance is brittle and porous bones, which can put patients at an increased risk for fractures.[1] Although nonpharmacologic considerations are an important aspect of osteoporosis management, pharmacologic treatment options, including bisphosphonates; the RANKL inhibitor denosumab; and the SERM raloxifene, are mainstays of treatment depending on patient history and risk.[8,10] This article will highlight the newer PTH analogues, teriparatide and abaloparatide, their mechanisms of action, as well as their place in the treatment of osteoporosis.

Pathophysiology, Epidemiology/Etiology, and Risk Factors

Osteoporosis is characterized by a decrease in bone density and mineralization, leading to porous and fragile bones that are at an increased risk of fracture. Osteoporosis is a multifactorial disease and can occur for varying reasons. Therefore, it is divided into different types: primary osteoporosis, further subdivided into type 1 and type 2; and secondary osteoporosis. Primary osteoporosis is the loss of bone density due to aging and decreased gonadal function; it is not due to any other chronic illness.[3] Type 1 primary osteoporosis occurs in postmenopausal women due to a drastic decline in estrogen production. Estrogen deficiency causes an activation of osteoclasts which leads to resorption pits in the bone. Osteoblasts cannot keep up with the high activity of osteoclasts, thus resulting in cortical and trabecular bone loss. Type 2 primary osteoporosis occurs in both men and women 70 years of age and older. It is caused by the progressive imbalance of bone resorption and formation as a result of hormone, calcium, and vitamin D deficiencies that occur with age. Like type 1, type 2 primary osteoporosis results in cortical and trabecular bone loss. Secondary osteoporosis is bone loss due to a chronic condition or medication; it is present in both men and women. Chronic conditions and medications that can lead to secondary osteoporosis are listed in Table 1.[4]

Bone strength relies heavily on bone quality and bone mineral density, which may be influenced by a variety of different factors including genetics, diet, lifestyle, hormonal status, medications and other medical conditions. Development of osteoporosis is more common with advanced age, and generally people older than 50 are most affected. Women are more likely to develop lower bone mass and osteoporosis than men. Therefore, two of the major risk factors include advanced age and gender (female). Other risk factors include race (White or Asian); body weight (less than 127 pounds) or small stature; estrogen deficiency before age 45; low physical activity; low calcium intake;

TABLE 1. Causes of Secondary Osteoporosis

Endocrine Disorders	Hyperparathyroidism or PTH excess, hyperthyroidism or thyroxine excess, hypogonadism, DM
Gastrointestinal Disorders	Inflammatory bowel disease, gastric bypass surgery, celiac disease
Hematologic Disorders	Multiple myeloma
Renal Disorders	CKD, idiopathic hypercalciuria
Autoimmune Disorders	RA, MS
Medications	Anticonvulsants, antidepressants (SSRIs), aromatase inhibitors, medroxyprogesterone, gonadotropin releasing hormone agonists, glucocorticoids, cytotoxic chemotherapy agents, thyroxine or thyroid hormone, immunosuppressants, antiretroviral agents, calcineurin inhibitors, PPIs, heparin, loop diuretics

cigarette smoking; 3 or more alcoholic beverages per day; an osteoporotic-related fracture; and rheumatoid arthritis.[5]

Patient Presentation and Diagnosis

Due to the silent nature of diminishing bone density, most patients will not present until they are post-fracture.[6] The most common areas for an osteoporotic fracture to occur are the hip, wrist, forearm, and vertebrae.[6] Patients may also present with symptoms such as pain, immobility, fear, or depression, although some fractures might also be asymptomatic.[6] Other signs of osteoporosis include shortened stature, kyphosis, lordosis, and an overall decrease in BMD.[6]

Assessment of BMD at multiple sites where osteoporotic fractures may occur is one of the most common methods for diagnosing osteoporosis.[6] DXA is considered the gold standard to predict bone mineral density and, thus, predict fracture risk.[6] Per the 2004 WHO Scientific Group on the Assessment of Osteoporosis at Primary Health Care Level, the standard for diagnosis based on BMD in men >/= 50 years old and postmenopausal women is a T-score 2.5 standard deviations or more below the normal range.[7] Per the AACE/ACE 2020 guidelines on postmenopausal osteoporosis, BMD testing is recommended in all women >/= 65 years old and younger postmenopausal women with an increased fracture risk.[8] Unless there are significant risk factors for diminished BMD, premenopausal women and otherwise healthy men are not recommended to undergo BMD measurement. BMD does remain the best indicator for fracture risk. However, BMD measurements should not be used alone. Combining BMD results with other fracture risk evaluations, such as the FRAX, might be recommended to help diagnose osteoporosis. FRAX is an algorithm applicable to men >40 years old and women at the age of menopause to calculate the 10-year probability of a hip or other osteoporotic fracture, with or without the bone mass density calculated at the femoral neck.[8] Risk factors included in FRAX are[8]:

- Ethnicity
- Age (must be between 40 and 90 years old)
- Sex
- BMI
- Family history of hip fractures
- Personal history of previous fractures considered fragile (radiographic vertebral fracture)
- Current or previous long-term glucocorticoid use
- Rheumatoid arthritis
- Current smoking

There are certain limitations to FRAX, which is why a combination of assessments to confirm diagnosis is best. FRAX does not account for how a vitamin D deficiency and recent or numerous falls might affect a patient's BMD. FRAX is also limited to patients who are treatment naïve, and assumes that a patient's fracture risk remains consistent over time.[9] Per the NOF 2014 guidelines on the prevention and treatment of osteoporosis, BMD testing should be performed via DXA in women >/= 65 years old, men >/= 70 years old, and postmenopausal women and men of younger ages who have other risk factors.[10] Based on the T-score, vertebral imaging may also be necessary. Vertebral imaging is necessary for women >/= 70 years old and men >/= 80 years old with a T-score </=-1, and postmenopausal women and men >/= 50 years old with certain risk factors, such as history of a trauma fracture, height loss, and long-term glucocorticoid treatment.[10] Annual height measurements should also be taken to observe whether there is any historical height loss of 1.5 inches or more.

Nonpharmacologic Treatment Options

There are a few non-pharmacologic treatments patients may incorporate into their lifestyles to help improve their bone health. These lifestyle modifications include limited alcohol intake, smoking cessation, weight-bearing and resistance exercise, fall prevention, and diet interventions.[6,9,11] There are several things to consider for dietary changes. As already stated, lower alcohol intake will benefit patients with osteoporosis. Excessive alcohol intake can lead to bone loss. Lowering caffeine and sodium intake will also yield some benefit. Caffeine may decrease calcium absorption, and high sodium intake will cause more calcium to be released, both of which can ultimately lead to lower bone density. Increased calcium and vitamin D may help with osteoporosis and can be found in foods like dairy products (milk, cheese, yogurt, etc.), leafy green vegetables (spinach, kale, etc.), soy beans, white beans, and certain types of fish. Patients may also consider including foods that are fortified to include more calcium, such as some orange juice and cereals. Foods that are rich in vitamin D include fatty fish (tuna, salmon, etc.), beef liver, cheese, and egg yolks. Just like calcium, there may also be certain foods fortified to include more vitamin D, such as dairy products, orange juice, and cereals.[9,11]

Calcium and Vitamin D Supplementation

Though increased dietary calcium and vitamin D intake is highly encouraged as the primary source, supplementation may be needed for most patients with osteoporosis to maintain calcium levels within normal limits. The daily recommended calcium and vitamin D supplement requirements are as follows[6,11]:

Calcium

Adolescents/Young Adults	1200-1500 mg
Men/Women Age 25-50	1000 mg
Men Age 51-70	1000 mg
Men Age >70	1200 mg
Women Age >50	1200 mg

Vitamin D

All Men	600 IU
Women Age 19-70	600 IU
Women Age >70	800 IU

Three different types of calcium are available for supplementation: calcium carbonate, calcium citrate, and tricalcium phosphate. When choosing among these types of supplements, providers and patients should consider cost, adverse effects, and patient preference. Calcium carbonate is typically the least expensive option for patients. However, this medication is best taken with food due to GI upset and requires adequate stomach acid to be well absorbed. Therefore, patients taking

stomach acid reducers such as proton pump inhibitors should refrain from using this source of calcium supplementation. For older patients, calcium citrate may be a better option, as it may be taken on an empty stomach and does not require stomach acid for absorption. Tricalcium phosphate is typically the agent used in most fortified foods and may be the most expensive supplementation option for patients. All products can cause adverse effects, including constipation, gas, and upset stomach. There is also an increased risk of kidney stone development from large calcium ingestion. Doses of calcium from all products should be limited to no more than 600 mg per dose.[6,9,11]

Treatment Guidelines

The AACE and ACE joint guidelines, along with the NOF guidelines, are the leading clinical references for guidance on the treatment of osteoporosis in men and postmenopausal women.[8,10] AACE/ACE guidelines include treatment recommendations for postmenopausal osteoporosis only, while the NOF guidelines also include recommendations for managing osteoporosis in men. The AACE/ACE and NOF guidelines differ slightly in their recommendations for when pharmacologic treatment for osteoporosis should be initiated. AACE/ACE guidelines recommend treatment initiation in patients with a T-score ≤-2.5 in the lumbar spine, femoral neck, total proximal femur, or ⅓ radius, in patients with low-trauma spine or hip fractures; and in patients with a T-score between -1 and -2.5 along with the presence of fragility fractures or high FRAX.[8] NOF guidelines recommend pharmacologic treatment initiation in patients with hip or vertebral fractures; in patients with a T-score ≤-2.5 at the femoral neck, total hip, or lumbar spine; and in men and women age 50 or older who have a T-score between -1 and -2.5 along with an elevated 10-year hip fracture probability based on FRAX.[10]

Prior to initiation of pharmacologic therapy, patients should be assessed for any secondary causes of osteoporosis, including endocrine, gastrointestinal, and medication-related causes, examples of which are listed in Table 1. Both the AACE/ACE and the NOF guidelines also recommend initiating the aforementioned nonpharmacologic treatment options, including smoking cessation, alcohol use reduction, and fracture risk assessment strategies for patients diagnosed with osteoporosis.[8,10] In addition, any calcium or vitamin D deficiencies should be corrected through diet or supplementation in order to maintain appropriate calcium intake as well as a serum 25-hydroxyvitamin D (25[OH] D) level ≥ 30ng/mL.[8,10]

The AACE/ACE guidelines include an algorithm to guide the treatment of osteoporosis in postmenopausal women, which stratifies treatment modalities based on history of fractures and risk for future fractures.[8] In patients with no history of prior fractures who are deemed to be at high risk, the bisphosphonates alendronate, risedronate, and zoledronate are considered first-line therapeutic options, along with the bone-modifying monoclonal antibody denosumab.[8] Bisphosphonates indirectly increase BMD by acting on osteoclasts and osteoclast precursors, which ultimately leads to inhibition of bone resorption.[12] Denosumab binds RANKL to prevent osteoclast formation and also leads to a decrease in bone resorption.[13] Alternative agents include the bisphosphonate ibandronate, and raloxifene, a SERM, which antagonizes bone tissue to prevent bone loss.[14] Patients should be assessed yearly for fractures and progression or improvement in BMD.[8] If there is improvement in BMD without the occurrence of fractures, clinicians should consider a drug holiday after five years of oral therapy and three years of IV therapy.[8] Therapy should be re-initiated in patients who develop fractures, have a significant decline in BMD, or have BTM that rise to pretreatment levels.[8]

Based on the AACE/ACE guidelines, high-risk patients without fracture history who have further bone loss or fracture occurrence on first-line therapies should be assessed for causes of inadequate therapeutic response.[8] Adherence, as well as the development of any secondary causes of osteoporosis, should be reviewed prior to

TABLE 2. Dosing and Administration Pearls for the Parathyroid Hormone Analogues[16,17]

Drug	*FDA Indication(s) and Dose(s)*	*Administration*
Teriparatide (Forteo)	Postmenopausal osteoporosis in women with a high fracture risk: • **Treatment:** 20mcg SQ daily Increase bone mass in males with primary or hypogonadal osteoporosis with a high fracture risk: • **Treatment:** 20mcg SQ daily Glucocorticoid-induced osteoporosis in men and women with a high fracture risk receiving ≥5mg/day of prednisone equivalent: • **Treatment:** 20mcg SQ daily	• For first administration, ensure patient is in an environment where they can sit/lie down in the event of orthostasis • Inject into thigh or abdominal wall • Can be administered without regard to time or meals • Can administer right after removal from refrigeration • Each device good for 28 days after first use • Can be used for up to 2 years
Abaloparatide (Tymlos)	Postmenopausal osteoporosis in women with a high fracture risk: • **Treatment:** 80mcg SQ daily	• For first administration, ensure patient is in an environment where they can sit/lie down in the event of orthostasis • Inject into the periumbilical region of the abdomen • Rotate injection site daily • Administer at the same time every day • Can be used for up to 2 years

therapeutic escalation. In the absence of any identifiable causes of disease progression, patients previously on oral agents should be switched to injectable antiresorptive agents, or transitioned to the parathyroid hormone analogues abaloparatide or teriparatide, or the sclerostin inhibitor romosozumab.[8] The pharmacology and mechanism of action of the parathyroid hormone analogues will be discussed shortly. Romosozumab is a monoclonal antibody that increases bone formation through activation of the Wnt/Beta-catenin signaling pathway.[15]

The AACE/ACE postmenopausal osteoporosis treatment algorithm also stratifies treatment for patients who have a history of prior fractures and are at a very high fracture risk, which includes patients who are frail, elderly, have an increased fall risk, who use glucocorticoids, or who have very low T-scores.[8] First-line agents for such patients include abaloparatide, denosumab, romosozumab, teriparatide, and zoledronate. Alternative agents include alendronate and risedronate.[8] These patients should also have yearly assessments to monitor adherence, disease progression, and fracture occurrence.[8] Patients should receive denosumab until they are no longer deemed to be very high risk, and should then be transitioned to an appropriate antiresorptive agent.[8] Romosozumab should be trialed for one year, and then patients should be transitioned to an appropriate IV or oral antiresorptive agent as well.[8] The parathyroid hormone analogues can be used for up to two years before transitioning to an antiresorptive agent, and zoledronate can be continued for up to six years before a drug holiday is recommended.[8] If patients do not respond, or experience fractures while taking zoledronate, they can be switched to a parathyroid hormone analogue or romosozumab in order to prevent further disease progression.[8]

PTH Analogue Pharmacology, Dosing, and Administration

The parathyroid hormone analogues teriparatide and abaloparatide are both FDA-approved for the treatment of postmenopausal osteoporosis in women with a high risk for fractures. Teriparatide is also FDA-approved to increase bone mass in men with hypogonadal osteoporosis, along with glucocorticoid-induced osteoporosis in both men and women. These agents contain a recombinant amino acid sequence that is identical to the N-terminal of parathyroid hormone, and thus increase BMD and bone mass through stimulation of osteoblast function.[16,17] Teriparatide and abaloparatide achieve their pharmacologic activity by increasing the concentration of cAMP upon binding to the PTH Type 1 receptor.[18] Although analogues of PTH, teriparatide and abaloparatide have a lesser effect on calcium compared to endogenous PTH.[18] Adverse effects of these agents include, headache, dizziness, nausea, and an increased risk for osteosarcoma.[16,17] In addition, their duration of therapy should not exceed 24 months.[16,17]

The Fracture Prevention Trial was the first randomized controlled trial that assessed the efficacy of teriparatide for the treatment of osteoporosis in postmenopausal women.[19] Neer and colleagues found that teriparatide could significantly reduce the incidence of VFxs and NVFxs by 65% and 53%, respectively, compared to placebo.[19] They also compared different doses of teriparatide, and found that both the 20mcg dose and the 40mcg dose significantly increased BMD at the LS, femoral neck, trochanter, intertrochanter, and total hip ($p<0.001$).[19] Originally planned for a duration of 24 months, the study was discontinued early due to the incidence of osteosarcoma in long-term rat toxicology studies.[19] The average treatment duration was 18 months; however, no human cases of osteosarcoma were reported.[19]

The VERO trial compared teriparatide 20ug daily versus risedronate 35mg weekly for the prevention of new VFx in postmenopausal women with osteoporosis.[20] Treatment lasted for up to 24 months, and subgroup analyses were performed to stratify outcomes based on the number of prevalent VFFxs, the severity of Fxs, the number of prevalent NVFxs, the use of glucocorticoids, and a history of prior pharmacologic treatment for osteoporosis.[20] For the entire study population, VFxs occurred in 5.4% of women in the teriparatide group and 12.0% in the risedronate group, with a RR 0.44 (95% CI: 0.29-0.68; $p=0.000094$).[20] Overall, about half as many patients who received teriparatide experienced a VFx compared to patients who had received risedronate.

The ACTIVE trial was a Phase III, double-blind, international RCT that compared the incidence of new VFx and NVFxs in osteoporotic postmenopausal women treated with either abaloparatide or placebo.[21] Postmenopausal women ≥65 years of age fulfilling the fracture and T-score criteria (≤2.5 SD and >5 SD) or those with severe osteoporosis without fracture (≤3.0 SD but >5 SD) were enrolled.[21] Abaloparatide treatment reduced the absolute risk of new morphometric VFx by 3.6% (0.6% vs. 4.2%) compared to placebo, corresponding to a relative risk reduction of 86% ($P < 0.001$).[21] Abaloparatide treatment after 18 months increased BMD for the total hip, femoral neck, and LS by 4.25%, 4.01%, and 10.4%, respectively, compared to placebo.[21]

The ACTIVExtend trial further expanded on the findings of the ACTIVE trial, and showed that patients who received alendronate after abaloparatide had a reduced risk of fracture at total hip, femoral neck, and LS compared to patients that had received placebo prior to alendronate therapy.[22] In addition, BMD at the spine and total hip continued to increase during the 24-month alendronate treatment period following the initial 18 months of abaloparatide therapy.[22] Discontinuation of abaloparatide led to more serious events in 9.9% of patients compared to placebo (6.1%) or teriparatide (6.8%).[22] Table 2 includes the specific dosing and administration recommendations for the FDA-approved indications for teriparatide and abaloparatide.

Conclusion

Osteoporosis is a spectrum of bone disease characterized by compromised bone integrity and an increased risk for fractures.[10] The development of osteoporosis is multifactorial, and often involves an interplay between environmental, genetic, and hormonal factors.[8,10] BMD measured through DXA is considered the gold standard for the diagnosis of osteoporosis, although FRAX can also be a useful tool to stratify fracture risk.[7] The NOF and the AACE/ACE guidelines provide recommendations on both nonpharmacologic and pharmacologic treatment approaches to osteoporosis, with an emphasis on ruling out secondary causes of osteoporosis and addressing underlying

calcium and vitamin D deficiencies prior to pharmacologic treatment initiation.[8,10]

Available as SQ formulations, teriparatide and abaloparatide are reserved for treatment-resistant and more severe cases of osteoporosis.[8] In patients without prior fracture history who are at a high risk for developing fractures, teriparatide and abaloparatide are second-line options for those who have worsening disease on first-line therapeutic options, such as bisphosphonates or denosumab.[8] In high-risk patients with a history of fractures, teriparatide and abaloparatide are considered first-line treatment options. Treatment duration of these agents is, however, limited to 2 years, at which point patients should be transitioned to an appropriate antiresorptive therapy.[8,16,17]

Alyssa Schaller and Austin Mondloch are Doctor of Pharmacy Graduates from the Concordia University of Wisconsin School of Pharmacy in Mequon, WI. Analeah Schwind is a 2nd Year Doctor of Pharmacy Candidate and Emily Mauer is a 4th Year Doctor of Pharmacy Candidate at the Concordia University of Wisconsin School of Pharmacy in Mequon, WI. Sarah Ray is an Associate Professor at the Concordia University of Wisconsin School of Pharmacy in Mequon, WI.

PR *This article has been peer-reviewed. The contribution in reviewing is greatly appreciated!*

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

References

1. Bonjour JP. Calcium and phosphate: a duet of ions playing for bone health. *J Am Coll Nutr.* 2011;30(5 suppl 1):438S-48S. doi:10.1080/07315724.2011.10719988
2. Feng X. Chemical and biochemical basis of cell-bone matrix interaction in health and disease. *Curr Chem Biol.* 2009;3(2):189-196. doi:10.2174/187231309788166398
3. Emily E. Nuss MD, Rachel Wright Heinle MD. Osteoporosis. In: Fred F. Ferri, eds. Ferri's Clinical Advisor 2021. *Elsevier*. 2020:1015-1019.e2.
4. Mirza F, Canalis E. Management of endocrine disease: secondary osteoporosis: pathophysiology and management. *Eur J Endocrinol.* 2015;173(3):R131-R151. doi:10.1530/EJE-15-0118
5. Phillips B. Osteoporosis in: Pharmacotherapy Principles and Practice. 2nd ed. New York, NY: McGraw Hill; 2010.

Patient Case

The patient (known as "PB") is a 71-year-old, postmenopausal (at age 53), White female. She has a history of high blood pressure, COPD, and GERD. No history of fracture. Her current medications include amlodipine 5 mg po daily, Combivent Respimat® 1 puff QID, hydrochlorothiazide 25 mg po daily, and pantoprazole 40 mg po daily. She does not take any over-the-counter medications. She denies any medication allergies or adverse drug reactions. Her calcium intake from her diet is estimated to be 200 mg daily.

She does not regularly exercise. She walks once weekly for 20 minutes.
Caffeine: 3 cups per day
Alcohol: 1 drink (wine or beer) 3 days per week
Tobacco: Former smoker, smoked 1 ppd for 15 years, quit 40 years ago.
Illicit drugs: Denies
PB weighs 120 pounds and is 63 inches tall.

Labs		**Reference Range**
WBC	6.7	3.7-10.5 k/mm3
Hemoglobin	14.2	11.9-15.5 g/dL
Hematocrit	41%	35-47%
Platelets	289	50-400 k/mm3
Red Blood Count	4.4	4.0-5.2 millions/mm3
RDWCV	11.3	9.0-14.5%
RDWSD	40.2	36.4-46.3 fL
MCV	88	82-99 femtoliters
MPV	10.9	9.4-12.3 fL
MCH	29	25-35 picograms
MCHC	33	32-36 g/dL RBC
Albumin	4.2	3.4-5.4 g/dL
Alk Phos	63	20-130 U/L
ALT	19	4-36 U/L
AST	22	8-33 U/L
BUN	16	6-20 mg/dL
Calcium	8.2	8.5-10.2 mg/dL
Chloride	100	96-106 mEq/L
CO2	25	23-29 mEq/L
Creatinine	1.2	0.6-1.3 mg/dL
Glucose	94	70-100 mg/dL
Potassium	4.3	3.7-5.2 mEq/L
Sodium	140	135-145 mEq/L
Total bilirubin	0.8	0.1-1.2 mg/dL
Total Protein	7.1	6-8.3 g/dL
TSH	4.2	0.5-6 uU/mL
Free T4	1.1	0.7-1.9 ng/dL
Free T3	400	230-619 pg/d
Total Cholesterol	190	125-199 mg/dL
LDL	80	<100 mg/dL
Triglycerides	140	<150 mg/dL
HDL	58	>50 mg/dL
Vitamin D	33 ng/mL	>20 ng/mL
T score (DXA spine)	-2.9	
T score (DXA femoral neck)	-2.7	
Creatinine Clearance	37 mL/min	

6. O'Connell M, Vondracek S. Osteoporosis and other metabolic bone diseases in : Pharmacotherapy: A Pathophysiologic Approach. 7th ed. New York, NY: McGraw Hill; 2008.
7. WHO Scientific Group on the Assessment of Osteoporosis at Primary Health Care Level. Published May 2004. https://www.who.int/chp/topics/Osteoporosis.pdf
8. Camacho PM, Petak SM, Binkley N, et al. American Association Of Clinical Endocrinologists/American College Of Endocrinology clinical practice guidelines for the diagnosis and treatment of postmenopausal osteoporosis-2020 update. *Endocr Pract*. 2020;26(suppl 1):1-46. doi:10.4158/GL-2020-0524
9. Rottman-Sagebiel R. Osteoporosis in : Koda-Kimble and Young's applied therapeutics: the clinical use of drugs. 10th ed. Philadelphia, PA: Lippincott Williams and Wilkins; 2013.
10. Cosman F, de Beur SJ, LeBoff MS, et al. Clinician's guide to prevention and treatment of osteoporosis [published correction appears in *Osteoporos Int.* 2015 Jul;26(7):2045-7]. *Osteoporos Int.* 2014;25(10):2359-2381. doi:10.1007/s00198-014-2794-2
11. Phillips B. Osteoporosis in: Pharmacotherapy Principles and Practice. 2nd ed. New York, NY: McGraw Hill; 2010.
12. Alendronate. Lexicomp. Wolters Kluwer. Updated December 18, 2020. Accessed January 3, 2021.
13. Denosumab. Lexicomp. Wolters Kluwer. Updated December 15, 2020. Accessed January 3, 2021.
14. Raloxifene. Lexicomp. Wolters Kluwer. Updated December 25, 2020. Accessed January 3, 2021.
15. Romosozumab. Lexicomp Wolters Kluwer. Updated December 13, 2020. Accessed January 26, 2021.
16. Teriparitide. Lexicomp. Wolters Kluwer. Updated December 18, 2020. Accessed January 3, 2021.
17. Abaloparatide. Lexicomp. Wolters Kluwer. Updated December 13, 2020. Accessed January 3, 2021.
18. Tella SH, Kommalapati A, Correa R. Profile of abaloparatide and its potential in the treatment of postmenopausal osteoporosis. *Cureus*. 2017;9(5):e1300. doi:10.7759/cureus.1300
19. Neer RM, Arnaud CD, Zanchetta JR, et al. Effect of parathyroid hormone (1-34) on fractures and bone mineral density in postmenopausal women with osteoporosis. *N Engl J Med.* 2001;344(19):1434-1441. doi:10.1056/NEJM200105103441904
20. Geusens P, Marin F, Kendler DL, et al. Effects of teriparatide compared with risedronate on the risk of fractures in subgroups of postmenopausal women with severe osteoporosis: The VERO Trial. *J Bone Miner Res*. 2018;33(5):783-794. doi:10.1002/jbmr.3384
21. Miller PD, Hattersley G, Riis BJ, et al. Effect of abaloparatide vs placebo on new vertebral fractures in postmenopausal women with osteoporosis: a randomized clinical trial [published correction appears in *JAMA.* 2017 Jan 24;317(4):442]. *JAMA.* 2016;316(7):722-733. doi:10.1001/jama.2016.11136
22. Bone HG, Cosman F, Miller PD, et al. ACTIVExtend: 24 months of alendronate after 18 months of abaloparatide or placebo for postmenopausal osteoporosis. *J Clin Endocrinol Metab*. 2018;103(8):2949-2957. doi:10.1210/jc.2018-00163

Assessment Questions

1. Which of PB's lab values is the most important to assess when evaluating PB for osteoporosis?
   a. Calcium
   b. Creatinine
   c. TSH
   d. Vitamin D

2. Which of the following medications could be contributing to PB's osteoporosis?
   a. Amlodipine
   b. Combivent®
   c. Hydrochlorothiazide
   d. Pantoprazole

3. How many risk factors for osteoporosis does PB have?
   a. 2
   b. 3
   c. 6
   d. 11

4. What is an appropriate calcium and vitamin D regimen to recommend for PB?
   a. Calcium carbonate 1200mg PO once daily and vitamin D 800 units once daily
   b. Calcium citrate 1200mg PO once daily and no vitamin D
   c. Calcium citrate 500mg PO BID and vitamin D 800 units once daily
   d. No supplementation is necessary

5. **True or False:** According to the AACE/ACE 2020 Postmenopausal Osteoporosis Treatment Algorithm, PB is considered at very high risk.
   a. True
   b. False

6. Which of the following is an appropriate first-line therapy for PB?
   a. Alendronate 70mg PO once weekly
   b. Calcitonin 200units IN daily
   c. Romosozumab 210mg SQ once monthly
   d. Teriparatide 20mg SQ once daily

7. Three years later, PB is admitted with a vertebral fracture, and her T-score is -3.4. PB's physician decides to start teriparatide 20mg SQ once daily. What is the expected length of teriparatide therapy?
   a. 6 months
   b. 1 year
   c. 2 years
   d. 5 years

8. Which of the following adverse effects is associated with teriparatide?
   a. Cardiac disorders
   b. Hypocalcemia
   c. Orthostatic hypotension
   d. Osteonecrosis of the jaw

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

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

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

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

17. If you answered "no" to question 16, please comment (email info@pswi.org).

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

Continuing Education Credit Information

The Pharmacy Society of Wisconsin is accredited by the Accreditation Council for Pharmacy Education as a provider of continuing pharmacy education. Continuing education credit can be earned by completing the self assessment questions. Questions may be completed online at www.pswi.org or by mailing completed answer form to PSW, 701 Heartland Trail, Madison, WI 53717. Participants receiving a score of 70% or better will be granted 0.75 hour (0.075 CEU) credit through CPE Monitor within 60 day of quiz completion. Accurate birth date (MMDD) and CPE Monitor ID must be provided in order to receive this credit as required by ACPE.

This CE offering is offered free-of-charge to all PSW members. Nonmembers are charged $20 for each exam submitted to cover administrative costs.

Submit Your CE Online!

www.pswi.org/Education/Journal-CE

Quiz Answer Form

circle one answer per question

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

November/December 2021
Osteoporosis: A Pathophysiology and Pharmacotherapy Review Highlighting the Parathyroid Hormone Analogues and their Place in Therapy

ACPE Universal Activity Number: 0175-0000-21-122-H04-P

Target Audience: Pharmacists
Activity Type: Knowledge-based
Release Date: November 1, 2021
(No longer valid for CE credit after November 1, 2024)

Name_____Designation (RPh, PharmD, etc.)_____

CPE Monitor #_____ DOB (MMDDYY)_____

Preferred Mailing Address_____

City_____State_____ Zip _____

Is this your home ☐ or work ☐ address?

ID CORNER

A Case of Varicella Zoster Virus Reactivation Post COVID-19 Immunization

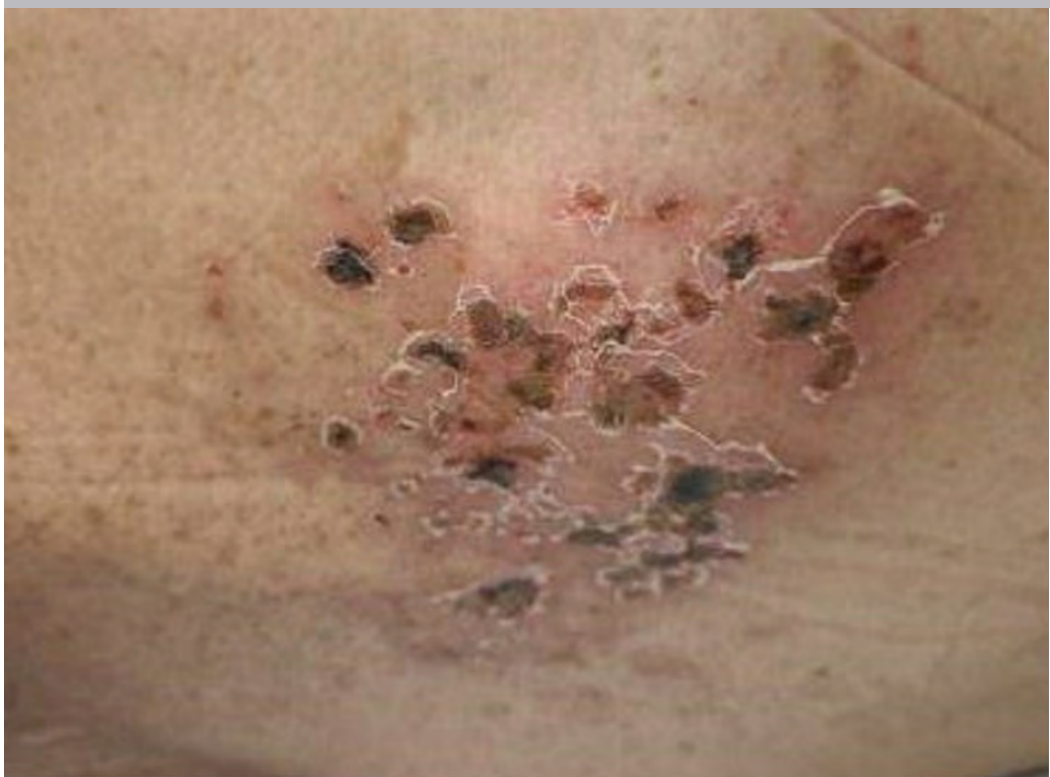
by Aaron Klysen, BSPS, 2022 PharmD Candidate, Kasey Arnhoelter, PharmD, BCPS

Recent efforts to slow the COVID-19 pandemic have focused largely on immunization. With COVID-19 vaccines being readily available, approximately 55% of the United States population is now fully vaccinated, with many citizens having received one of the two available mRNA products. Both mRNA vaccines, produced by Pfizer and Moderna, have proven to be safe and effective in clinical trials.[1,2] Since their introduction to the public, under Food and Drug Administration Emergency Use Authorization, the Vaccine Adverse Events Reporting System (VAERS) has continued to collect data on adverse events surrounding COVID-19 vaccination. Furthermore, anecdotal case reports have been published throughout the vaccination period on potential, but rare, adverse effects. Below, we present a case of herpes zoster status –post-COVID-19 vaccination with Pfizer's BNT162b2 vaccine.

A 67-year-old male presented to the hospital with an erythematous, blistering rash under the right axilla, reported to have developed over the past week. Significant past medical history for the patient included renal transplant with subsequent immunosuppression using tacrolimus and prednisone; hypertension; and type II diabetes mellitus. It was noted that the patient received his second dose of Pfizer's BNT162b2 mRNA COVID-19 vaccine 29 days prior to the rash development. Upon physical examination, the rash appeared macerated with scab formation, and the patient reported associated pain and fatigue. The patient was diagnosed with herpes zoster and prescribed both oral valacyclovir 1 gram 3 times daily and oral cephalexin 500 mg 3 times daily for 7 days. The lesions became dry and closed within 3 weeks, with pain persisting for several months. Of note, the patient had not been vaccinated against herpes zoster in the past.

After primary infection, often manifested as chicken pox, varicella zoster virus (VZV) resides latently in the dorsal-root ganglia and cranial-nerve.[3] Potential reactivation as herpes zoster, typically in older persons and immunocompromised states, often leads to the development of painful cutaneous lesions. Neurologic complications of herpes zoster may include postherpetic neuralgia, cranial or peripheral nerve palsies, meningitis, or encephalitis.[4] Although a direct link between VZV reactivation and COVID-19 immunization has not been established, several case reports have been identified in literature. This includes herpes zoster development post-mRNA inoculation in individuals taking immunosuppressive medications, similar to our case.[5] In a systematic review of herpes zoster activation post-COVID-19 vaccination, the mean time to symptom onset was 4-9 days post-vaccination across included studies, earlier than our case.[6] Furthermore, the systematic review highlighted an imbalance in the number of patients presenting with active herpes zoster after each dose of the studied 2-dose vaccines, with more patients developing active infection after the first dose. Currently, case reports of herpes zoster development post-COVID-19 inoculation include reports related to Astrazeneca-Oxford's ChAdOx1 vaccine, Pfizer's BNT162b2 vaccine, and Moderna's mRNA-1273 vaccine.[7] However, the mRNA-based products, particularly from Pfizer, have been implicated in most of the presently available case reports, possibly owing to its higher global utilization.[8-11] No report of post-inoculation herpes zoster development in phase 3 trial data for any vaccine was

Below: *67-year-old male noted to have macerated rash with scab formation post VZV treatment with valacyclovir.*



found.[1,2,12]

In conclusion, more research is needed before establishing any concrete association between herpes zoster and COVID-19 immunization. While dozens of herpes zoster cases status-post COVID-19 inoculation have been described in literature, primarily from mRNA-based products, no definitive link has been identified. Thus, it cannot be said with certainty whether the case presented today is the result of COVID-19 immunization or mere coincidence.

Aaron Klysen is a 4th Year Doctor of Pharmacy Candidate at the University of Wisconsin-Madison School of Pharmacy in Madison, WI. Kasey Arnhoelter is a Clinical Pharmacy Coordinator at Advocate Aurora Health.

Corresponding Author: kasey.arnhoelter@aah.org.

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

PR *This article has been peer-reviewed. The contribution in reviewing is greatly appreciated!*

References

1. Baden LR, El Sahly HM, Essink B, et al. Efficacy and safety of the mRNA-1273 SARS-CoV-2 vaccine. *N Engl J Med.* 2021;384(5):403-416. doi:10.1056/NEJMoa2035389
2. Polack FP, Thomas SJ, Kitchin N, et al. Safety and efficacy of the BNT162b2 mRNA covid-19 vaccine. *N Engl J Med.* 2020;383(27):2603-2615. doi:10.1056/NEJMoa2034577
3. Gilden DH, Kleinschmidt-DeMasters BK, LaGuardia JJ, et al. Neurologic complications of the reactivation of varicella-zoster virus. *N Engl J Med.* 2000;342(9):635-645. doi:10.1056/NEJM200003023420906
4. Clinical overview of herpes zoster (shingles). Centers for Disease Control and Prevention. Published October 5, 2020. Accessed September 23, 2021. https://www.cdc.gov/shingles/hcp/clinical-overview.html#complications
5. Furer V, Zisman D, Kibari A, et al. Herpes zoster following BNT162b2 mRNA covid-19 vaccination in patients with autoimmune inflammatory rheumatic diseases: a case series. *Rheumatology.* 2021;keab345. doi:10.1093/rheumatology/keab345
6. Katsikas Triantafyllidis K, Giannos P, Mian IT, et al. Varicella zoster virus reactivation following covid-19 vaccination: a systematic review of case reports. *Vaccines.* 2021; 9(9):1013. https://doi.org/10.3390/vaccines9091013
7. Alpalhão M, Filipe P. Herpes zoster following SARS-CoV-2 vaccination - a series of four cases. *J Eur Acad Dermatol Venereol.* 2021;10.1111/jdv.17555. doi:10.1111/jdv.17555
8. Eid E, Abdullah L, Kurban M, et al. Herpes zoster emergence following mRNA covid-19 vaccine. *J Med Virol.* 2021;93(9):5231-5232. doi:10.1002/jmv.27036
9. Santovito LS, Pinna G. A case of reactivation of varicella-zoster virus after BNT162b2 vaccine second dose? *Inflamm Res.* 2021;70(9):935-937. doi:10.1007/s00011-021-01491-w
10. Channa L, Torre K, Rothe M. Herpes zoster reactivation after mRNA-1273 (Moderna) SARS-CoV-2 vaccination. *JAAD Case Rep.* 2021;15:60-61. doi:10.1016/j.jdcr.2021.05.042
11. Ritchie H, Mathieu E, Rodés-Guirao L, et al. Coronavirus (COVID-19) vaccinations - statistics and research. Our World in Data. Published March 5, 2020. Accessed September 29, 2021. https://ourworldindata.org/covid-vaccinations
12. Voysey M, Clemens SAC, Madhi SA, et al. Safety and efficacy of the ChAdOx1 nCoV-19 vaccine (AZD1222) against SARS-CoV-2: an interim analysis of four randomised controlled trials in Brazil, South Africa, and the UK. *Lancet.* 2021;397(10269):99-111. doi:10.1016/S0140-6736(20)32661-1

WISCONSIN PHARMACY QUALITYCOLLABORATIVE
an initiative of the pharmacy society of wisconsin

Impact of the United Way and PSW Collaboration to Bring Pharmacist Comprehensive Medication Reviews to Community Settings

by Kara Mudd, PharmD, Samuel Taylor, Emily Jaeger, PharmD, Colin Pearson, PharmD, Kari Trapskin, PharmD, Helene McDowell, MS, Amanda Margolis, PharmD, MS, BCACP

Comprehensive medication reviews (CMRs) delivered by community pharmacists are known to improve clinical outcomes, as demonstrated by a review including 35 systematic reviews.[1] This is especially true for improvements in outcomes for patients with diabetes, hypertension, or hypercholesterolemia. Kallio and colleagues also conducted a systematic review that demonstrated the positive effect of interventions and recommendations identified during community-based CMRs on reducing the incidence of adverse drug events (ADEs) and improving overall patient health outcomes.[2] Despite the benefits of pharmacist-conducted CMRs, not all eligible patients are able to participate.[2,3] For example, one community pharmacy experienced a 25% dropout rate, with lack of time and becoming household bound among the top reasons for patients being unable to access a CMR.[4]

In Wisconsin, two organizations are working together to provide one of the most populous counties with a way to access CMRs using a novel community model. In Dane County, Wisconsin, The Pharmacy Society of Wisconsin (PSW) and The United Way of Dane County (UWDC) have been working together since 2011 to reach patients through the provision of CMRs by Wisconsin Pharmacy Quality Collaborative (WPQC)-certified pharmacists at convenient locations for patients.[5,6] By bringing pharmacists to convenient community-based locations instead of requiring patients to travel to a pharmacy, the goal of this service was to increase the number of patients who have access to CMRs.

WPQC is "a network of accredited pharmacies throughout Wisconsin that are committed to higher standards of medication management, patient education, quality assurance and patient safety."[7] Pharmacists undergo additional training by PSW to provide CMRs to complex patients with multiple chronic conditions in order to become WPQC-certified. The community-based CMRs offer patients a one-on-one, 60-minute appointment with a WPQC-certified pharmacist to assess adult medication regimens, including use of prescription and over-the-counter (OTC) medications, use of supplements, lifestyle factors, and individual patient goals. The pharmacist listens to and addresses patient concerns, then makes recommendations to both the patient and their primary care provider with the goal of preventing ADEs, reducing fall risk, and improving the patient's quality of life. The objective of this evaluation was to determine the number of community-based CMRs delivered, the types of interventions recommended by pharmacists, and patient satisfaction from the community-based CMR program.

Methods

Community-based organization (CBO) partners that participated in this program were identified and engaged based on their organizational mission and the populations they served. Initially, partners included senior centers and neighborhood senior coalitions. However, as the program grew, new CBO partners included neighborhood community centers, churches, and various social service agencies. The PSW program coordinator and the WPQC-certified pharmacists traveled to community settings to provide the CMRs. Wisconsin Medicaid provided authorization and compensation for CMRs provided to eligible Medicaid recipients.

The PSW program coordinator and the community partner collaborated to

TABLE 1. Baseline Characteristics

Age	#	%
50-59	28	19.6
60-69	26	18.2
70-79	35	24.5
80-89	32	22.4
90+	8	5.6
Not Reported	14	9.8
Sex	**#**	**%**
Female	98	68.5
Male	39	27.3
Not Reported	6	4.2
Race/Ethnicity	**#**	**%**
Caucasian	86	60.1
African American	44	30.8
Asian	1	0.7
Latino	1	0.7
Not Reported	11	7.7
Number of Persons Living in Home	**#**	**%**
1	46	32.2
2	32	22.4
3 or more	13	9.1
Not Reported	52	36.4
Who Manages the Patient's Medications	**#**	**%**
Self	72	50.3
Spouse/Significant Other	7	4.9
Professional Service	6	4.2
Child	3	2.1
Other	4	2.8
Not Reported	51	35.7
Number of Medications Taken (Mean +/- SD)	**# ± SD**	
Prescription (n=107)	7.3 ± 4.3	
Over-the-Counter (n=106)	3.4 ± 3.2	

TABLE 2. Pharmacist-proposed Interventions by Category

Proposed Intervention	#	%
Medication Addition	90	20.7
Immunization	89	20.5
Medication Device Instruction/Education	71	16.4
Dose/Dosage Form/ Duration Change	54	12.4
Medication Deletion	46	10.6
Adherence	34	7.8
Therapeutic Interchange	27	6.2
Labs Due	15	3.5
Dose Consolidation	8	1.8

provide this unique community-based CMR model in neighborhoods where at-risk, underserved, and older adults lived. The program coordinators served as education, outreach, and intake coordinators. CMRs were initially offered to individuals age 60 or older; however, following discussions with the CBOs, coordinators realized there was a greater need for the program. The criteria were expanded to include low-income and older adults with complex medication regimens in Dane County.

Patient information (demographics, income, primary care provider(s), pharmacy information, Medicaid or other insurance status, falls risk assessment data, and HIPAA authorization) was collected and provided to the pharmacist prior to the CMR. This information informed the pharmacist about the patients, and helped ensure that the appropriate number of WPQC-certified pharmacists were recruited for each day. Of note, this program also included UW-Madison pharmacy students, who assisted the pharmacists in the patient intake process.

Each visit began with patient intake by the PSW program coordinator, during which the patient was educated about the visit, was given HIPAA privacy notices, and consented to the service. The pharmacist then conducted the CMR using an approved electronic documentation platform and any written materials per their professional judgement. For the purposes of this evaluation, the pharmacists also had paper forms to record the nature of their recommended interventions. Patients were initially asked for their personal goals, and pharmacists followed a standardized process within the clinical documentation platform. PSW pharmacy student interns received the list of pharmacist recommendations for each patient seen at a community CMR event, and recorded and categorized the interventions.

The primary outcome of this evaluation was the number of CMRs the service was able to provide. Secondary outcomes included the recommended interventions, and patient satisfaction. Recommended interventions were documented by the pharmacists during the CMRs. Intervention categories included adherence, dose consolidation, dose/dosage form/duration change, labs due, medication addition, medication deletion, medication device instruction/education, immunization, and therapeutic interchange. Patient satisfaction was measured via a patient interview with the PSW program coordinator. Patient satisfaction with pharmacist performance during the CMR visit was measured using a satisfaction survey consisting of seven questions using a five-point scale (poor, fair, good, very good, and excellent). This was collected following the CMR appointment but prior to the patient leaving.

Following the CMR, patients were contacted via telephone by PSW pharmacy student interns at 14, 30, and 90 days post-CMR. Each telephone call was attempted up to three times. During this interview, the PSW student intern would determine the patient's acceptance of pharmacist recommendations. A script was used to collect this information (available upon request) and the information was documented in REDCap, a HIPAA-compliant web-based database.[8] Given the difficulty of consistently contacting patients via phone, many patients received a 14- or 30-day phone call, and therefore only the 30-day results are reported. Descriptive statistics were calculated as means and counts. As this project was undertaken for programmatic evaluation, it did not meet the federal definition of research and per the UW-Madison Health Sciences IRB, full IRB review was not required.

Results

An initial pharmacist visit was documented for a total of 143 patients, and 102 patients (71.3%) responded to the one-month follow-up call between April of 2019 and January of 2020. To offer this service, 15 pharmacists and 22 pharmacy student volunteers served patients at 12 community-based locations. The patients enrolled in this program were predominately female (68.5%) and had approximately even representation across the decades aged 50–89 years, with only 5.6% of patients aged 90 years or older (Table 1). The majority of patients lived alone (32.2%) or with one other person (22.4%). Most patients managed their own prescriptions (50.3%), with others receiving help from family members or professional services. Patients reported taking an average of 11 medications. This included a mean of 7.3 ± 4.3 prescription medications and a mean of 3.4 ± 3.2 over-the-counter medications.

Pharmacists made 434 recommendations during the community-based CMRs (Table 2). This was a mean of 3 recommendations

TABLE 3. Patient Satisfaction with Pharmacist Performance During CMR (% Patients Responding)

Survey Question	Poor	Fair	Good	Very Good	Excellent
Pharmacist's ability to answer your questions?	0.0	0.0	7.1	23.1	69.8
Pharmacist's ability to provide you with information about your medicines?	0.0	0.5	6.6	29.1	63.7
Pharmacist helping you to understand the purpose of your medicines?	0.6	0.0	5.1	27.0	67.4
Pharmacist helping you to understand how to take your medicines to prevent problems?	0.6	0.0	6.9	25.7	66.9
Pharmacist's ability to be clear when explaining suggested changes to your medicines?	0.0	0.0	6.6	25.7	67.7
Overall care you received from the pharmacist?	0.0	0.0	3.8	22.5	73.6

Of note, instances where participants chose not to answer a question are removed from the percentages.

per patient. Medication additions (90) and immunizations (89) were the two most frequent recommendations made by the pharmacists. Pharmacists also frequently recommended or provided medication device instruction/education (71), a change in dose/dosage form/or duration (54), and medication deletions (46). Of the recommendations with a known definitive outcome at the 30-day follow-up call, 162 (74%) were accepted and implemented while 57 (26%) had been declined.

When surveyed following the CMRs, patients reported high levels of satisfaction regarding the pharmacist's performance (Table 3). The majority of patients ranked the pharmacist's performance as "excellent" for each aspect of performance, and greater than 90% of patients ranked the performance as "very good" or "excellent" across each criterion.

Discussion

The outcomes of this community-based CMR service demonstrate the impact pharmacists can have on increasing patient access to CMRs and optimizing medication regimens in at-risk patient populations. By traveling to convenient locations for patients, pharmacists were able to make significant interventions and reach patients who might not have been able to go to a pharmacy. Additionally, the rate of accepted interventions in this evaluation was consistent with previously published literature. In a systematic review by Kallio and colleagues, 76% of pharmacist-recommended interventions were accepted, which was similar to the percentage after this community-based CMR service of 74%.[2]

Notably, pharmacists were able to provide numerous recommendations for patient intervention, including both medication and non-medication recommendations. The most common medication recommendations provided were the addition of a medication or a dose and/or dosage form change. The most frequent non-medication recommendations were for immunizations and education on how to use a medication device. Based on these results, our community-based CMR service proved to be useful, as a majority of patients accepted and implemented the pharmacist-proposed interventions.

Overall, patients appeared to be satisfied with pharmacist performance during CMRs, rating the majority of components on the satisfaction survey as "excellent" or "very good." Patients were most satisfied with the pharmacist's ability to answer questions and clearly explain recommended interventions. Some respondents (0.5%) gave a "fair" rating to "pharmacist's ability to give you information about your medications." Improvements could be made in this area, perhaps by encouraging more incorporation of motivational interviewing techniques into this component of the CMR, and by using methods such as "teach-back" to ensure patient understanding. The "teach-back technique" allows providers to assess patient comprehension, providing increased patient satisfaction during patient-provider interactions.[9]

There were several limitations to this service model. First, the size of the cohort included in the analysis was relatively small and comprised of a limited population of patients who had the ability to visit the senior centers where the CMRs were conducted. Additionally, numerous patients were lost to follow-up, which limited the ability to determine whether those patients implemented the recommended interventions. One factor that may have reduced the number of patients reached for follow-up was the limited availability of pharmacy interns to conduct calls on a regular basis. Furthermore, when conducting CMRs, we did not ask pharmacists to specify the medication changes in a measurable way. This information could have provided details on potentially preventable ADEs. Lastly, our work did not include a control arm, which restricted our ability to determine whether our delivery method further improved patient outcomes compared to the traditional method of having the patient travel to the pharmacy for CMR services.

In the future, we hope to expand delivery of our services in order to improve access for patients to attend CMR events. Possible methods to do so include providing services at additional community sites outside of Dane County, offering in-home visits, and creating a telehealth option. Additionally, we see the potential to extend our services to younger populations who are considered at high-risk, with resources and funding available from the Wisconsin ForwardHealth (Medicaid) Medication Therapy Management program, in addition to UWDC. Lastly, we hope to better balance resources and staff availability to improve our overall follow-up with patients after making initial interventions.

Conclusions

This unique CMR delivery method has been demonstrated to be an effective way to provide services to at-risk patient populations. Further expansion of services and more consistent follow-up with patients is necessary to provide more detailed information on the impact of this service to reduce ADEs in at-risk patient populations.

Kara Mudd is a PGY-1 General Practice Pharmacy Resident at the William S. Middleton Memorial Veterans Hospital in Madison, WI. Samuel Taylor is a 4th Year Doctor of Pharmacy Candidate at the University of Wisconsin-Madison School of Pharmacy in Madison, WI. Emily Jaeger is a PGY1 HSPAL Resident at M Health Fairview - University of Minnesota Medical Center in Minneapolis, MN. Colin Pearson is a PGY-2 HSPAL Resident at the University of Minnesota Medical Center-Fairview-East Bank in Minneapolis, MN. Kari Trapskin is the Vice President of Health Care Quality Initiatives at the Pharmacy Society of Wisconsin in Madison, WI. Helene McDowell, is the Senior Manager of Pharmacy Quality and Community Outreach at the Pharmacy Society of Wisconsin in Madison, WI. Amanda Margolis is an Assistant Professor at the University of Wisconsin-Madison School of Pharmacy in Madison, WI.

PR *This article has been peer-reviewed. The contribution in reviewing is greatly appreciated!*

Acknowledgements: The authors would like to thank the Dane County WPQC pharmacists and community center partners who have donated their time and expertise to this program and the individuals it serves. The authors would also like to thank United Way of Dane County for their continued support of this important work.

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

References

1. Jokanovic N, TanECK, Sudhakaran S, et al. Pharmacist-led medication review in

community settings: an overview of systematic reviews. *Res Social Adm Pharm.* 2017;13(4):661-685. doi: 10.1016/j.sapharm.2016.08.005
2. Kallio SE, Kiiski A, Airaksinen MSA, et al. Community pharmacists' contribution to medication reviews for older adults: a systematic review. *J Am Geriatr Soc*. 2018;66(8):1613-1620. doi:10.1111/jgs.15416
3. Benson M, Murphy D, Hall L, Vande Kamp P, Cook DJ. Medication management for complex patients in primary care: application of a remote, asynchronous clinical pharmacist model. *Postgrad Med*. 2021;133(7):784-790. doi: 10.1080/00325481.2021.1934492
4. Twigg MJ, Wright D, Barton GR, Thornley T, Kerr C. The four or more medicines (FOMM) support service: results from an evaluation of a new community pharmacy service aimed at over-65s. *Int J Pharm Pract*. 2015;23(6):407-414. doi:10.1111/ijpp.12196
5. Pearson C. Serving the underserved: the partnership between WPQC and the United Way of Dane County to promote patient education and healthy aging. *J Pharm Soc Wis.* 2018;21(5):22-25.
6. Martin A, Lopina S, Trapskin K. WPQC update: expansion of the United Way of Dane County Safe and Healthy Aging Community-Based Program to the health system. *J Pharm Soc Wis.* 2018;21(5):22-25.
7. WPQC overview. Pharmacy Society of Wisconsin Website. Accessed October 5, 2021. https://www.pswi.org/Resources/Wisconsin-Pharmacy-Quality-Collaborative-WPQC
8. REDCap. Accessed October 5, 2021. https://www.project-redcap.org/resources/citations/
9. Wick JY. Checking for comprehension: mastering teach-back techniques. Consult Pharm. 2013;28(9):550-554. doi:10.4140/TCP.n.2013.550

Immunization Training for Pediatric and Adult Vaccinations Available for Pharmacists and Technicians

\Training for Pharmacists: PSW's Immunization Delivery for Pharmacists course is an ACPE accredited program that meets Wisconsin's training requirements for pharmacists interested in providing immunizations in an effort to improve public health. This training program also includes education on non-vaccine injections, enabling you to begin administering medications as a part of your pharmacy practice.

The course consists of several online modules that can be completed at your availability. Course content will include:

- Immunology & Vaccine Basics
- Operating & Expanding Your Immunization Program
- Patient Care for Immunizing Pharmacists
- Vaccines & Vaccine Preventable Diseases
- Special Populations
- Case Discussion
- Non-Vaccine Injections (a separate but linked & required 1 CE activity)

Registration is $325 for PSW members and $425 for non-members.

If you're already completed the training, but just need training on pediatric vaccination administration in order to vaccinate below age 6, click here. Registration is $100.

Training for Technicians: The PSW Technician Immunization Delivery for Pharmacy Technicians course provides certified technicians with the concepts and terminology of immunization, vaccine administration techniques and safety procedures, as well as documentation requirements, proper product handling, and adverse reaction management to expand their support of pharmacy practices.

Each technician participant will complete three online modules (including a final exam) and a vaccine administration assessment at their home practice site. Participants must complete the online modules and assessment in their entirety and submit a current BLS/CPR certification (with documentation) before receiving immunization certification. Upon completing all components of the course, certified technicians are eligible to administer vaccines (under pharmacist supervision and to patients age 6 and older) in the state of Wisconsin.

The cost of the program is $175 for members and $275 for non-members.

For more Immunization continuing education credit, click here.
Please email info@pswi.org with any questions.

Original Work

Quality Assurance of Offering Comprehensive Medication Reviews to 90-Day Medication Synchronization Patients

by Blair A. Baillio, PharmD, Amanda Margolis, PharmD, MS, BCACP, Denise Garner, 2022 PharmD Candidate Abbigail Linde, PharmD

Abstract

Background: Medication synchronization (med sync) and comprehensive medication reviews (CMRs) have each been found to improve patient outcomes. Beaver Dam Hometown Pharmacy has been successful in implementing both services, but there is an opportunity to improve follow-up CMR visits. The Beaver Dam Hometown Pharmacy already has quarterly contact with patients receiving 90-day med sync; therefore, coordinating CMR follow-ups with med sync may have a synergistic benefit. The objective of this evaluation is to assess the change in CMRs as well as patient satisfaction after combining these two services.

Methods: Eligible patients were identified through the Pioneerx© pharmacy software. To qualify for CMR visits, patients had to be enrolled in Medicaid, have 4 or more medications for 2 or more disease states, and at least one medication on a 90-day fill in the med sync service. Attitudes of patients toward the services were assessed after completion via a Likert scale with values ranging from "poor" to "excellent." Effects of the services on tracked pharmacy outcomes were also measured, including professional supplement sales and eCare Plans completed.

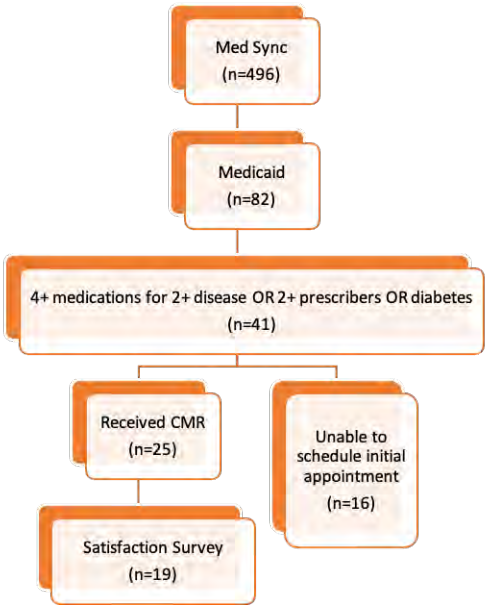
Results: A total of 41 patients were selected for the evaluation. Of those, 24 have completed the initial CMR at the time of their med sync date. Nineteen patients have recorded satisfaction data associated with their experience. Initial and follow-up CMRs increased by 50% compared to the same time period in the previous year. Patient satisfaction was also shown to be high.

Conclusions: The Beaver Dam Hometown Pharmacy was able to increase the number of CMRs completed following coordination of CMRs with med sync. Survey results also demonstrated high patient and satisfaction with the service.

Comprehensive medication reviews (CMRs) are an efficient way to manage a patient's medications and disease states. Community pharmacists can conduct CMRs using their clinical skills to find and solve drug-related problems, improve patient knowledge of medications, increase adherence, and improve patient satisfaction.[1] A study by Doucette et al. found that over 90% of patients feel CMRs are important for their health.[2] CMRs do not only increase patient health, but are also an added revenue stream for pharmacies. Medicaid reimburses pharmacies for the CMRs they conduct. Although Medicaid has strict enrollment and qualification guidelines, it can be useful in helping patients who are at higher risk of experiencing drug-related problems. Medicaid also reimburses pharmacies for three additional follow-up CMR visits per year.

Another way to optimize patient care is through medication synchronization (med sync). Med sync ensures that patients can pick up all their prescriptions at one time every month or every three months. This is convenient not only for the patients, but for the pharmacy staff as well. The pharmacy staff can limit the time they spend refilling certain medications and can spend more meaningful time with patients each month. It saves resources, and reduces the amount of calls the pharmacy staff must answer for refill requests. Plus, expensive medications are only ordered when patients confirm that they need them. Not only does med sync benefit pharmacy workflow and patient convenience, but it has also been shown to improve patient adherence. Lester et al. found that patients who refilled their medications though standard refill methods were adherent to their medications 73.6% to 76.4% of the time compared to patients who filled with automatic refill, who were adherent to their medications 77.5% to 83.6% of the time.[3] In another study, White found that patients enrolled in med sync had a 3.4 to 6.1 times greater odds of adherence compared to unenrolled patients.[4] Some pharmacies have found that using appointment-based med sync allows pharmacies to foster better relationships with their patients and work on improving

FIGURE 1. Participant Disposition



Med sync = Medication synchronization; CMR = comprehensive medication review

patient treatments.[5]

Although both CMRs and med sync offer improved outcomes for patients, combining the services may lead to better care overall. There is currently a gap in the literature addressing the possibility of increase in CMR completions when directly linked to a med sync program. Patients picking up their medications monthly or quarterly can optimize their trips to the pharmacy through scheduling CMR visits. This would allow patients to pick up their prescription medications as well as discuss any health-related items, including their disease states, drug-related problems, nutraceutical supplements, and nutrition support.

The staff at Hometown Pharmacy in Beaver Dam, Wisconsin, strives to improve how they care for their patients. They do this is by offering services like CMRs and med sync. In 2020, the pharmacy enrolled a substantial number of patients into med sync to help ensure regular patient contact as well as better patient adherence. They also carry high-quality nutraceutical supplements and provide counseling on nutritional support based on a patient's medication profile. Recognizing the opportunity for greater efficiency and improved patient care, the Beaver Dam Hometown Pharmacy combined CMRs and med sync to provide better care to their patients and save both the pharmacy's and the patients' time. The goal of this project was to assess the change in CMR completions compared to the previous year when tied to med sync. The secondary objective was to determine patient and employee satisfaction after combining services.

Methods

A report of pharmacy patients was filtered to include those who were enrolled in the med sync program, had 90-day fills, and received Medicaid. The CMR service was performed by phone and combined with a call to determine fill needs for a 90-day med sync. CMRs were allowed by phone due to COVID. A clinical services pharmacist had dedicated time to perform these calls. To qualify, patients needed to be enrolled in Medicaid and meet 1 of the following 3 criteria: have 4 or more medications covering 2 or more specific disease states; have 2 or more prescribers; or have diabetes. In September of 2020, patients were identified, and a schedule was created to perform the combined CMR/med sync call. The designated time period for counting CMRs and follow-up visits based on sync cycles fell between October 2020 and January 2021.

Patients received a satisfaction survey 2-4 weeks after the CMR/med sync. These surveys were performed over the phone by a pharmacy student not associated with the CMRs or Beaver Dam Hometown Pharmacy to allow for more objective data collection. Patients were asked 6 satisfaction questions based on a 5-point Likert scale with values of poor, fair, good, very good, or excellent (see Figure 4 for a list of specific questions asked). Investigators performed three informal interviews with the pharmacy staff to understand changes in workflow and workload following the combination of CMRs with med sync.

The number of CMRs was pulled from the Pioneerx© software and analyzed. Because the documentation process changed from the previous year, initial versus follow-up visits were not clearly labeled. Therefore, this comparison was unable to determine directly the number of new versus follow-up CMRs. Because nutraceuticals are an important part of the pharmacy, number of items sold during the evaluation periods were collected from the Catapult© point of sale software. These data were compared to the same time period from the previous year (October 2019 to January 2020).

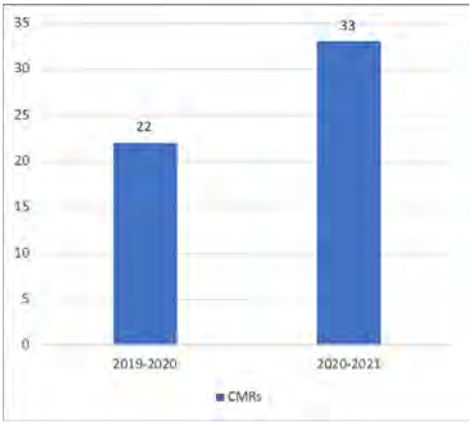
Results

Of the 496 patients enrolled in med sync, 41 were found to meet inclusion criteria (Figure 1). CMR appointments were lined up with med sync appointments for 25 patients, of whom 19 received a post-CMR satisfaction survey. Sixteen patients could not be reached to perform the CMR and 6 patients were lost to follow-up.

During the period of October 2020 to January 2021, an increase of 11 CMRs performed was observed compared to the same time period from the previous year (Figure 2). There was an increase of 54 items sold compared to the previous year (Figure 3); however, it is not certain that this increase was directly tied to performing the CMR/med sync services.

Results of the patient survey showed 53% of the overall responses were "excellent." Eighty percent of the responses

FIGURE 2. CMRs Completed



CMR = comprehensive medication review

FIGURE 3. Nutraceuticals Sold

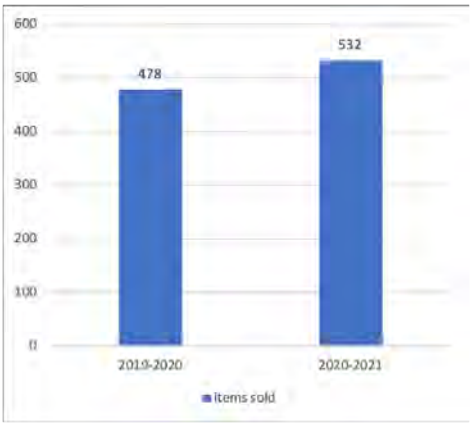


FIGURE 4. Patient Satisfaction Survey Results

averaged as very good or better (Figure 4).

From informal interviews with three members of the pharmacy staff who were involved in the med sync and CMR programs, it was discovered that combining the services extended the reach of the pharmacy. Effectiveness and efficiency were improved. The clinical services pharmacist identified how easy it is to flow from a med sync call into a CMR call.

> ***Pharmacist 1:*** *"Combining these services has allowed us as a pharmacy to reach our patients with more of our services. The tools we have available to help our patients are being maximized through this program."*
>
> ***Pharmacist 2:*** *"It's much easier catching these CMR opportunities. It flows smoothly from a med sync call to reviewing changes we discussed last time."*
>
> ***Technician:*** *"This program really makes things more efficient. We're able to contact patients just once rather than several times for similar services."*

Discussion

After combining med sync and CMR services, an increase was seen in the number of CMRs completed and the number of nutraceutical supplement sales made. Combining med sync and CMR services optimized pharmacy efforts, allowing for multiple beneficial services while minimizing resources required for each individual service. For example, during the time of this project, CMRs could be performed over the phone, which was typically a 25- to 30-minute phone call. Many of the patients that qualified for this study had more than 4 medications. A separate med sync phone call for the same patient would also take a significant amount of time. By combining these services, the pharmacy staff was able to optimize their time spent on the phone.

Patient and pharmacy satisfaction with the program was high. It is logical that patients would feel satisfied with the combined service. They receive close attention to their medications and have time to ask questions. They receive multiple services from the pharmacy that help them feel cared for. For example, one patient expressed her satisfaction having switched to this pharmacy. She felt the whole staff gave her the attention she needed. For the pharmacy, staff can maximize resources and redistribute workflow. The clinical services pharmacist can alleviate additional work for other staff members. Billable services are better organized and extended to their full potential.

Limitations

The small study size is a limitation. As a single pharmacy serving a small community, the population of the study was fairly homogeneous, which can limit external validity.

Quantification of health outcomes was not assessed in this study. This study specifically addressed the number of completed CMRs following coordination of CMRs and med sync, and did not address potential benefits of combining these services such as increased adherence, increased patient safety, and improved health outcomes for patients.

It is unclear whether CMR follow-ups had a direct impact on nutraceutical sales. The CMR recipients in this evaluation were often on Medicaid, and therefore are likely lower-income households. The nutraceutical supplements the pharmacy sells are more expensive than standard over-the-counter supplements, so Medicaid patients may have needed to make significant adjustments to their budget to afford these supplements. Even though the clinical pharmacist recommended supplements during CMR appointments, it is unlikely that performing the CMR follow-ups had a direct impact on nutraceutical sales. It is possible that the clinical pharmacist recommending supplements to other patients at the pharmacy or other concurrently running initiatives had a greater impact.

Future Direction

This 3-month period only begins to capture how well med sync calls catch follow-up CMR opportunities. Historically, patients at this pharmacy have not always received the optimal number of follow-up CMRs. With the synergy of combing CMRs with med sync, the likelihood that patients will continue to receive the benefits of clinical pharmacist care is increased.

Beaver Dam Hometown Pharmacy will continue to track follow-ups for CMRs to ensure patients continue to receive the highest possible care and services available. Accepted interventions will also be tracked and monitored over time. The pharmacy will expand the program to all qualifying patients. Plans also exist to share this process with other in-network pharmacies. Through video-based and in-person presentations, other pharmacies will learn how to find qualifying patients and extend the CMR benefit within their current workflow.

Conclusions

At Beaver Dam Hometown Pharmacy, combining med sync and CMR services led to an increase in the number of CMRs completed compared to previous years. Survey results also showed high patient and pharmacy staff satisfaction. Future directions include determining the proportion of interventions that are accepted, and expansion of the pairing of CMRs with med sync at other pharmacies.

At the time of this article, Blair Baillio, was a University of Wisconsin-Madison School of Pharmacy Community Pharmacy Resident at Beaver Dam Hometown in Beaver Dam, WI. Amanda Margolis is an Assistant Professor at the University of Wisconsin-Madison School of Pharmacy in Madison, WI. Denise Garner is a 4th Year Doctor of Pharmacy Candidate at the University of Wisconsin-Madison School of Pharmacy in Madison, WI. Abbigail Linde is a Clinical Pharmacist at Beaver Dam Hometown Pharmacy in Beaver Dam, WI.

PR *This article has been peer-reviewed. The contribution in reviewing is greatly appreciated!*

Disclosure: The authors have had no actual or relevant financial relationships to create a potential conflict of interest in relation to this program. This project was submitted through the UW-Madison IRB self-determination tool and it was determined not to meet the federal definition of research and determined to be a quality assurance assessment.

References

1. Kallio SE, Kiiski A, Airaksinen MSA, et al. Community pharmacists' contribution to medication reviews for older adults: a systematic review. *J Am Geriatr Soc.* 2018;66(8):1613-1620. doi:10.1111/jgs.15416

2. Doucette WR, Zhang Y, Chrischilles EA, et al. Factors affecting Medicare Part D beneficiaries' decision to receive comprehensive medication reviews. *J Am Pharm Assoc* (2003). 2013;53(5):482-487. doi:10.1331/JAPhA.2013.12233

3. Lester CA, Mott DA, Chui MA. The influence of a community pharmacy automatic prescription refill program on Medicare Part D adherence metrics. *J Manag Care Spec Pharm.* 2016;22(7):801-807. doi:10.18553/jmcp.2016.22.7.801

4. White ND. Pharmacy medication synchronization service works to improve medication adherence. *Am J Lifestyle Med.* 2016;10(6):385-387. doi:10.1177/1559827616660687

5. Dao N, Lee S, Hata M, Sarino L. Impact of appointment-based medication synchronization on proportion of days covered for chronic medications. *Pharmacy (Basel).* 2018;6(2):44. doi:10.3390/pharmacy6020044

Original Work

Impact of a Direct Oral Anticoagulant Population Management Tool in a Pharmacist-Led Outpatient Anticoagulation Service

by Jessica A. Wedel, PharmD, Carla E. Staresinic, PharmD, BCACP, Jillian Kolasinski, 2022 PharmD Candidate, Amanda Margolis, PharmD, MS, BCACP, Andrea L. Porter, PharmD

Abstract

Background: Clinical guidelines indicate that direct oral anticoagulants (DOACs) require periodic monitoring but do not define the optimal workflow for this required monitoring.

Objectives: To evaluate the impact of a population management tool (PMT) on pharmacist interventions compared to traditional management of DOACs in an outpatient pharmacist-led anticoagulation (AC) service. Pharmacist time spent and occurrence of bleeding and thromboembolism were reviewed as secondary objectives.

Methods: A retrospective analysis was conducted of patients on DOAC therapy managed by a pharmacist-led AC clinic. A query of the health-system pharmacy database was performed to identify all patients initially prescribed a DOAC from April 2016 to April 2017, to represent pharmacist monitoring using a traditional model, and from April 2018 to April 2019, to represent monitoring with a PMT. Patients were randomly selected from each respective monitoring model for chart review. Pharmacist interventions, including lab ordering, were tracked as the primary outcome. Pharmacist time invested per patient encounter and safety outcomes were assessed as a secondary outcomes.

Results: A total of 150 patient charts (n=75 for each model) were reviewed. The traditional model yielded more overall interventions than the PMT model (249 vs. 127, respectively). However, if routine lab ordering was excluded, the PMT model yielded a higher number of clinical interventions (66 vs. 82, respectively). Besides lab monitoring, there were statistically significant differences in DOAC discontinuation, DOAC dose change, and changes to GI prophylaxis captured between models.

Conclusions: DOAC monitoring using the PMT approach may offer an effective alternative to traditional monitoring to reduce the need for unnecessary lab ordering while still capturing necessary clinical interventions.

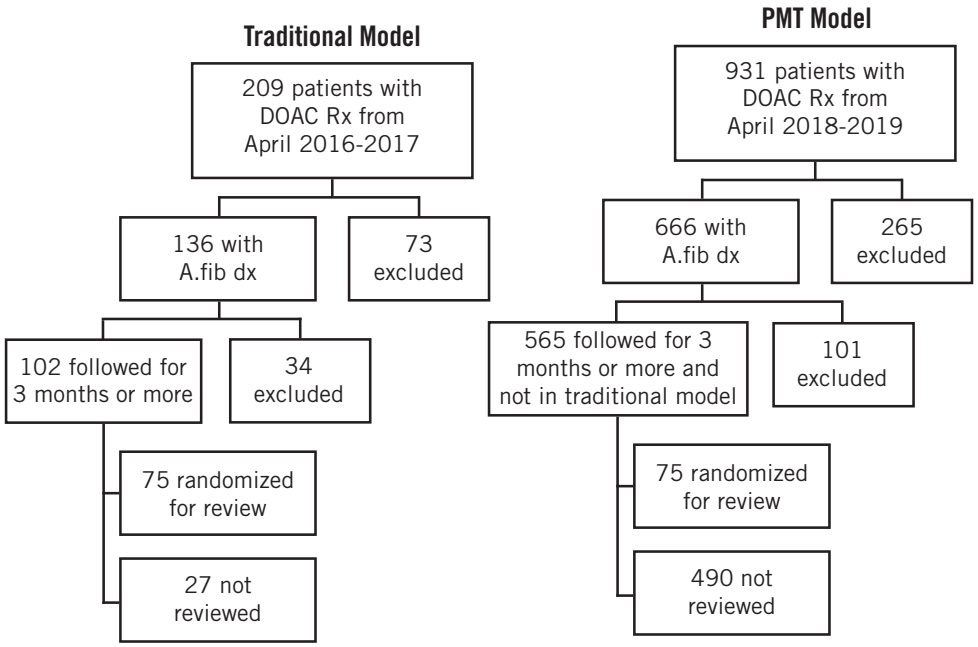
Direct oral anticoagulant (DOAC) therapies were first approved by the U.S. FDA in 2010.[1] Since their introduction, multiple societies have worked to provide guidance on appropriate monitoring of DOAC therapies. The Canadian Cardiovascular Society created a monitoring checklist to ensure topics such as adherence, bleeding risk, renal function, and drug interactions are being assessed during follow-up visits.[2] The American Heart Association and European Heart Rhythm Association published practice guidelines recommending routine monitoring for DOACs at least every six months.[3,4] Even with these practice recommendations available, the ideal management strategy for DOACs has yet to be determined.

Given this gap in knowledge regarding optimal DOAC management, monitoring of these therapies has become very site specific. At the William S. Middleton Memorial Veterans Hospital, the outpatient anticoagulation clinic (AC) is primarily managed by clinical pharmacy specialists (CPS). A CPS operates as an advanced practice provider within a defined scope of practice to manage anticoagulant medications and order necessary labs. Direct oral anticoagulants are among the medications managed by the AC clinic, and their use increased more than 200% at this site from May 2017 to May 2018.

Historically, the traditional method of DOAC monitoring in the AC clinic included an initial, educational visit followed by a phone call at two weeks to assess medication tolerability. Within three months of DOAC initiation, a complete blood count and serum creatinine labs were drawn to monitor therapy safety. These labs were repeated six months after initiation and every six months thereafter, or more frequently if determined clinically necessary. Not every patient contacted via phone by a CPS needed a clinical intervention. It remained unclear if this resource-intensive method for DOAC management was ideal, because there were no clear guidelines for the optimal frequency of clinician follow-up.

Evidence regarding the use of clinical dashboards, such as a population management tool (PMT), in health care environments has demonstrated better

FIGURE 1. Participant Flow



Direct Oral Anticoagulant (DOAC), Prescription (Rx), Atrial Fibrillation (A.fib), Diagnosis (dx)

immediate access to patient information, in addition to improving care processes and patient outcomes.[5] Population management tools have been found useful in the management of chronic disease states such as diabetes.[6] Two Veterans Affairs (VA) hospitals collaboratively developed a PMT for DOACs that electronically tracked data and determined when a clinical intervention was needed based on predefined clinical parameters.[7] The PMT tracked critical labs, drug-drug interactions, appropriateness of therapy dose and duration based on indication, and overdue refills and labs. A prospective study comparing routine, scheduled DOAC monitoring versus use of the PMT showed the PMT reduced the amount of pharmacist time required to perform a clinical intervention by 48 minutes.

The William S. Middleton Memorial Veterans Hospital AC implemented the VA DOAC PMT in July 2018 to streamline management of patients receiving DOACs by electronically tracking and flagging when a potential intervention was needed. The PMT monitoring diverges from the traditional monitoring model after the third month, where, instead of scheduled labs every six months, unscheduled patient encounters occur when the PMT alerts the CPS to a necessary intervention. The purpose of this evaluation was to determine the impact of a population management tool (PMT) compared to traditional follow-up for management of direct oral anticoagulants (DOACs) in a pharmacist-led anticoagulation (AC) service, with a primary focus on number of pharmacist interventions.

Methods

This single-center retrospective evaluation reviewed patients managed by a pharmacist-led AC clinic. A query of the health-system pharmacy database was performed to identify all patients initially prescribed a DOAC from April 2016 to April 2017 (traditional model) and from April 2018 to April 2019 (PMT model). Patients were eligible for review if they had a DOAC prescription managed by the William S. Middleton Memorial Hospital VA outpatient AC clinic. Patients were excluded from the evaluation if they had a DOAC indication other than atrial fibrillation or atrial flutter, due to variable durations of therapy and transition periods to the DOAC PMT for long-term management. Patients were also excluded if DOAC therapy was managed for less than 3 months.

In both the traditional and PMT model, a convenience sample of 75 patients was randomly selected for review from a total of 209 patients in the traditional model and 931 patients in the PMT. The convenience sample was performed due to time constraints of the reviewers, and randomization was performed using a random number generator. Chart reviews of AC clinical notes were performed by two investigators. Inter-rater reliability was completed every 5 patients. AC clinical notes for each patient were reviewed for a one-year period beginning three months after initiation of therapy. A start date of three months after DOAC initiation was selected to capture the differences between the traditional and PMT models, as this was when the monitoring strategies diverged. Charts were reviewed to collect the following demographics: age, gender, indication for DOAC, CHA2DS2-VASc score, DOAC used, history of major bleed, previous oral anticoagulant use, and concurrent antiplatelet therapy.[8] Interventions tracked included identification of drug interactions, DOAC dose adjustments, change in DOAC therapy or discontinuation, ordering of necessary labs, referral for additional care, adherence issues, peri-procedural management, discontinuation of antiplatelets, and addition or removal of gastrointestinal (GI) prophylaxis such as proton-pump inhibitors or histamine-2 receptor antagonists.

The total number of interventions captured in each model were reviewed with and without ordering labs included. Lab ordering in the PMT model was not performed on a scheduled basis. Any labs ordered by a VA provider (including annual labs ordered by a primary care provider) were automatically tracked by the tool, therefore reducing the lab ordering burden from the AC pharmacist. Since lab ordering was a routine part of the traditional model, total interventions captured in each model excluding labs might be a more accurate assessment of clinically needed interventions being made.

Major bleeding and thromboembolic episodes during the chart review period were assessed as secondary safety outcomes. Definition of major bleeding was defined as fatal or symptomatic bleed into brain, spine, eye, retroperitoneal, or intramuscular with compartment syndrome, or bleed leading to hospitalization or transfusion of two or more units of packed red blood cells.[9] An additional secondary outcome was pharmacist time spent per patient.

TABLE 1. Baseline Demographics / Safety Outcomes

	Traditional (n=75)	*PMT (n=75)*	*P-value*
Mean Age (SD)	73 (9.6)	75 (7.6)	0.31
Gender - Male (%)	72 (96)	72 (96)	1.00
Medication (%) Dabigatran Rivaroxaban Apixaban	 30 (40) 36 (48) 9 (12)	 4 (5) 32 (43) 39 (52)	 <0.001 0.62 <0.001
Previous OAC (%) Warfarin DOAC	 45 (60) 22 (29)	 30 (40) 21 (28)	 0.02 1.00
History of major bleed (%)	6 (8)	6 (8)	1.00
History of VTE (%)	5 (7)	6 (8)	1.00
Antiplatelet (%) Aspirin Clopidogrel	 31 (41) 4 (5)	 29 (39) 7 (9)	 0.87 0.53
GI prophylaxis (%)	35 (47)	30 (40)	0.51
Mean CHA2DS2-VASc (SD)	3.3 (1.8)	3.7 (1.5)	0.09
Major Bleeding n, (%)	7 (9%)	2 (3%)	0.19
Thromboembolism n, (%)	0	0	1.00

Footnote: Oral Anticoagulant (OAC), Direct Oral Anticoagulant (DOAC), Venous Thromboembolism (VTE), Gastrointestinal (GI), Population Management Tool (PMT)

TABLE 2. Counts of Interventions Captured

	Traditional (n=75)	*PMT (n=75)*	*P-value*
Ordering of labs	183	45	<0.001
Periprocedural Management	26	30	0.38
Referrals	10	15	0.45
Adherence	7	12	0.96
DOAC discontinuation	7	1	0.03
Drug Interaction	6	2	0.15
Antiplatelet discontinuation	4	2	0.63
Switch DOAC agent	4	5	0.73
Addition or removal of GI prophylactic agent	2	9	0.03
DOAC dose change	0	6	0.01

Footnote: Population Management Tool (PMT), Direct Oral Anticoagulant (DOAC), Gastrointestinal (GI)

The William S. Middleton Memorial Veterans Hospital AC clinic previously performed a time and motion analysis in December 2018 to determine pharmacist time spent for various anticoagulation clinic DOAC activities including scheduled and unscheduled patient encounters. The unpublished results from that time study were used to determine CPS time spent for each patient encounter. No additional time was designated for specific interventions. Assumptions from the time study included the following: unscheduled follow-ups where patient was not reached (5 minutes), unscheduled follow-up where patient was reached (20 minutes), scheduled follow-up where patient was not reached (7 min), scheduled follow-up where patient was reached (21 minutes).

Baseline demographics were determined using descriptive statistics. Comparison of the traditional and PMT models used Students T-test and Fisher's Exact Test for continuous and binominal results, respectively. A linear regression analysis was performed for CPS time spent to account for any differences in baseline statistics. Statistical analysis was conducted using STATA version 14.1. P-values <0.05 were considered statistically significant and there were no adjustments made for repeated analysis. This project was determined not to meet the federal definition of research and full institutional review board review was not required.

Results

Patient charts (n=75 for each model) were reviewed for a median of 10 months (Figure 1). Baseline demographics demonstrated a primarily older adult male population (Table 1). Dabigatran use was higher in the traditional mode, whereas apixaban use increased in the PMT model. Prior warfarin use was also statistically significantly different between the traditional and PMT models. Other demographic characteristics were similar between the two groups.

The traditional model yielded more overall interventions than the PMT model (249 vs. 127, respectively). However, if routine lab ordering was excluded, the traditional model yielded 66 interventions compared to 82 in the PMT model. Besides lab monitoring, there were statistically significant differences in DOAC

discontinuation, DOAC dose change, and changes to GI prophylaxis captured between models (Table 2). In terms of the secondary outcome of pharmacist time invested, the total time spent per patient was 15 minutes shorter in the PMT model. This was consistent with the regression analysis; the PMT model still showed a similar time savings of 18 minutes (p=0.006).

The secondary safety outcome of major bleeding episodes revealed more bleeding episodes in the traditional model; however, this was not statistically significant (Table 1). No thromboembolic episodes were noted in either model during the time period review.

Discussion

In general, use of the PMT model maintains the number of clinical interventions detected while saving pharmacists' time. More widespread use of PMTs for DOAC monitoring may lead to clarification of the best DOAC monitoring strategy to adopt.

Based on a time savings of about 18 minutes per patient during the evaluation period, a facility could determine how much annual CPS time could be saved. For example, at the Madison VA, there are about 1900 patients on DOAC therapies. Therefore, by switching to the PMT model, the AC clinic could save around 570 hours per year. From an impact standpoint, this has system-wide implications from a cost-savings perspective. The William S. Middleton Memorial Veterans Hospital AC implemented a pharmacy technician in the AC clinic to assist with more administrative tasks between the two time periods reviewed, which could have improved CPS efficiency and be a confounding variable in the time savings. Of note, the prospective study performed at another VA looked at the amount of pharmacist time required to perform a clinical intervention (48 minutes) whereas this evaluation looked at the time savings between the two different models of monitoring.[7]

There were some differences in baseline characteristics between the traditional and PMT models. The decrease in prior warfarin use during the PMT model could be attributed to increased provider comfort with DOAC prescribing as time progressed as well as changes in the local prior authorization process for DOACs. During the time of the traditional model, dabigatran was used more frequently and this shifted to apixaban at the time of the PMT model. We suspect this also influenced the type of interventions made. For instance, there is more flexibility in apixaban dosing and dabigatran has the potential for GI side effects which could have swayed the likelihood for DOAC discontinuation versus dose changes.

Strengths of this evaluation include the random selection of patients, inclusion of inter-rater reliability, and use of regression analysis to account for differences in baseline characteristics. One limitation of retrospective chart reviews is that quantifying interventions and time requirements is based on documentation. If an intervention was performed but not documented, or if a patient's chart was reviewed to determine appropriateness of an intervention but no note was placed, then this could be an underestimation of the true results in either model. Other limitations include a relatively small sample size and the use of time estimates from a previous study.

Conclusion

Use of the DOAC PMT resulted in similar non-laboratory monitoring interventions captured and less time spent monitoring per patient compared to the traditional model of scheduled encounters with a CPS. While this model could improve pharmacist monitoring efficiency for DOACs, institutions need to consider safety and feasibility prior to implementation.

Jessica Wedel is a Staff Pharmacist at Froedtert Home Delivery & Specialty Pharmacy in Menomonee Falls, WI. Carla Staresinic is a Clinical Pharmacist at the William S. Middleton Veterans Hospital in Madison, WI. Jillian Kolasinski is a 4th Year PharmD Candidate at the University of Wisconsin-Madison School of Pharmacy in Madison, WI. Amanda Margolis is an Assistant Professor at the University of Wisconsin-Madison School of Pharmacy in Madison, WI. Andrea Porter is an Assistant Professor at the University of Wisconsin-Madison School of Pharmacy in Madison, WI.

PR *This article has been peer-reviewed. The contribution in reviewing is greatly appreciated!*

Disclosures: The authors declare no real or potential conflicts or financial interest in any product or service mentioned in the manuscript, including grants, equipment, medications, employment, gifts, and honoraria. The corresponding author had full access to all the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis.

References

1. van Ryn J, Stangier J, Haertter S, et al. Dabigatran etexilate – a novel, reversible, oral direct thrombin inhibitor: interpretation of coagulation assays and reversal of anticoagulant activity. *Thromb Haemost,* 2010;103(6):1116-1127.
2. Gladstone DJ, Geerts WH, Douketis J, Ivers N, Healey JS, Leblanc K. How to monitor patients receiving direct oral anticoagulants for stroke prevention in atrial fibrillation: a practice tool endorsed by thrombosis Canada, the Canadian stroke consortium, the Canadian cardiovascular pharmacists network, and the Canadian cardiovascular society. *Ann Intern Med.* 2015;163:382-385.
3. Steffel J, Verhamme P, Potpara TS, et al. The 2018 European Heart Rhythm Association Practical Guide on the use of non-vitamin K antagonist oral anticoagulants in patients with atrial fibrillation. *Eur Heart J*. 2018;39(16):1330-1393.
4. Chen A, Stecker E, Warden BA. Direct oral anticoagulant use: a practical guide to common clinical challenges. *JAHA.* 2020;9:e017559.
5. Dowding D, Randell R, Gardner P, et al. Dashboards for improving patient care: review of the literature. *Int J Med Inform*. 2015;84(2):87-100.
6. Watts B, Lawrence RH, Drawz P, Carter C, Hirsch Schumaker A, Kern EF. Development and implementation of team-based panel management tools: filling the gap between patient and population systems. *Popul Health Manag*. 2016;19(4):232-239.
7. Valencia D, Spoutz P, Stoppi J, et al. Impact of a direct oral anticoagulant population management tool on anticoagulation therapy monitoring in clinical practice. *Ann Pharmacother.* 2019;53(8):806-811.
8. Lip GYH, Nieuwlaat R, Pisters R, et al. Refining clinical risk stratification for predicting stroke and thromboembolism in atrial fibrillation using a novel risk factor-based approach: the euro heart survey on atrial fibrillation. *Chest* 2010;137:263-272.
9. Schulman S, Kearon C. Definition of major bleeding in clinical investigations of antihemostatic medicinal products in non-surgical patients. *J Thromb Haemost*. 2005;3:692-694.

Original Work

Successful Use of Catheter-Directed Low Dose Alteplase Infusion for Mitral Valve Thrombus: A Case Report

by Austin M. Padilla, PharmD, Jared M. Frost, PharmD, BCCP, James S. Mathia, PharmD, BCPS, Ryan M. Servais, PharmD, BCPS, BCCCP, BCCP

Abstract

We describe a patient case of the successful use of catheter-directed alteplase 25 mg IV administered over 25 hours to treat a thrombosis in a mechanical mitral valve.

Mechanical prosthetic valve thrombosis (PVT) is a rare but serious complication of valve replacement. Optimal treatment is controversial and depends on the cause of the obstruction and the hemodynamic status of the patient. The therapeutic treatment options include systemic anticoagulation, thrombolysis, surgery, or optimization of current anticoagulation strategy. In this case, the patient presented with a nonobstructive mitral valve thrombus and was initiated on catheter-directed low dose alteplase infusion, 25 mg IV over 25 hours, and subsequent bridging with IV heparin infusion to warfarin long-term therapy. Systemic heparin was monitored by activated partial thromboplastin time (aPTT) with a goal range of 45–70 seconds for a total duration of 5 days. Repeat echocardiographic imaging was done and showed complete resolution of the clot. There were no bleeding complications from anticoagulation. On discharge, the patient's international normalized ratio (INR) goal was 2.5-3.5 and the patient continues to be followed at our institutional anticoagulation clinics.

Prosthetic valve thrombosis (PVT) is a rare but serious complication of valve replacement. PVT can cause obstructive and nonobstructive complications, and both have significant morbidity and mortality rates. The incidence of obstructive PVT for mechanical valves is 0.3–1.3% incidence per patient years.[1] Nonobstructive PVT is more common, with reported findings as high as 10% during the early post-operative period. Roudaut et al described the variation in the incidence of PVT, with the first post-operative year marked by a 24% incidence of thrombosis and a subsequent decrease of approximately 15% between the second and fourth years.[1] The diagnosis of PVT can be challenging, because patients can present with varying signs and symptoms. The different therapeutic modalities available for PVT include heparin, fibrinolysis, surgery, or optimization of anticoagulation. Surgical treatment is usually preferred in obstructive PVT but largely influenced by the presence of several factors, including valvular obstruction, valve location, thrombus size, and clinical status. Anticoagulation is necessary to minimize complications from subsequent thromboses, but the optimal treatment strategy remains controversial.[1]

Alteplase, a recombinant tissue-type plasminogen activator (t-PA), is a thrombolytic agent that is FDA-approved for the treatment of acute ischemic strokes, pulmonary embolism, acute myocardial infarction, and catheter occlusion. Other indications include treatment of deep vein thrombosis, catheter-directed thrombolysis in the treatment of peripheral arterial occlusive disease, and treatment of prosthetic valve thrombosis.[2] Alteplase thrombolysis works by binding to fibrin in a thrombus, causing the conversion of plasminogen to plasmin. Alteplase has a high affinity for fibrin and will produce limited conversion of plasminogen in the absence of fibrin.[3]

Case Report

A 47-year-old female was seen in clinic in October 2019 with a complaint of shortness of breath and dyspnea on exertion. The patient's past medical history included chronic warfarin therapy for mechanical mitral valve replacement (2011), atrial fibrillation, heart failure with reduced ejection fraction, rheumatic fever, nonischemic cardiomyopathy, and hyperlipidemia. Family history included hyperlipidemia in her father and cardiovascular disease in her mother. Her social history was unremarkable.

Per the patient's report, she intermittently took her warfarin therapy and eventually stopped taking it due to social, financial, and location difficulties for proper management. At the time of presentation, she had been off warfarin therapy for at least four years, as reported by the patient. During the initial workup, providers ordered a chest x-ray, which showed mild pulmonary edema. She was taken for a transthoracic echocardiogram and was found to have severe left ventricular dysfunction (ejection fraction 25%) and improper function of her mitral valve (mean gradient 7.8 mmHg). A transesophageal echocardiogram was completed and a nonobstructive thrombus (1.7 cm x 1.2 cm) was found on the septal annulus adjacent to the medial disc. Her left ventricular ejection fraction (LVEF) was severely decreased from her previous exam (LVEF 65% from 2015). The clinic physician advised the patient to be admitted to the intensive care unit and

start thrombolysis. However, she refused any medical treatment, and left against medical advice. After further worsening of her symptoms, she then presented to our hospital for further care.

On admission, the patient was well compensated. Her systolic blood pressure ranged between 150 and 160 mmHg; her heart rate was 70 beats per minute; her respiratory rate was 14–18 breaths per minute; and she was afebrile. Her oxygen saturation was 98% on room air. Her INR was 1.1, which was expected, since her last reported warfarin dose was several years earlier. An EKG was ordered and showed the patient in sinus rhythm with 1st degree AV block.

Initially, the patient was started on IV heparin, but that was stopped on the same day and switched to alteplase catheter-directed infusion, 1 mg per hour for 25 hours with no initial bolus. The concentration of the alteplase infusion was alteplase 10 mg in sodium chloride 0.9% 250 mL (25 mL/hour). After the alteplase infusion, the patient was then re-initiated on IV heparin infusion (no initial bolus) 11 units/kg/hour and eventually titrated per institutional protocol to 15 units/kg/hour based on aPTT goal range of 45-70 seconds. During the heparin infusion, the patient was bridged to warfarin with an INR goal of 2.5-3.5. The patient remained on heparin infusion for 5 days with no bleeding complications noted. She denied any further symptoms such as shortness of breath, chest pain, or palpitations. No adverse effects were noted from the alteplase. Two days after the alteplase infusion, a repeat transesophageal echocardiogram was completed and showed complete clot resolution. The patient was discharged on warfarin with a therapeutic INR and continues to follow up with our institutional anticoagulation clinic.

Discussion

PVTs can present as an acute, subacute, or chronic thrombus, with the latter being more common. Thrombus formation is complex; they are typically formed of multiple clot layers with varying degrees of organization.[1] In relation to Virchow's triad, endothelial, hemodynamic, and hemostatic factors can predispose thrombus formation. With regard to the prosthetic valve, endothelial factors represent the interaction between the prosthesis and suture zone. The hemodynamic factors include the cardiac hemodynamic status of the patient and the characteristics of the prosthesis. Hemostatic factors involve anticoagulation management, which is often a challenging balance, especially during the early post-operative period. The balance between excessive anticoagulation and hemorrhagic complications, versus suboptimal anticoagulation and thrombosis must be evaluated on a case-by-case basis.[1]

According to the 2020 ACC/AHA Guideline for the Management of Patients with Valvular Heart Disease for acute mechanical prosthetic valve thrombosis presenting with symptoms of valve obstruction, urgent initial treatment with either slow-infusion low-dose fibrinolytic therapy or emergency surgery is recommended.[4] The level of evidence was updated to Level B-NR, which includes moderate-quality evidence from one or more well-designed, well-executed nonrandomized studies, observational studies, or registry studies. Slow-infusion fibrinolytic therapy has higher success rates and lower complication rates than historically used high-dose regimens, and is effective in patients previously thought to require urgent surgical intervention.[5] The overall 30-day mortality rate with surgery is 10% to 15%, with an even lower mortality rate (<5%) in patients with New York Heart Association (NYHA) class I/II symptoms.[4,5] Prior to 2013, studies that evaluated fibrinolytic therapy showed an overall 30-day mortality rate of 7% and hemodynamic success rate of 75%. Furthermore, thromboembolism rates were as high as 13%, major bleeding rates 6%, and intracerebral hemorrhage 3%.[6,7] However, recent reports have suggested that slow-infusion low-dose fibrinolytic protocols have high success rates (>90%), with embolic event rates <2% and major bleed rates <2%.[4,5,8] These fibrinolytic therapy regimens can be successful even in patients with advanced NYHA class and larger-sized thrombi. The decision for emergency surgery versus fibrinolytic therapy should be individualized, as there have not been randomized controlled trials comparing the two interventions.[5]

The best treatment strategies for prosthetic valve thrombosis remain controversial. The TROIA trial was conducted to find the safest and most effective regimen among different thrombolytic treatment strategies.[8] This was a single-center study from 1993 to 2003 that included 182 patients with 220 episodes of mechanical PVT. The trial compared five regimens: rapid streptokinase administration (1.5 million units over 3 hours, group I); slow streptokinase (1.5 million units over 24-hours, group II); high-dose 100 mg tissue plasminogen activator (t-PA) (group III); half-dose 50 mg and slow infusion (6 hours) of t-PA without bolus (group IV); and a low dose (25mg) and slow infusion (6 hours) of t-PA without bolus (group V).

This trial showed that t-PA 25 mg over 6 hours was as efficacious as the other treatment regimens but had lower complication rates in patients with PVT. Complication rates varied between groups I-IV but did not differ significantly (37.5%, 24.4%, 33.3%, and 29.6%; $p>0.05$ for each comparison) but was significantly lower in group V (10.5%, $p<0.05$ for each).[8] Specifically, for this patient case, the low dose alteplase infusion strategy was chosen based on the PROMETEE trial. The PROMETEE trial was conducted to test whether further prolongation of the alteplase infusion time would reduce complication rates without reducing success rates.[9] This was a single-center study from 2009 to 2013 that included 114 patients with PVT in 120 different episodes. Outcomes for the PROMETEE trial found a success rate of 20% after the first thrombolytic therapy session (25 mg over 25-hour infusion). More than one t-PA session was required in 93 episodes (77.5%) and there were two median thrombolytic sessions.

Ultimately, there was a 90% success rate after the eighth session (maximum alteplase dose of 200 mg). The presence of atrial fibrillation, NYHA class IV status, higher baseline thrombus area, and greater duration of suboptimal anticoagulation (DSA) were associated with a lower likelihood of success by univariate analyses.[9] Of note, the majority of the study population was NYHA classes I and II, and only 35% were NHYA class III and IV. The median age was 49 years, and PVT was nonobstructive in 36% and obstructive in 64% of patients. Four patients had NYHA class IV, one underwent surgery due to unsuccessful thrombolytic therapy, one developed an

embolism, one died from heart failure, and another had an ischemic stroke. The authors surmised that the poor outcomes in this group might have been due to a limited time interval to achieve thrombolysis.[9]

Compared to those patients, our patient had a history of atrial fibrillation and NYHA class III. Another similar characteristic was the thrombus size; in the PROMETEE trial, the average mitral thrombus size was 1.5 cm, and this patient's was 1.7 cm, as noted by an echocardiogram.[9] One major difference from this case report and the PROMETEE trial was the DSA. The trial included patients with an average DSA of 7 months, but this patient had a DSA at 48 months. The DSA reflects the elapsed time since a thrombus formation, and the PROMETEE trial predicted that an earlier thrombus might have a better response to thrombolytic therapy. In comparison, thrombolytic therapy to an organized thrombus (longer DSA) may have a higher likelihood of unsuccessful outcomes.[9]

Furthermore, increased thrombus area is another independent predictor of complications, and was associated with unsuccessful outcomes of thrombolytic therapy. This is attributed to more severe valvular obstruction and higher NYHA class in patients with greater thrombus area.[9]

Despite the longer DSA, this patient had successful thrombus resolution after one round of alteplase infusion (25 mg over 25 hours), followed by IV heparin and warfarin. In terms of complication rates from the PROMETEE trial, these were relatively low and were comparable to previous published studies.[8,10] The rates of embolism and major and minor hemorrhage were 1.7%, 1.7%, and 2.5%. The rates of complications did increase with the number of thrombolytic therapy sessions, and 67% of complications were seen after completion of the second thrombolytic session.[9] For our patient case, there were no documented complications, which is likely attributed to only one thrombolytic session being performed.

One limitation of this case report is that there was a lack of follow-up during the four years during which the patient reported she wasn't taking warfarin. Based on the information provided by the patient, it is unclear whether warfarin was taken intermittently or not at all. From a pathophysiologic standpoint, the longer DSA suggests more fibrin cross-linking and a stronger thrombus, which would make alteplase less successful. We would expect this patient would require more thrombolytic sessions to completely resolve the thrombus, which further suggests the patient had been taking warfarin intermittently.

The outcome of this case report supports the findings from the PROMETEE trial, in that catheter-directed low dose alteplase infusion over 25 hours is a feasible option for a patient with a mechanical mitral valve thrombus.

Austin Padilla is an Advanced Heart Failure and Cardiothoracic Transplant Pharmacist at Nebraska Medicine, Omaha, NE. Jared Frost is a Specialty Pharmacy Coordinator, Cardiology at Advocate Aurora Health – St. Luke's Medical Center, Milwaukee, WI. James Mathia is a Senior Clinical Pharmacist at Advocate Aurora Health – St. Luke's Medical Center, Milwaukee, WI. Ryan Servais is a Specialty Pharmacy Coordinator at Advocate Aurora Health – Aurora Sinai Medical Center, Milwaukee, WI.

PR *This article has been peer-reviewed. The contribution in reviewing is greatly appreciated!*

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

References

1. Roudaut R, Serri K, Lafitte S. Thrombosis of prosthetic heart valves: diagnosis and therapeutic considerations. *Heart*. 2007;93(1):137-142. doi: 10.1136/hrt.2005.071183.
2. Hughes R, Tadi P, Bollu P. StatPearls. TPA therapy. Updated July 2021. Accessed April 2021. https://www.ncbi.nlm.nih.gov/books/NBK482376/
3. Genentech, Inc. Activase. Updated February 2015. Accessed April 2020. https://www.accessdata.fda.gov/drugsatfda_docs/label/2015/103172s5203lbl.pdf
4. Otto C, Nishimura R, Bonow R, et al. 2020 ACC/AHA guideline for the management of patients with valvular heart disease: a report of the American College of Cardiology/American Heart Association Joint Committee on Clinical Practice Guidelines. *J Am Coll Cardiol*. 2021;77:e25-197. doi: 10.1016/j.jacc.2020.11.018
5. Nishimura R, Otto C, Bonow R, et al. 2017 AHA/ACC focused update of the 2014 AHA/ACC guideline for the management of patients with valvular heart disease. *Circulation*. 2017;135:1159-1195. doi: 10.1161/CIR.0000000000000503
6. Roudaut R, Lafitte S, Roudaut MF, et al. Management of prosthetic heart valve obstruction: fibrinolysis versus surgery. early results and long-term follow-up in a single-centre study of 263 cases. *Arch Cardiovasc Dis*. 2009;102:269-277. doi: 10.1016/j.acvd.2009.01.007
7. Caceres-Loriga FM, Perez-Lopez H, Morlans-Hernandez K, et al. Thrombolysis as first choice therapy in prosthetic heart valve thrombosis. A study of 68 Patients. J *Thromb Thrombolysis.* 2006;21:185-190. doi: 10.1007/s11239-006-4969-y
8. Özkan M, Gündüz S, Biteker M, et al. Comparison of different TEE-guided thrombolytic regimens for prosthetic valve thrombosis: the TROIA trial. *JACC Cardiovasc Imaging.* 2013;6(2):206-216. doi: 10.1016/j.jcmg.2012.10.016
9. Özkan M, Gündüz S, Gürsoy O, et al. Ultraslow thrombolytic therapy: a novel strategy in the management of PROsthetic MEchanical valve Thrombosis and the prEdictors of outcomE: The Ultra-slow PROMETEE trial. *Am Heart J*. 2015;170(2):409-418. doi: 10.1016/j.ahj.2015.04.025
10. Özkan M, Kaymaz C, Kirma C, et al. Intravenous thrombolytic treatment of mechanical prosthetic valve thrombosis: a study using serial transesophageal echocardiography. *J Am Coll Cardiol*. 2000;35(7):1881-1889. doi: 10.1016/s0735-1097(00)00654-9

Original Work

Lessons Learned in The Evaluation of Hospital Admissions for Patients with Heart Failure Seen by a Pharmacist in Addition to a Nurse Practitioner, Compared to a Nurse Practitioner Alone

by : Alexis T. Mowry, PharmD, Karrie A. Stanke, PharmD, BCPS

Abstract

Objective: Compare hospital admission rates for patients seen by a pharmacist in collaboration with a nurse practitioner, versus a nurse practitioner alone.

Methods: Two evaluators collaborated in a retrospective chart review of patients with congestive heart failure (CHF) who were seen in an outpatient cardiology clinic. The first evaluator selected 40 patients: 20 who saw a nurse practitioner (NP) and a pharmacist (RPh), and 20 who saw an NP alone. The evaluator matched the groups according to a heart failure admission risk score. A second evaluator, who was blinded to the groups, performed the data collection and analysis. The primary outcome was the number of hospital admissions at 30, 60, and 90 days post-cardiology clinic visit. A two-tailed student's t-test was used to detect statistically significant differences in the number of all-cause admissions between the two groups, with a p-value of less than 0.05 considered significant.

Results: The number of hospital admissions was lower in the RPh+NP group compared to the NP-only group at 30 (2 admissions RPh+NP vs. 4 admissions NP; p=0.389), 60 (4 admissions RPh+NP group vs. 5 admissions NP; p=0.714), and 90 days (4 admissions RPh+NP vs. 7 admissions NP; p=0.300) post-cardiology clinic visit, but not statistically significantly different for any of the time points evaluated.

Conclusions: Although not statistically significant, there were fewer hospital admissions in the interdisciplinary group compared to the NP-only group, which could support an expansion of pharmacist services in the outpatient cardiology clinic.

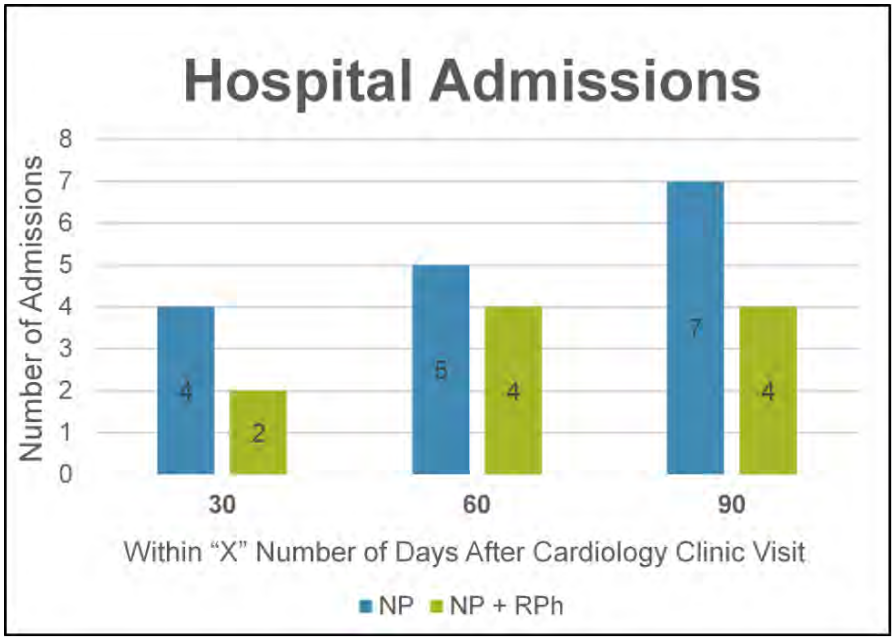
In 2014, heart failure admissions were estimated to cost the United States' health systems more than 11 billion dollars.[1] National initiatives such as the Hospital Readmissions Reduction Program and health-system specific interventions have emerged to reduce the frequency and cost of these admissions. One such initiative that has gained popularity in recent years is the addition of pharmacists to the care of patients with congestive heart failure (CHF) in ambulatory settings. Pharmacists can perform a variety of services in these ambulatory settings, including providing disease state, pharmacologic, and non-pharmacologic management and monitoring, performing medication histories, and providing medication recommendations to clinic providers.

Previous studies have evaluated pharmacist involvement in the care of CHF patients.[2-7] Many of these studies focus on pharmacists independently, or collaboratively meeting with CHF patients who have recently been discharged from the hospital to provide disease and medication-specific information, titrate medications to optimal doses, and perform medication histories. These studies suggest that pharmacist involvement decreases emergency room visits, decreases hospitalizations, and increases medication adherence. Focusing on heart failure admissions, one systematic review and meta-analysis of 12 studies including 2060 patients found that pharmacist involvement in the care of CHF patients significantly lowered all-cause (OR 0.71; 95% CI 0.54-0.94) and heart failure-specific hospital admissions (OR 0.69, 95% CI 0.51-0.94) compared with the control group.[2] Two smaller studies also found favorable effects, including at least a 50% reduction in hospitalizations after patients established care in ambulatory settings with a clinical pharmacist.[3,4]

Despite primarily positive findings in the literature, pharmacist expansion in ambulatory cardiology clinics has been slow. At the institution where this study was conducted, pharmacists are only allotted 0.125 full-time equivalents (FTE) to staff in the cardiology clinic, which equates to one day a week, every other week. The workflow in the clinic is drastically different

when the pharmacist is present compared to when the pharmacist is absent. The appointment length remains 30 minutes regardless of whether the pharmacist is present in clinic, but when the pharmacist is present, the pharmacist sees the patient first, performs a medication history, provides medication and lifestyle-specific education, and then verbally hands off their findings to the nurse practitioner (NP). When absent, the patient only sees the NP, and less time is devoted to medication-specific information. The purpose of this evaluation is to compare 30-, 60-, and 90-day hospital admissions between patients who see both the pharmacist (RPh) and the NP, versus the nurse practitioner alone. If the data supports it, next steps could include expanding the pharmacist FTE in the cardiology clinic.

FIGURE 1. Number of Hospital Admissions 30-, 60-, and 90 days After Cardiology Clinic Visit for Nurse Practitioner Only versus Nurse Practitioner and Pharmacist Groups



NP = Nurse Practitioner; NP + RPh = Nurse Practitioner and Pharmacist

Methods

Design

Two evaluators were involved in the data collection and synthesis of this retrospective chart review. The first evaluator selected patients for enrollment. To be eligible, patients had to have a diagnosis of CHF, and had to have been seen in the cardiology clinic between January and May 2020. Any patient with a diagnosis of CHF was eligible for inclusion, regardless of their ejection fraction being considered reduced (ejection fraction less than 40%), or preserved (ejection fraction greater than 50%). A total of 40 patients were selected (to reach 20 patients per group). Because admissions were evaluated through 90 days, patients in the RPh+NP group were selected in reverse chronological order by selecting patients who reached 90 days out from their cardiology clinic visit and then continued back in time to reach a total of 20 patients. Each of these 20 patients were scored based on heart failure admission risk, using a score that is calculated in the electronic medical record. This calculated score provides an estimated 1-year risk of being admitted to the hospital for heart failure, and ranges from 1% to 12%. The score defines a risk of 1-3% as low risk of admission, 4-9% as moderate risk, and 10-12% as high risk. To create groups with similar admission risk and thereby reduce the likelihood of confounding variables, the other group was selected to have admission risk scores that matched the first group (6 low, 12 medium, and 2 high risk patients respectively). Patients were excluded if they were deceased within 90 days of the visit, did not have a risk of heart failure admission score, or were selected for the NP-only group but met with a pharmacist within the previous year of their visit date. The other evaluator, who was blinded, conducted the retrospective chart review and documented the number, dates, and reasons for admission for each patient. Reasons for admission were documented and evaluated by consensus by the two evaluators to determine if they were elective versus non-elective procedures. Elective procedures (e.g. colonoscopies) were omitted from the final data as the intent of the evaluation was to reduce unintentional hospitalizations. All pharmacists who saw patients in the cardiology clinic had their Doctor of Pharmacy (PharmD) degrees, but no additional ambulatory care training.

Data Analysis

A two-tailed student's t-test was used to detect statistically significant differences in the number of admissions between the group seen by the RPh+NP versus the NP alone for 30, 60, and 90 days after cardiology clinic visits. A p-value of less than 0.05 was considered significant. This study was exempt from institutional review board (IRB) approval because it was a retrospective chart review.

Results

The number of hospital admissions was lower in the RPh+NP group compared to the NP-only group at 30 (2 admissions RPh+NP vs 4 admissions NP; p=0.389), 60 (4 admissions RPh+NP group vs 5 admissions NP; p=0.714), and 90 days (4 admissions RPh+NP vs 7 admissions NP; p=0.300) post-cardiology clinic visit, but not statistically significant for any time point evaluated (Figure 1). One patient underwent an elective colonoscopy during the study period from the NP only group, which was excluded from the final analysis. No patients were admitted multiple times during the study period.

Discussion

Comparison To Other Studies

The reduction in hospital admissions in the RPh+NP group compared to the NP alone group was approximately 43% by the end of the study. This is similar to previous studies that showed approximately a 50% reduction in hospital admissions with the addition of a pharmacist in this setting.[3,4] The results of this trial may be used to expand the FTEs of the pharmacist in the cardiology clinic. Furthermore, it can add to the growing literature that demonstrates the benefit of the addition of pharmacists to ambulatory cardiology clinics and other primary care settings.

Limitations

There are several limitations of this evaluation. First, this evaluation was not randomized, which could have introduced bias. Attempts were made to limit bias by blinding the evaluator who performed the chart review, although it is possible the evaluator inadvertently saw notes in the chart that may have indicated which group the patient belonged to. Second, hospital admissions may have been missed if patients sought care outside of the facility where the evaluation was conducted (and that facility did not communicate via Epic's Care Everywhere functionality). Third, patients were matched between the two groups based on a risk of heart failure admission score. Although this score might have created similar admission risk for heart failure-specific admissions, the primary endpoint of this evaluation was all-cause hospital admissions. The decision to choose all-cause hospital admissions was twofold. Much of the available literature reports all-cause admissions and not heart failure-specific admissions, which would allow comparisons to similar studies. Second, the health system tracks quarterly heart failure admissions (which are classified as admissions within 30 days for any reason, except for scheduled elective procedures). Therefore, to prove a benefit of the pharmacist in the cardiology clinic at an institutional level, the investigators chose a variable that closely matched what would be evaluated by the health system. Lastly, the results of this evaluation are likely only applicable to low- or medium-risk patients, because patients who were deceased within 90 days were excluded (likely the patients with the most advanced disease), and only two high-risk patients were included in each group at baseline.

Choice Of Statistical Test

The initial trial design was to use Fisher's exact test to determine if there was a statistically significant difference in the percentage of patients admitted versus not admitted in each of the groups. After realizing the potential for multiple admissions during the study period, the decision was made to switch to the student's t-test to evaluate the difference in the number of admissions between the two groups. Although no patients were admitted multiple times during the evaluation period, future evaluation would benefit from using the student's t-test to evaluate similar data to account for multiple admissions.

Conclusions

The addition of a pharmacist to an outpatient cardiology clinic may reduce hospital admissions through 90 days post-cardiology clinic visit. Future studies could evaluate the effect on hospital admissions for longer durations (e.g. 6 months to 1 year), and with larger sample sizes. Ideally, a randomized trial could be conducted to minimize selection bias in future studies.

Alexis Mowry is a PGY-1 Pharmacy Resident at Reedsburg Area Medical Center in Reedsburg, WI. Karrie A Stanke is a Clinical Pharmacist at Aurora BayCare Medical Center in Green Bay, WI.

PR *This article has been peer-reviewed. The contribution in reviewing is greatly appreciated!*

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

References

1. Jackson SL, Tong X, King RJ, Loustalot F, Hong Y, Ritchey MD. National burden of heart failure events in the United States, 2006 to 2014. *Circ Heart Fail.* 2018;11(12):e004873. doi:10.1161/CIRCHEARTFAILURE.117.004873
2. Koshman SL, Charrois TL, Simpson SH, McAlister FA, Tsuyuki RT. Pharmacist care of patients with heart failure: a systematic review of randomized trials. *Arch Intern Med.* 2008;168(7):687-694. doi:10.1001/archinte.168.7.687
3. Schumacher C, Moaddab G, Colbert M, Kliethermes MA. The effect of clinical pharmacists on readmission rates of heart failure patients in the accountable care environment. *J Manag Care Spec Pharm*. 2018;24(8):795-799. doi:10.18553/jmcp.2018.24.8.795
4. Ingram A, Valente M, Dzurec MA. Evaluating pharmacist impact on guideline-directed medical therapy in patients with reduced ejection fraction heart failure. *J Pharm Pract.* 2021;34(2):239-246. doi:10.1177/0897190019866930
5. Hale GM, Hassan SL, Hummel SL, Lewis C, Ratz D, Brenner M. Impact of a pharmacist-managed heart failure postdischarge (bridge) clinic for veterans. *Ann Pharmacother.* 2017;51(7):555-562. doi:10.1177/1060028017698974
6. Gattis WA, Hasselblad V, Whellan DJ, O'Connor CM. Reduction in heart failure events by the addition of a clinical pharmacist to the heart failure management team: results of the Pharmacist in Heart Failure Assessment Recommendation and Monitoring (PHARM) Study. *Arch Intern Med.* 1999;159(16):1939-1945. doi:10.1001/archinte.159.16.1939
7. Murray MD, Young J, Hoke S, et al. Pharmacist intervention to improve medication adherence in heart failure: a randomized trial. *Ann Intern Med.* 2007;146(10):714-725. doi:10.7326/0003-4819-146-10-200705150-00005

Original Work

Impact of Professional Continuous Glucose Monitors in an Ambulatory Clinic

by Ashley Moore, PharmD, Julie Bartell, PharmD, BCACP

Continuous glucose monitoring (CGM) systems have been rapidly gaining popularity over the last few years, as they serve as alternatives to traditional self-monitoring blood glucose (SMBG) methods. CGMs automatically measure interstitial glucose levels every few minutes through a microfilament sensor inserted under the patient's skin. The capability of CGMs to provide daily glycemic trends is a valuable tool to help guide clinical decision-making. This technology can help patients and providers make informed decisions based on glucose trends and offers an advantage over SMBG, which is limited by the need for frequent testing and the difficulty of reporting accurate results.

The first CGM system was approved for professional use by the United States Food and Drug Administration (FDA) in 1999. Since then, technological advancements in accuracy, usability, and duration of wear have given rise to a variety of CGM devices for both personal and professional use. Medicare and most private insurers have covered clinician use of professional CGMs for therapeutic management in diabetes for more than a decade; however, most professional CGM devices had historically required regular calibration with finger-stick blood glucose values to ensure their

TABLE 1. Baseline Demographics

Patients	22
Age in Years, Median (range)	60 (21-85)
Female (%)	13 (59.1)
Insulin Therapy (%)	20 (90.1)

TABLE 2. Baseline Control

	Average Hemoglobin A1c (%)	*Average Hypoglycemic Events Per Week*
Combined (n = 22)	**8.9 ± 1.6**	**0.7 ± 1.2**
Hemoglobin A1c		
>10 (n = 5)	11.3 ± 0.8	0.8 ± 1.6
9.0 - 9.9 (n = 5)	9.4 ± 0.3	0.0 ± 0.0
8.0 - 8.9 (n = 5)	8.4 ± 0.2	1.0 ± 1.3
7.0 - 7.9 (n = 4)	7.7 ± 0.3	1.3 ± 1.3

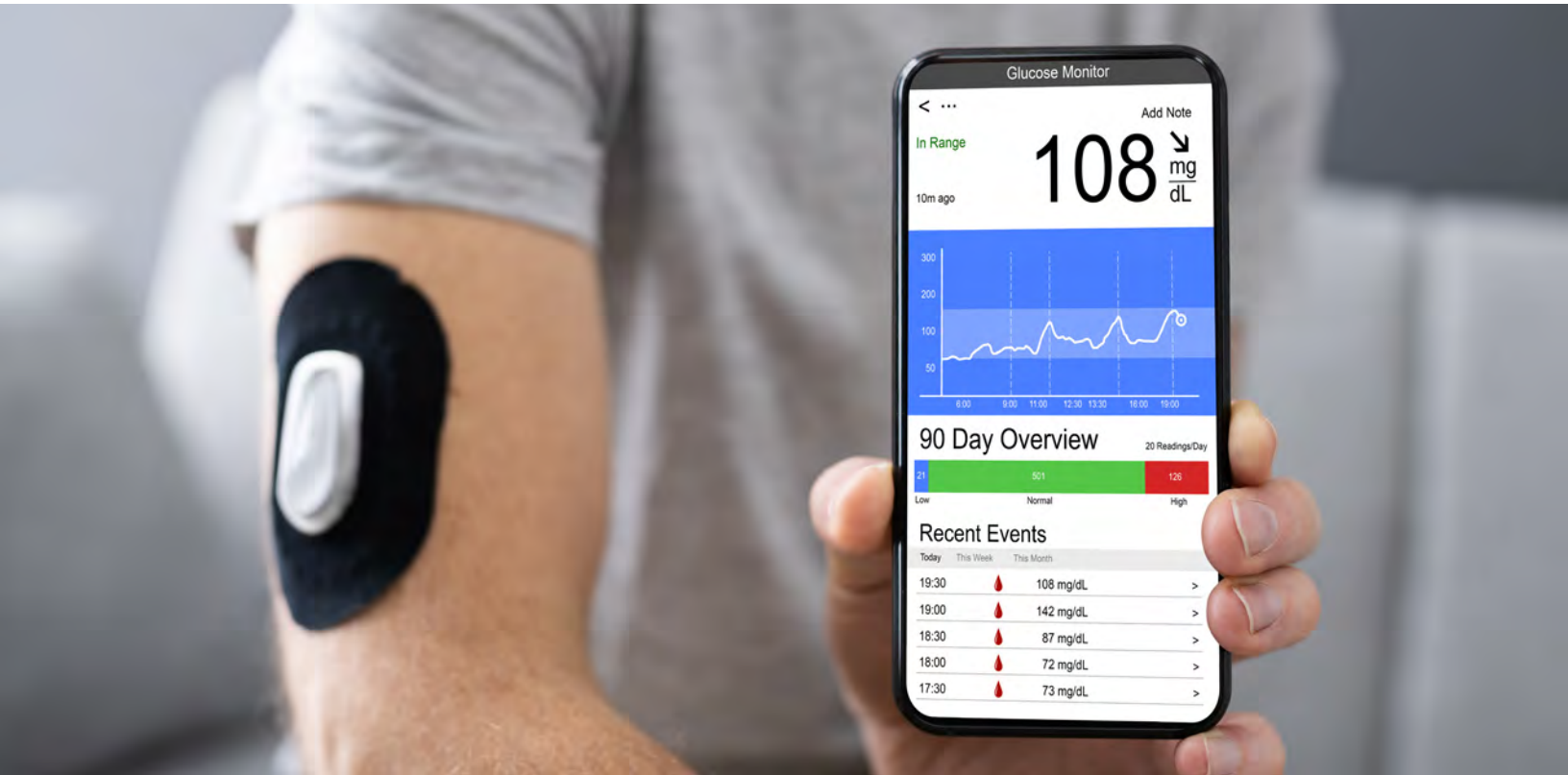
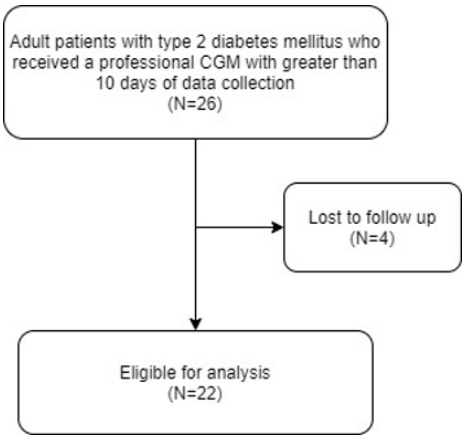


FIGURE 1. Patient Inclusion Flowchart



CGM: Continuous glucose monitor

accuracy.[1] The FreeStyle Libre Pro flash glucose monitoring system was approved by the FDA in 2016 for use by health care professionals in the management of patients with diabetes treated with insulin. It was the first professional CGM system to not require finger-stick calibration.[2]

The American Diabetes Association (ADA) Standards of Care state that CGMs have an important role in assessing the effectiveness and safety of treatment in subgroups of patients with type 1 diabetes mellitus (T1DM) and in selected patients with type 2 diabetes mellitus (T2DM).[3] These subgroups include patients who are not achieving glycemic targets, and those with hypoglycemic unawareness and/or frequent hypoglycemic episodes. While the ADA guidelines provide data demonstrating improved hemoglobin A1c (HbA1c) lowering and reduced frequency of hypoglycemia, the evidence was mostly derived from clinical trials of T1DM patients using real-time CGM.[4-7] 2021 ADA Standards of Care now recommend CGM as useful for people with diabetes on multiple daily injections, continuous subcutaneous insulin infusions, and other forms of insulin therapy despite age or type of diabetes.[3] Guidance provided by the American Association of Clinical Endocrinologists (AACE) and the American College of Endocrinology (ACE) 2016 Outpatient Glucose Monitoring Consensus Statement reported that data on CGM use, real-time or retrospective, in patients with T2DM using insulin, sulfonylureas, or meglitinides is limited and additional studies are recommended to evaluate its role in T2DM management.[8] A follow-up consensus conference by AACE/ACE concluded that the benefits of CGM in patients with T1DM are likely to be replicated in patients using intensive insulin therapy, regardless of the type of diabetes.[9] It was also recommended that real-world analyses of health care use for acute and chronic complications affect the impact of both personal and professional CGM on potential cost savings and health-related quality of life. Consequently, clinicians would benefit from further guidance on the value of professional CGM in the management of patients with both type 1 and type 2 diabetes.

There is currently minimal research on the value of professional CGM in patients with diabetes. Furthermore, there is limited literature describing the effectiveness of clinical pharmacist-led professional CGM services in the ambulatory setting.

Today, both professional and personal CGMs are available to the general public. One of the largest drawbacks of a CGM is cost. Professional CGM placements are billed as a procedure through medical insurance, while personal CGMs are typically billed through drug insurance. Patients' out-of-pocket costs can vary based on their insurance plans. When affordable, professional CGMs are an effective way of getting a two-week snapshot of a patient's glycemic control when a personal CGM is not an affordable option. In addition, they can be used as a bridge until a patient is approved for a personal CGM. For more information on CGMs in general, please refer to the contining education available in the July/August 2021 issue of The Journal of the Pharmacy Society of Wisconsin.[10]

SSM Health Monroe Clinic is a rural health system located in southern Wisconsin, which consists of a 58-bed hospital and several multispecialty clinic practices. There are seven satellite branch clinics located throughout southern Wisconsin and northern Illinois. Ambulatory care pharmacists (pharmacotherapists) at the Monroe Clinic are uniquely positioned in the pharmacotherapy department to manage chronic disease states, including diabetes. This is achieved through broad scopes of practice and collaborative practice agreements (CPAs), allowing the pharmacotherapists to adjust medications, order labs, and follow up with the patients at their discretion.

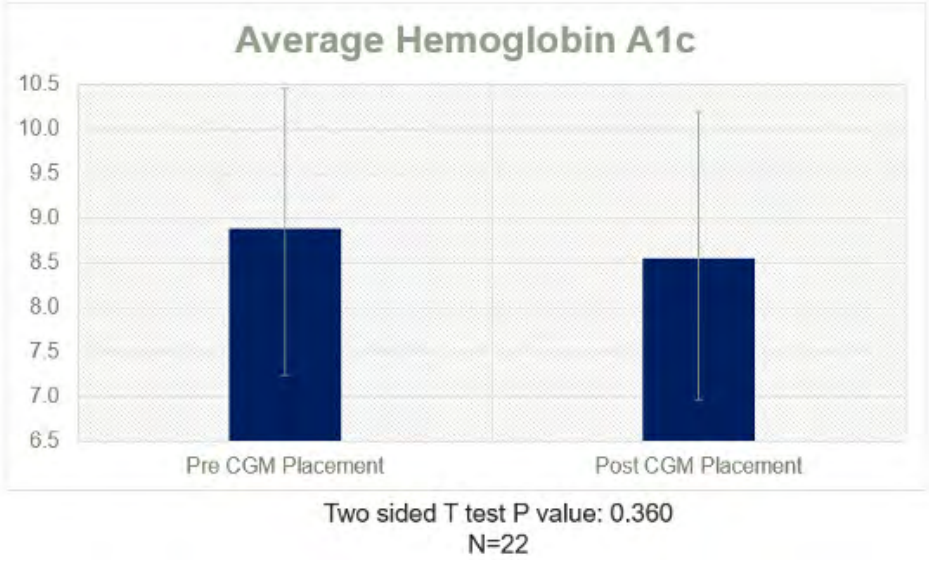
Methods

This is a retrospective, pre-post, cohort analysis conducted from September 1, 2020–February 28, 2021 at the SSM Health-Monroe Clinic pharmacotherapy department. This study was determined to be exempt from IRB review.

Outcomes

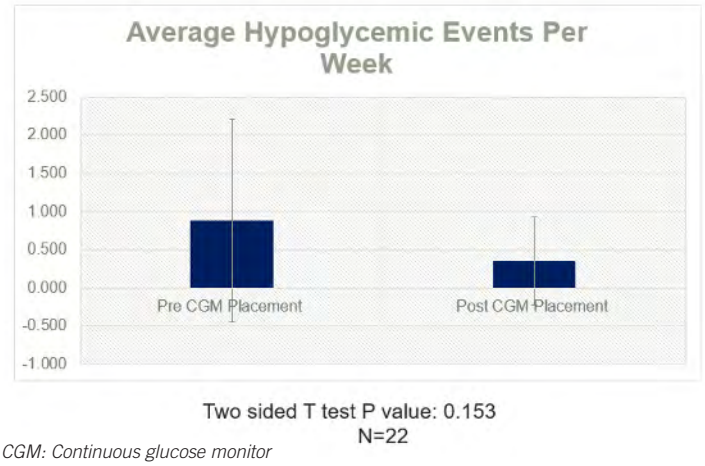
The objective of this project was to evaluate the clinical and economic impact of professional CGMs on the management of patients with type 2 diabetes by ambulatory

FIGURE 2. Change in Hemoglobin A1c



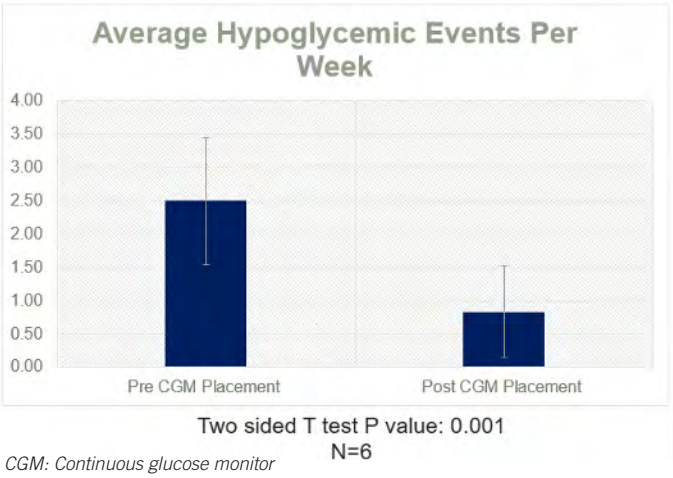
CGM: Continuous glucose monitor

FIGURE 3. Overall Change in Hypoglycemic Events



CGM: Continuous glucose monitor

FIGURE 4. Change in Hypoglycemic Events in Patients Experiencing Hypoglycemia



CGM: Continuous glucose monitor

care pharmacists. Clinical impact was measured through glycemic control and change in hypoglycemic events. Glycemic control was defined as the change in the most recent HbA1c prior to CGM placement, and the first HbA1c after CGM placement. The change in incidence of hypoglycemia was defined as any patient-reported episodes requiring treatment or self-monitored blood glucose of less than 70 mg/dL reported within a timeframe of 3 months prior to and 3 months post CGM placement. Paired t-tests were used to compare the change from baseline to post-intervention HbA1c and hypoglycemic events.

Data collection

Starting in September 2020, pharmacotherapists began offering FreeStyle Libre Pro CGM devices for professional use to patients with type 2 diabetes over the age of 18 years. A nurse-only encounter was scheduled for CGM placement by nursing staff, and a follow up appointment for CGM removal and data download by nursing staff was scheduled approximately 14 days later. Pharmacotherapists then met with patients to discuss CGM results and adjust antihyperglycemic therapy based on interpretation of the ambulatory glucose profile (AGP). Current Procedural Terminology (CPT) code 95250 was used within the EHR to bill for professional CGM placement.

All clinical data was extracted from patients' electronic medical records, while reimbursement data was provided by the Monroe Clinic's billing department. Insurance reimbursement to the healthcare system was also collected and analyzed.

Results

Upon review of electronic medical records, 26 patients had a professional CGM placed within the 6-month study period. A total of 22 patients were included for analysis (Figure 1). The majority of the study population was female and had a mean age of 60 years, with most patients receiving supplemental insulin. (Table 1).

The primary outcome of glycemic control is summarized in Figure 2. The mean difference between pre- and post-intervention HbA1c was 0.3% (p=0.360). Overall, there was a decline in weekly hypoglycemic events (Figure 3). A subgroup analysis (Figure 4) was performed on six patients experiencing hypoglycemic events prior to CGM placement which showed a statistically significant decrease from 2.5 to 0.8 weekly events (p=0.001).

All CPT codes associated with the professional CGM placement were submitted by the pharmacotherapists. Reimbursement data for CPT code 95250 was available for all patients and the mean payment amount was $107.42 ± $157.12 per patient, which was greater than CGM unit acquisition costs and encounter expenses.

Discussion

Adjustment of antihyperglycemic therapy was implemented in 21 of the 22 patients during the study period, demonstrating a mean decrease in HbA1c of 0.3%. While this was not a statistically significant difference, it did show clinical improvement. More significantly, pharmacotherapists were able to use CGM data to make medication adjustments, which resulted in reducing hypoglycemic events by over 65%. Professional CGMs also created a new form of revenue for the department. This study supports that CGMs are a beneficial tool in patients with T2DM.

These documented medication interventions did not include lifestyle recommendations that were implemented as a result of professional CGM use. While not measured directly, patients were able to visualize how lifestyle habits, such as dietary choices or medication adherence, impacted blood glucose levels throughout the day when reviewing CGM reports with their pharmacotherapist. These variations in glycemic control that would have been otherwise undiscovered by intermittent SMBG values allowed patients to recognize the effects of positive and negative lifestyle habits and implement behavioral changes with the pharmacotherapist's guidance.

Patients with T2DM have become a substantial portion of patients seen in the pharmacotherapy department at SSM Health- Monroe Clinic. This number will continue to grow through the roll out of the Diabetes Center for Excellence. With this program, any patient who is referred to diabetes education with an HbA1c greater than 8 is automatically referred to the department and seen by a pharmacotherapist.

A limitation of this study was the small sample size and short timeframe. It is likely that all results would reach statistical

significance given more time and CGM placements.

Conclusion

A major barrier in clinical practice is motivating patients to perform SMBG at appropriate and consistent intervals that allow for effective adjustments to antidiabetic regimens. This gap in care has prompted the expansion of both professional and personal-use CGMs in clinical practice. Professional CGMs can provide a useful bridge for patients and providers to improve patient care and are covered under patients' insurance plans as a medical procedure. Overall, professional CGMs are a financially beneficial tool to guide medication adjustments for patients with T2DM to improve glycemic control.

Ashley Moore is a Pharmacy Resident at SSM Health – Monroe Clinic in Monroe, WI. Julie Bartell is the Residency Director at SSM Health – Monroe Clinic in Monroe, WI.

PR *This article has been peer-reviewed. The contribution in reviewing is greatly appreciated!*

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

References

1. Telgener PC, Lowe S. A look at the current reimbursement environment for continuous glucose monitoring (CGM): understanding the fundamentals. *J Diabetes Sci Technol.* 2008;2(4):681-684. doi: 10.1177/193229680800200419
2. Libre Pro flash glucose monitoring system FDA summary of safety and effectiveness data. Accessed December 26, 2020. http://www.accessdata.fda.gov/cdrh_docs/pdf15/P150021B.pdf
3. American Diabetes Association. 7. Diabetes technology: standards of medical care in diabetes-2021. *Diabetes Care.* 2021;44(suppl 1):S85-S99. doi: 10.2337/dc21-S007
4. Tamborlane WV, Beck RW, Bode BW, et al. Continuous glucose monitoring and intensive treatment of type 1 diabetes. *N Engl J Med.* 2008; 359(14):1464-1476. doi: 10.1056/NEJMoa0805017
5. Lind M, Polonsky W, Hirsch IB, et al. Continuous glucose monitoring vs conventional therapy for glycemic control in adults with type 1 diabetes treated with multiple daily insulin injections: the GOLD randomized clinical trial. *JAMA.* 2017;317(4):379-387. doi: 10.1001/jama.2016.19976
6. Beck RW, Riddlesworth T, Ruedy K, et al. Effect of continuous glucose monitoring on glycemic control in adults with type 1 diabetes using insulin injections: The DIAMOND randomized clinical trial. *JAMA.* 2017;317(4):371-378. doi: 10.1001/jama.2016.19975
7. Wong JC, Foster NC, Maahs DM, et al. Real-time continuous glucose monitoring among participants in the T1D exchange clinic registry. *Diabetes Care.* 2014;37(10):2702-2709. doi: 10.2337/dc14-0303
8. Bailey T, Grunberger G, Bode B, et al. American Association of Clinical Endocrinologists and American College of Endocrinology 2016 outpatient glucose monitoring consensus statement. *Endocr Pract.* 2016;22(2):231-261. doi: 10.4158/EP151124.CS
9. Fonseca VA, Grunberger G, Anhalt H, et al. Continuous glucose monitoring: a consensus conference of the American Association of Clinical Endocrinologists and American College of Endocrinology. *Endocr Pract.* 2016;22(8):1008-1021. doi: 10.4158/EP161392.CS
10. Blake W, Rivera V, Woloszyn C, Patel K, Srivastava S. Review of continuous glucose monitors: technology and beyond. *J Pharm Soc Wis.* 2021;24(4):4-13.

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

The Importance of USP <797>: Teaching Proper Aseptic Technique and Implementation of Standard Operating Procedures

by Katie Fermanich, 2022 PharmD Candidate, Melissa Smith, 2023 PharmD Candidate, Elizabeth Braun, 2023 PharmD Candidate, McKay Carstens, 2024 PharmD Candidate

Compounded medications—medications that are combined, mixed, or have altered ingredients to tailor the medication to the needs of an individual patient—are estimated to make up 1% to 3% of all prescriptions, despite a lack of tracking of their exact volume.[1,2] Although compounded medications are a small portion of the overall number of dispensed prescriptions, the impact of an error in compounding one of these medications can result in dramatic consequences. In 2012, contaminated preparations of a preservative-free methylprednisolone acetate injection prepared in a compounding pharmacy caused a meningitis outbreak in 20 states.[3] Fourteen thousand people were exposed to the contaminated injections, resulting in 751 cases of fungal meningitis, other infections, and strokes, and 64 deaths, making this one of the largest healthcare-related outbreaks in the United States. In fact, over the past 40 years, there have been a significant number of cases of contaminated compounded products that have caused various adverse events, including infections, blindness, and deaths.[4] Great advances have been made since the development of compounding guidelines, and survey data from 2007 reveal that 96% of pharmacy schools provided some didactic and laboratory instruction about sterile compounding.[5] However, variation in the depth of this education among schools of pharmacy and space for interpretation within the guidelines poses a risk for compounding errors. In this article, we aim to emphasize the importance of the aseptic technique and explore its strengths and weaknesses, to highlight the importance of sterile-compounding education in both pharmacies and pharmacy schools.

USP <797>

The United States Pharmacopeia (USP) is an independent, nonprofit organization whose founding purpose was to devise standards for the quality and safety of medicines to protect the health of the public.[6] That mission is still the driving force for USP today. For sterile compounded preparations (CSPs), USP <797> is the governing chapter. One important element of this document is its thorough breakdown of several sections, especially CSP microbial contamination risk levels, which provides an in-depth assessment and examples of corresponding aseptic manipulations.[7] Another notable feature is its mention of rigorous testing methods for ensuring compounders are performing aseptic technique adequately. For example, USP <797> mentions using media fill tests as the method for evaluating the quality of aseptic manipulation skills of personnel, and requires that the test is performed under the most challenging or stressful conditions by the personnel being evaluated.[7] Additionally, a recent revision to USP <797> in 2018 included biannual testing of sterile techniques, as opposed to only annual testing, using the media-fill tests in addition to yearly testing of core competencies through either written exam, observed demonstration, or both.

However, an ostensible gap in USP <797> is its level of ambiguity, where it explains what must be done for proper aseptic technique but not how it must be done, which means it is up to the best judgment, interpretation, and training experience of compounders. Furthermore, other areas of ambiguity rely on the instruction of more experienced personnel rather than thoroughly written out techniques. For example, USP <797> mentions under its "Responsibility of Compounding Personnel" heading that all CSPs are to be prepared sterilely and with minimal introduction of particulate matter, and refers to both compounders and compounding supervisors as the parties responsible for ensuring this goal is met.[7] However, despite the extensive duties of the compounding personnel, compounders must rely on direct measurement and judgment of the compounding supervisor, or unspecified appropriate information sources as a means to fulfilling these requirements. This further raises the question of how aseptic technique is facilitated by personnel beyond the compounder.

Aseptic technique is a practice used by healthcare professionals where its purpose is to prevent the contamination of sterile compounded medications with microbial pathogens, bacterial endotoxins, and unintended chemical and physical contaminants.[7] The set of rules governing aseptic technique minimize the risk of causing infection; bodily harm via chemical contaminants or physical particles; or death to patients being administered compounded sterile preparations, surgical operations using sterile equipment, or exposure to medical tools designed to enter the body.[7,8] Healthcare professions who apply aseptic technique include pharmacists, pharmacy technicians, physicians, nurses, and a multitude of others whose position is to handle sterile medications or equipment.

In pharmacy practice, aseptic technique is important for producing sterilely compounded medications. However, when it comes to the oversight of these products, what responsibilities does the pharmacist

take? Patricia C. Keinle, a pharmacist and leading medication safety expert at Cardinal Health, argued in 2020 that the role of the pharmacist in sterile compounding is patient safety and being aware of risks associated with compromised sterile preparations.[9] Pharmacists can work with other pharmacy personnel to help see that sterile preparations are being compounded using the safest and most effective techniques and processes.

Proper aseptic technique leads to fewer incidences of contamination, as indicated by Austin and Elia in their 2013 study that compared a pharmacy operator with more training in aseptic technique to nurses who have less instruction in this area.[10] When tasked with preparing parenteral intravenous dose syringes, the pharmacy operator outperformed the nurses by making more syringes, faster, and with much less contamination. This emphasized the importance of using proper aseptic technique when preparing intravenous doses, because doing so leads to fewer occurrences of contamination. In 2002, van Grafhorst et al. further represented the impacts of aseptic technique by seeing it from another perspective.[11] This study compared syringes made by pharmacy technicians under standard aseptic conditions to intensive care unit nurses practicing under ICU standard procedures. It was found that the deficiency of proper aseptic technique and the lack of an aseptic environment led to high rates of contamination with Gram-positive bacteria. Both incidents suggest that using proper aseptic technique promotes fewer occurrences of contamination and yields safer compounded products.

Hospital/Clinic

Any community pharmacy, institutional pharmacy, specialty pharmacy, etc. has the creative ability to develop an aseptic compounding procedure. What's more, these compounding sites need to follow USP <797> to the best of their ability, despite the guideline being largely open to interpretation. A standard operating procedure (SOP) is one way aseptic technique and USP <797> can be organized and customized to fit each pharmacy's specific practices and needs. Standard operating procedures are beneficial to the success of aseptic compounding and have the potential to benefit different pharmacy settings. One important idea is that aseptic compounding is a skill that should be continuously improved upon by using standard operating procedures to promote the advancement of safety and efficacy.[12] Standardized training programs have the ability to properly train staff while reducing variability among staff members.

Aurora Health Care (AHC), located in eastern Wisconsin, performs sterile compounding at 15 of its 16 hospitals and 22 specialized cancer-care clinics.[12] Before 2016, AHC did not have a standardized process for sterile compounding, leading to different procedures, techniques, knowledge, and skills that varied among sites. AHC worked to fix this by identifying super users at each site, who attended an in-person, one-day refresher course focusing on key concepts related to USP <797> and <800>. Before the training, there was a pre-intervention stage that assessed super users' current knowledge of aseptic technique. The assessments included a written sterile-compounding knowledge-based exam; a media-fill challenge test; and a rubric-based observation assessment of aseptic technique, done in conjunction with the media-fill challenge test. After the pre-intervention assessments, trainees participated in a one-day refresher training intervention, which included a one-hour online review of related calculations, a 30-minute online review of beyond-use date (BUD) assignment, and a live training course focused on aseptic technique and major knowledge-based concepts within USP Chapter <797>.

A main focus of this training was to instill standardized knowledge across all sites.[12] After all training had been completed, a post-intervention assessment was conducted that included the same assessments given in the pre-intervention. Trainees passed if they received a score of 80% or higher for the knowledge-based exam, and if their media-fill test was negative for contamination. Overall, there was a statistically significant improvement on all assessments that were included in the pre- and post-intervention (written exam scores $P < 0.0001$; written exam pass rates $P < 0.0001$; aseptic technique observations pass rates $P < 0.0001$; media fill with aseptic technique evaluation for matched pair only $P < 0.0002$). These statistically significant results demonstrated an increased retention of sterile-compounding knowledge and better performance of aseptic compounding, leading to reduced microbial contamination. After the course, the super users brought their valuable knowledge back to their sites, to distribute the information and perform evaluations of other personnel who perform sterile compounding. From this study, a new sterile-compounding training program was developed. It incorporated a refresher training course, online learning modules, and repeated evaluations.

Schools of Pharmacy

Pharmacy school is one place where future pharmacists can learn sterile compounding, and the manner of teaching has evolved over time. In late 2016, a survey was sent to 139 schools of pharmacy across the United States to gain information about their compounded sterile products curriculum.[13] This study was an update to one completed by Hellums et al. in 2007.[5] The survey measured elements of course structure, compounding environment, and compounding experience.[13] In the ten years between surveys, there was a significant increase in schools teaching beyond use dating and incorporating a laboratory aspect to teach aseptic technique. After passing written competencies, sterile compounding is generally guided by technique and skill more than knowledge. Implementing experiences to practice the concepts learned in lecture reinforces those teachings. Learning and practicing proper aseptic compounding processes in pharmacy school creates a foundational experience students will take into their careers. Students may also receive further guidance at their workplace when sterile compounding plays a role in their practice.

Rural Areas

Smaller critical access hospitals (CAHs) have needs for sterile compounding as well. When these products are needed, it is essential to follow USP standards. Crawford et al. surveyed 40 rural hospitals in Illinois to determine compliance with USP <797>, the availability of sterile compounding practices, and where the compounding is done.[14] Results showed that 75% of the hospitals surveyed were in compliance with USP <797>, while 17.5% were unsure of their compliance status; the remaining hospitals did not respond.

Furthermore, the most common areas for sterile compounding in the CAHs were in a glove box (47.8%); in a laminar flow hood in a clean room (30.4%); and in a laminar-airflow hood in a separate I.V. room (17.4%). The glove box affords a sterile environment about the size of a desk for staff to prepare medications in places where space may be limited. Data from this survey demonstrates that there is ample room to implement SOPs to ensure practices are up to date with USP <797> at rural hospitals despite challenges they may face.

Conclusion

While SOPs create a standardized process, that uniformity only extends to the specific institution for which it was developed. Furthermore, there is great variability among institutions with respect to available resources and sterile compounding volume, so a one-size-fits-all approach is not appropriate. Regardless of the details of implementation, the crucial factor in developing high-quality aseptic technique is the implementation of an SOP itself, along with the administrative support needed to create and maintain it. Additionally, rules are best learned and retained when they are continuously reinforced.[15] Therefore, it is important that sterile compounding be integrated into pharmacy school curriculum. Students who learn aseptic technique early in their careers can implement these standards into their future pharmacy practice, and work to prevent future healthcare outbreaks and consequences for patients.

Katie Fermanich is a 4th Year Doctor of Candidate, Melissa Smith is a 3rd Year Doctor of Pharmacy Candidate, Elizabeth Braun is a 3rd Year Doctor of Pharmacy Candidate, and McKay Carstens is a 2nd Year Doctor of Pharmacy Candidate at the University of Wisconsin-Madison School of Pharmacy in Madison, WI.

PR *This article has been peer-reviewed. The contribution in reviewing is greatly appreciated!*

Acknowledgements: Thank you to Nate Menninga for his mentorship and guidance in the writing of this manuscript.

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

References

1. FDA's human drug compounding progress report: three years after enactment of the Drug Quality and Security Act. U.S. Food and Drug Administration. Published January 2017. Accessed April 15, 2021. https://www.fda.gov/drugs/human-drug-compounding/fdas-human-drug-compounding-progress-report-three-years-after-enactment-drug-quality-and-security
2. Watson CJ, Whitledge JD, Siani AM, Burns MM. Pharmaceutical compounding: a history, regulatory overview, and systematic review of compounding errors. *J Med Toxicol.* 2021;17(2):197-217. doi:10.1007/s13181-020-00814-3
3. Multistate outbreak of fungal meningitis and other infections. Centers for Disease Control and Prevention. Published October 30, 2015. Accessed April 15, 2021. https://www.cdc.gov/hai/outbreaks/meningitis.html
4. Myers CE. History of sterile compounding in U.S. hospitals: learning from the tragic lessons of the past. *Am J Health Syst Pharm*. 2013;70(16):1414-1427. doi:10.2146/ajhp130112
5. Hellums M, Alverson SP, Monk-Tutor MR. Instruction on compounded sterile preparations at U.S. schools of pharmacy. *Am J Health Syst Pharm*. 2007;64(21):2267-2274. doi:10.2146/ajhp060531
6. United States Pharmacopeial Convention. From guesswork to standards: the history of medicine quality. Accessed April 17, 2021. https://www.usp.org/200-anniversary/history-of-medicine-quality#:~:text=The%20U.S.%20Pharmacopeia%20was%20first,entry%20with%20tools%20to%20identify
7. United States Pharmacopeial Convention. General chapter <797> pharmacopeial compounding – sterile preparations. Accessed September 6, 2020. https://online.uspnf.com/uspnf/document/1_GUID-A4CAAA8B-6F02-4AB8-8628-09E102CBD703_6_en-US
8. The Joint Commission. Preventing central line–associated bloodstream infections: useful tools, an international perspective. Nov 20, 2013. Accessed April 19, 2021. https://www.jointcommission.org/-/media/tjc/documents/resources/health-services-research/clabsi-toolkit/clabsi_toolkit_tool_3-8_aseptic_versus_clean_techniquepdf.pdf
9. Kienle PC. Sterile compounding safety: the pharmacist's responsibility. *Am J Health Syst Pharm*. 2020;77(11):811-813. doi:10.1093/ajhp/zxaa055
10. Austin P, Elia M. Improved aseptic technique can reduce variable contamination rates of ward-prepared parenteral doses. *J Hosp Infect*. 2013;83(2):160-163. doi: 10.1016/j.jhin/2012.009
11. van Grafhorst JP, Foudraine NA, Nooteboom F, Crombach WH, Oldenhof NJ, van Doorne H. Unexpected high risk of contamination with staphylococci species attributable to standard preparation of syringes for continuous intravenous drug administration in a simulation model in intensive care units. *Crit Care Med*. 2002;30(4):833-836. doi:10.1097/00003246-200204000-00019
12. Loomis M, Kosinski T, Wucherer S. Development and implementation of a standardized sterile compounding training program. *Hosp Pharm.* 2019;54(4):259-265. doi:10.1177/0018578718788841
13. Cooper C, Almgren MM, Maxwell WD, Baker JL. Instruction on compounded sterile preparations at schools of pharmacy. *Am J Health Syst Pharm.* 2018;75(12):845-847. doi:10.2146/ajhp170641
14. Crawford SY, Schumock GT, Ursan ID, Walton SM, Donnelly AJ. Comparison of pharmacy services at critical access hospitals and other rural and small hospitals in Illinois. *Am J Health Syst Pharm*. 2013;70(15):1313-1321. doi:10.2146/ajhp120442
15. Bromage BK, Mayer RE. Quantitative and qualitative effects of repetition on learning from technical text. *J Ed Psych.* 1986;78(4):271-278. doi:10.1037/0022-0663.78.4.271

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

Pharmacogenetic Testing in Psychiatric Pharmacy: Background, Clinical Relevance, and Barriers

by Sarah A. Fierek, 2022 PharmD Candidate, Amy M. Genisot, 2022 PharmD Candidate, Rachel A. Hawley, 2022 PharmD Candidate, Molly A. O'Connell, 2023 PharmD Candidate, Amy M. Wolff, 2023 PharmD Candidate

Pharmacogenetics is the study of how variations in inherited DNA sequences affect individual responses to medications.[1] Identifying gene variants is important, because variants can alter the pharmacokinetic and pharmacodynamic properties of drugs, thus impacting metabolism.

Approximately 1 in 5 prescriptions are affected by actionable pharmacogenes, meaning the presence of gene variants may influence how an individual responds to a medication.[2] Many psychotropic drugs, such as antidepressants, anxiolytics, and antipsychotics, are metabolized by enzymes that vary in activity based on one's genes. Although the use of medications affected by actionable pharmacogenes is common, preemptive pharmacogenetic testing is not yet widespread due to lack of access, affordability, utility, and necessity.[3]

Genes Targeted During Pharmacogenetic Testing

Cytochrome P450 (CYP) enzymes are responsible for the metabolism of many drugs. Namely, 90% of drugs are metabolized by six CYP enzymes: 1A2, 3A4, 3A5, 2C9, 2C19, and 2D6.[4] Genetic variability of CYP enzymes may lead to differences in how a patient responds to a particular drug. For example, a genotype that increases the activity of a CYP enzyme that metabolizes a drug will result in a lower concentration of the active drug in circulation, decreasing efficacy. Alternatively, a genotype that decreases the activity of a CYP enzyme that metabolizes a drug will lead to a higher concentration of drug in circulation, producing toxicity. Additionally, in the case of prodrugs, the effects on drug metabolism will be the opposite of those previously mentioned. That is, a genotype that induces metabolism of the prodrug will effectively result in an increase in active drug in circulation. However, a genotype that inhibits the metabolism of the prodrug will result in a decrease in active drug in circulation. This information has been incorporated into clinical practice guidelines to help clinicians predict how a patient will respond to a particular drug therapy.

Genotypes describe changes in the number of copies present of a gene encoding a functional CYP enzyme. In general, more functional copies of the gene result in an increased level of metabolism, while fewer functional copies of the gene result in a decreased level of metabolism. Using this idea, when individuals are genotyped, they can be placed into one of up to five phenotype groups. These groups are based on the number of functional copies of the gene they have, corresponding with the metabolic activity seen in their designated genotype. These groupings are: poor metabolizers (PM), intermediate metabolizers (IM), normal metabolizers (NM), rapid metabolizers (RM), and ultrarapid metabolizers (UM).[5] Individuals with two nonfunctional copies of a gene are considered poor metabolizers. There is little to no metabolic activity seen within this genotype. Individuals who have one functional copy of a gene and one nonfunctional copy are considered intermediate metabolizers. Within this group, there is more metabolic activity compared to the poor metabolizers, but less than in normal metabolizers. Individuals

TABLE 1. CYP Phenotypes[5]

Phenotype	*Example*	*Effect on Metabolism*
Poor Metabolizer (PM)	Individuals who are homozygous for a gene that results in a nonfunctional enzyme	Decreased activity of the enzyme resulting in little to no metabolism of the substrate
Intermediate Metabolizer (IM)	Individuals who are heterozygous for a gene that results in one functional copy and one nonfunctional copy of an enzyme	Decreased activity of the enzyme resulting in lower levels of metabolic activity than normal metabolizers, but greater activity than normal metabolizers
Normal Metabolizer (NM)	Individuals who are homozygous for a gene that results in two functional copies of an enzyme	Normal enzyme activity which results in normal levels of metabolism of the substrate
Rapid Metabolizer (RM)	Individuals who are heterozygous for a gene that results in one increased function copy and one normal function copy of an enzyme	Increased activity of the enzyme which results in an increased level of metabolism of the substrate
Ultrarapid Metabolizer (UM)	Individuals who have more than two functional copies of an enzyme	Increased activity of the enzyme which results in an increased level of metabolism of the substrate

who have two fully functioning copies of a gene are considered wild-type, and are normal metabolizers. They have what is considered normal metabolic activity of the enzyme. Lastly, those with genes conferring greater than normal level function (e.g., more than two functional copies of a gene) are described as rapid or ultrarapid metabolizers, depending upon the gene and level of activity. The metabolic activity of the enzyme for these groups is greater than that of the normal metabolizers. See Table 1 for a summary of the CYP phenotypes and their effects on substrate metabolism.

Clinicians should look to evidence-based guidelines created by organizations like the Clinical Pharmacogenetics Implementation Consortium (CPIC) and the Food and Drug Administration (FDA) for guidelines concerning prescribing medications with actionable pharmacogenes.[6,7] The CPIC and FDA provide information for over 200 medications and dosing guidelines regarding these drugs. These medications are used to treat many different disease states (i.e. anticoagulation, oncology, etc.) and involve a variety of CYP enzymes. However, only CYP2D6 and CYP2C19 provide clinicians with guidance for prescribing psychiatric medications within the CPIC guidelines.[6] These guidelines are specific for dosing of tricyclic antidepressants (TCAs) and selective serotonin reuptake inhibitors (SSRIs). In terms of FDA guidelines, there are 40 neuropsychiatric medications with listed pharmacogenetic considerations.[7] For these 40 medications, information recommending that the dosage be modified if the patient has a known specific CYP variant and metabolizer status can be found in the package insert.[8] Pharmacists and clinicians often use additional resources that summarize pertinent dosing recommendations from CPIC and the FDA to increase efficiency during clinical encounters. One of these references is the *CPIC and FDA Labeling Guidelines Pocket Guide* created by Dr. Vincent Wartenweiler and Dr. Cody Wenthur, also published in this issue of *The Journal*.[9] This pocket guide contains information on genotypes, dosing recommendations based on phenotype, strength of recommendation, and additional information to note when dosing the given medication.

Clinical Relevance

Precision medicine is defined as targeting treatments to the needs of individual patients on the basis of genetic, biomarker, phenotypic, or psychosocial characteristics that distinguish a given patient from another with similar clinical presentations.[10] Advancement in precision medicine has led to improved clinical outcomes for specific patient populations. For example, precision medicine has been used in various disease states including cancer, cardiovascular disease, metabolic disease, smoking cessation, and psychiatry. The determination of treatment required for many of these disease states not only requires various biomarkers, but also genetic testing. Clinically actionable pharmacogenetic testing is used by clinicians to make prescribing recommendations when providing care to patients.[11] In practice, this testing has become more prevalent with one study of 11 million insured patients finding utilization to have nearly doubled between 2013 and 2017, increasing from 1,955 to 3,946 tests performed.[12]

For major depressive disorder, pharmacogenetic testing has the potential to reduce disease severity, decrease adverse drug reactions, improve response time to therapy, and provide cost savings to patients.[13] Further, studies of pharmacogenetic testing in other psychiatric conditions demonstrate evidence of clinical improvement with easy-to-administer tests and little risk to the patient.[14] Clinically, pharmacogenetic testing can be used in psychiatric patients when starting a particular medication to determine appropriate doses based on the patient's metabolic enzyme activity. Testing is also used in patients who have tried and failed multiple medication therapies, a common occurrence in psychiatric medications. Although the absolute utility of pharmacogenetic testing in psychiatry is still being determined, promising results for its use in specific patient populations were observed when analyzing adults less than 60 years old, diagnoses with moderate to severe depression, or diagnoses between 1 and 5 years in length.[15] Pharmacogenetic testing led to statistically significant reductions in

TABLE 2. Pharmacogenetic Resources

Resource	*Website Link*	*Description*
Clinical Pharmacogenetics Implementation Consortium (CPIC)[6]	https://cpicpgx.org/guidelines/	• This website provides clinical practice guidelines regarding how genetic test results can be used to optimize pharmacotherapy. • These guidelines are peer-reviewed and evidence-based.
Dutch Pharmacogenetics Working Group (DPWG)[26]	https://www.pharmgkb.org/page/dpwg	• This link provides access to the DPWG homepage. • DPWG provides a key describing how they rank evidence quality of a drug-gene interaction, as well as the clinical relevance of that interaction. • Through this website, specific clinical recommendations can be found on the KNMP website.
U.S. Food and Drug Administration (FDA)[7]	https://www.fda.gov/medical-devices/precision-medicine/table-pharmacogenetic-associations	• This website links to the FDA's Table of Pharmacogenetic Associations. • This document highlights three categories of pharmacogenomic associations with currently approved medications.
Pharmacogenomics Knowledge Base (PharmGKB)[27]	https://www.pharmgkb.org/	• This website links to the homepage for PharmGKB. • There are annotations provided by PharmGKB for drug labels, clinical guidelines, curated pathways, and drugs. • The annotations can be used by clinicians and researchers to understand how genetic variation impacts drug response.

baseline depressive severity scores in patients with these characteristics when compared to adults of different ages, diagnosis, and diagnoses lengths.

Guidelines created by CPIC suggest how to apply the results of pharmacogenetic testing to tailor medication prescribing, but often lack recommendations on appropriateness.[11] Overall, more progress needs to be made in clinical studies comparing the use of prescribing guided by pharmacogenetic testing to medication decisions not guided by pharmacogenetic testing. This includes high-quality studies of adverse effect profiles and cost-effectiveness to prove clinical utility. With these improvements, clinicians will be provided with appropriate clinical guidance and reduced barriers to implementation to help guide psychiatric medication decisions.

Barriers to Pharmacogenetic Testing

The clinical implementation of pharmacogenetic testing in psychiatry has the potential to improve patient outcomes. However, many challenges exist concerning patient access to and provider execution of pharmacogenetic testing. In psychiatry, there is often a delay between a patient's treatment and their response to psychotropic medications.[16] Results from pharmacogenetic testing may optimize pharmacotherapy by maximizing therapeutic benefits and minimizing adverse effects for patients. Notable challenges for patients and providers in pharmacogenetic testing implementation in psychiatry include: cost-effectiveness; availability of resources and clinical guidelines; and provider preparedness.[16-19]

The cost-effectiveness of pharmacogenetic testing in psychiatry is not clearly defined, which has prevented widespread clinical implementation.[17] However, a systematic review of the utility of pharmacogenetic testing in psychiatry found five studies that evaluated cost-effectiveness.[18] Every study found a reduction in medical costs, ranging from 9.5% to 28%; these reductions were the result of fewer treatment failures and adverse events for patients. In addition, there is a lack of data regarding the availability of insurance coverage for pharmacogenetic testing. For patients with private insurance, coverage may vary depending on their insurance plan, the pharmacogenetic testing done, the lab completing the test, and the reason for testing.[20] The coverage of pharmacogenetic testing for Medicare and Medicaid beneficiaries can also vary based on a variety of factors, including necessity for testing and which gene is being analyzed.[21] To solve the insurance coverage barrier to testing, insurance companies must be provided with an incentive. This can be done by improving and expanding the current literature in pharmacogenetics to demonstrate that an upfront cost of pharmacogenetic testing can result in future savings for the insurance companies.[16]

Increased awareness of the clinical guidelines and other educational resources available to providers is important.[22] Mental health providers may include psychiatrists, nurse practitioners, primary care providers, or pharmacists under collaborative practice agreements. These clinicians, in addition to genetic counselors and other professionals, require training and support for pharmacogenetic delivery to be successful.[16] Research is currently underway to improve provider understanding of when pharmacogenetic tests should be ordered and how their results should be interpreted.[22] In 2018, a publication detailed the successful implementation of pharmacogenetic services in the inpatient psychiatry service over the course of 14 years at Cincinnati Children's Hospital Medical Center.[23] The use of a multidisciplinary team contributed to the success of implementing pharmacogenetic services, further proving the necessity of educating providers on pharmacogenetics.

Pharmacists, with their expertise in medication use, have the potential to serve as key resources in pharmacogenetics for both providers and patients.[19,24] In recent years, education for pharmacists on pharmacogenetics has increased. The Accreditation Council for Pharmacy Education (ACPE) 2016 Standards for the Doctor of Pharmacy curriculum require pharmacogenetics as an element of training.[25] In addition, practicing pharmacists can use the following resources, as mentioned previously, to improve their understanding of pharmacogenetics testing: CPIC, FDA, Dutch Pharmacogenetics Working Group (DPWG), and PharmGKB.[6,7,26,27] These resources are described in detail in Table 2.

Pharmacogenetic Spotlight

Marshfield Clinic Health Systems, Inc.

Some pharmacists in Wisconsin are using pharmacogenetic testing at their practice sites. One of these is Marshfield Clinic Health Systems, Inc., where Dr. Emili Leary, PharmD, specializes in pharmacogenetic testing and runs a pharmacogenetic bootcamp. The bootcamp (more formally known as the Marshfield Clinic Pharmacogenomics Certificate Program), started in 2018 and is a two-week, 80-hour intensive program. Throughout the program, participants learn about methods of DNA evaluation, and genes pertinent to pharmacogenetics. The participants engage in topic discussions, lectures, and clinical practice applications such as case studies. To make the experience more impactful and relatable, learners are offered the opportunity to complete and examine their own genetic test. Additionally, participants learn how to provide actionable recommendations based on pharmacogenetic test results to patients and providers. Currently, the program is offered to pharmacy residents, genetic counseling students, other internal Marshfield Clinic employees, and pharmacy students. In the future, the program will hopefully be expanded to include medical students and residents, as well as other professional students.

Clinically, Dr. Leary's job responsibilities include providing recommendations to practitioners after patients receive their pharmacogenetic test results. In practice, these genetic tests are used most often for disease states of anxiety and depression after multiple therapies have been ineffective or caused adverse effects. CYP2D6 and CYP2C19 are highly polymorphic drug metabolizing enzymes that can result in poor efficacy of psychiatric medications. In her practice, Leary's recommendations may include choosing a new medication that is not processed by those specific enzymes. Additionally, dosage adjustments can also be made. To help patients understand their results, Leary suggests that pharmacists use patient-friendly language and analogies.

Less than 1% of the clinic population at Marshfield Clinic uses pharmacogenetic testing. Cost is a significant barrier to these tests, with an average price around

$300-$400. After pharmacogenetic testing, 30-50% of patients have potentially actionable findings and may end up having their medication regimen modified. Marshfield Clinic is one of the first health systems to implement a pharmacist role in pharmacogenetic testing in Wisconsin; however, there is still room for expansion. Leary envisions that community pharmacies could use a patient's genetic results with the CPIC website to identify drug-gene interactions. Pharmacists would then be able to call the prescriber and intervene.

The work by Leary and her colleagues at Marshfield Clinic provides an excellent example of how pharmacogenetic testing can be implemented into practice to find more effective drug therapies for patients.

Sarah A. Fierek, Amy M. Genisot, and Rachel A. Hawley are 3rd Year Doctor of Pharmacy Candidates at the University of Wisconsin-Madison School of Pharmacy in Madison, WI. Molly A. O'Connell and Amy M. Wolff are 2nd Year Doctor of Pharmacy Candidates at the University of Wisconsin-Madison School of Pharmacy in Madison, WI.

PR *This article has been peer-reviewed. The contribution in reviewing is greatly appreciated!*

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

References

1. Aneesh TP, M SS, Jose A, Chandran L, Zachariah SM. Pharmacogenomics: the right drug to the right person. *J Clin Med Res.* 2009;1(4):191-194. doi:10.4021/jocmr2009.08.1255
2. Dunnenberger HM, Crews KR, Hoffman JM, et al. Preemptive clinical pharmacogenetics implementation: current programs in five US medical centers. *Annu Rev Pharmacol Toxicol.* 2015;55:89-106. doi:10.1146/annurev-pharmtox-010814-124835
3. Moaddeb J, Haga SB. Pharmacogenetic testing: current evidence of clinical utility. *Ther Adv Drug Saf.* 2013;4(4):155-169. doi: 10.1177/2042098613485595
4. Lynch T, Price A. The effect of cytochrome P450 metabolism on drug response, interactions, and adverse effects. *Am Fam Physician.* 2007;76(3):391-396.
5. Roden DM, McLeod HL, Relling MV, et al. Pharmacogenomics. *Lancet.* 2019;394(10197):521-532. doi:10.1016/S0140-6736(19)31276-0
6. Clinical Pharmacogenomics Implementation Consortium. Guidelines. Updated March 26, 2021. Accessed October 9, 2021. https://cpicpgx.org/guidelines/
7. FDA: Food and Drug Administration. Table of Pharmacogenetic Associations. Updated May 5, 2021. Accessed October 9, 2021. https://www.fda.gov/medical-devices/precision-medicine/table-pharmacogenetic-associations
8. Gross T, Daniel J. Overview of pharmacogenomic testing in clinical practice. Ment Health Clin. 2018;8(5):235-241. doi:10.9740/mhc.2018.09.235
9. Wartenweiler V, Wenthur C. Pocket guide - CPIC and FDA labeling guidelines. *J Pharm Soc Wis.* 2020;24(6):44-45.
10. Jameson JL, Longo DL. Precision medicine--personalized, problematic, and promising. *N Engl J Med.* 2015;372(23):2229-2234. doi:10.1056/NEJMsb1503104
11. Caudle KE, Klein TE, Hoffman JM, et al. Incorporation of pharmacogenomics into routine clinical practice: the Clinical Pharmacogenetics Implementation Consortium (CPIC) guideline development process. *Curr Drug Metab.* 2014;15(2):209-217. doi:10.2174/1389200215666140130124910
12. Anderson HD, Crooks KR, Kao DP, Aquilante CL. The landscape of pharmacogenetic testing in a US managed care population. *Genet Med.* 2020;22(7):1247-1253. doi: 10.1038/s41436-020-0788-3
13. Rosenblat JD, Lee Y, McIntyre RS. does pharmacogenomic testing improve clinical outcomes for major depressive disorder? A systematic review of clinical trials and cost-effectiveness studies. *J Clin Psychiatry.* 2017;78(6):720-729. doi:10.4088/JCP.15r10583
14. Espadaler J, Tuson M, Lopez-Ibor JM, Lopez-Ibor F, Lopez-Ibor MI. Pharmacogenetic testing for the guidance of psychiatric treatment: a multicenter retrospective analysis. *CNS Spectr.* 2017;22(4):315-324. doi:10.1017/S1092852915000711
15. Menchon JM, Espalder J, Tuson M, et al. Patient characteristics driving clinical utility in psychiatric pharmacogenetics: a reanalysis from the AB-GEN multicentric trial. *J Neural Transm.* 2018; 126:95-99 https://doi.org/10.1007/s00702-018-1879-z
16. Brown L, Eum S, Haga SB, Strawn JR, Zierhut H. Clinical utilization of pharmacogenetics in psychiatry – perspectives of pharmacists, genetic counselors, implementation science, clinicians, and industry. *Pharmacopsychiatry.* 2020;53(4):162-173. doi:10.1055/a-0975-9595
17. Zanardi R, Prestifilippo D, Fabbri C, Colombo C, Maron E, Serretti A. Precision psychiatry in clinical practice. *Int J Psychiatry Clin Pract.* 2021;25(1):19-27. doi:10.1080/13651501.2020.1809680
18. Gardner KR, Brennan FX, Scott R, Lombard J. The potential utility of pharmacogenetic testing in psychiatry. *Psychiatry J.* 2014;e730956. doi:10.1155/2014/730956
19. Kennedy MJ. Personalized medicines - are pharmacists ready for the challenge? *Integr Pharm Res Prac.* 2018;7:113-123. doi:10.2147/IPRP.S133083
20. Pharmacogenomics: drug-gene testing. Mayo Clinic. Accessed January 17, 2020. https://www.mayo.edu/research/centers-programs/center-individualized-medicine/patient-care/pharmacogenomics/drug-gene-testing
21. Medicare coverage database. Centers for Medicare & Medicaid Services. Updated August 12, 2020. Accessed January 17, 2021. https://www.cms.gov/medicare-coverage-database/details/lcd-details.spx?lcdid=38435&ver=6&keyword=P450&keywordType=starts&areaId=s57&docType=NCA,CAL,NCD,MEDCAC,TA,MCD,6,3,5,1,F,P&contractOption=all&sortBy=relevance&bc=AAAAAAQAAAAA&KeyWordLookUp=Doc&KeyWordSearchType=Exact
22. Zierhut HA, Campbell CA, Mitchell AG, Lemke AA, Mills R, Bishop JR. Collaborative counseling considerations for pharmacogenomic tests. *Pharmacotherapy.* 2017;37(9):990-999. doi:10.1002/phar.1980
23. Ramsey LB, Prows CA, Zhang K, et al. Implementation of pharmacogenetics at Cincinnati Children's Hospital Medical Center: lessons learned over 14 years of personalizing medicine. *Clin Pharmacol Ther.* 2019;105(1):49-52. doi:10.1002/cpt.1165
24. Haidar CE, Petry N, Oxencis C, Douglas JS, Hoffman JM. ASHP Statement on the pharmacist's role in clinical pharmacogenomics. *Am J Health Syst Pharm.* 2021;zxab339. doi:10.1093/ajhp/zxab339.
25. Accreditation Council for Pharmacy Education. Accreditation standards and key elements for the professional program in pharmacy leading to the Doctor of Pharmacy degree. 2015. Accessed January 17, 2021. https://www.acpe-accredit.org/pharmd-program-accreditation/
26. DPWG: Dutch Pharmacogenetics Working Group. Accessed October 9, 2021. https://www.pharmgkb.org/page/dpwg
27. PharmGKB: Pharmacogenomics knowledge base. Accessed October 9, 2021. https://www.pharmgkb.org/

Review Article

Pocket Guide - CPIC and FDA Labeling Guidelines

by Vincent Wartenweiler, PharmD, Cody Wenthur, PharmD, PhD

In support of healthcare providers at William S. Middleton Memorial Veterans Hospital, the following document was generated as a reference for clinical decision making for commonly prescribed psychiatric medications. The prescribing frequency of psychiatric medications at the Madison VA was assessed to determine any trends in the prescription distribution. Following this data review, the most prescribed psychiatric medications were selected to be included in the final document. The goal of the pocket guide is to offer a simple, centralized collection of information concerning safety and efficacy implications for selected psychiatric medications with pharmacogenetic dosing considerations. The intended use of the pocket guide is primarily referential, not prescriptive. This list is not all inclusive and review of the pocket guide is not an acceptable substitute for the clinical evaluation of a licensed healthcare provider.

Vincent Wartenweiler is a 2021 Doctor of Pharmacy Graduate from the University of Wisconsin-Madison School of Pharmacy in Madison, WI. Cody Wenthur is an Assistant Professor at the University of Wisconsin-Madison School of Pharmacy in Madison, WI.

Drug name	Type of interaction	Diplotypes (i.e. genotypes)	Alternatives/next steps	Strength of Recommendation	Additional monitoring/ follow-up
Ex. clopidogrel	*Safety*	*CYP2C19 *1/*17*	*Standard dosing of clopidogrel*	*Strong*	*None*
Carbamazepine (CBZ)#	Safety (**SERIOUS ADR**)	**HLA-A and HLA-B** HLA-B*15:02 negative HLA-B*15:02 positive HLA-A*31:01 negative HLA-A*31:01 positive	**HLA-A and HLA-B** Double negative: use standard dose B*15:02(-) and A*31:01(+): use alternative if CBZ naĭve B*15:02(+) and any A*31:01: use alternative if CBZ naĭve	Strong Strong Strong	Possibility of developing SJS/ TEN even if patient is double negative pheotype. Exercise caution and monitor closely for s/sx of rash.
Doxepin+	Pharmacokinetic (↑ side effects and ↓ response)	**CYP2C19** *17/*17 *1/*17 *1/*1 *1/*2, *1/*3, *2/*17 *2/*2, *2/*3, *3/*3 **CYP2D6** (*1/*1)xN, (*1/*2)xN, (*2/*2)xN *1/*1, *1/*2, *2/*2, *1/*9, *1/*41, *41/*41, *1/*5, *1/*4 *4/*41, *5/*9, *4/*10 *4/*4, (*4/*4)xN, *3/*4, *5/*5, *5/*6	**CYP2C19** UM: avoid tertiary amines OR consider a non-2C19 medication RM: “ “ NM: use standard dose IM: use standard dose PM: avoid tertiary amines OR consider a 50% dose reduction **CYP2D6** UM: choose a non-2C19 medication or increase target dose NM: use standard dose IM: consider a 25% dose reduction or alternative PM: avoid TCAs OR consider a 50% dose reduction if warranted	Optional Optional Strong Optional Optional Optional Strong Optional Optional	IF you are considering amitriptyline as an alternative, be aware that there is appreciable metabolism by BOTH CYP2C19 AND CYP2D6. See Table 4 of CPIC Guidelines on for CYP2D6 and CYP2C19 Genotypes and Dosing of Tricyclic Antidepressants: 2016 Update.+
(Es) citalopram^	Pharmacokinetic (↑ side effects)	**CYP2C19** *17/*17, *1/*17 *1/*1 *1/*2, *1/*3, *2/*17 *2/*2, *2/*3, *3/*3	**CYP2C19** UM: choose non-2C19 medication NM: use standard dose IM: use standard dose PM: consider 50% dose reduction or alternative	Moderate Strong Strong Moderate	Consider monitoring Na+ labs.
Oxcarbazepine (OXC)#	Safety (**SERIOUS ADR**)	**HLA-B** HLA-B*15:02 negative HLA-B*15:02 positive	**HLA-B** HLA-B*15:02 negative: use standard dose HLA-B*15:02 positive: use alternative if OXC naĭve	Strong Strong	Possibility of developing SJS/ TEN even if patient is double negative pheotype. Exercise caution and monitor closely for s/sx of rash."
Sertraline^	Pharmacokinetic (↑ side effects)	**CYP2C19** *17/*17, *1/*17 *1/*1 *1/*2, *1/*3, *2/*17 *2/*2, *2/*3, *3/*3	**CYP2C19** UM: use standard dose NM: use standard dose IM: use standard dose PM consider a 50% dose reduction or alternative	Optional Strong Strong Optional	Consider monitoring Na+ labs.

^ Hicks JK, Bishop JR, Sangkuhl K, et al. Clinical Pharmacogenetics Implementation Consortium (CPIC) Guideline for CYP2D6 and CYP2C19 Genotypes and Dosing of Selective Serotonin Reuptake Inhibitors. Clin Pharmacol Ther. 2015;98(2):127-134. doi:10.1002/cpt.147
# Phillips EJ, Sukasem C, Whirl-Carrillo M, et al. Clinical Pharmacogenetics Implementation Consortium Guideline for HLA Genotype and Use of Carbamazepine and Oxcarbazepine: 2017 Update. Clin Pharmacol Ther. 2018;103(4):574-581. doi:10.1002/cpt.1004
+Hicks JK, Sangkuhl K, Swen JJ, et al. Clinical pharmacogenetics implementation consortium guideline (CPIC) for CYP2D6 and CYP2C19 genotypes and dosing of tricyclic antidepressants: 2016 update. Clin Pharmacol Ther. 2017;102(1):37-44. doi:10.1002/cpt.597
For more information see: https://cpicpgx.org/guidelines/
Last updated: 9/16/2020

UM = ultrarapid metabolizer
RM = rapid metabolizer
NM = normal metabolizer
IM = intermediate metabolizer
PM = poor metabolizer

Drug name	Type of interaction	Diplotypes (i.e. genotypes)	Alternatives/next steps	Strength of Recommendation	Additional monitoring/ follow-up
Clopidogrel	*Safety*	*CYP2C19 *1/*17*	*Standard dosing of clopidogrel*	*Strong*	*None*
Clozapine	Pharmacokinetic (↑ side effects)	**CYP2D6** *1/*1xN, *1/*2xN, *2/*2xN *1/*1, *1/*2, *1/*4, *1/*5, etc. *4/*10,*4/*41, *5/*9 *3/*4, *4/*4, *5/*5, *5/*6	**CYP2D6** UM: no recommendation NM: no recommendation IM: no recommendation PM: Results in higher systemic concentrations. Dosage reductions may be necesary.	Level 2B and Actionable	Continue to monitor ANC and target drug concentrations as indicated.
D-amphetamine salts	Pharmacokinetic (↑ side effects)	**CYP2D6** *1/*1xN, *1/*2xN, *2/*2xN *1/*1, *1/*2, *1/*4, *1/*5, etc. *4/*10,*4/*41, *5/*9 *3/*4, *4/*4, *5/*5, *5/*6	**CYP2D6** UM: no recommendation NM: no recommendation IM: no recommendation PM: May affect systemic concentrations and adverse reaction risk. Consider lower starting dosage or use alternative agent.	Level 3 and Informative	None
(Des)venlafaxine	Pharmacokinetic (↑ side effects)	**CYP2D6** *1/*1xN, *1/*2xN, *2/*2xN *1/*1, *1/*2, *1/*4, *1/*5, etc. *4/*10,*4/*41, *5/*9 *3/*4, *4/*4, *5/*5, *5/*6	**CYP2D6** UM: no recommendation NM: no recommendation IM: no recommendation PM: Alters systemic parent drug and metabolite concentrations. Consider dosage reductions.	Venlafaxine: Level 2A and Actionable Desvenlafaxine: Informative only	Consider monitoring Na+ labs.
Donepezil	Pharmacokinetic (↑ side effects)	**CYP2D6** *1/*1xN, *1/*2xN, *2/*2xN *1/*1, *1/*2, *1/*4, *1/*5, etc. *4/*10,*4/*41, *5/*9 *3/*4, *4/*4, *5/*5, *5/*6	**CYP2D6** UM: alters systemic concentrations NM: no recommendation IM: no recommendation PM: alters systemic concentrations	Level 3 and Actionable	None
Risperidone	Pharmacokinetic (↑ side effects)	**CYP2D6** *1/*1xN, *1/*2xN, *2/*2xN *1/*1, *1/*2, *1/*4, *1/*5, etc. *4/*10,*4/*41, *5/*9 *3/*4, *4/*4, *5/*5, *5/*6	**CYP2D6** UM: no recommendation NM: no recommendation IM: no recommendation PM: Alters systemic parent drug and metabolite concentrations.	Level 1B and Informative	Continue to monitor metabolic panels (i.e. FLP, A1c, PRL etc.) as indicated.

For more information: https://www.fda.gov/medical-devices/precision-medicine/table-pharmacogenetic-associations
Last updated: 9/16/2020

UM = ultrarapid metabolizer
RM = rapid metabolizer
NM = normal metabolizer
IM = intermediate metabolizer
PM = poor metabolizer

2021 PSW Annual Meeting

2021 PSW Annual Meeting Recap

by Amber Patt, 2022 PharmD Candidate, Kaitlin Ledvina, 2023 PharmD Candidate

Just as life has adapted to the progression of the COVID-19 pandemic, so too did the 2021 PSW Annual Meeting. Unlike last year's virtual-only platform, the 2021 meeting (which was held September 17-18) offered attendees the option to join virtually or in person. More than 280 students, technicians, and pharmacists gathered in person at the Hyatt Regency in Green Bay, honoring social distancing and mask policies. Forty-seven participants joined virtually from the comfort of their own homes and offices, making this year's conference a truly hybrid experience. Upon registering for the event, members had access to the conference content through the PSW app. On the app, members could access on-demand virtual content, the schedule of events, speaker biographies, and more. They could even post photos and comments on the 2021 PSW annual meeting activity stream. Echoing the 2020 PSW virtual meeting, topics for this year's meeting addressed the fluidity of the pharmacy landscape due to the COVID-19 pandemic, but also focused on recognizing leadership qualities both within oneself and within the team.

The PSW app's on-demand content gave members access to 10 pre-recorded sessions on a variety of pharmacy topics, from the impact of ambulatory care pharmacists on medication adherence to assessing beta-lactam allergies. Pharmacists and technicians could also collect CE credits while learning how to improve patient care and the patient experience, and how to maximize performance.

Friday afternoon kicked off the conference with four forums: Ambulatory Care, Community Pharmacy, Health-System Pharmacy, and Leadership Development. Each forum covered topics unique to its respective practice area during the three-hour session, and all included a speaker-led discussion, networking opportunities, and an update on PSW work toward provider status. Attendees at the ambulatory care practice and community practice forums received PSW clinical toolkits, which included updated information on various disease states and special patient populations. The toolkits covered topics like tobacco cessation, asthma, diabetes management, hypertension, heart failure, healthy lifestyle, collaborative practice agreements, and pharmacogenomics, as well as a new toolkit on pediatrics.

The Ambulatory Care Practice forum, led by Dr. Julie Bartell and Dr. Maria Wopat, gave attendees a chance to deliver feedback about resources from the Ambulatory Care Advisory Committee. Those resources include podcasts, toolkits, residency worksheets, and rotation/residency preceptor manuals. These items help guide pharmacy students during residency and support pharmacy care providers in making the best patient-care decisions in the clinic setting. Additionally, Dr. Eric Matey of Mayo Clinic in Rochester, MN, spoke on

> **"Very few organizations are willing to take on the challenge of delivering a 'hybrid' conference to provide an in-person and virtual experience. PSW rose to the challenge and provided a great experience for members wherever they joined us from." David Hager, UW Health**

The New Era of Medication Prescribing: What Clinicians Need to Know- The Role of Pharmacogenomics. Dr. Matey provided information to the audience on how to practice at the top of their profession through utilizing pharmacogenomic testing, when to consider testing and how to identify resources to support pharmacogenomics in practice.

Dr. Dimmy Sokhal and Dr. Nicole Shreiner led the Community Pharmacy Practice forum and provided a platform for attendees to discuss and share ideas surrounding best practices and difficulties seen in the community pharmacy. Topics included hypertension and blood pressure monitoring; influenza and COVID-19 vaccine administration and billing; and technician vaccination training. Dr. Dave Mott of the UW-Madison School of Pharmacy presented "Community Pharmacist Access to Health-System EHS," where he addressed barriers and facilitators to EHR access, best practices, and strategies that could be implemented to facilitate future access to health system EHRs by community pharmacists.

The Health-System Pharmacy forum discussed two major topics in current pharmacy practice: labor and pharmacy technician shortages, and practice advancement initiatives. The Student and PSW Outreach PALT subgroup (Dr. Moataz Ali, Dr. Robert Lolcoma, and Dr. Matt Wong) discussed the current shortages in the healthcare workforce, specifically pharmacy technicians. They offered possible solutions to this dilemma and held a question and answer (Q&A) session to hear from attendees about shortages at their practice sites. The practice advancement initiative topic, presented by Dr. Kofi Andoh, Dr. Drew Dretske, and Dr. Shannel Gallard, gave audience members recommendations and resources for adapting to the ever-changing pharmacy practice models and meeting the demands of patient care needs.

"Cultivating Your Career" was the topic of the Leadership Development forum, presented by Dr. Brook DesRivieres of Vizient. Dr. DesRivieres spoke about creating a personal brand and using social media, like LinkedIn, for creating original contentt. She described the personal brand's four elements: personal appearance, personality, competencies, and unique values that differentiate you from others. She then offered LinkedIn and networking tips.

Friday evening concluded with a welcome dinner and reception, held at the Johnsonville Tailgate Village at Lambeau Field. Attendees had the unique opportunity to tour Lambeau Field and visit the field through the players' tunnel.

After a memorable evening of networking at the reception, Saturday was full of the PSW general sessions. Dr. Melissa Theesfeld, former PSW President, welcomed guests to the conference and introduced Dr. Brandon Jennings, Founder, President, and CEO of Abilyn Consulting, LLC. Dr. Jennings cpresented "Become a Leader Worth Following: Discover Your Leadership Voice." Jennings spoke about identifying your foundational leadership voice through the Leadership Voice Quiz, and how to be a "liberating leader" while understanding your team's dynamic, and everyone's dominant voice. Deborah Biddle, Founder and Chief Consultant with The People Company, presented "Inclusive Leadership: Unconscious Bias, Trust and Decision-Making." She encouraged the audience to be aware of their own biases, and prevent those biases from interfering with their behaviors, opinions, and decisions.

Following the general sessions, Dr. Sarah Sorum, Vice President and CEO of PSW, and Danielle Womack, Vice President of Public Affairs for PSW, gave an update on PSW advocacy efforts. They focused on the push for provider status; contraceptive access expansion; pharmacy technician registration; and the passing of the PBM reform and pharmacy immunization laws.

Dr. Theesfeld delivered her presidential remarks and thanked the PSW members who were transitioning from office. The newest board members were inducted, and Dr. Ellina Seckel was installed as the 2021-2022 PSW President and gave her presidential remarks.

The afternoon featured the Exhibit Showcase, with 40 exhibitors who shared pharmacy knowledge and expertise with attendees. At the Poster Session, 17 posters lined the central hallway of the conference rooms as pharmacy students and pharmacists presented their work. Throughout the conference there were several exhibit theaters, including AstraZeneca, describing therapy for stoke or transient ischemic attack and management of uncontrolled asthma; Incyte, describing Monjuvi in combination with lenalidomide; and DrFirst, describing AI improvements for medication history.

The afternoon featured the Residency Showcase, where 19 residency programs met one-on-one with students and spent time answering questions, discussing program specifics, and making personal connections. Other afternoon programming included "Medication Management Standards Compliance," "Preventing your Immature Leadership Voice from Undermining Your Influence," "Application of a Hypertension Management Program," and "When You've Exhausted First Line Therapies for Chronic Pain Management," as well as a COVID response panel.

The PSW Annual Meeting 2021 was a tremendous success, despite challenges surrounding the COVID-19 pandemic. The meeting's hybrid approach delivered substantial content to both online and in-person attendees and demonstrated that the pharmacy community is dedicated to improving the lives of patients in the state of Wisconsin and beyond.

"Thank you so much for a great conference. I really enjoyed the weekend. You put together meaningful programming in a very challenging year. I appreciate all you do for PSW and all that you did for me and others to make the weekend great!!" Janet Fritsch, Hometown Pharmacy

Amber Patt is a 3rd Year PharmD Candidate and Kaitlin Ledvinais a 2nd Year PharmD Candidate at the Medical College of Wisconsin School of Pharmacy in Milwaukee, WI.

PSW Educational Programming Committee

by Marisa Goninen, PharmD, BCACP

Change is a constant, and we have seen an enormous amount of change in pharmacy, healthcare, and the world in the past couple years. So much so that 'unprecedented' was named the People's Choice 2020 Word of the Year by Dictionary.com. While pharmacy practice evolved during the pandemic, we know that pharmacy practice has always been constantly evolving and will continue to do so.

With changes in clinical guidelines, scope of practice, and authorization of new therapies, it is imperative that our pharmacy community never stops learning–and that's why education is a core component of PSW.

Like many members, my first exposure to PSW educational programming was through attending conferences. I remember going to my first Annual Meeting and being blown away by how many sessions there were to choose from! I always love reading through upcoming meeting agendas to see all the new information there is to learn, and I'm continually impressed by the breadth of educational offerings. Beyond conference sessions, members can engage in webinars, online CE, and journal CE.

Who's behind all this? Our amazing PSW members develop and present educational content through these various avenues. Over the course of my PSW membership, I've been grateful for opportunities to present posters and an on-demand presentation. In 2020, I wanted to find a way to give back to the organization a bit more after all the benefits I have and continue to receive. Joining the Educational Programming Committee allowed me to do just that!

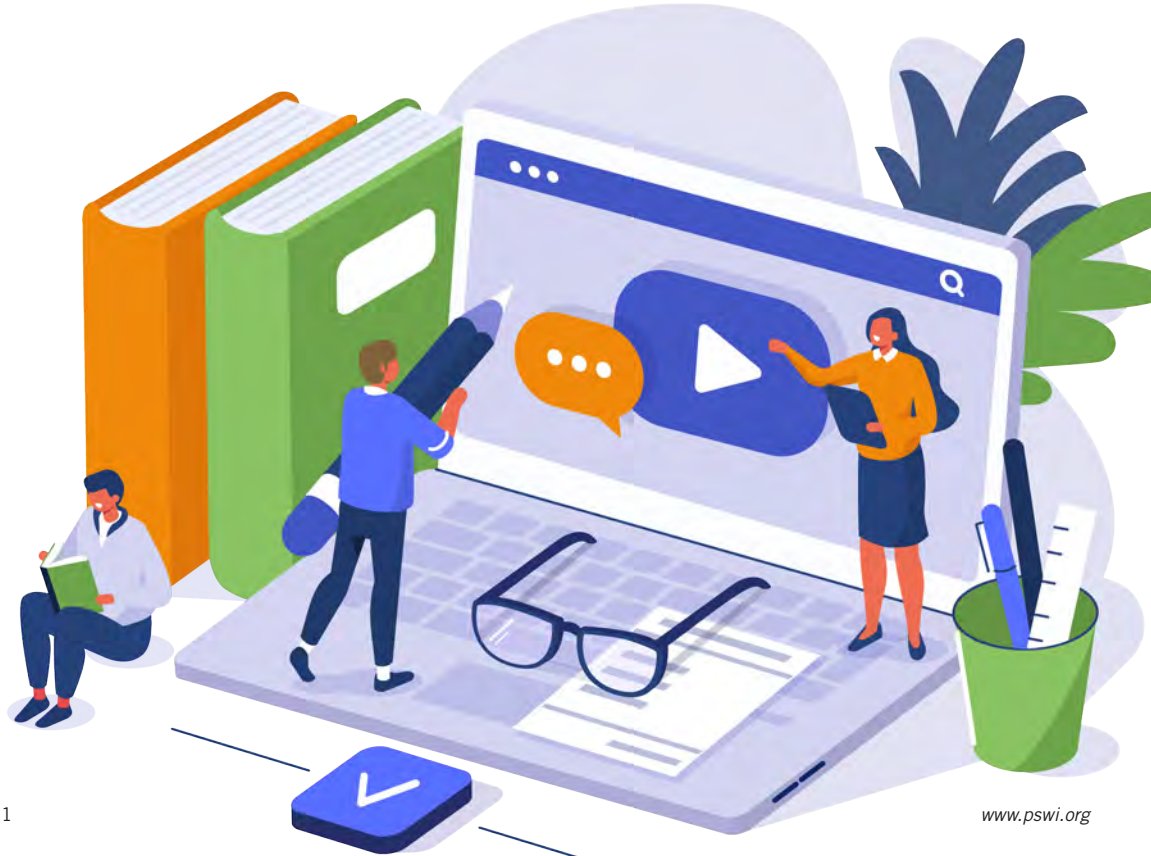
The Educational Programming Committee oversees and supports the development and delivery of educational programming. We collect Requests for Proposals for new educational content and support members as they create and provide presentations. We are also refining the Mission of PSW Continuing Pharmacy Education and evaluating compliance with ACPE standards to maintain PSW's status as an accredited CPE provider. It is a priority of PSW to address Diversity, Equity, and Inclusion (DEI) and this committee collaborates with the DEI workgroup to ensure speakers, presenters, and topics are appropriately incorporated into educational programming. The committee also oversees the work of the Wisconsin Pharmacy Residency Conference. Committee members serve staggered two-year terms with possible reappointment to an additional term. Meetings are held monthly for one hour via video/phone conference.

How can I get more involved, you ask? In many ways!

- **Engage in educational offerings.** Access CE On Demand on the PSW website, CE in JPSW, and attend PSW conferences.
- **Present at a PSW Conference.** Submit your program idea for consideration by completing the Request for Proposal application at https://www.pswi.org/Education/Present-at-a-Conference. Applications are reviewed by the committee and applicants are notified of acceptance within 6-8 weeks.
  - » Deadline for Educational Conference: December 15, 2021
  - » Deadline for Annual Meeting: May 1, 2022
- **Serve on the Educational Programming Committee.** Submit your interest and short bio or CV to info@pswi.org by December 1 of each year.

With education being a core tenet of PSW, and multiple avenues and levels of involvement available, educational programming is a fantastic way to get more involved in PSW. We look forward to working with you!

Marisa Goninen is the incoming Vice Chair of the Educational Programming Committee of the Pharmacy Society of Wisconsin in Madison, WI.



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

PSW Member Spotlight: Lucas Schulz

by Ashley Srb, 2023 PharmD Candidate, Amy Nadine Bowman, 2023 PharmD Candidate, Alexa Bekkerus, 2023 PharmD Candidate

Lucas Schulz, PharmD, BCIDP, is the Clinical Coordinator of Infectious Disease at UW Health in Madison, Wisconsin. At UW Health, Schulz completed a PGY-1 pharmacy practice residency and PGY-2 residency in an area he was passionate about: critical care After treating critically ill patients, many with septic shock, an infectious disease position opened and Schulz saw an opportunity to match his enthusiasm for the treatment of septic shock with his commitment to life-long learning. This new position challenged him to learn about the broad spectrum of infectious disease conditions in acute and ambulatory care, through on-the-job training and many nights of research and self-directed learning. He expanded his knowledge base by applying his learning during daily prospective patient reviews and patient care projects, and with the assistance of his pharmacist and physician colleagues. Early mentors, like Jeff Fish, PharmD; Philip Trapskin, PharmD; Barry Fox, MD; and David Andes, MD guided Schulz's development. An infectious diseases and stewardship focused program called Making A Difference in Infectious Disease (MAD-ID) strengthened his role in antimicrobial stewardship and infectious diseases. To this day, life-long-learning and continuous professional development remain important to Schulz's practice philosophy..

"A-Typical" Day

For Schulz, every day is different and presents a new challenge. As the clinical coordinator, he enjoys balancing strategic thinking and planning with finding creative solutions to the "little fires" that arise daily. His work is always guided by improving patient care and advancing pharmacy practice activities for patients across the UW Health enterprise. He is responsible and accountable for antimicrobial prescribing for inpatients, the emergency department, and ambulatory clinics. Prospective antimicrobial prescribing audits help keep Schulz knowledgeable about changing patient care practice. Monitoring prescribing trends and identifying when practice standards deviate is the key to ensuring all patients receive high-quality care. Schulz standardizes antimicrobial use by writing guidelines, creating order sets, and developing pharmacist and nursing delegation protocols. After setting pharmacy practice standards and putting clinical pharmacists in a position to succeed, he monitors to ensure that guideline interpretation, order set use, and delegated acts are appropriate. Finally, Schulz tracks and reports antimicrobial use and resistance trends across the enterprise. Creative solutions that improve patient outcomes; reduce the impact or development of antimicrobial resistance; or improve the financial health of the system are shared through scholarly activity. Schulz has over 100 published manuscripts and abstracts and an equal number of presentations.

When asked about work-life balance, Schulz prefers the term "work-life integration." "When you are a professional, you don't stop thinking about your patients and how to improve their care," says Schulz. "It is important to have time to relax and be away from work, but I find myself answering a call or page often to help a patient or physician in need." Infectious disease impacts all patient populations at UW Health. It is ubiquitous and covers every patient group, because "every patient is at risk" according to Schulz. He relies on a team of pharmacists to care for all the patients, and he interacts with his team daily. Infectious diseases pharmacists and physicians, surgeons, critical care and general medicine teams, microbiology lab directors and technicians, nursing teams, administrators, and patient care advocates all work together to solve complex problems caused by microscopic pathogens. Education regarding the misuse of antimicrobials, and how misuse drives antimicrobial resistance, is communicated to patients, caregivers, and hospital administration. His goal is to find the safest, most effective, and most fiscally responsible antimicrobial regime to treat

patients. Balancing safety, efficacy, cost, and social responsibility (selecting the antimicrobial least likely to drive resistance), is the basis of his daily work.

COVID-19 brought infectious diseases issues to the forefront of public discourse. Serving as an infectious diseases expert is also part of Schulz's role. Schulz is often asked for his professional opinion regarding the virus. As a volunteer youth baseball coach for his youngest children, he became a resource for parents on all things health and COVID-19-related. Schulz presents often for PSW and other state and national organizations as a content expert and enjoys being active and available when needed. He takes any opportunity he can get to go to legislative day and annual meetings, so he can continue to expand the pharmacist's role by talking to policy makers and networking with fellow pharmacists.

Setting Higher Standards

As a healthcare professional, it is crucial to improve patient outcomes via practice advancement. Schulz believes relationship development is the first step. For example, Schulz recently worked with the microbiology lab to increase pharmacists' roles in reacting to and modifying treatment based on results of rapid diagnostic tests. In another example, Schulz led a project resulting in pharmacists increasing their accountability to the management of patients receiving certain medications, like vancomycin. Schulz says these practice advancement opportunities give UW Health pharmacists the ability to lead patient care management based on their unique professional knowledge and judgment, which results in increased job satisfaction. The success of clinical pharmacists in these spheres will continue to strengthen support for expansion of pharmacy services in other care settings. Schulz views pharmacy practice advancement through a value lens, constantly identifying opportunities to share value-added activities with hospital colleagues. Daily, he creates value by optimizing antimicrobials to provide the best patient outcomes (safety and efficacy) at the least cost to the patient and health system. He analyzes data comparing old antimicrobials to new antimicrobials and identifies what is best for the patient.

Continuous practice development and advancement started early in Schulz's career and is driven by improving patient outcomes and sharing success. Schulz and his team of ID pharmacists are residency trained, completing either one or two years of training, and board-certified infectious disease specialists. Schulz continues to expand his knowledge by routinely interacting with and learning from information technology professionals, many of whom are pharmacists who transitioned into the technical world. The culmination of developing innovative and leading infectious diseases practice provides ample opportunities to publish their research so others can learn from shared success.

Adapting to Changing Times and Challenging the Status Quo

Navigating the healthcare system's complexities is challenging; COVID-19 magnified old challenges and exposed new ones. Schulz led the UW Health COVID-19 treatment guideline workgroup. This workgroup was charged with identifying treatment strategies based on emerging literature. Responding to rapidly evolving data about treatment strategies required Schulz to lead a large interdisciplinary team, which identified, evaluated, and disseminated contemporary recommendations. While treatment

guideline creation and implementation was not new, the pace of change was atypical. Relying on prior change-management experience was critical.

Schulz summarized his experience with change like this: First, change begins with identifying a problem. Ideas for new programs often occur organically for Schulz while discussing problems with infectious diseases colleagues and leaders. Membership in state and national societies, like PSW, are excellent resources for connecting with associates who experience common problems. Next, you need to generate a sense of urgency about the problem—why do we need to fix the problem and why is it important? Solution development requires collaboration across teams of healthcare professionals. Program implementation can be the most challenging, as this step requires risk-taking. Patient and/or provider response is unknown until this step. The program is evaluated based on benefits and how well it is perceived. Programs are never perfect and changes are always made to accommodate the ever-changing needs of patients.

Action Drives Motivation

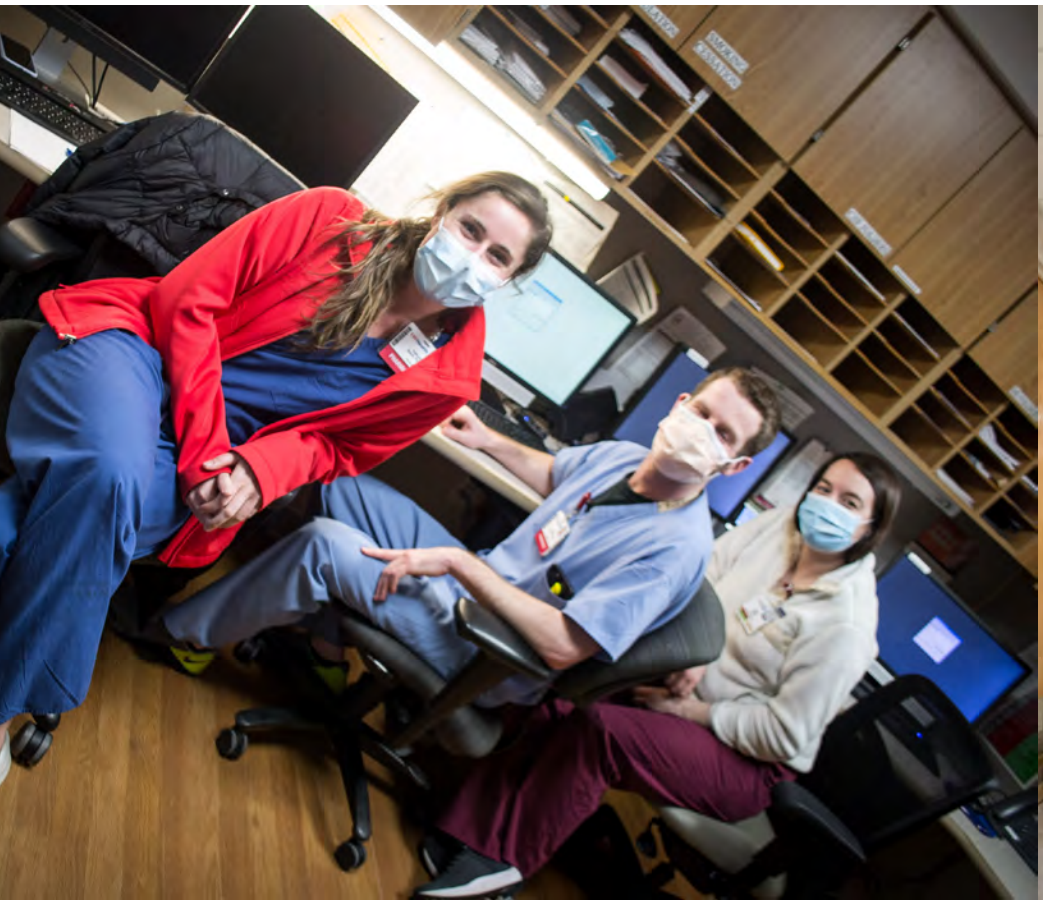
What motivates Schulz's continued focus on improvement? "Action drives motivation. Advancement is achieved by setting a big goal and taking small steps to get to the finish," says Schulz. Taking action on each step, whether successful or unsuccessful, motivates Schulz to the next stage. Learning from missteps and analyzing why a project did not go as planned is as important as a smooth and successful project.

Schulz sees wonderful opportunities for the pharmacy profession. Pharmacists should have full responsibility and accountability for patient outcomes associated with medication use across the spectrum of care. From acute care to ambulatory care and across transitions of care, a pharmacist should be present and engaged in the healthcare team. Pharmacists are starting to do this in infectious diseases with active participation in hospitals, ambulatory care, home health, long-term care, academia, and industry. Schulz values growing partnerships between academic medical centers and small and rural hospitals. He partners with industry leaders and policy-makers to determine and demonstrate the value of new antimicrobials. Pharmacists should be present whenever decisions about medications are discussed and made.

Schulz did not follow a traditional path into infectious disease, but he took a chance on a job opening that led him to a career that he enjoys and that places him in situations to develop and improve pharmacy practice opportunities each and every day.

Ashley Srb, Amy Nadine Bowman, and Alexa Bekkerus are 3rd Year Doctor of Pharmacy Candidates at the University of Wisconsin-Madison School of Pharmacy in Madison, WI.

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



Spotlight

WPQC Spotlight: Dana Whittlinger

by Moua Lee, 2022 PharmD Candidate

The Wisconsin Pharmacy Quality Collaborative (WPQC) encourages pharmacists to perform comprehensive medication review and assessment (CMR/A) services by combining financial and professional incentives. This spotlight focuses on a pharmacist who has shifted her role over time and is leading the way in providing WPQC CMR/A services at her pharmacy location.

Dana Whittlinger, PharmD, BCACP, and a graduate of UW-Madison's School of Pharmacy 2002, is a medication expert expanding her role. After graduation, she chose to move to the Eau Claire area with her husband, Michael Whittlinger, also a pharmacist. She currently practices in the outpatient pharmacy at Mayo Clinic Health System in Eau Claire, where she is given opportunities to expand pharmacy clinical services. With support from her leadership and director, she became WPQC-certified and began providing medication therapy management (MTM) services in her department. She has been participating in a cardiovascular- and diabetes-focused program that provides CMR/A services to Medicaid members with support from the local public health department and PSW. She now lives in Fall Creek with her husband and two teenage sons.

Interview with Whittlinger

What has been the most rewarding part of providing CMR/A services to Medicaid members?

Professional satisfaction. We learned about CMRs years ago in training, and now I am one of the pharmacists practicing it. I am in a position to use my pharmacist knowledge. I'm being challenged with learning new tasks and processes, including learning and utilizing the electronic health record (EHR) and telehealth to be more effective and efficient. I have a supportive team of professionals around me. All this inspires me to be a better clinician.

What has been the most challenging part of this process?

The no-shows. There is a ton of behind-the-scenes work that goes into a visit. It's frustrating to coordinate everything, compile documentation and background information for the patient, arrange for time and space for the visits, schedule an appointment, call for an approval, send reminders, review patient history, and then have a no-show. When patients don't show up it can feel very defeating for me.

What public health interfaces have you been able to implement?

We are providing [blood pressure] monitors and teaching to those that need it. We discovered some patients need an extra-large size to be able to read their blood pressures, and we were able to start providing that. We are getting reimbursed for these services offered by the pharmacy. I've provided transportation resources to those who need it. I've provided a CMR/A for a non-English-speaking patient using an interpreter service. I've connected patients with social services to help them

Left: *Dana Whittlinger.* ***Below:*** *Dana Whittlinger and family.*

make appointments and coordinate other care, as some patients may not know how to navigate this with today's technology. We have MTM pharmacists in other departments, and I have been able to coordinate with them with regards to consistent documentation and communication about mutual patients.

What do you see the WPQC program growing into?

I'm hoping to involve more pharmacists at my institution to provide CMR/As for our patients or even to help identify patients. We will have an ambulatory pharmacy resident starting in 2022, and I hope that individual can become involved as well. We are looking at getting other commercial insurance plans to support this service in addition to the Medicare and Medicaid patients we offer this for.

What would you like to tell other pharmacists who may be hesitant or do not know WPQC?

I know it may feel difficult to start and complete projects in a busy retail or clinic setting, but PSW does listen and will help you find solutions for a real-world pharmacy. PSW staff Helene McDowell and Kari Trapskin are available for questions if they should arise. PSW has great resources. Participating in their trainings and pilot programs has been helpful. Having support from your own institution is also essential. My director, Michele Richmond, has provided connections, staffing flexibility, and sometimes emotional support when I'm questioning my efforts. My team in the pharmacy permits me time to work, space in the pharmacy to meet [and] support billing, and more. The MTM pharmacists in our other departments were willing to let me shadow their MTM visits and well as provide instruction for EHR documentation and more.

Moua Lee is a 4th Year Doctor of Pharmacy Candidate at the University of Wisconsin-Madison School of Pharmacy, WI.

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