Volume 26 • Issue 3 www.pswi.org

May/June 2023

The Journal

of the Pharmacy Society of Wisconsin

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The Journal of the Pharmacy Society of Wisconsin is the official publication of the Pharmacy Society of Wisconsin. 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.

What is Your Origin Story?

by Janet Fritsch, RPh

This is the question I ask all of my guests on PSW's series of Member Meet Up podcasts. On this podcast, I have been interviewing PSW members and staff. What fun it has been!! I have learned about Melissa Theesfeld's time with the UW Marching Band and her first job out of college. Sarah Sorum talked about her connections to Iowa. Ryan Miller told me about working in IT and how that benefits pharmacy staff and ultimately gives better patient care. I talked to Danielle Womack about advocacy in PSW and how we can all be involved, and heard about her new baby. I was moved by Ellina's story of her family. Each person has a unique origin story just as each member brings something of themselves to PSW.

In my own story there are two major themes: number 1 is the great work that PSW does for the pharmacy profession; number 2 is the relationships and friendships I enjoy because of my involvement in PSW. I need both to keep me involved. The initiatives and strategic goals of PSW are productive and important for the profession of pharmacy. Working on these activities satisfies me and enhances my practice of pharmacy. It continues to make me better at what I do. The relationships and friendships due to PSW are just plain fun. Yes, of course, there is an element of networking and all of that, but mostly I just enjoy seeing these people.

I love serving as President of PSW. I have learned much and have met many new people. I have spent some time thinking about networking, relationships, and friendships. When you ask someone about the benefits of PSW, you almost always hear "networking" on the list. Networking is absolutely a benefit of PSW. At every PSW event, you meet many pharmacists and pharmacy technicians doing many different types of jobs in various places and practice sites, all in the profession of pharmacy. Any of these professionals could potentially be your next co-worker, your next boss, your next employee—and could certainly be your new friend.

At the PSW Member Engagement Committee meetings, we brainstorm about possible events and new ways to involve members. We talk about ways to reach out to pharmacists and pharmacy technicians who are not members. We talk about telling our story. How do we tell the story of PSW, and how does each of us tell our individual story? Storytelling is impactful. Storytelling demonstrates our involvement in PSW and our "why."

So, what is your origin story with PSW? Who can you share it with? Who will feel the impact of your story? Only you can tell your story.

What's next? Check out some stories on the podcast and then tell your own story.

Click here to listen to the PSW Member Meet Up Podcast.

Janet Fritsch is the current President of the Pharmacy Society of Wisconsin and the Owner of Baraboo Corner Drug Hometown Pharmacy in Baraboo, WI.

PSW Welcomes Kate Hartkopf

Kate Hartkopf received her Doctor of Pharmacy degree at the University of Wisconsin-Madison in 2008 and completed a PGY-1 community pharmacy practice residency with University of Wisconsin Hospital and Clinics in 2009. She has been a clinical pharmacist at UW Health in the community pharmacy and ambulatory care areas, the Supervisor of Clinical Education and Program Expansion for the UW Health ambulatory pharmacies, and most recently the Pharmacy Manager of Ambulatory Care Services and PGY2 Ambulatory Care Pharmacy Residency Program Director. Her responsibilities have included expansion and oversight of pharmacist services in community pharmacies, primary care, and specialty clinics; involvement in UW Health's Population Health program development; and collaboration for patient transitions of care with an emphasis in the ambulatory care setting. Her professional interests include implementation and advancement of pharmacist services in the ambulatory care setting, team-based care collaboration, population health strategies, and adult learning principles.

Kate has also served as a preceptor for student pharmacists and pharmacy residents throughout her professional career and has assisted as a co-coordinator for the UW-Madison School of Pharmacy Resident Teaching Certificate Program. Formal leadership positions have included the New Practitioner Representative for the UW-Madison School of Pharmacy and the Wisconsin Pharmacy Alumni Association; appointed member of the PSW Ambulatory Care Advisory Committee; and Region A Director of the PSW Board of Directors. Kate is a 2011 participant of the Decker/Temple Leadership Pharmacy Conference. She has been awarded the UW-Madison School of Pharmacy Alumni Association Young Alumna of the Year award and the American Association of Colleges of Pharmacy Master Preceptor Recognition.

Outside of work, Kate keeps busy with family activities. She and her husband, Eric (also a pharmacist and PSW member!), are the proud parents of two daughters, Josie (7) and Cecilia (4). As a family, they stay very busy following the girls' many co-curricular activities, including dance, gymnastics, swimming, skating, softball/t-ball, and music. This year, they enjoyed their first Badger hockey games as a family of four and the time-honored tradition of singing "Varsity." They enjoy annual family vacations to Door County and LOVED their Disney Cruise in 2022; a fan favorite that will likely be repeated. They live in Waunakee and often enjoy local performances and sporting events, play dates, the neighborhood pool, and Governor Nelson State Park when the weather cooperates.

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

Leadership Spotlight: Kate Hartkopf

by Doha Awad, 2025 PharmD Candidate, Mara Gosch, 2025 PharmD Candidate

Editor's Note:
Since the time of this interview, Dr Hartkopf has taken a role with the Pharmacy Society of Wisconsin. She started April 1, 2023 at PSW. See the previous article "PSW Welcomes Kate Hartkopf" for her introduction.

Kate Hartkopf, PharmD, BCACP is the Pharmacy Manager of Ambulatory Care Services and PGY-2 Ambulatory Care Residency Program Director at UW Health. With a vision for advancing pharmacy practice while delivering high quality patient-centered care, Harktopf has dedicated her career to mentoring students, growing pharmacist services, and supporting pharmacists' efforts at an administrative level in addition to clinical practice.

Harkopf graduated from the UW-Madison School of Pharmacy in 2008 and completed her postgraduate year one (PGY1) community pharmacy residency at UW Health. Post-residency, Hartkopf gained experience in the community and clinic setting at UW Health as a clinical pharmacist before transitioning into the role of Supervisor for Education and Program Expansion. In the initiative to move forward with many elements of the Wisconsin Pharmacy Quality Collaborative (WPQC), Hartkopf worked with providers to develop delegation protocols as well as dedicated many efforts to expand direct pharmacist-patient care such as vaccination services. For the past six years, her role has evolved into providing oversight for pharmacists in the ambulatory care setting and accelerating the implementation of pharmacist services in primary care.

More recently, she has been working in partnership with primary care providers and population health departments to increase pharmacists' delegated authority. Such efforts have been particularly influential during the pandemic as pharmacists supported the treatment of COVID-19-positive patients who required outpatient oral and infused therapies. Delving into more novel patient care responsibilities she developed a drive-through influenza vaccine service, and upon the availability of COVID-19 monoclonal antibody treatment, she also served as a liaison for eligible patients. Until the start of the pandemic, Hartkopf had continued her clinical practice in community pharmacies and the anticoagulation clinic. Now through her current role, she supports pharmacists in their delivery of efficient, patient-centered care and facilitates the expansion of pharmacist services.

Hartkopf's unique journey also includes her dedicated involvement with PSW. As a new member she gave presentations, attended poster sessions, and attended meetings. Her involvement further increased as a PGY-1 resident, then later becoming a member of PSW's Ambulatory Care Advisory Committee before her election to the Board of Directors.

Expanding Pharmacist Services

One of the current challenges Hartkopf has faced in expanding pharmacist services has been raising awareness on the training pharmacists receive that makes them exceptionally qualified to support medication management activities within primary care services. She shares the pharmacist perspective with other health professionals, emphasizing the missed improvements in the patient care experiences when pharmacists' roles are limited to medication renewals and technical functions. She educates professionals about the unique perspective pharmacists bring to the care team and their qualification as the medication experts, demonstrated by their certification with the Board of Pharmacy Specialties (BPS) within two years of onboarding at UW Health.

Hartkopf recognizes these efforts in advocacy take time, patience, and bravery. Although it may be difficult to keep the momentum going in these ongoing pursuits, seeing some of the fruits of this labor has been rewarding and many unexplored practice advancement areas remain. Hartkopf sees opportunity for pharmacists to expand their role to areas in which data demonstrates improved patient care. She also knows pharmacists can facilitate care team interactions within primary clinic areas, as well as within specialty clinic areas where the outcomes can be very impactful for patients. Finally, Hartkopf notes pharmacogenomics as an innovative and growing priority at UW Health where there is potential for pharmacists to be a "precise and careful component of the patient care team". Through advocating for the value pharmacists bring to all these areas of patient care and challenging uninformed perspectives, Hartkopf has patiently and bravely led the conversations that are shaping the expanding role of clinical pharmacists.

Paying It Forward

Hartkopf has dedicated a significant portion of her career to mentoring and precepting aspiring student pharmacists. She was recently recognized as a 2022 Master Preceptor by the American Association of Colleges of Pharmacy (AACP). Hartkopf cites the award as one of her proudest professional achievements because it reflects her strong commitment to the UW-Madison School of Pharmacy and well-rounded professional organizational involvement through PSW.

Feeling incredibly humbled by this recognition, Hartkopf expresses her strong admiration for the preceptors and mentors who helped shape her own interactions with student pharmacists. She finds the compilation of work that has led her towards this accomplishment

to be a reflection of their teachings. Now recognized for her positive influence on students, she hopes she is paying it forward.

Hartkopf views the students she interacts with more as colleagues than learners. She believes each learner brings a fresh perspective with different lived experiences, priorities, values, and strengths. She enjoys seeing her students perform at a highly-independent level, offering them the space to think creatively and "set [their own] roadmap". Hartkopf is proud to observe the professional and personal growth of her students over the course of their rotations and careers as they stay in touch.

Advice to Future Leaders in Pharmacy

Hartkopf encourages aspiring leaders in pharmacy to have a flexible frame of mind as they navigate the opportunities presented to them. She believes there is "no one way to get to any endpoint" and urges students to re-evaluate their goals after each experience. Hartkopf references a conversation early in her career with former preceptor and mentor David Zilz who challenged her to consider what she wanted her legacy to be. This conversation helped Hartkopf align her career aspirations with her values of patient care, professional advocacy, and leadership. Since taking on the role of the mentor herself, she encourages students to develop professional goals informed by their values and to review them often throughout their careers to ensure they are in alignment with their desired legacy.

Sharing another valuable piece of advice she once received, Hartkopf notes that it would be remiss to evaluate one's progress while forgetting to acknowledge the wins. With the challenges to expanding pharmacist services in mind, Hartkopf stresses the importance of celebrating progress and success, no matter how incremental. She reminds us, "it's okay to celebrate and pat ourselves on the back. It propels us forward for those new opportunities."

Doha Awad and Mara Gosch are 2025 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.

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PHARMACIST CE:

Updates on Glucagon-Like Peptide-Based Medications: Current, New, and Pipeline Agents

by Elizabeth A. Buckley, PharmD, CDCES, Francesca Napolitano Johnson, PharmD, MEd, Denise Walbrandt Pigarelli, PharmD, BC-ADM

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Learning Objectives

- Compare and contrast the currently available glucagon-like peptide-1 receptor agonists (GLP1-RA)
- Describe the mechanism and advantages of tirzepatide
- Identify trends in pipeline GLP1-RA-based-medications

Finding the best therapeutic agent to help millions of people manage type 2 diabetes and hyperglycemia, reduce clinical and economic burden, and prevent macro- and microvascular complications continues to be a priority. It can be challenging to find an appropriate agent to help achieve glycemic goals and support heart and kidney risk reductions while limiting adverse drug reactions, intolerability and cost. Since the first glucagon-like peptide-1 receptor agonist (GLP1-RA) was approved in 2005, subsequent incretin agents have been developed with advantages such as extended dosing duration (once weekly) and cardiorenal risk reduction. The drug class has significantly and positively impacted the management of type 2 diabetes, as evidenced by its increasingly prominent role as an important therapeutic choice to decrease blood glucose, body weight, risk of major adverse cardiac events (MACE) in people at high risk for or established atherosclerotic cardiovascular disease (ASCVD), and risk of kidney dysfunction.[1] Current standards of care pathways and algorithms recommend specific agents in this class as first-line for people with these co-morbidities and risks, regardless of hemoglobin A1C (A1C) at diagnosis.[2,3] In addition, the American Diabetes Association (ADA) Standards of Care recommend initiating GLP1-RAs before prandial insulin due to their efficacy to lower glucose without the risks of hypoglycemia or weight gain. This article will review and compare the Federal Drug Administration (FDA)-approved indications, advantages, and disadvantages of current agents within this class; highlight the mechanisms and advantages of the newest incretin agent to enter the market; and preview pipeline agents.

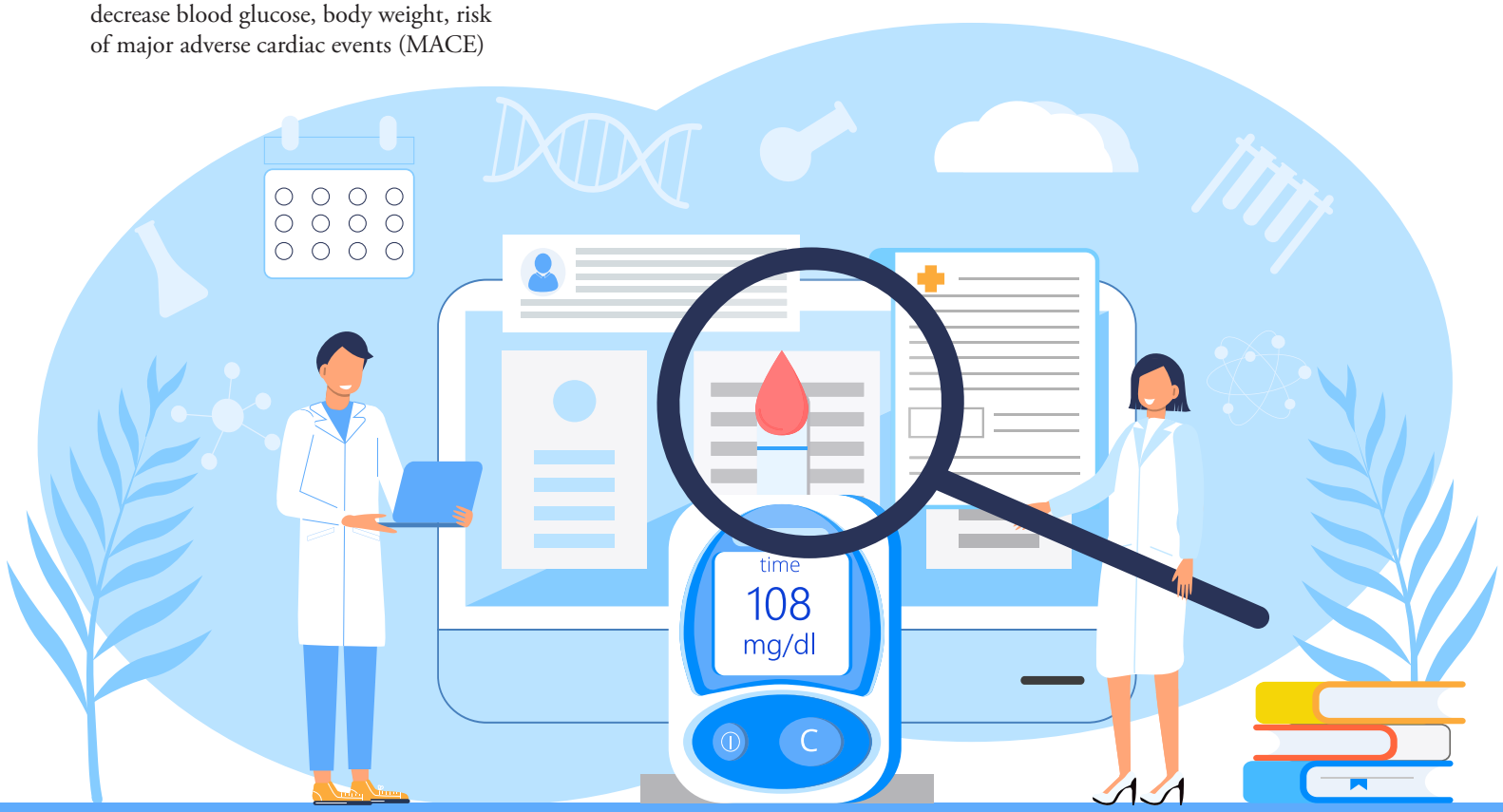

TABLE 1. Comparison of Currently Available GLP1-RA and GIP/GLP1-RA Medications[5,7–16]

Drug	Indication	Comparative Weight Loss	Efficacy ~A1C decrease	Frequency	Starting Dose (Sub-Q)	Titration schedule (As tolerated)	Approximate Similar Doses					
Tirzepatide (Mounjaro®)	T2DM - Adults	~ 11.2 kg	2.3%	Weekly	2.5 mg	Every 4 weeks	2.5 mg	5 mg	7.5 mg	10 mg	12.5 mg	15 mg
Dulaglutide (Trulicity®)	T2DM > 10 yo MACE reduction	~2.5-4.6kg	1.8%	Weekly	0.75 mg	Every 4 weeks		0.75 mg	1.5 mg	3 mg	4.5 mg	
Exenatide (Byetta®)	T2DM - Adults	~ 2 kg	0.9%	BID	5 mcg Before meals	Every 4 weeks	5 mcg	10 mcg				
Exenatide ER (Bydureon®)	T2DM > 10 yo	~ 2 kg	1.5%	Weekly	2 mg	No titration			2 mg			
Liraglutide Victoza®	T2DM MACE reduction	~ 2.5 kg	1.5%	Daily	0.6 mg	Weekly	0.6 mg	1.2 mg	1.8 mg			
Liraglutide Saxenda®	Obesity > 12yo	~ 9.5 kg		Daily	0.6 mg	Weekly	0.6 mg	1.2 mg	1.8 mg	2.4 mg	3 mg	
Semaglutide Ozempic®	T2DM MACE reduction	~ 4 kg	2.3%	Weekly	0.25 mg	Every 4 weeks		0.25 mg	0.5 mg	1 mg	2 mg	
Semaglutide Wegovy®	Obesity > 12yo	~ 16 kg		Weekly	0.25 mg	Every 4 weeks		0.25 mg	0.5 mg	1 mg	1.7 mg	2.4 mg
Oral semaglutide (Rybelsus®)	T2DM	~ 2.5 kg	1.3%	Daily	3 mg PO empty stomach	Every 30 days	3 mg	7 mg	14 mg			

Abbreviations: A1C = hemoglobin A1C, GIP = gastric inhibitory polypeptide, GLP1-RA = glucagon-like peptide-1 receptor agonist, MACE = major adverse cardiac events, Sub-Q = subcutaneous, T2DM = type 2 diabetes mellitus

Current GLP-1RAs

GLP1-RA agents mimic the action of endogenous GLP-1, a glucoregulatory hormone that is released from the gastrointestinal (GI) system in response to food ingestion.[4] GLP1-RA agents bind to the receptors on several organ systems and work in a multimodal manner to reduce blood glucose in response to food:

1. Pancreas - enhances beta cell insulin secretion and alpha cell glucagon suppression
2. Liver - decreases glucose production
3. Brain - increases satiety
4. Stomach - slows gastric emptying time
5. Peripheral tissue - increases insulin uptake via weight loss

There are currently five FDA-approved GLP1-RA agents for the treatment of type 2 diabetes in the United States4 (Table 1). The medications are commonly differentiated by duration of action, with the shorter-acting agents having more of an effect on gastric emptying, thereby decreasing post-prandial glucose yet resulting in a higher incidence of GI effects.[4] The longer-duration agents (weekly injectables) affect both fasting and post-prandial glucose due to continuous receptor activation, which leads to greater reductions in A1C values. In general, the GLP1-RA with the highest efficacy to decrease A1C is semaglutide, followed by dulaglutide, liraglutide, and exenatide. In addition, exenatide is an exendin-4-derived agent that does not have the same effect on MACE outcomes as the other agents. The agents that do have evidence of improved cardiovascular outcomes are derived from modified human GLP-1, and include dulaglutide, liraglutide, and semaglutide. Interestingly, semaglutide was developed from modification of liraglutide to extend its duration of action. Each of these modified human GLP-1 agents has an FDA indication to reduce the risk of MACE in adults with type 2 diabetes and ASCVD. There is also strong published evidence that these agents can reduce MACE in adults with multiple risk factors for ASCVD, although at this time dulaglutide is the only agent to have an FDA-approved indication for it.[5,6]

Oral Formulation

As injectable incretin agents continue to come to market, there is only one oral GLP1 agonist currently available. In 2019, semaglutide (Rybelsus®) became the first oral GLP1 treatment approved by the FDA.[17] Although this dosage form is usually preferred over injectables, in order for it to be properly absorbed, it requires specific adherence to taking the tablet at least 30 minutes before the first intake of the day (food/beverages/medications) with no more than four ounces of plain water.[13] This is based on the addition of an absorption enhancer, Sodium-N-[8-(2-hydroxybenzoyl) amino] caprylate (SNAC), that works locally as a pH buffer in the stomach and enables the large structure of semaglutide to be absorbed orally before being degraded by gastric enzymes.[18] In addition, this dosage form does not have equal glycemic efficacy or data to support a reduction in cardiovascular or renal complications. However; there is currently a phase III study researching the effects on A1C and weight loss of oral semaglutide at 25 mg and 50 mg which may yield improved A1C and weight

loss potential.[19]

New Indications

A major focus of the updated joint ADA/European Association for the Study of Diabetes (EASD) and the stand-alone ADA Standards of Care 2023 is on the treatment of obesity as a health condition, with an emphasis on weight management being as important as glucose management in people with prediabetes and diabetes.[2] GLP1-RA agents have proven efficacy to reduce body weight in the majority of individuals that utilize this therapy.[4] This is related to their actions in the brain and the stomach. GLP1-RA mechanisms in the brain enhance hypothalamic satiety, reduce hunger, and suppress energy intake. GLP1-RA effects on the stomach slow GI motility and contribute to feeling full. However, the satiety and absorption delay signals can lead to nausea and vomiting, the most common side effects with agents in this class. Two of these agents, liraglutide and semaglutide, have separate, branded products and FDA-approved indications for the treatment of obesity/overweight in adolescents > 12 years old and adults (Table 1).[10,14] In general, based on clinical trial information, weight loss is as follows: semaglutide > liraglutide > dulaglutide > exenatide. The efficacy of these agents led to a shortage of all GLP1-RAs beginning in August 2022, which has prevented many people with diabetes from procuring their medications. Table 1 gives approximately similar doses of the agents and can be a useful tool in times of shortage or when switching between products for formulary issues. When making a switch, it is suggested to start with the approximately similar or a lower dose and titrate up as tolerated.[16]

Precautions

All agents within this class have similar adverse drug reaction profiles, warnings, and contraindications. Due to development of thyroid C-cell tumors in rats and mice during clinical trials, all GLP1-RAs are contraindicated in people with a personal or family history of medullary thyroid carcinoma (MTC) and multiple endocrine neoplasia syndrome type 2 (MEN 2), and all people taking GLP-1RA should be counseled on the symptoms of thyroid tumors.[5,7–14,20] Other warnings include monitoring for pancreatitis, hypoglycemia when used in combination with insulin or secretagogues, kidney impairment during dehydration, hypersensitivity reactions, and acute gallbladder disease.

TABLE 2. Incretin Effects at the Organ/Tissue Level[20,21]

Organ/Tissue	*GLP1*	*GIP*
CNS	Decreases caloric intake significantly	Decreases caloric intake
Heart	Increases in heart rate	
Pancreas – beta cells	Increases Insulin secretion	
Pancreas – alpha cells	Decreases glucagon secretion	Increases glucagon secretion
Stomach	Slows gastric emptying and chylomicron production	No prominent effect
Adipose Tissue	No prominent effect	Increases glucose uptake Increases triglyceride uptake and storage
Kidneys	Transient sodium excretion decreases	No prominent effect
Bones	Increases meal-associated bone remodeling	Increases meal-associated bone remodeling significantly
Liver (indirect effects)	Glucose uptake, glycogen increases, hepatic glucose production decreases	

CNS = central nervous system, GIP = gastric inhibitory polypeptide, GLP1 = glucagon-like peptide-1

Adverse Reactions

The most common adverse reactions within the class have some differences in frequency among agents: GI-related nausea, vomiting, diarrhea, decreased appetite, dyspepsia, and constipation.[5,9,11-13] Due to the mechanism of delaying gastric emptying, shorter-acting agents can affect the absorption of concomitantly administered oral medications, and people taking these medications should be educated on consistency of dosing intervals.

New Incretin

Addition of GIP to GLP-1 RA: Tirzepatide

Tirzepatide (Mounjaro®) was FDA approved in 2022 and is an agonist at both the glucose-dependent insulinotropic polypeptide (GIP) and GLP-1 receptors.[7] It is the first "twincretin" to come to market, based on evidence from the SURPASS trials. For more details on the SURPASS trials, please see the "Review of Effect of Tirzepatide on Glycemic Control and Weight Loss" article in this issue. GIP is another incretin secreted from the intestines in response to ingestion of carbohydrates.[20] The activation of GIP receptors enhances GLP-1RA effectiveness and further decreases A1C and body weight in people with type 2 diabetes. See Table 2 for comparative effects on the body. People with type 2 diabetes have a reduced incretin effect, with a slight GLP1 impairment and an almost complete lack of GIP response.[20] Initially, GIP did not seem to have the same effectiveness as GLP1 on increasing insulin secretion, so it did not progress as a therapeutic agent until research showed the synergistic effect of using them together.

Tirzepatide is a once-weekly subcutaneous injection that has a higher efficacy (A1C reduction > 2%) and a more profound weight loss (> 10 kg on average) than comparators of semaglutide 1 mg weekly (not maximum dose), insulin degludec, insulin glargine, and combination therapy in persons with increased cardiovascular (CV) risk.[7] The side effects, contraindications, and precautions for tirzepatide are similar to other agents in the GLP1-RA class.[7] In addition, due to the effect on gastric emptying, labeling for tirzepatide includes a precaution about potential reduced efficacy of oral contraceptives, and recommends a backup form of contraception for the first four weeks of use. Drugs with a narrow therapeutic window such as warfarin

and levothyroxine should be monitored carefully, and people taking acetaminophen should be educated on the possibility of decreased efficacy and delayed time for pain relief. There is a positive impact on CV-associated risk factors such as weight, blood pressure, and lipids. However, the medication's impacts on MACE and prevention of adverse kidney outcomes will be determined via results from ongoing trials.[22] A sub-analysis of SURPASS-4 did show a significant decrease in albuminuria, estimated glomerular filtration (eGFR) rate of decline, and risk of end stage kidney disease.[23]

Pipeline Incretin Medications

The following sections will highlight incretin agents that are currently being studied in phase II or III clinical trials.

Pipeline Oral Incretins

Orforglipron (LY3502970) is a once-daily oral GLP1-RA in the pipeline that completed Phase II studies in fall of 2022.[24] During phase I trials, the medication was found to have pharmacodynamic profiles similar to injectable GLP1-RA, pharmacokinetics enabling once daily administration, and up to a 3.6 kg weight reduction in 29 days.[25] Although finalized data from phase II has not been formally released, preliminary results shared during the investor meeting demonstrated a dose-dependent A1C reduction of up to 2.1% and weight loss of up to 9.6% in patients with diabetes over a 26 week period, and Eli Lilly and Company plan to move this medication into phase III studies in 2023.[26]

Danuglipron (PF-06882961) is a twice daily oral GLP1-RA in the pipeline for which Pfizer Inc. presented phase II study results at the 2022 EASD Annual Meeting.[27] The phase 2a results found mean A1C reductions up to 1.57% and body weight reductions up to 5.38 kg over 16 weeks and had efficacy and safety data in line with phase II data for other GLP1-RAs. The phase 2b results found a mean A1C reduction of up to 1.15%, mean fasting plasma glucose reductions of up to 31.93 mg/dl, and mean weight loss of up to 4.6 kg over 16 weeks.

TABLE 3. Pipeline Dual- and Tri- Agonists in Phase II or III[33–35]

Medication	Route, Frequency, and MOA	Company	Current Status and Relevant Publications/Studies
BI 456906	Subcutaneous once to twice weekly GCGR/GLP1-R dual agonist	Zealand Pharma	Phase II Completed 11/14/2021 https://clinicaltrials.gov/ct2/show/NCT04153929
Oxyntomodulin (OPK88003)	Weekly subcutaneous GCGR/GLP1-R dual agonist	OPKO Health	Phase II Completed 6/27/2019 https://clinicaltrials.gov/ct2/show/NCT03406377
Retatrutide (LY3437943)	Weekly subcutaneous GIP/GLP1/GCGR tri-agonist	Eli Lilly	Phase II completed 12/28/2020 https://doi.org/10.2337/db21-104-OR https://doi.org/10.1016/S0140-6736(22)02033-5 https://doi.org/10.2337/db22-340-OR

GCGR = glucagon receptor, GIP = gastric inhibitory polypeptide, GLP1-R = glucagon-like peptide-1 receptor, MOA = mechanism of Action

PIPELINE Incretin Combinations with Semaglutide

Novo Nordisk currently has two incretin combinations in phase II that utilize a combination with semaglutide both orally and subcutaneously. CarigSema is a once weekly subcutaneous injection that includes cagrilinitide and semaglutide, with a phase II trial that was completed in July 2022.[28]

Cagrilintide is a long-acting acylated amylin analogue that agonizes amylin and calcitonin receptors.[28] Amylin is a peptide hormone secreted from the pancreatic β-cell in addition to insulin that can function similarly to GLP1 by inhibiting glucagon secretion, delaying gastric emptying, and causing satiety.[29] What differentiates the action of amylin from a GLP1RA is that it does not cause beta-cell insulin release.

When utilized alone, the investigational amylin agonist cagrilintide has been found to reduce food intake and weight in a dose-dependent manner in people with excess body weight without diabetes who experienced weight reductions up to 10.8% in 26 weeks; however, there was no change in A1C or fasting glucose from baseline to week 26.[30] Although the phase II trial results for weight loss efficacy of CarigSema are not available yet, there seems to be a potential for significant weight loss with the combination of cagrilintide with semaglutide as compared to GLP1-RA monotherapy, while maintaining A1C lowering due to the inclusion of semaglutide.

FDC Sema – OW GIP (NNC0480-0389) is a once weekly subcutaneous injection that includes a novel GIP agonist in combination with semaglutide. A phase II trial of this investigational combination agent for people with type 2 diabetes began in November 2021, and study completion is expected in March 2023.[31] Little information is currently available about this product; however, in the future, it may provide people with type 2 diabetes additional A1C and weight loss efficacy, compared to a GLP1-RA alone.

Pipeline GLP1, GIP, GCGR Dual- and Tri- Agonists

With the success of GLP1-RA agents and the introduction of a dual GLP1/GIP RA into the market, there are additional dual, triple, or other unique modifications of the glucagon receptor (GCGR) on the horizon.[32] Agonizing GCGR can reduce appetite, increase energy expenditure to promote weight loss, decrease gastrointestinal motility, enhance hepatic fatty acid oxidation and lipolysis, and stimulate insulin secretion during times of hyperglycemia.[33]

Studies demonstrating the synergistic weight-loss mechanisms of GLP-1 and glucagon have led to development of dual-agonists.[32] Several candidates have been in the pipeline for treatment of type 2 diabetes; however, a recent review of pharmaceutical companies' pipeline websites revealed that the intended use for many of these agents has been changed to treatment of nonalcoholic fatty liver disease (NAFLD) and/or obesity. Three agents for type 2 diabetes are currently in phase II or beyond, as described in Table 3.

Tri-agonism of GLP1-R, GIP-R, and GCGR in pre-clinical and clinical

studies demonstrated weight reductions and improved glycemic parameters.[32,34,35] Multiple agents are being explored for obesity and NAFLD, and one tri-agonist has completed a phase II trial for type 2 diabetes, as seen in Table 3. Results from the phase II trial of retatrutide demonstrated a mean A1C reduction of up to 1.9% and mean weight loss of up to 8.65 kg (10.1% decrease from baseline) at 12 weeks, which could be a competitive addition to the market.[33]

Conclusion

This is a dynamic time for diabetes pharmacotherapeutics. The introduction of GLP1-based medications into the market has been transformative in providing effective A1C and weight reductions for people with Type 2 diabetes. Additionally, the most recent ADA guidelines highlight weight management as a compelling factor when selecting diabetes pharmacotherapy. Several GLP1-based therapies are currently available, and there are additional, exciting products in the pipeline.

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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.

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Assessment Questions

1. Which of the following is true regarding the mechanism of GLP1-RA?
   a. Decreases beta cell insulin secretion in the pancreas
   b. Decreases glucose production in the liver
   c. Decreases satiety
   d. Increases gastric emptying time

2. **True or False:** Once daily GLP1-RA medications are more effective than once weekly
   a. True
   b. False

3. Patient MR is a 45-year-old male with type 2 diabetes. He was previously well managed on metformin 1000 mg BID and Farxiga 10 mg daily, however his A1C today was elevated at 8 %. MR has had the following BMI values over the last year: 32.4 kg/m^2 (today's visit), 30.2 kg/m^2 (6 months ago), 28.6 kg/m^2 (12 months ago). Due to his rising BMI, you would like to start a GLP1-RA. Assuming no contraindications to therapy or insurance barriers, which GLP1-RA would have the best efficacy for weight loss?
   a. Dulaglutide
   b. Exenatide
   c. Liraglutide
   d. Semaglutide

4. Which of the following is NOT approved for use in adolescents WITH diabetes?
   a. Dulaglutide
   b. Tirzepatide
   a. Liraglutide
   b. Semaglutide

5. Which of the follow medications do NOT have an FDA approval for MACE
   a. Dulaglutide
   b. Exenatide
   a. Liraglutide
   b. Semaglutide

6. Which of the following is unique about the mechanism of GIP compared to GLP1?
   a. GIP does not affect the kidneys
   b. GIP slows gastric emptying
   c. GIP increases glucagon secretion
   d. GIP does not affect the adipose tissue

7. Which of the following is an advantage of tirzepatide compared to other GLP1-RA medications?
   a. Oral administration
   b. Once monthly administration
   c. Lower risk of drug interactions
   d. More effective for weight loss

8. The common adverse gastrointestinal reactions of nausea, vomiting, diarrhea or constipation are primarily due to which mechanism of GLP1-RAs?
   a. Delayed gastric emptying
   b. Change in intestinal biome
   c. Increased insulin secretion and uptake in peripheral tissues
   d. Increased satiety in the CNS

9. Which of the following is TRUE about the ORAL formulation of semaglutide?
   a. It has higher efficacy
   b. It has a more profound weight loss
   c. It needs to be taken on an empty stomach with up to 4 ounces of water
   d. It can be taken with food if it causes nausea

10. **True or False:** Including GCGR agonism in combination with GLP1/GIP-RA can increase weight loss potential due to increased energy expenditure.
    a. True
    b. False

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

12. 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.

13. 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.

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

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

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

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

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

19. Please indicate the amount of time it took

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PRECEPTING SERIES:

Inclusive Precepting: Strategies to Promote Safety and Inclusion

by Charlene Williams, PharmD, BCACP, CDCES

Many preceptors have a strong desire to help create experiential learning environments that foster psychological safety and inclusion. Some preceptors have just started their precepting journey and may not have access to strategies that can help with this focus, and some are already doing great work in this space and want to add to the work they are doing. This article aims to equip new and advanced preceptors with tools and strategies that can be personalized to help foster an inclusive learning environment.

Bias and discrimination manifest in overt as well as unconscious ways.[1] FitzGerald and Hurst note that implicit biases "involve associations outside conscious awareness that lead to negative evaluation of a person on the basis of irrelevant characteristics such as race or gender," which influence our judgements and behaviors.[2] Sue and colleagues defined microaggressions as "commonplace verbal, behavioral, or environmental indignities, whether intentional or unintentional that communicate hostile, derogatory, or negative…slights and insults" to target persons based on their marginalized or group membership."[3] Some subtler examples of these include, "You are so articulate," "Where were you born?" and "As a __ person, I know what you must go through as a __ person," though other examples may be more explicit. Note that the terminology around microaggressions is evolving, as there is recognition that the term "micro" could be perceived as dismissive and minimize the receiving person's experience as well as deemphasize the harms these insults pose.[4] At the time of this writing, there is not consensus on updated terminology. "Exclusionary behavior" is one alternative term that has been proposed.[4] Health professions students are not exempt from receiving these behaviors. In medical training, for example, a meta-analysis found that more than half of trainees experienced at least one form of harassment or discrimination.[5] A group of pharmacy students at a midwestern college of pharmacy described examples of feeling othered and the presence and negative impact of pervasive microaggressions.[6] There is growing awareness of the significant negative impact exclusionary behaviors and implicit biases have on health disparities, patient care, patient-provider relationships, provider and learner health and well-being, cognition, and academic performance.[7,8]

Supporting the social and emotional dimensions of students positively influences learning and performance.[9] Inclusive learning practices promote these elements. However, the best evidence-based strategies for preceptors to use to respond to exclusionary behaviors are currently unclear, and more research needs to be done in this space. What follows are some strategies preceptors can use to create psychologically safe, inclusive learning spaces for their learners and some frameworks to help guide responses to exclusionary behaviors from team members and patients. Psychological safety, where team members feel safe to be vulnerable and take risks without fear of consequences, has been found to be a crucial element of successful teams (Table 1).[10] These tools below are not all-encompassing, but they give preceptors a place to start. We suggest adapting these strategies for one's own use with personalized language and action, so they feel comfortable and

genuine, and supplementing with other resources as appropriate.

There are a number of communication tools that have been developed to help individuals interrupt and/or respond to exclusionary behaviors. Examples of these include: ACTION; INTERRUPT; Stop, Talk, and Roll; 6 Ds; OFTD; VITAL(S); ARISE; ERASE; XYZ; and PEARLS.[15-24] Some of these tools can be used by recipients of exclusionary behaviors, as well as allies (including ACTION; 6 Ds; Stop Talk, and Roll; OFTD; and XYZ).[15,17-19,24] Tools that can be used by bystanders/allies/upstanders who witness exclusionary behaviors include INTERRUPT, OFTD, VITALS(S), ARISE, and ERASE.[16,20-23] An additional tool that can be used to support someone after they experience an exclusionary behavior is PEARLS.[25] A communication tool that can be used by the source of the exclusionary behavior is ASSIST.[22] At the time of this writing, it appears that none of the tools of have been researched in real-time precepting environments for outcomes to discern the optimal approach in experiential environments. However, a number of them have demonstrated a change in participants' knowledge, awareness, and/or confidence after training.[16,17-19,22,23,25]

Recognize that there is not one "right" way to respond. We suggest adapting these tools to what feels natural for one's personal use and the situation. Preceptors are encouraged to visit the source materials for additional context, as the examples provided in this article are based on the author's interpretation. Many of the tools are available in open-access formats with supplementary materials.[7,16,18,20,22,24] There are common themes connecting a number of the frameworks. Below is a summary of some similar actions that appear in many of the communication tools; those actions are organized with the acronym ISEEAPPES.[7,15-24] This summary framework includes steps for recipients, bystanders, and sources of exclusionary behaviors as the situation requires. All steps will not apply to every situation.

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TABLE 1. Some Tips to Promote a Psychologically Safe and Inclusive Learning Environment[11-14]

Action	*Examples*
Respect names, name pronunciation, identities, and pronouns that individuals share (do not require to share all details though sharing yours may invite that it is safe to share)	"My name is ___. You may address me as ___. My pronouns are ___. How do you wish to be addressed? Did I pronounce your name correctly? I want to honor your name- please help me say your name correctly. Is that correct?"
Get to know your learners holistically insofar as they are willing to share	[In a more casual setting if possible] "I'd like to take some time to get to know each other better." [Share your introduction] "If you feel comfortable sharing, I would love to learn more about your interests, strengths and areas of growth, learning goals, long-term goals, and how I can best support you."
Communicate your desire to create a space that values learners and others for who they are and what they bring	"It is my goal to create a learning experience where you feel safe to learn and are valued for your contributions."
Encourage your learner to come to you with any concerns	"Please feel free to reach out if you feel uncomfortable or have concerns about myself, a team member, or patient."
Create space for discussions and feedback to occur	"Let's schedule a weekly time to check in to see how the rotation experience is going for you and to share feedback with each other."
Acknowledge that tragic events impact people in different ways and may negatively impact performance and engagement	"I've seen some difficult things in the news this week affecting various communities. I am not sure if they impact you or not, but I am willing to talk if needed or learn if there is something I can do to support you."
Share resources and support available at school and practice sites around diversity equity and inclusion	"Here are our site's diversity, equity, and inclusion policies and resources that I share with every learner on my rotation. If you have a concern, these are steps you can follow to get assistance. I understand that you also may have resources available to you at your school. Please let me know if you have any questions after you have had a chance to review."
Discuss how health disparities are addressed at your site	"Here are resources we have at our site to support equitable access to care."
Recognize that learners may bring fears and emotions into the experiential environment	"I noticed that after that patient interaction, you seemed quiet for the rest of the afternoon. If you need to talk, some additional space, or additional support, please let me know. Sometimes things that happen in patient care or with team interactions can bring personal things up, and that is ok. I am here to support if needed."
Acknowledge and interrupt exclusionary behaviors	Please see the next section on communication models/frameworks to intervene, respond to, and support others in the midst of exclusionary behaviors.
Use inclusive language and person-first language	Use "person with diabetes" vs. "diabetic," or "person experiencing bipolar disorder" vs. "manic-depressive," for example
Use non-gendered terms when possible	Use "you all" instead of "you guys." Use "significant other" or "partner" instead of "wife/husband" or "girlfriend/boyfriend."
Investigate Universal Design for Learning techniques to incorporate into the experience to optimize learning for all individuals (such as choice in activities/assignments, use of different modes of teaching, and providing resources in a variety of formats)	Learn more at UDL Guidelines: https://udlguidelines.cast.org/

TABLE 2. ISEEAPPES

Individual	*Action*	*Example phrases*
Recipient, bystander	**I - Interrupt/acknowledge** exclusionary behaviors nonjudgmentally with curiosity	"I'm curious about what you mean when you say __." "It seems like you may have concerns about the care you are receiving. Could you tell me more about that?" Note that recipients may not always be comfortable speaking up due to possible power differentials.
Recipient	**S- Seek** assistance	"I am feeling uncomfortable with that statement. I am going to consult with my preceptor or supervisor."
Bystander, recipient, source	**E- Empathize** nonjudgmentally	"It sounds like you may be concerned about ___. Is that correct?" "When I said__, I noticed your body language changed. Would you be willing to share what came up for you when ___ said ___?"
Bystander, recipient	**E- Explore** impact to self and or others and educate with "I" statements	"I am concerned about that statement because it made me feel or think ___ because ___." "I don't think you meant to cause harm, but this language could be perceived as a harmful stereotype and could be detrimental to our team's ability to work together effectively to care for our patients."
Bystander, source	**A- Apologize** and alleviate biases	"I am really sorry that I caused pain." "I am so sorry that you experienced that." Participate in ongoing work to learn more about biases and how to mitigate them. For example, Project Implicit offers Implicit Association Tests (IAT) to help assess conscious and unconscious attitudes on a variety of topics. https://implicit.harvard.edu/implicit/research/
Bystander, recipient	**P-Probe** further and debrief	Offer space for the recipient to share their experience in private, insofar as they are comfortable. As a learner, ask to talk through the situation with a preceptor/supervisor. Share personal feelings as comfortable. "Would you like to talk about what happened earlier?" "When the patient said ___, I felt uncomfortable because ___, and I am hoping we can talk through the situation together."
Bystander, recipient, source	**P- Partner** on solutions	"What do you think are our next steps moving forward?" "I have some ideas on how to proceed and would like to hear from you what you think would be helpful."
Bystander, source	**E- Endorse/validate** person's experience and recognize their contributions	"Thank you for sharing that. I can see from your perspective why you would feel that way." "You are a valued member of this team."
Bystander, recipient	**S- Support;**- Encourage a positive climate and explore resources	"It is my aim that all learners feel safe in their learning environment. I want to support you when things like this happen. Please come to me if any other uncomfortable situations occur. There are resources at your school that we can connect you to if you would like." A learner might share, "I'm still having trouble processing what happened, and I am wondering if you can help me get connected with additional support at the school."

Disclosure: 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.

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WPQC UPDATE:

WPQC Spotlight: Matt Huppert

Fitchburg Family Pharmacy Tuberculosis Dispensing Partnership and Guideline Review

by Dan Funk, PharmD, Sommer Gay, PharmD, Hunter Furley, 2023 PharmD Candidate

Tuberculosis (TB), caused by *Mycobacterium tuberculosis*, is one of the most common infectious diseases worldwide, infecting roughly 23% of the global population.[1] However, in the United States, TB infection is much less prevalent, impacting only 2.2 per 100,000 people.[2] According to the Wisconsin Department of Health Services (DHS), there were only 66 reported cases of TB in Wisconsin in 2021, 6 of which occurred in Dane county.[3] It is imperative that these patients be treated appropriately, so DHS assumes full responsibility for the management of care for these patients, from diagnosis to cure.

Given the relative rarity of TB in Wisconsin, coordinating the dispensing of the medications to treat TB can be challenging. Many pharmacies do not regularly carry the medications necessary to treat TB. Having to order these medications as needed from a distributor can result in delays in treatment initiation. In addition, pharmacists who do not routinely dispense TB treatment may not be prepared to assess the safety and efficacy of regimens involving medications such as isoniazid or rifapentine.

Considering these challenges, DHS partners with a single regional pharmacy to dispense treatment for the small number of its patients with TB. This helps prevent delays in treatment, ensures appropriate turnover of TB medications from pharmacy shelves, and allows the pharmacists on site to become regional experts in evaluating TB treatment. When the Wisconsin DHS sought a new pharmacy partner in the Dane County area, they reached out to Fitchburg Family Pharmacy (FFP) based on both agencies' previous experience collaborating to address the COVID-19 pandemic. In the following Q&A, Matt Huppert, PharmD, shares his experience establishing this TB dispensing partnership with DHS.

Q&A with Matt Huppert

Q: How did the idea for this partnership come about?

A: We received an email from the Public Health Supervisor for Dane County asking Thad Schumacher, the owner, if we at Fitchburg Family Pharmacy could provide dispensing services for the TB program. We said we could help to ensure the patient was getting the medications they needed.

Q: What previous experiences prepared you for this partnership?

A: Our pharmacy has been working with other branches of Wisconsin DHS to provide COVID vaccinations and testing. We also felt that we could provide medications to patients in an efficient manner based on the culture of our pharmacy.

Q: What steps did you take to get started?

A: We called the coordinator to set up a date to meet. We then set up a meeting to meet with all the nurses involved with the TB drug dispensing program.

Q: How does this partnership work and what is your role in the partnership?

A: The TB nurses send us prescriptions for TB medications. They provide us with insurance information, labs, and other information for us to provide safe and effective medications. Our role is to provide the medication in a logistically efficient manner to treat TB.

Q: What barriers did you face with implementing the partnership?

A: We hadn't stocked or dispensed TB drugs previously. We also were unsure about reimbursement and payment of patient copays. We needed to be reimbursed for the medication and the time it takes to ensure the medication is safe and effective for the patient.

For another perspective on partnerships with local health departments, consider listening to PSW's 2022 Emerging Leaders Podcast episode "Working with Your Local Health Department." Here, Joshua Davis, PharmD, BCACP, discusses his experience building a relationship with the Iowa Department of Public Health and providing services such as HIV testing and COVID immunizations. The Emerging Leaders Podcast series can be found on PSW's website: https://www.pswi.org/Communications/PSW-Podcasts

Q: How did you overcome these barriers?

A: We utilized 4th-year pharmacy students to ensure our staff was updated on how to provide TB medications safely and effectively. We also did a cost analysis on how much medication we would need to stock in the pharmacy. We wanted to make sure that our pharmacy would not be spending too much money on inventory to provide this service for patients.

Q: How will this partnership help FFP and the community?

A: We want to ensure patients are receiving their medications in a timely fashion to reduce risks of disease progression. We feel this partnership is important to ensure we are taking care of patients in our community. Access to healthcare is a major barrier for patients. Both adherence and safety can be affected due to low access to healthcare. Our pharmacy is attempting to provide as much access as possible to improve this social determinant of health. Providing services like this to patients may help our pharmacy by showing what pharmacists are able to do to help our communities.

Tuberculosis Guideline Review

Most commonly, TB affects the lungs, but the bacteria can attack anywhere in the body.[4] Symptoms can include cough, fever, fatigue, or night sweats. However, it is important to recognize that not everyone infected with TB becomes sick, due to latent TB infections (LTBI). Along with LTBI, there are other factors that impact the treatment of TB, including drug susceptibility and resistance, as well as human immunodeficiency virus (HIV) status. As a result, multiple guidelines exist to aid in the treatment of TB.

Drug Susceptible TB Treatment

The American Thoracic Society (ATS), Centers for Disease Control and Prevention (CDC), and Infectious Diseases Society of America (IDSA) released a clinical practice guideline in 2016 regarding the treatment of drug-susceptible TB.[5]

Preferred Treatment Regimen

The preferred regimen for drug-susceptible TB in adults caused by organisms that are not known or suspected to be drug-resistant consists of an intensive phase for 2 months, followed by a continuation phase of 4 months, as outlined in tables 1 and 2.

When using isoniazid (INH), pyridoxine (vitamin B6) is added to prevent neuropathy. Doses of 25-50 mg daily are appropriate if the patient does not already have neuropathy. This is especially important in those at high risk of neuropathy, such as those pregnant or breastfeeding, patients with HIV, diabetes, alcoholism, malnutrition, chronic renal failure, or advanced age. If the patient experiences neuropathy, the dose may be increased to 100 mg per day.

Administration Schedule

The preferred frequency of this treatment regimen is once-daily dosing for both the intensive and continuation phases; however, there have been a variety of studies that have looked at the administration of antituberculosis drugs using directly observed therapy (DOT). This is the practice of observing the patient swallow their medications 5-days-a-week. Experts believe that both approaches to treatment are appropriate and should be decided on based upon patient-specific factors and preferences. Treatment regimen medications typically are administered together at one dosing period and the bioavailability of all the medications is greatest when taken on an empty stomach.

Alternative Treatment Regimens

When patients are intolerant to first-line medications or there is a presence of mono-resistance, alternative regimens may be used.

- If pyrazinamide (PZA) cannot be used, INH, rifampin (RIF), and ethambutol (EMB) should be used for 2 months followed by 7 months of RIF and INH.

For treatment of latent TB, please see: Guidelines for the Treatment of Latent Tuberculosis Infection: Recommendations from the National Tuberculosis Controllers Association and CDC, 2020

TABLE 1. Intensive Phase Regimen

Intensive Phase	*Dosing*	*Duration*
Rifampin* (RIF)	10 mg/kg/day (typically 600 mg)	7 days/week for 8 weeks (56 doses) or 5 days/week for 8 weeks (40 doses)
Isoniazid (INH)	5 mg/kg/day (typically 300 mg)	
Pyrazinamide (PZA)	40-55 kg: 1000 mg daily 56-75 kg: 1500 mg daily 76-90 kg: 2000 mg daily	
Ethambutol (EMB)	40-55 kg: 800 mg daily 56-75 kg: 1200 mg daily 76-90 kg: 1600 mg daily	
**Rifampin analogs rifapentine and rifabutin can be used in select patients*		
Rifabutin	5 mg/kg/day (typically 300 mg)	
Rifapentine	10–20 mg/kg/day	

TABLE 2. Continuation Phase Regimen

Continuation Phase	*Dosing*	*Duration*
Rifampin (RIF)	10 mg/kg/day (typically 600 mg)	7 days/week for 18 weeks (126 doses) or 5 days/week for 18 weeks (90 doses)
Isoniazid (INH)	5 mg/kg/day (typically 300 mg)	

- If EMB or INH cannot be used, moxifloxacin or levofloxacin can be used in their place for a minimum of 6 months in duration. It is also important to note that the use of moxifloxacin and levofloxacin has not been established in clinical trials.
- If RIF or its analogs cannot be used, it is recommended to follow the Official ATS/CDC/ERS/IDSA Clinical Practice Guideline for the Treatment of Drug-Resistant Tuberculosis.[5]

For treatment in special situations including HIV infection, tuberculous pericarditis, tuberculous meningitis, culture-negative pulmonary tuberculosis in adults, or other special situations, please see the full drug-susceptible tuberculosis treatment guidelines.

Follow-up & Monitoring

At baseline, it is recommended that patients with suspected TB have 3 sputum specimens collected for evaluation and culture, with at least 1 specimen for rapid molecular testing. Susceptibility testing should also occur for INH, RIF, EMB, and PZA if the initial culture is positive, regardless of the source. Patients also should receive a chest radiograph or similar imaging. Baseline liver function tests are obtained and if results are normal, continued monitoring does not need to occur unless symptoms consistent with hepatotoxicity develop, or for patients who chronically consume alcohol, take other hepatotoxic medications, have viral hepatitis or liver disease, or HIV. At baseline, patients should also be screened for HIV, hepatitis B and C, and diabetes. For patients being initiated on EMB, it is important that baseline visual acuity and color discrimination tests are completed, followed by monthly monitoring.

During treatment, a sputum specimen is collected for an acid-fast bacilli (AFB) smear and cultured monthly until 2 consecutive specimens are negative. When initiating the continuation phase, it is crucial that the patient obtain a sputum specimen once completing the intensive phase if a negative sputum culture has not already been documented, as the culture results tend to correlate with the likelihood of relapse after completing therapy. It is also recommended that once a patient has been on treatment for 3 months or longer, drug susceptibility tests are completed to identify any treatment failures. Also, it is important to assess adherence and monitor for improvement in TB symptoms as well as the development of medication adverse effects such as jaundice, dark urine, nausea, vomiting, abdominal pain, fever, rash, anorexia, malaise, neuropathy, or arthralgias. Weight should be monitored monthly to adjust medication doses as needed.

Management of Treatment Interruptions

Treatment interruptions can lead to serious outcomes such as treatment resistance and potentially the need to restart treatment from the beginning, especially if the break is early in therapy or long in duration. In general, if the treatment interruption occurs during the intensive phase and is less than 14 days in duration, continue treatment until the planned number of doses is completed. If the interruption is greater than 14 days in duration, drug therapy will need to be restarted from the beginning. If the interruption occurs during the continuation phase, and the patient has received at least 80% of doses and had a negative AFB smear on initiation, further therapy may not be warranted. If the patient has received at least 80% of doses and the AFB smear was positive initially, continue drug therapy until all doses are complete. If the patient has not received at least 80% of doses, and the accumulative lapse is less than 3 months, the patient may continue therapy until all doses are complete. If the patient has not received at least 80% of doses and the accumulative lapse is greater than 3 months, the patient needs to restart therapy from the beginning of the intensive phase.

Management of Common Adverse Events

As mentioned previously, potential adverse effects that may develop from these treatment regimens include jaundice, dark urine, nausea, vomiting, abdominal pain, fever, rash, anorexia, malaise, neuropathy, or arthralgias.

Gastrointestinal Adverse Effects: Gastrointestinal (GI) adverse reactions are common with these treatment regimens. To minimize symptoms of nausea or epigastric distress, patients may take the medications at bedtime. When GI intolerance is not related to hepatotoxicity, antacids may be used as they interfere less with drug absorption as compared to food. If patients are still experiencing intolerances, a low-fat snack may be utilized to minimize side effects.

Rash: A rash may also be a common side effect experienced by patients using antituberculosis medications. If the rash is considered mild (mainly itchy without mucous membrane involvement or systemic symptoms (fever)), patients can use antihistamines and their TB regimen can be continued. If the rash is considered a petechial rash or a generalized erythematous rash, or if fever and/or mucous membrane involvement develops, medications should be stopped. Systemic corticosteroids may be used to treat severe systemic rashes. When symptoms have improved greatly, medications can be individually restarted in intervals of 2-3 days. RIF should be restarted first, then INH, then EMB or PZA. If at any point the rash reoccurs, the last medication added should be stopped immediately. Once 3 medications have been restarted without the recurrence of a rash, the fourth medication should not be added unless the medication is essential, and the rash was considered mild.

Fever: Drug fevers can be caused by multiple factors when treating TB. If patients have a body temperature of ≥ 39°C but feel well, superinfection is generally not suspected. Stopping the medications should resolve the fever in approximately 24 hours. Once the patient is not experiencing a fever, reinitiate medications individually every 2-3 days, similar to the process used for rechallenging medications due to a rash.

Hepatotoxicity: The most frequent serious adverse reaction to RIF, INH, and PZA is drug-induced liver injury. When alanine transaminase (ALT) is ≥ 3 times the upper limit of normal (ULN) with symptoms of hepatitis such as jaundice, dark urine, nausea, vomiting, abdominal pain, or ≥ 5 times the ULN in the absence of symptoms, drug-induced liver injury is suspected. If drug-induced liver injury is suspected, hepatotoxic medications should be stopped immediately. Once ALT is < 2 times the ULN, medications may be restarted individually, typically starting with RIF since it is less likely to cause hepatotoxicity than INH or PZA. After 1 week, if there is no increase in ALT, INH can be restarted. Similarly, if there is still no increase in ALT after 1 week, PZA can

be initiated. If at any point ALT increases or symptoms reoccur, the last medication added should be stopped immediately.

Drug-Drug Interactions

Drug-drug interactions are very common when treating TB. It is uncommon for antituberculosis drug concentrations to substantially change and affect the treatment of TB, but it is very common for antituberculosis medications to cause changes in concentrations of other medications. Many of these interactions are due to induction of CYP isozymes by rifamycins. For a detailed list of drug-drug interactions, please see the full drug-susceptible tuberculosis treatment guidelines.

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Disclosure: 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.

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Original Work

Evaluating the Implementation of a Pharmacist-Driven Epilepsy Telehealth Education Program in an Epilepsy Specialty Clinic

by Magdalena M. Siodlak, PharmD, BCACP, Barry E. Gidal, PharmD, Stephanie Hunter-Banks, PharmD, Judith Thompson, PharmD, MPH, Robert J. Kotloski, MD, PhD, Amanda Margolis, PharmD

Abstract

Objective: In patients with epilepsy, disease self-management skills may improve seizure control, quality of life, and medication adherence. A patient education and adherence program was developed to empower patients to manage their epilepsy. This pilot assessed the feasibility of implementing the five-module educational book series (Exploring Epilepsy) as a pharmacist-driven telehealth program in an ambulatory care epilepsy clinic and its effect on clinical outcomes.

Methods: This was a prospective cohort study of patients was enrolled at the William S. Middleton Memorial Veterans Hospital Epilepsy Clinic in Madison, WI. A study pharmacist scheduled and conducted five telephone encounters to review the educational modules. Clinical assessments compared baseline to 3 months post-intervention: Epilepsy Self-Efficacy Scale (ESES), Epilepsy Self-Management Scale (ESMS), Patient Weighted Quality of Life in Epilepsy inventory-10 (QOLIE-10-P), Generalized Anxiety Disorder-7 (GAD-7), Neurological Disorders Depression Inventory in Epilepsy (NDDI-E), and a modified Patient-Physician Interactions survey.

Results: Twenty patients were enrolled; 14 (70%) completed the five-module series. Appointments lasted on average 25±9 minutes. There were no statistically significant differences in ESES, ESMS, QOLIE-10-P, GAD-7, nor NDDI-E (n=10). All participants completing assessments found the facilitator helpful. At least 70% of patients reported improved comfort in discussing epilepsy and understanding various self-management aspects of epilepsy.

Conclusion: Implementation of this epilepsy education program is feasible in a clinic setting. Patients reported high satisfaction with the service and endorsed enhanced understanding of self-management strategies. Although there were no statistical improvements in clinical questionnaires, the small sample size is not powered to detect clinically significant differences. Future investigations could consider organizing the program in a group setting to facilitate peer support and discussion.

In 2015, the Centers for Disease Control and Prevention estimated that 3.4 million people in the United States were living with epilepsy, the majority of whom are adults.[1] In addition, an estimated $US 15.5 billion are spent yearly on healthcare costs in this patient population. In the veteran population, epilepsy is more common because of the higher incidence of traumatic brain injury (TBI), which is one of the risk factors in developing this disease. Post-traumatic epilepsy was reported in 35% to 45% of veterans with combat-related TBI during World War I, World War II, and the Korean War.[2] High rates of post-traumatic epilepsy were also found in veterans of Afghanistan and Iraq with TBI following Operation Enduring Freedom and Operation Iraqi Freedom, respectively. In this veteran population, the estimated risk for epilepsy among those with penetrating TBI was nearly 18 times greater than among those without TBI.[3]

It is well documented that patients with epilepsy often lack the support and information necessary to properly self-manage their disease. Studies have shown a significant knowledge gap between what patients and their caregivers wish to learn about epilepsy-related morbidity and mortality and the information that is shared with them by their healthcare providers.[4-6] In a cross-sectional study, low levels of disease understanding among patients with epilepsy were reflected by low general knowledge as well as limited details of the patient's own epilepsy diagnosis (e.g., etiology, seizure type).[7] Other studies have reported low understanding of epilepsy-related information and lifestyle management,[8] and low self-management practices among patients from underserved populations.[9] Shortcomings in disease self-management contribute to suboptimal outcomes for patients. For instance, patients with epilepsy often struggle to take their medications consistently and adherence rates can be as low as 30% to 50%.[10] This low adherence results in poor patient outcomes including decreased quality of life, limited seizure control, increased morbidity and mortality including sudden unexpected death in epilepsy,[11] and a significant increase in health-care costs. In a claims database analysis, medication nonadherence among patients with epilepsy increased the risk of mortality (hazard ratio [HR] 3.32, 95% confidence interval [CI] 3.11-3.54), emergency department visits

(relative risk [RR] 1.50, 95% CI, 1.49-1.52), and hospital admissions (RR 1.86, 95% CI 1.84-1.88).[10] Taken together, these findings highlight the need for educational interventions in epilepsy management, including the creation of seizure action plans that can improve key elements of patient and caregiver education and help patients and caregivers better manage their epilepsy.[12,13] Community and ambulatory care pharmacists are well positioned to provide such interventions because they are accessible health-care providers who routinely interact with patients with chronic diseases without requiring formal appointments. Pharmacist involvement in chronic disease state management has been shown to improve patient outcomes.[14-16] Unfortunately, epilepsy has not been a focus of pharmacist-driven medication therapy management (MTM) programs in the past.

Educational programs can help patients with epilepsy improve self-management of their condition as well as medication adherence. A 2017 meta-analysis investigated various educational interventions in patients with epilepsy and measured their effects on adherence rates.[17] Two trials included in the analysis showed a significant benefit of these educational programs, such as improved adherence rates and improved scores on an adherence questionnaire.[18,19] Interventions included one-on-one educational sessions with providers, online educational sessions, and full-day group sessions with providers. The programs helped educate patients with epilepsy to better understand their condition and improve their epilepsy management. However, pharmacists were involved in only one of the included studies.[20] Pharmacists are medication experts and if patients struggle with medication use and adherence, pharmacists can play a vital role in improving these aspects of treatment. If it is feasible for pharmacists to implement an educational program into a clinical practice, it could help patients with epilepsy improve their self-care and ultimately reduce morbidity, mortality, and health-care costs. To evaluate the health benefits a pharmacist-run educational program can make in patients with epilepsy, it is first important to measure if it is feasible to incorporate these programs into clinic workflow, including barriers and perceived benefits.[21]

TABLE 1. Patient Toolkit: Exploring Epilepsy Modules

Section	Content
Module 1: Epilepsy 101	Overview of epilepsy including pathophysiology, types, signs and symptoms, concerns across the lifespan, healthcare team members, and questions to ask health-care professionals
Module 2: Epilepsy Medication Therapy	Overview of the medications for epilepsy, treatment goals and challenges, ways to optimize treatment
Module 3: Epilepsy Support and Non-Medication Management	Overview of non-medication strategies to optimize well-being, including potential safety issues, managing lifestyle, understanding triggers and risk factors, improving quality of life, and establishing a community of support
Module 4: Medication Action Plan	Introduces an individual MAP developed by the patient to ensure adherence and compliance to the treatment regimen
Module 5: Follow-up Pharmacotherapy Consultation	Guidance for discussion with health-care professional for one-on-one follow-up to continue to discuss the MAP and make any necessary changes

MAP = Medical Action Plan.

The primary objective of this prospective cohort study was to determine the feasibility, including barriers and perceived benefits, of implementing Exploring Epilepsy as a pharmacist-driven program for patients with epilepsy within an ambulatory care clinic. Secondary objectives included assessing patient acceptability of this intervention and the effect on patient clinical outcomes.

Methods

Exploring Epilepsy Program Development

Human-centered design is a problem-solving methodology that uses co-creation with end users or those impacted by the product, service, system or process to develop a solution. In this study, the materials were developed with a diverse working group including patients, pharmacists and physicians. In the first phase of Exploring Epilepsy development, a working group was convened of patients with epilepsy, clinical pharmacists, nurses, nurse practitioners, physician assistants who work in or have expertise in epilepsy, and physicians or health-care professionals actively involved in educational programs for patients with epilepsy. This group worked with the UCB Pharma team over a 3-month period to identify unmet needs in the epilepsy journey leveraging MTM programs in other disease states as a foundation, with input from involved parties (i.e. patients with epilepsy and health-care providers). The working group held two virtual meetings and one in-person meeting to discuss the program outline, content type, topics, program operations and delivery, as well as outcome measures of interest. The feedback was integrated into the final program pilot, ensuring that the participant experience and quality of care was aligned with program expectations.

These collaborations resulted in the creation of modular content during phase 2 development, yielding the Exploring Epilepsy Patient Toolkit and a Facilitator's Guide. The Exploring Epilepsy Patient Toolkit comprised an educational book series with five modules: Epilepsy 101, Medication Therapy Review, Disease Management Support, Medication Action Plan, and Follow-up Pharmacotherapy Consultation (Table 1). The Toolkit contained resources specifically designed to aid patients as they progress through their journey in living with epilepsy. The content of the patient toolkit was visually stimulating, included videos, and was designed to tell a visual story across ability levels (e.g. to those with impaired cognition, low general and health literacy, those who speak English as a second language, and older adults; thus, written at a 6th- to 8th-grade literacy level) to activate patient empowerment and enhance self-management through pharmacist-facilitated discussions, disease education, a personalized action plan, and a high level of interactivity. The Facilitator's Guide for the health-care professionals administering

the program was created to provide detailed guidance and tips for leading patients through the program. The guide also provided health literacy and plain-language tips for communicating with patients, and useful links including a patient welcome letter, patient baseline self-questionnaires, reporting for adverse events, a shared decision-making approach, and a teach-back method for patients to demonstrate their understanding of the content (Table 2).

In the third phase of program development, a secure, interactive website was created to house the patient toolkit as an eBook. Materials are publicly available at https://www.exploringepilepsytoday.com/ and include modules 1 through 3 as of December 2022. In the fourth stage of development, the program was piloted in an ambulatory setting, with a target enrollment of 35 participants.

TABLE 2. Facilitator Guide

Section	Content
Introduction to the Exploring Epilepsy Program	• Purpose/Objectives/Appropriate Patients • Overview of Exploring Epilepsy Program • Program Execution Timing • Program Logistics and Patient Flow • Patient Communication Tips and Tools
Module 1: Epilepsy 101	• Exploring Epilepsy program content, with guidance and tips to help lead patients through the program • Health literacy and plain-language tips for communicating with patients
Module 2: Epilepsy Medication Therapy	
Module 3: Epilepsy Support and Non-Medication Management	
Module 4: Medication Action Plan	
Module 5: Follow-up Pharmacotherapy Consultation	

Clinical Setting

This pilot study was conducted at the Epilepsy Center of Excellence (ECoE), William S. Middleton Memorial Veterans Hospital, Madison, Wisconsin (hereinafter referred to as the Madison VA). The Veterans Affairs (VA) health-care system offers numerous services to their patients through the ECoE. The ECoE at the Madison VA is one of 17 VA ECoEs across the country that provide patient and clinician education regarding epilepsy treatment and disease management. The ECoE at the Madison VA provides epilepsy care to approximately 400 veterans each year. As a Level 4 Epilepsy Center, the ECoE receives referrals from other VA centers and provides high-quality epilepsy care, including treatment with new antiseizure medications (ASMs), neuromodulation devices, and resective surgeries. A Clinical Pharmacist Practitioner (CPP), epileptologist, psychiatrist, medical and pharmacy fellows and residents, medical support assistants, nurse practitioner, and nurses are members of a multidisciplinary team providing individualized care. Integrated into the Madison VA Epilepsy Clinic in 1991, the CPP works at the highest level of clinical practice, providing comprehensive medication management following initial epilepsy diagnosis (e.g. prescribing medications, ordering laboratory tests and diagnostic studies, performing physical assessments, counseling, mental health triage, and referral). The Madison VA Epilepsy Clinic meets 1 day per week for 4 hours, during which 14 in-person patient and telehealth appointments are available.

Recruitment

Patients with diagnosed epilepsy established at the Madison VA Epilepsy Clinic who were at least 18 years of age and had provided informed consent during regularly scheduled appointments with the epilepsy clinic were eligible for participation in the Exploring Epilepsy pilot. Those enrolled in another study or without functional capacity as determined by their health-care provider were excluded. This study received approval from the University of Wisconsin-Madison Institutional Review Board and the Madison VA Research and Development Committee.

Study Design: 12-week Education Intervention

Upon enrollment, patients received the Exploring Epilepsy Patient Toolkit from a health-care professional. Enrolled patients were scheduled for five, individualized 30-minute educational sessions with the pharmacist via telephone. The purpose of these sessions was to review each of the five modules. Appointments for module review were scheduled every 2 weeks, with the intention of the program being completed within a 12-week period from enrollment. Patients were discharged from the study after three consecutive, failed attempts at scheduling session phone appointments.

In leveraging the expertise and availability of pharmacist practitioners during the one-on-one consultations, patients received a customized, co-created action plan by the end of the module appointments. Throughout the program, participants received tips on how to enhance other health-care provider discussions, a holistic approach to epilepsy management, and how to educate others in the event of a seizure.

Outcome Measures

The primary outcome was the feasibility of program implementation,[22] which was measured by encounter completion time, patient completion rates, and proportion of patients requiring appointment rescheduling.

Secondary assessments included four validated surveys that patients completed regarding their epilepsy at baseline and at 3 months after completing the Exploring Epilepsy education series. Change in survey results from baseline to 3 months post-intervention was used to assess the effect of Exploring Epilepsy on clinical outcomes and acceptability. The four epilepsy-related patient surveys were the Epilepsy Self-Efficacy Scale (ESES), the Epilepsy Self-Management Scale (ESMS), the Patient Weighted Quality of Life in Epilepsy inventory-10 (QOLIE-10-P), and the Neurological Disorders Depression Inventory in Epilepsy (NDDI-E). The ESES is a 33-item questionnaire using an 11-point Likert scale with 0 being "I cannot do at all" to 10 being "sure I can do," with higher scores indicating increased self-

efficacy.[23] The ESMS is a 38-item survey with a five-point rating scale, with 1 being "never" and 5 being "always"; higher scores indicate increased frequency in epilepsy self-management behaviors.[24] The QOLIE-10-P is a 10-item survey that measures a patient's perceived effect of epilepsy on quality of life,[25] and the NDDI-E is a six-item tool scored over the previous 2 weeks using a four-point scale, with 4 being "always or often" and 1 being "never."[26] NDDI-E scores over 13 indicate potential major depressive disorder.[27]

Patients completed three additional surveys. The first was the Generalized Anxiety Disorder-7 (GAD-7), a validated seven-item survey where patients indicate the effect of symptoms over the previous 2 weeks using a four-point scale, with 0 being "not at all" and 3 being "nearly every day," with a total score of 5 indicating mild anxiety.[28] The Perceived Efficacy in Patient-Physician Interactions (PEPPI) instrument, which measures older adults' self-efficacy in interacting with physicians,[29] has been previously modified to describe interactions with pharmacists and includes the addition of several questions with good reliability, as shown by Cronbach's alpha ranging from 0.94 to 0.97.[30] This modified PEPPI instrument was used to assess patient-pharmacist interactions. After series completion, patients evaluated the program using a patient satisfaction and perception survey that contained nine questions about various aspects of Exploring Epilepsy delivery. The survey used a four-point Likert scale of "strongly agree" to "strongly disagree," and also allowed participants to report no opinion.

Individuals identified through NDDI-E or GAD-7 scores as at risk of major depression or anxiety, respectively, were referred to appropriate resources for intervention.

Statistical Analysis

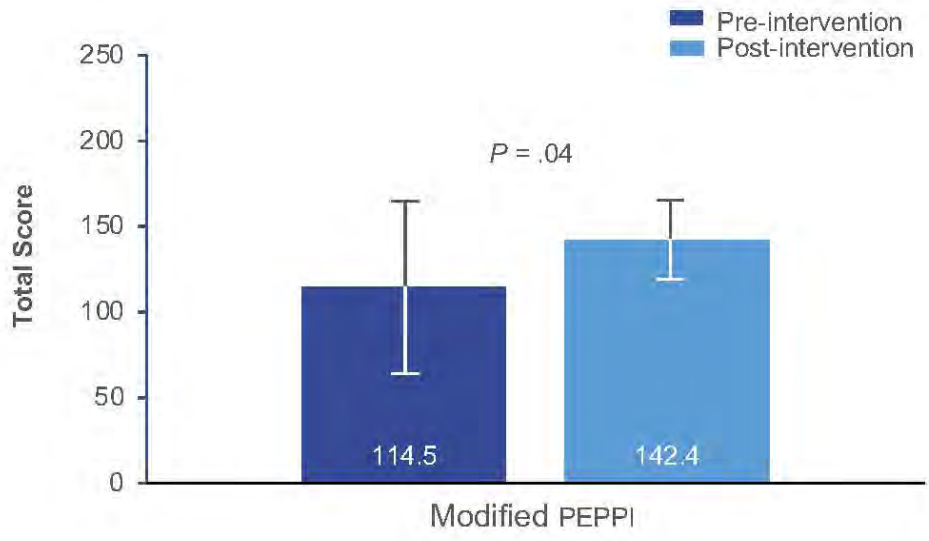
Statistical analyses were performed using STATA version 14.2 (StataCorp LP, College Station, TX, USA). Descriptive statistics were used as appropriate (i.e. means, standard deviations, and proportions). Continuous variables were assessed with the Wilcoxon Signed-Rank test. Imputation was used to manage missing data and was conducted through averaging the patient's score from the remaining questions on the scale. Results were tested for statistical significance using a two-sided alpha level of 0.05 without adjustment for repeated testing.

Results

Feasibility of Implementation

Between February 2019 and October 2019, a total of 20 patients were enrolled in the Exploring Epilepsy pilot program at the VA ambulatory clinic. Participants

FIGURE 1. Total Scores for Epilepsy and Quality of Life Assessments (n = 10)



ESES = Epilepsy Self-Efficacy Scale; ESMS = Epilepsy Self-Management Scale; QOLIE-10-P = Patient Weighted Quality of Life in Epilepsy inventory-10.

TABLE 3. Demographic and Clinical Characteristics at Baseline (2019)

Characteristic	*Value (n = 20)*
Age (years), mean (SD)	57.8 (12.3)
Male, n (%)	17 (85)
Race and ethnicity, n (%)	
American Indian/Native Hawaiian	1 (5)
Hispanic/Latino	1 (5)
White	16 (80)
Declined to answer	2 (10)
Medications, mean (SD)	
Scheduled	7.8 (5.6)
As needed	1.4 (1.7)
Specific comorbid conditions,a n (%)	
Depression	7 (35)
Hearing loss	7 (35)
Osteoporosis	2 (10)
Post-traumatic stress disorder	2 (10)
Traumatic brain injury	2 (10)
Health-care utilization in past 12 months, n (%)	
Emergency Department	11 (55)
Hospitalization	3 (15)
ASM use, mean (SD)	1.6 (0.8)
Patients on specific ASM, n (%)	
Levetiracetam	8 (40)
Gabapentin	4 (20)
Lamotrigine	3 (15)
Brivaracetam	2 (10)
Carbamazepine	2 (10)
Divalproex sodium	2 (10)
Lacosamide	2 (10)
Perampanel	2 (10)
Phenytoin	2 (10)
Cannabidiol	1 (5)
Valproic acid	1 (5)

ASM = antiseizure medication; SD = standard deviation; VA = Veterans Administration.
aReflect comorbid conditions that are common (depression), important for telephonic delivery (hearing loss), possibly induced by epilepsy/ASM (osteoporosis), and common to the VA population (post-traumatic stress disorder, traumatic brain injury).

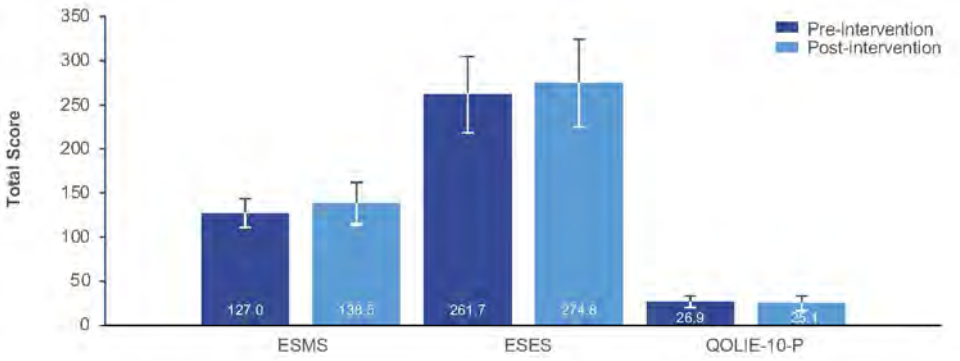
were primarily White men, as is typical for the Madison VA population. Additional baseline characteristics including specific comorbidities and ASM use are summarized in Table 3.

The five-module series was completed by 14 participants (70%). One patient withdrew consent for participating in the program, and five patients were discharged after three consecutive failed attempts at scheduling follow-up. The average time for module session completion was 25±9 minutes. Most patients (13/20; 65%) required rescheduling efforts for at least one of their scheduled sessions.

Clinical Outcomes

Total survey scores pre-intervention and post-intervention were compared for the 10 patients who completed the questionnaires assessing clinical outcomes. Numerical improvements in pre-intervention versus post-intervention scores were noted for the ESMS and the ESES; however, the differences were not statistically significant (Figure 1). No significant differences between pre- and post-intervention scores were noted for the QOLIE-10-P (Figure 1). There were no significant changes in depression and anxiety scores (NADDI-E, 9.0 [5.6] vs 11.4 [4.4], p=0.73; and GAD-7, 4.7 [4.1] vs 4.8 [4.2], p=1.0) pre- versus post-intervention. The modified PEPPI, assessing interactions with pharmacists, increased significantly from pre- to post-assessment (p=0.04) (Figure 2).

FIGURE 2. Total Score for Patient-Pharmacist Interactions (n = 10)



PEPPI = Perceived Efficacy in Patient-Physician Interactions.

Patient Acceptance

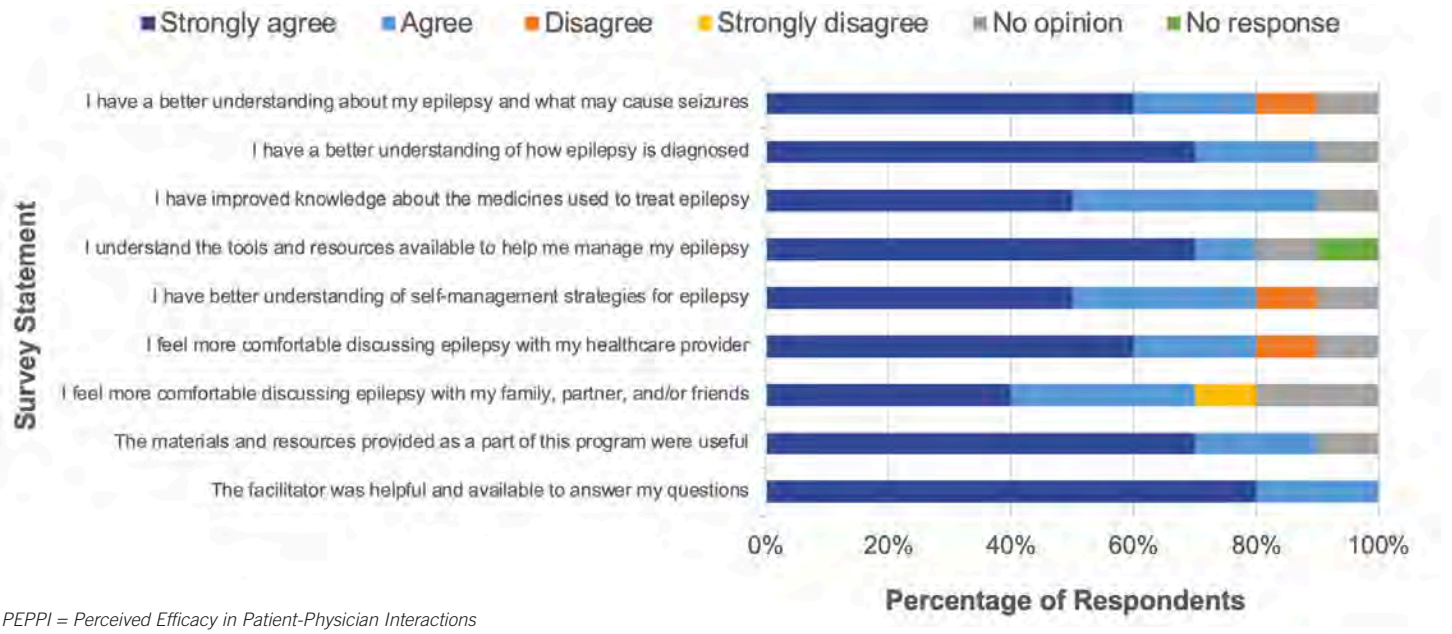
Ten patients completed the patient satisfaction and perception survey after completion of the Exploring Epilepsy pilot study. Based on the Likert scale, a large percentage (70-100%) of patients "strongly agreed" or "agreed" with statements about their level of comfort discussing epilepsy with others or understanding various self-management strategies as a result of their participation in Exploring Epilepsy (Figure 3). All patients "strongly agreed" or "agreed" that the materials were useful. Most patients (90%) "strongly agreed" or "agreed" that the facilitator was useful.

Discussion

Feasibility of Exploring Epilepsy Use in an Ambulatory Clinic

Our analysis of the implementation of Exploring Epilepsy shows that pharmacists can effectively lead an epilepsy education program within an ambulatory clinic setting. In the VA ambulatory clinic, 70% of enrolled patients completed the five-module series that was based on newly developed materials focusing on facilitating discussion with the patient. Patients attended scheduled telephone appointments with the pharmacist, though rescheduling efforts were needed for over half of the patients. The average time spent on these appointments was in line with facility standards for patient care appointments, which typically allot 30 minutes for an

FIGURE 3. Patient Satisfaction and Perception Survey (n = 10)



PEPPI = Perceived Efficacy in Patient-Physician Interactions

office visit.[31,32] Several strategies can be employed to increase pharmacist time for direct patient care activities, including using administrative staff support to handle appointment scheduling responsibilities.

The majority of patients who completed the program evaluation questionnaire "strongly agreed" or "agreed" that the pharmacist facilitators as well as the educational material were helpful. Participants found the telephone format acceptable despite over 30% of participants having some level of hearing loss. Additionally, over 70% of patients completing post-intervention questionnaires "strongly agreed" or "agreed" that the program increased patient understanding of various aspects of self-management strategies and aspects of epilepsy management. These findings suggest that participants found this program beneficial in promoting various aspects of self-management skills. An increase in the modified PEPPI score was also observed, indicating increasing participant confidence in interacting with the pharmacist over the course of the five telephone discussions. This result is consistent with the post-intervention question regarding finding the facilitator (i.e. pharmacist) helpful.

There were no statistically significant differences found between various epilepsy-specific clinical questionnaires. There was an improvement in self-management, self-efficacy, and quality of life scores; however, these were not statistically significant, likely because of the small sample size. No improvements in the anxiety and depression scale scores post-intervention were anticipated because this program was not designed to improve these areas; i.e. it did not employ psychotherapy approaches such as mindfulness exercises, which have been shown to be beneficial for anxiety and depression in patients with epilepsy.[33] In addition, a longer study would be needed to observe changes in these areas.

This program was conducted before the significant changes that occurred in health-care delivery as a result of the COVID-19 pandemic, which necessitated a shift to telemedicine. This shift is reflected by results from a survey of neurology providers; whereas less than 40% of providers used telehealth before the pandemic, nearly 90% used it after pandemic onset.[34] As telehealth has become a common modality for health-care interactions since COVID-19 onset, it is interesting to speculate whether this increased familiarity with telehealth would help to improve response rates in the Exploring Epilepsy program.

Limitations

This pilot program had several limitations. First, participants were selected from normal clinic flow for inclusion in the study; however, recruitment was difficult given the time-intensive baseline questionnaires that had to be completed. Thus, the sample size for this feasibility study was limited and did not reach the target enrollment number. This lower than anticipated sample size also left this study underpowered. Additionally, some questionnaires were missing answers, which were completed using imputation. This approach potentially limits the validity of the available data. Given the chronic nature

of epilepsy, a longer study may be needed to reveal continued changes over time, particularly with anxiety and depression. The study showed the feasibility of the program within a VA population; however, this population may not be representative of patients with epilepsy in general, and the sub-specialty focus of the clinic may be different from general neurology or primary care clinics.

Future Directions

Data from this pilot program can be compared with those from other sites to assess common themes in the larger epilepsy population. It would be interesting to examine the effect of Exploring Epilepsy in populations with psychiatric comorbidities, as well as to repeat questionnaires after a longer duration post-intervention to assess longer-term effects on patient outcomes. It would be advantageous to conduct this study with a larger, appropriately powered sample, potentially across multiple VAs confirm the benefit of the Exploring Epilepsy program. Additionally, it would be useful to complete an analysis quantifying the effect on medication adherence rate and other health outcomes following the intervention on self-management strategies. Finally, this program could be explored in a group clinic setting to maximize pharmacist time while facilitating dialogue between patients.

Pharmacists are underutilized health-care providers who can effectively facilitate patient-centered learning about various self-management strategies. This pilot program shows that a pharmacist-led epilepsy education initiative is feasible with appropriate planning and that patients are highly satisfied with the service.

Conclusion

Implementation of Exploring Epilepsy within an epilepsy clinic is feasible through telehealth modalities. Patients reported high satisfaction with the service and enhanced understanding of various self-management strategies. Although preliminary data did not show statistical improvements in various clinical questionnaires, the sample size of this feasibility study is small and not powered to detect clinically significant differences. Future considerations for operationalizing this program include leveraging the clinic scheduling team for administrative tasks that would maximize the health-care professional's time on direct patient care activities. Additional considerations include organizing the program in a group setting to facilitate peer support and discussion.

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

Acknowledgments: This work was supported by UCB Pharma (Smyrna, GA, USA). UCB Pharma was not involved with data collection.

The authors would like to acknowledge the following individuals for their assistance in developing the Exploring Epilepsy program: Jacquelyn Bainbridge, PharmD (University of Colorado, Aurora, CO); Alan Ettinger, MD (Safe Passage Diagnostics, New York, NY); Mikiko Yamada-Takeda, PharmD (University of New Mexico, College of Pharmacy, Albuquerque, NM); and Todd Woodard, PharmD (Peach State Health Plan, Atlanta, GA). The authors would also like to thank the following individuals for their assistance with data collection at the Madison VA Epilepsy Clinic: Andrew Cannon, Katherine Davenport, Hannah Hecht, and Carlie Wilke. The authors thank the patients and their caregivers in addition to the investigators and their teams who contributed to this pilot program.

The authors acknowledge Kathleen Richards, PhD (UCB Pharma, Smyrna, GA, USA) for managing the development of the manuscript and Lynne Isbell, PhD, CMPP (Evidence Scientific Solutions, Philadelphia, PA, USA) for writing assistance, which was funded by UCB Pharma.

The contents do not represent the views of the U.S. Department of Veterans Affairs or the United States Government. Preliminary results from the Madison VA Epilepsy Clinic were presented as a poster at the American Society of Health-System Pharmacists Midyear Clinical Meeting 2019, and the Annual Meeting of the American Epilepsy Society 2020.

Disclosure: AM.M. Siodlak, R.J. Kotloski, and A. Margolis report no relevant disclosures. B.E. Gidal has served as a consultant and speaker for Aquestive Therapeutics, Eisai Co., Ltd., Greenwich Biosciences, UCB Pharma, and SK Bioscience. J. Thompson is an employee of UCB Pharma. S. Hunter-Banks was an employee of UCB Pharma at the time of this study and is currently with Hunter B Consulting Group, LLC (Marietta, GA). A. Margolis 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.

Data-sharing statement
Data from noninterventional studies is outside of UCB Pharma's data-sharing policy and is unavailable for sharing.

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Original Work

Characterization of Population Health Management Activities and Barriers of Wisconsin Pharmacists

by Michael W. Nagy, PharmD, BCACP, Mikayla Bell, 2023 PharmD Candidate

Abstract

As the clinical responsibilities of pharmacists grow, the use of population health management (PHM) activities may enhance the efficient and impactful provision of patient care. Characterization of current pharmacy practice trends regarding PHM may identify pharmacists roles, explore perceived barriers, and guide future expectations. The primary objective of this study is to characterize the frequency in which Wisconsin pharmacists perform PHM. Secondary objectives include identifying the percent of pharmacists incorporating pharmacy learners in PHM and identifying barriers for incorporation of PHM. This mixed-methods exploratory study used an investigator-developed survey. All active Wisconsin pharmacists within Pharmacy Practice Enhancement and Action Research Link (PearlRx) were provided the survey to investigate the frequency, type, and incorporation of PHM activities into daily practice, barriers, as well as inclusion of pharmacy learners. Survey participants had the option to partake in a follow-up 30-minute semi-structured interview. Fifty-four pharmacists voluntarily completed the survey, of which 40 (75%) perform PHM activities using, on average, 10% of their allotted practice time and 27 (50%) incorporate learners. Identified barriers include lack of time, the need for stakeholder support from outside the pharmacy profession, and lack of awareness. Ideas to overcome barriers included increasing collaborative efforts on interdisciplinary teams, development of practice resources, and establishing the value of PHM activities return on investment for stakeholders. Training of current and future pharmacists on the basic processes of PHM and health information technology resources is needed. Wisconsin pharmacists are in an early adoption phase of incorporating PHM into practice.

The improvement of health data technology has led to the creation and use of datasets within health systems. These datasets allow health care providers to proactively target evidence-based interventions within their patient populations, a method known as population health management (PHM).[1] As the responsibilities of pharmacists grow in the clinical management of disease states, the use of PHM may help expand pharmacist scopes of care in an efficient and impactful manner.[2,3]

Examples of PHM activities that pharmacists perform vary based on practice setting. Community-based pharmacists may perform adherence monitoring, deprescribing initiatives, or screening of cardiovascular risk and statin appropriateness. For example, patients over age 70 on aspirin for primary prevention could be flagged for a risk and benefit discussion with the community pharmacist. Inpatient pharmacists may perform antimicrobial stewardship, where a pharmacist has a list of patients who have been prescribed broad-spectrum antibiotics when susceptibility tests indicate the ability to narrow the spectrum. Finally, clinic-based pharmacists may focus their efforts on medication management for patients with poorly controlled chronic diseases—for example, identifying patients with type 2 diabetes and heart failure with reduced ejection fraction who are not prescribed a sodium-glucose cotransporter 2 inhibitor. Leveraging PHM strategies may allow for identification of the highest-need patients who may need additional attention and help alleviate some of the burden from primary care providers.[4]

Emphasizing the importance of pharmacist-led PHM services, the 2021 American Society of Health System Pharmacist Foundation Pharmacy Forecast recommends that systems "define the roles of pharmacist in ambulatory and population health management."[5] Moreover, pharmacists who adopt PHM principles may be well positioned to address the Quintuple Aim, which modified the Institute for Healthcare Improvement's Triple Aim.[1,6-8] The Quintuple Aim involves improving patient access to care and quality of care, while potentially reducing per capita health care costs, improving the work lives of health care providers, and addressing health equity. Pharmacists who incorporate PHM may find specific patients who lack access to care or who are not meeting metrics of high-quality care. At the same time, PHM could limit extraneous visits where clinical interventions do not exist. Additionally, PHM provides an opportunity to evaluate populations for inequity of care related to medication optimization.[7,8]

Even with the recognized benefits and strategic priorities related to the use of PHM and data analytics, the current state of adoption of PHM principles within pharmacy practices is unknown. Therefore, we aim to characterize current pharmacy practice trends regarding PHM, which may

identify pharmacists' roles, explore perceived barriers, and guide future expectations.

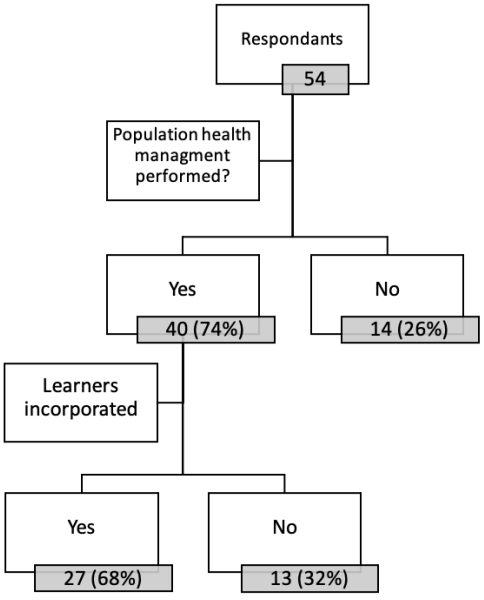
Methods

This mixed-methods exploratory study used an investigator-developed survey. The primary objective of this study is to characterize the frequency with which Wisconsin pharmacists perform population health management. Secondary objectives include identifying the percent of pharmacists incorporating pharmacy learners in PHM and identifying barriers for the incorporation of PHM into practice.

Participants

All active Wisconsin pharmacists within Pharmacy Practice Enhancement and Action Research Link (PearlRx) were provided the survey via an email for voluntary completion with submission of the survey interpreted as informed consent to participate. There were two reminder emails spaced out in monthly intervals. PearlRx is a network of pharmacists, technicians, and students across the state of Wisconsin, and at the time of this study consisted of 535 actively practicing pharmacists who were eligible to complete the survey. PearlRx members voluntarily join with the goal to promote and conduct collaborative, patient-centered research across all pharmacy settings.

FIGURE 1. Consort Diagram Participant Responses



Study Design

The survey was open for participant responses from January 2021 to March 2021. The survey tool consisted of 19 questions including: eight multiple-choice questions, one slider scale, two Likert matrixes, and two short-answer sections. Data collected included demographics as well as frequency, type, and incorporation of PHM principles into daily practice, as well as the inclusion of pharmacy learners. Participants were asked to identify possible barriers to the implementation of PHM activities at their site. The survey was reviewed by a research committee and piloted by two pharmacists prior to distribution.

Following the completion of the survey, participants had the option to indicate interest to participants in a virtual, one-on-one, 30-minute semi-structured recorded interview with study investigators to provide additional perspective. Interviews were completed in July of 2021 with participants randomly selected, and each interview consisted of eight identical open-ended questions with the ability for investigators to ask follow-up questions when appropriate.

Data Analysis

Survey responses were analyzed with descriptive statistics and summary analysis for open response data. Summary analysis was performed through transcription of the interviewee's recorded verbal responses into written format. Data was then evaluated with attention to repeated phrases and concepts, and similar ideas were grouped together.

This research was approved by the Medical College of Wisconsin institutional review board. This study was conducted in collaboration with PearlRx of Wisconsin, a statewide pharmacist practice-based research network, which is in part supported by the Clinical and Translational Science Award (CTSA) program, the National Institute of Health (NIH) National Center for Advancing Translational Sciences (NCATS), grant UL1TR002373, and the Pharmacy Society of Wisconsin.

Results

A total of 54 pharmacists voluntarily completed the survey. Forty respondents (75%) performed PHM activities in their practice, of which 27 (68%) incorporated pharmacy learners (Figure 1). Stratification of respondents into population density and practice site showed that most respondents who perform PHM work in areas with higher population density (Table 1). Across all practice areas, respondents reported that similar PHM tasks are being performed. Most respondents identified that the largest barrier to completion of PHM activities was lack of time allotted (71%) with an average allotment of 0.1 of a pharmacist's full time equivalent (FTE) dedicated to performing

TABLE 1. Demographics Of Participants who perform population health management (n=40)

Characteristic	*Response, N (%)*
Practice Area	
Academia	6 (15)
Ambulatory Care	8 (20)
Community-Large Chain	0 (0)
Community Independent	7 (17.5)
Hospital Inpatient	10 (25)
Hospital Administration	3 (7.5)
Hospital Outpatient	2 (5)
Industry	1 (2.5)
Long Term Care	1 (2.5)
Managed Care	2 (5)
Clinical Experience	
Less than 2 years	2 (5)
2-5 years	9 (22.5)
6-10 years	7 (17.5)
11-15 years	7 (17.5)
16-20 years	7 (17.5)
20+ years	8 (20)
Precepting Experience	
IPPE Student	28 (70)
APPE Student	33 (82.5)
PGY1 Resident	26 (65)
PGY2 Resident	12 (30)
Student Intern or Technicians	16 (40)
Population Density	
Rural, non-metro (>2,500 people)	4 (10)
Rural, metro (2,500 – 50,000 people)	7 (17.5)
Urban (>50,000 people)	29 (72.5)
Region in Wisconsin	
Northern	2 (5)
Northeast	2 (5)
South Central	15 (37.5)
Southeast	15 (37.5)
West Central	6 (15)

Abbreviations: introductory pharmacy practice experience (IPPE), advanced pharmacy practice experience (APPE), post-graduate year 1 (PGY1), post-graduate year 2 (PGY2)

PHM activities. Based on the design of the survey, this was the smallest possible increment of FTE available to choose on the survey (Table 2).

As learners progress from introductory to advanced pharmacy practice experiences (APPE) and continue to post-graduate residencies, the PHM tasks delegated to them by practicing pharmacists shifted from an observatory to an active role (Figure 2). For example, respondents shared that students on introductory pharmacy practice experiences (IPPE) most commonly shadowed pharmacists (70%) or performed health record screens or medication histories (45%), while 75% of respondents have APPE students perform and document PHM encounters. Limitations to the ability to incorporate learners within PHM activities include lack of time in the pharmacist workload (66%) and need for training learners on the processes (57%), as reported by respondents (Table 2).

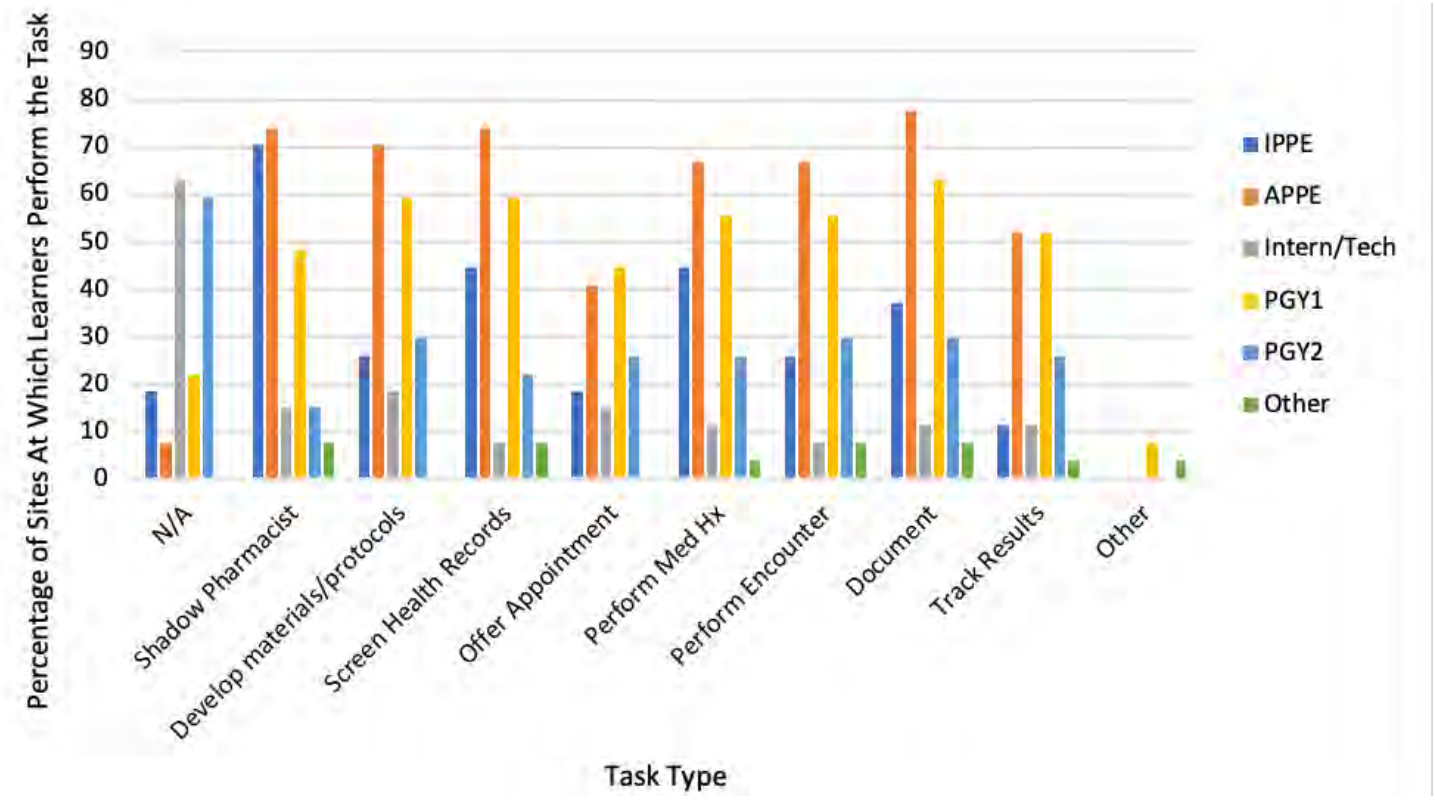
A total of four interviews were conducted with pharmacists and a summary analysis revealed the perceived benefits of PHM to include increasing access to care and meeting the needs of the population with specialized services (Table 3). While each pharmacist was involved in some form of PHM activities, none had achieved their perception of the ideal role in terms of scope or access. In general, interviewees agreed with survey findings that APPE students and residents could handle the higher-level functions to conduct activities with more independence compared to IPPE students.

Interviewees identified workload capacity as a barrier for incorporating PHM activities, especially in the community setting where COVID vaccinations were taking priority. The summary analysis highlighted additional barriers to focus on, including stakeholder support from outside the pharmacy profession, advocacy, support from statewide institutions, and increasing awareness and communication. One specific point that stood out was the need

TABLE 2. Pharmacists Perceived Barriers for Implementation of PHM at Site (n=40)

In pharmacist practice		*To incorporate pharmacy learners*	
Lack of time	71%	Workload at site with lack of time	66%
Lack of training on how to perform Population Health Management	34%	Training the learner for the logistical process	57%
Ability to identify populations or metrics to target	29%	Clinical readiness of the learner	49%
Lack of administration support	29%	Time and schedule of the learner (job, school, exams, breaks)	49%
Lack of provider engagement	18%	Lack of pharmacy learners at your site	29%
Lack of perceived benefit	18%	Level of interest of the learner	17%
Lack of interest	13%		

FIGURE 2. Type of Population Health Management Tasks performed by Level of Learner (n=27)



Abbreviations: introductory pharmacy practice experience (IPPE), advanced pharmacy practice experience (APPE), post-graduate year 1 (PGY1), post-graduate year 2 (PGY2)

to frame these activities as a cooperative effort and not as a pharmacist attempting to supersede the scope of another provider. Ideas to overcome some of these barriers included increasing collaborative efforts on interdisciplinary teams; development of resources (education, grant funding, outcome metrics, and electronic health record access in community pharmacies); and establishing the value of PHM activities to prove there is a return on investment for stakeholders.

Discussion

This exploratory study found that most respondents are incorporating some PHM activities within their practice and that half of respondents incorporate learners. The key barriers for future growth include time allocation, training of learners, and advocacy for interdisciplinary stakeholder support. Ideas to overcome these barriers were identified and focus mainly on resource development and establishing the financial value of PHM to gain the support of stakeholders more easily.

To date, multiple systematic reviews and

TABLE 3. Summary Analysis of Pharmacist Interviews

Focus Area	*Pharmacist Ideas*
Definition of PHM	• Resources directed towards a group based on data to help meet goals • Identification of a patient population in need of a specialized service • Providing access in a user-friendly way • Improved access to care outside of a physical setting
Current Involvement at Practice Site	• Identification of patients outside of goal, onboarding to the program, collaborate until control established and can self-manage • Optimization of prescribing for patients to lower adverse events, increase quality, and provide naloxone for patients in need • Statistics determine group for additional resources which is expedited by collaborative practice agreements • Help patients who have been diagnosed by a provider to manage their disease state which will reduce cost expenditure
Ideal role at practice site	• Prioritization of specialized tasks such as medication management and tasks that are unable to be completed by our health care colleagues due to time constraints or lack of training • Need to be well integrated, trusted, and supported team members when currently defining the purpose and duties of a pharmacist may be blurry to some health care peers • To be able to provide services within one setting to be accessible for the patient which can be accomplished with CPA
Learner involvement	• Students provide valuable benefit by carrying an increasing amount of the workload independently • Students assist in reminder calls and improving workflow and documentation • Student's knowledge of technology can assist with communicating services • APPE students are primarily involved in tasks due to the higher-level work required
Current barriers	• Support from stakeholders outside the pharmacy profession especially if identified services overlap with another team member • Advocacy work internally and externally in the state to be included equally in opportunities and discussions with providers • Current barriers are defining the process to perform population health management • Raising awareness and increasing participation is not competition, but rather a cooperative effort to increase pharmacist roles • Barriers are two-fold in obtaining CPAs to provide services and communication that of the services that are available • Capacity is a concern as the pharmacist to patient ratio and pharmacist to provider ratio is far from ideal • Focus on COVID vaccinations leaves little time to focus on providing additional services • Due to the cost saving nature of the activity, expending money, training people, and including pharmacists is a barrier
Ideas to overcome barriers	• Current barriers are overcome by interdisciplinary meetings, flexible staffing, and fostering familiarity • Resources needed are education of technicians and medical assistants to support pharmacist workload to facilitate prioritization • Value/necessity of pharmacists to complete focused PHM needs to be established to prove return on investment • Obtaining the resources needed to prove the worth can be started with grants or stakeholders outside of pharmacy • Metrics to establish return on investment for a service that is cost avoidant need to be defined to prove quality from not only a patient perspective but also a payer perspective • Metrics are needed to prove a positive financial outlook and need to focus on underserved and expensive disease states • Connecting with uninsured or underinsured patients can be done via PSW platform to perform CMM
Future thoughts	• Plans include increasing pharmacist areas of focus, expanding patient populations, and allowing PHM to become its own discipline • Future goals are expanding focus areas and providing more community outreach and education • Plans involve improving patient access by completing medication reviews in the pharmacy and providing home services • PHM has a demonstrated need which can be implemented with the assistance of technicians and students to avoid introducing gaps in care and inequalities • Plans involve creating a partnership to solve the lack of resources problem which will allow expansion of focus areas to underserved areas like med adherence and rural opioid stewardship

Abbreviations: advanced pharmacy practice experience (APPE), Pharmacy Society of Wisconsin (PSW), collaborative practice agreement (CPA), comprehensive medication management (CMM), population health management (PHM).

meta-analyses demonstrated positive clinical outcomes of pharmacist involvement within the management of a variety of chronic disease states.[9-13] The benefits were consistent whether interventions occurred in person or via telehealth.[11,14] Beginning with the Ashville Project in 2003 and expanding since then, economic analysis of pharmacist chronic disease management shows positive returns when exploring both cost avoidance and return on investment, with the Hickory Project showing a return on investment of almost 5 to 1.[15-20] Since traditional pharmacist services have not been billable activities, PHM activities targeting value-based metrics have been used to show positive results through cost avoidance and meeting clinical outcome metrics for value-based payments.[21-24] However, with provider status becoming more widespread for pharmacists at the state level and recently being signed into law in the State of Wisconsin, the possibility of revenue streams may further enhance the possible return on investment.

When comparing PHM to more traditional chronic disease management, the economics for pharmacist return on investment might be even higher. In fact, a return on investment of 12.4 to 1 was demonstrated when incorporating technology-guided PHM for pharmacists within a Medicaid population.[25] Additionally, pharmacists leveraging PHM have been shown to maximize value through education, population-level data analysis, and medication management within accountable care organizations.[26] This pre-existing literature supporting PHM activities could be leveraged by pharmacists, such as those interviewed in this study, to support proposals to stakeholders for increasing future allocation of resources. Furthermore, systems-based care and population health is one of the competency domains highlighted by the American College of Clinical Pharmacists' competencies, which signify the need to develop PHM compared to traditional chronic disease management models.[27]

Even with these positive findings, barriers identified within this study and described within the PHM literature will need to be addressed for pharmacists to be able to consistently incorporate PHM into normal practice. Commonly identified PHM barriers include the lack of health information technology infrastructure, especially in the community setting; lack of formal billing codes; lack of formal training; and a need for outreach, scheduling, and maintaining patient appointments.[28,29] Currently, most pharmacist-led PHM examples occur within health systems or in models consistent with patient-centered medical homes.[22, 24,30-32] The concentration in these settings is likely due to access limitations in the community pharmacy setting. However, PHM achievements in community-based pharmacy settings exist and need to be further optimized within the health care system.[29,33]

Given the limited resource of time, pharmacists have utilized pharmacy learners (i.e., students or residents) or technicians to perform PHM activities and act as a pharmacist extender.[34-36] The ability of student pharmacists to describe and develop population-based care is considered an essential skill for practice by the Accreditation Council for Pharmacy Education.[37] Furthermore, the Center for Advancement of Pharmacy Education suggests that pharmacy students should "participate in population health management by evaluating and adjusting interventions to maximize health."[38]

Whether woven into an introductory or advanced experiential rotation or during post-graduation training, learners who perform PHM mutually benefit via trainee education while adding to pharmacists' workload capacity.[34-36]

Literature is supportive of pharmacist disease state management and highlights the benefit of targeted use of PHM to further increase cost effectiveness. To advance resources provided to pharmacists, the existing data needs to be collected and organized for frontline pharmacists, so they have the tools necessary to market to their stakeholders. By leveraging existing literature, hopefully the pharmacy profession can move beyond the requirement of additional pilot studies demonstrating the clinical and economic benefits of pharmacists' services. Instead, it should become a priority for pharmacists to focus on the implementation science for establishment of resources to train and carry out PHM activities, as well as utilization of pharmacy organization networks to build consistent health information technology infrastructure.

Given this study is the first characterization of how pharmacists have incorporated PHM into their workflow, it provides a starting point for further exploration. Utilization of the PearlRx network allowed for a statewide distribution of the survey to mitigate regional bias. Furthermore, the analysis recognized barriers and identified targeted solutions.

This study was limited by the low response rate of participants due to the voluntary nature of the survey without the use of incentives. While PearlRx membership includes pharmacists statewide with a self-identified interest to potentially participate in research, it consists of only a fraction of all practicing Wisconsin pharmacists. Moreover, some participants failed to complete the survey after starting, which may have led to a self-selection bias. For example, pharmacists who incorporate PHM into practice may be more likely to take the time to respond, which could lead to their overrepresentation.

Information gained from this study highlights the need for formalized training within pharmacy education to conduct PHM. Potential future considerations include the creation and dissemination of a PHM and data analytics elective course for pharmacy students. Additionally, development of training tools, resources, and advocacy on a state-wide level to assist pharmacist expansion into PHM may be necessary. To achieve these goals, it is essential to create partnerships with pharmacists in all practice settings and across pharmacy organizations. This could allow for the removal of barriers, such as gaining access to electronic health records. Furthermore, the collection and dissemination of prior studies exploring financial considerations, such as return on investment for PHM activities, can empower frontline pharmacists to advocate for the expansion of dedicated time and resources. Finally, future studies should explore how recent laws in the State of Wisconsin surrounding provider status for the Medicaid population may strengthen the sustainability of PHM activities.

Conclusion

Most pharmacists are performing PHM activities and include a pharmacy learner in the process. However, an opportunity exists to increase the portion of time dedicated to PHM tasks in current practice. Furthermore, there is a need for training of current and future pharmacists on the basic processes of PHM and health information technology resources. Overall, Wisconsin pharmacists are in an early adoption phase of incorporating PHM into practice.

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

Acknowledgements: The authors would like to thank Marisa Goninen, PharmD and James Kotek, PharmD for their critical review and edits of the final manuscript.

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

Data Transparency: Michael Nagy had full access to all the data in the project and takes responsibility for the integrity of the data and accuracy of the data. De-identified data available upon request, please email study author Michael Nagy.

Previous presentations of the work: This work was presented at the Pharmacy Society of Wisconsin educational conference in April of 2021 as a poster with initial analysis of survey data.

Funding support: This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

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Review of Effect of Tirzepatide on Glycemic Control and Weight Loss

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Abstract

Tirzepatide (Mounjaro) is a new to market glucose-dependent insulinotropic polypeptide/glucagon-like peptide 1 receptor agonist. It has shown to substantially decrease hemoglobin A1c as demonstrated in the SURPASS trials. Additionally, the SURMOUNT-1 trial showed the impact tirzepatide can have on weight reduction independent of diabetes. Tirzepatide has just been implemented into the American Diabetes Association guideline recommendations for type 2 diabetes management with emphasis on weight reduction as of 2023. The current clinical data and upcoming trials have promising evidence to make a significant impact for patients with type 2 diabetes and/or obesity. In this article, we review the clinical trial data for tirzepatide and the applications for pharmacy practice.

Type 2 diabetes mellitus (T2DM) is a chronic health condition characterized by hyperglycemia, insulin resistance, and an impairment in insulin secretion.[1] The CDC estimates that over 37 million people in the United States live with diabetes and that 41.9% of the population is obese, with this being a risk factor of developing T2DM.[2] Roughly 90% of patients with T2DM are classified as overweight or obese and continue to trend up.[3] In 2019, it was estimated that 1.5 million deaths worldwide were directly related to diabetes, making it the ninth leading cause of death in the world.[4] Given the scope of T2DM and the link with obesity, improvements in management of these two concurrent disease states, including pharmaceutical options, is of high value to the health care community.

Currently, GLP-1 receptor agonists are approved for T2DM and two have indications for weight loss (liraglutide, semaglutide). Tirzepatide is a first-in-class glucose-dependent insulinotropic polypeptide/glucagon-like peptide-1 (GIP/GLP-1) receptor agonist approved by the U.S. Food and Drug Administration (FDA) on May 13, 2022.[5] The GLP-1 agonist component acts as an incretin hormone and has a role in the central nervous system, pancreatic islet cells, and stomach by decreasing food intake, increasing insulin secretion in hyperglycemic states, inhibiting glucagon secretion, and delaying gastric emptying thus increasing satiety.[6] Unlike other GLP-1 receptor agonists on the market, the addition of GIP receptor agonism action makes this a dual mechanism medication. It is thought that GIP receptor agonism will further decrease appetite and food intake, increase insulin sensitivity in adipose tissues, alter nutrient metabolism, increase insulin secretion, and alter glucagon secretion.[7] The dual mechanism action of this medication may lead to clinical significance when determining an antidiabetic regimen.

Patients with diabetes often require multiple anti-diabetic agents to reach and maintain their hemoglobin A1c (HbA1c) goal.[8] Even with multiple agents, meeting a HbA1c goal can be difficult. The dual mechanistic nature of tirzepatide has demonstrated evidence for use in both lowering HbA1c and overall body weight in the SURPASS trials and SURMOUNT-1.[9-14] This literature review analyzes current clinical data by outlining the safety profile, adverse effects, and evidence for use of the novel drug tirzepatide in the management of both T2DM and obesity.

Clinical Data/Literature Review

Tirzepatide has been studied for use in T2DM in a series of phase III randomized-controlled trials known as the SURPASS trials.[9-13] Within these trials, three different tirzepatide doses were evaluated in five clinical trials investigating the use as a stand-alone or add-on therapy with other diabetes medications. The SURPASS-1 and SURPASS-5 trials were conducted versus placebo in which HbA1c changes from baseline were analyzed following a 40-week period of weekly tirzepatide administration at doses of 5, 10, or 15 mg.[9,13] Patients in SURPASS-1 were on diet and exercise alone at baseline whereas in SURPASS-5 patients at baseline were on basal insulin with or without metformin. Additionally, three SURPASS studies compared tirzepatide to standard anti-hyperglycemic medications in effort to prove non-inferiority via ability to reduce HbA1c from baseline over 40- or 52-week periods.[10-12] These studies compared tirzepatide to semaglutide, insulin degludec, and insulin glargine for SURPASS-2, SURPASS-3, and SURPASS-4, respectively. Each of the studies showed statistically significant mean change in HbA1c versus the comparator as shown in Table 1.

A crucial secondary endpoint to each SURPASS trial was reduction of body weight in which tirzepatide was able to significantly outperform each comparator group as well. Tirzepatide demonstrated dose-dependent weight loss ranging from 7 kg on the lower dose to 13 kg on the highest dose (Table 1).[9-13] Safety analyses were conducted on tirzepatide in each of the trials in which diarrhea and nausea were

TABLE 1. Summary of SURPASS Trials Examining Tirzepatide in Patients with Type 2 Diabetes

	SURPASS-1[9]	*SURPASS-2*[10]	*SURPASS-3*[11]	*SURPASS-4*[12]	*SURPASS-5*[13]
Objective	Safety, efficacy, and tolerability in patients with poor glycemic control in addition to diet and exercise	Safety and efficacy in patients with poor glycemic control with metformin	Safety and efficacy in patients with poor glycemic control with metformin ± a sodium glucose-like transporter-2 inhibitor	Safety and efficacy in patients with high cardiovascular risk and poor glycemic control+	Safety and efficacy in patients with poor glycemic control with baseline insulin glargine ± metformin
Comparator	Placebo	Semaglutide 1 mg	Insulin degludec	Insulin glargine	Placebo
Primary Endpoint	Mean change in HbA1c from baseline at 40 weeks	Mean change in HbA1c from baseline at 40 weeks	Mean change in HbA1c from baseline at 52 weeks	Mean change in HbA1c from baseline at 52 weeks	Mean change in HbA1c from baseline at 40 weeks
Primary Results (%)	Tirzepatide 5 mg (- 1.87)	Tirzepatide 5 mg (- 2.01)	N/A	N/A	Tirzepatide 5 mg (- 2.11)
	Tirzepatide 10 mg (- 1.89)	Tirzepatide 10 mg (- 2.2)	Tirzepatide 10 mg (- 2.20)	Tirzepatide 10 mg (-2.43)	Tirzepatide 10 mg (- 2.40)
	Tirzepatide 15 mg (- 2.07)	Tirzepatide 15 mg (- 2.30)	Tirzepatide 15 mg (- 2.37)	Tirzepatide 15 mg (-2.58)	Tirzepatide 15 mg (- 2.34)
	Placebo (+ 0.04)	Semaglutide 1 mg (- 1.86)	Insulin degludec (-1.34)	Insulin glargine (-1.44)	Placebo (- 0.86)
Mean body weight change from baseline (kg)	Tirzepatide 5 mg (- 7.0)	Tirzepatide 5 mg (-7.6)	N/A	N/A	N/A
	Tirzepatide 10 mg (- 7.8)	Tirzepatide 10 mg (- 9.3)	Tirzepatide 10 mg (- 10.7)	Tirzepatide 10 mg (- 9.5)	Tirzepatide 10 mg (- 7.5)
	Tirzepatide 15 mg (- 9.5)	Tirzepatide 15 mg (- 11.2)	Tirzepatide 15 mg (- 12.9)	Tirzepatide 15 mg (- 11.7)	Tirzepatide 15 mg (- 8.8)
	Placebo (- 0.7)	Semaglutide 1 mg (- 5.7)	Insulin degludec (+ 2.3)	Insulin glargine (-1.9)	Placebo (- 1.6)
Safety Profile, Intervention vs. control (%)	Nausea 12-18 vs. 6	Nausea 17-22 vs. 18	Nausea 23-24 vs. 2	Nausea 12-23 vs. 2	Nausea 13-18 vs. 3
	Diarrhea 12-14 vs. 8	Diarrhea 13-16 vs. 12	Diarrhea 16-17 vs. 4	Diarrhea 13-22 vs. 4	Diarrhea 12-21 vs. 10
	Pancreatitis 0 vs. 0	Pancreatitis 0.4 vs. 0.6	Pancreatitis 0 vs. 0	Pancreatitis 0.3-0.9 vs. 0.3	Pancreatitis 0 vs. 0
	Cholelithiasis 1 vs. 0	Cholelithiasis 0.9 vs. 0.4	Cholelithiasis 1.1 vs. 0	Cholelithiasis 0.3 vs. 0.3	Cholelithiasis 0.9 vs. 0
	Retinopathy 0 vs. 0	Retinopathy 0.4 vs. 0	Retinopathy 0.8 vs. 0	Retinopathy 2 vs. 2	
Hypoglycemia (blood glucose < 54 mg/dL) N, (%)	Tirzepatide 5 mg 0 (0)	Tirzepatide 5 mg 3 (0.6)	Tirzepatide 5 mg 5 (1.4)	Tirzepatide 5 mg 29 (8.8)	Tirzepatide 5 mg 18 (15.5)
	Tirzepatide 10 mg 0 (0)	Tirzepatide 10 mg 1 (0.2)	Tirzepatide 10 mg 4 (1.1)	Tirzepatide 10 mg 20 (6.1)	Tirzepatide 10 mg 23 (19.3)
	Tirzepatide 15 mg 0 (0)	Tirzepatide 15 mg 8 (1.7)	Tirzepatide 15 mg 7 (1.9)	Tirzepatide 15 mg 27 (7.9)	Tirzepatide 15 mg 17 (14.2)
	Placebo 1 (1)	Semaglutide 2 (0.4)	Insulin degludec 26 (7.3)	Insulin glargine 191 (19.1)	Placebo 15 (12.5)

HbA1c= hemoglobin A1c
+Allowed for combination with metformin, sulfonylurea, or sodium-glucose co-transporter 2 inhibitor

the most common, albeit transient, adverse effects. Notably, each of the SURPASS trials distinguished incidence and rate of hypoglycemia as well as the more rare but serious adverse effects such as cholelithiasis, pancreatitis, and retinopathy (Table 1). Incidence of hypoglycemia below 54 mg/dL was rare in tirzepatide monotherapy. However in SUPRASS-4 and SURPASS-5 which allowed concurrent use with sulfonylureas or basal insulin, incidence of significant hypoglycemia increased. The overall incidence of adverse effects within the SURPASS trials for tirzepatide show a dose-dependent relationship and are generally consistent with other GLP1 agents on market.

Another study, the SURMOUNT-1 trial, addressed the potential for tirzepatide as a treatment option for weight loss in overweight or obese patients without a history of diabetes.[14] The phase III trial provided intervention in patients with a BMI greater than 30 kg/m^2 or 27 kg/m^2 with weight-associated complications by administering once weekly tirzepatide (5, 10, or 15 mg) for a 72-week period. Co-primary endpoints of the study assessed patient's percent weight change from baseline and proportion of participants reaching an overall weight reduction of at least 5% of baseline body weight. Results showed significant, dose-dependent, weight reduction in each of the three dosage cohorts -15.0% in tirzepatide 5 mg [P<0.001, 95% confidence interval (CI) -15.9 to -14.2], -19.5% for tirzepatide 10 mg [P<0.001, 95% CI -20.4 to -18.5], and -20.9% for tirzepatide 15 mg [P<0.001, 95% CI -21.8 to -19.9] compared to -3.1% in the placebo group [P<0.001, 95% CI -4.3 to -1.9]. The co-primary endpoint, weight reduction of 5% or more, found 85% [P<0.001, 95% CI 82 to 89], 89% [P<0.001, 95% CI 86 to 92], and 91% [P<0.001, 95% CI 88 to 94] of patients achieving this measurement for 5,10, and 15 mg of weekly tirzepatide, respectively, compared to 35% for placebo.

Application to Practice

The recent FDA approval of tirzepatide, the first GLP-1/GIP dual-agonist on market, provides exciting opportunity and advancement in the realm of diabetes and weight loss as early results from randomized clinical trials are promising. Tirzepatide has been shown to decrease HbA1c on average between -1.87% and -2.58%.[9-13] The 2023 American Diabetes Association (ADA) guidelines have recently modified their treatment algorithm for the management of T2DM.[1] Treatment options are now chosen based on what types of personalized goals the patient has when it comes to their disease state. Tirzepatide is included in the guidelines for patients that wish to achieve and maintain glycemic and weight management goals, with the highest efficacy rating.

Furthermore, even at its lowest therapeutic dose, tirzepatide has demonstrated greater weight loss from baseline compared to semaglutide, a GLP-1 with an FDA indication for weight loss, reducing weight by 7.6 kg and 5.7 kg, respectively.[10] However, it should be noted that in SURPASS-2, the maximum semaglutide dose was 1 mg which is less than what is maximally available (up to 2.4 mg weekly). Additional SURMOUNT trials examining tirzepatide's weight loss potential are expected to be published in 2023. As of October 2022, Eli Lilly received US FDA fast track designation for the investigation of tirzepatide for the treatment of adults with obesity, or overweight with weight-related comorbidities.[15]

The GLP-1 receptor agonists with proven cardiovascular benefit are considered first line in patients with T2DM and a history of cardiovascular disease.[1] A cardiovascular outcomes trial (CVOT) for tirzepatide is currently being conducted with estimated completion in October 2024.[16] Results from CVOT are measuring the time it takes for the composite of death from cardiovascular causes, a myocardial infarction, or stroke in patients who are taking tirzepatide versus dulaglutide. Results of this trial may alter tirzepatide's place in therapy within the ADA guidelines to assist those with cardiovascular disease.

While initial results from SURPASS and SURMOUNT-1 seem promising, there are several barriers to acknowledge when it comes to medication access and tolerability. Tirzepatide is sold as brand name only, Mounjaro®, which raises cost concerns. Additionally, due to the dual mechanistic nature of tirzepatide, the medication may result in a varying degree of tolerability and will require close post-marketing observation. Tirzepatide should only be increased by 2.5 mg increments every 4 weeks to improve tolerability.[17] Tirzepatide pens are single use ranging from 2.5 to 15 mg with a self-contained needle. This can be helpful for patients performing injections with poor eyesight or limited dexterity. Due to the high demand of tirzepatide for weight and HbA1c management, keeping tirzepatide in stock has been difficult for many pharmacies since the fall of 2022. For now, tirzepatide usage may be limited by the above factors.

Conclusion

The addition of tirzepatide to the 2023 ADA treatment guidelines for patients desiring glycemic control and weight management fits the initial data from the SURPASS trials. Forthcoming CVOT and additional SURMOUNT trials should provide additional information on the impact of tirzepatide for patients with T2DM, obesity, and cardiovascular disease. The initial demonstrations of the weight loss potential and HbA1c lowering ability of tirzepatide may lead to a paradigm shift for treatment of T2DM and obesity.

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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.

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MEDICAL COLLEGE OF WISCONSIN SCHOOL OF PHARMACY STUDENT WRITING CLUB:

Breaking Barriers with Aducanumab: Examining Alzheimer's Treatments and Implications for Patients

by Zoe E. Green, 2025 PharmD Candidate, Elena M. Hofbauer, 2025 PharmD Candidate, Riley Q. Hall, 2025 PharmD Candidate, Brandon B. Johnson, 2025 PharmD Candidate

Abstract

Alzheimer's disease is a neurodegenerative disorder affecting millions of patients worldwide, yet treatment options remain limited. For years, the mainstay of treatment has been cholinesterase inhibitors to increase concentrations of acetylcholine to stabilize cognitive function. Aducanumab (Aduhelm®) is a newly approved medication that targets beta-amyloid plaques, a hallmark of the disease. However, its approval has been surrounded by controversy, ultimately leaving a consensus on the medication's efficacy in question. Excessive costs and adverse reactions associated with treatment also have significant implications for patients and their caregivers. The purpose of this piece is to review current treatment recommendations for Alzheimer's disease, focusing on the recently approved monoclonal antibodies.

Alzheimer's disease (AD) is a common type of dementia and is most prevalent in geriatric patients.[1] In 2023, the number of affected patients in the United States (US) was 6.7 million, with projections to reach 12.7 million by 2050. It is estimated that 1 in 9 US adults (10.8%) 65 years or older have AD. In 2021, the US population over 65 was 58 million, and it is expected to grow to 88 million by 2050, leading to rising concerns about effective treatment options for AD patients.[2]

Patients with AD typically present with beta-amyloid plaques. While lifestyle factors may not directly contribute to the likelihood, onset, or pathological presentation of AD, these can impact the patient's (and their caregivers') quality of life.[3] The Alzheimer's Association (https://www.alz.org) offers resources to support both patients and caregivers, including a helpline and online tools.[2] While this neurodegenerative disease has been recognized throughout history, only more recently has there been a focus on new research, specifically for medications targeting the beta-amyloid plaques.[4]

Beta-Amyloid

Amyloid proteins in the brain can produce beta-pleated sheets that are resistant to protein breakdown.[5] These proteins can be either alpha or beta subunits, but they all begin as an alpha-beta-fragment. The congregation of these fragments stimulates the formation of amyloid plaques that can be deposited in the brain. Plaque concentrations and deposition can vary among AD cases.

A 2006 University of Minnesota study started linking beta-amyloid assembly with the impairment of memory.[6] These findings spurred a new focus area in AD research, although recent reports raised concerns about data manipulation, leaving patients and healthcare providers with questions about study validity.[7]

Current Treatments

The current guidelines for the management of early AD recommend the use of cholinesterase inhibitors.[8,9] The goal of therapy is to improve or stabilize memory and cognitive function by preventing or reducing the degradation of acetylcholine through inhibition of acetylcholinesterase, thereby increasing concentrations of acetylcholine. The United States Food and Drug Administration (FDA) has approved cholinesterase inhibitors for AD, including donepezil, rivastigmine, and galantamine.

Donepezil is a reversible and noncompetitive acetylcholinesterase inhibitor; rivastigmine is a pseudo-irreversible inhibitor; and galantamine is a competitive and reversible inhibitor.[8,10-12] The choice of cholinesterase inhibitor is based on several factors, including ease of use, patient preference, cost, safety issues, and potential drug-drug interactions.[8] Acetylcholinesterase inhibitors are titrated to help with adverse effects such as nausea, vomiting, diarrhea, or constipation.[13] Adverse effects such as bradycardia and insomnia may limit their use for older adults with AD.

Due to AD's progressive nature, adjusting a patient's therapy may become necessary as part of treatment. As the benefits of the cholinesterase inhibitor decline, a next appropriate step may be the use of memantine, an N-methyl-D-aspartate receptor (NMDA) antagonist, which is approved for moderate to severe AD.[8,14] Overstimulation of glutamate may lead to excitotoxicity and neuronal cell death, and while memantine can control this, it does not affect normal neurotransmission. Memantine is slowly titrated to reduce mild adverse effects such as headache, constipation, confusion, and

dizziness, which can be problematic in older patients.[8] Memantine combined with cholinesterase inhibitors has been shown to slow the cognitive and functional decline, compared to cholinesterase monotherapy.[15] To date, studies of memantine alone and in combination with cholinesterase inhibitors in mild AD have provided insufficient evidence to support an indication for mild AD.[16]

A New Therapy: Aducanumab

Since beta-amyloid plaques are a pathophysiological feature of AD, one theory for delaying progression is to interrupt plaque formation. Aducanumab is a monoclonal antibody and an anti-amyloid medication used to reduce and decelerate the progression of AD by targeting beta-amyloid.[17] It targets the plaques by binding to soluble oligomers and insoluble fibrils to mark them for elimination by microglial cells.[18] Aducanumab differs from other immunotherapies for AD because of its selective binding and ability to target oligomers and not monomers. Beta-amyloid monomers have physiological roles in the brain, while the oligomers and plaques are thought to be potentially neurotoxic.

Aducanumab is only available by IV and has a complex dosing schedule.[19] The patient receives a 1-hour infusion every 4 weeks, with a minimum interval of 21 days, due to its long half-life of 24.8 days. The goal maintenance dose is 10 mg/kg, based on actual body weight, but this is titrated up. The first and second infusions are 1 mg/kg, the third and fourth are 3 mg/kg, and the fifth and sixth are 6 mg/kg. After the first six infusions, the patient receives the 10 mg/kg maintenance dose.

Adverse reactions to aducanumab include headache, diarrhea, falling, and altered mental status.[19] The most significant adverse reactions are amyloid-related imaging abnormalities (ARIA). These are changes in the brain seen on magnetic resonance imaging (MRI) scans. ARIA-Edema (ARIA-E) is related to cerebral edema, and ARIA-Hemosiderin deposition (ARIA-H) is related to cerebral microhemorrhages and iron deposits called hemosiderosis. Both are believed to be related to increased cerebrovascular permeability and leakage of the blood vessels. In clinical trials, ARIA-E occurred in 35% of patients receiving aducanumab and only 3% of patients receiving placebo.[17] ARIA-H occurred in 15% of patients receiving aducanumab and only 3% of patients receiving placebo. Both ARIA presentations are typically present around the initial eight infusions and generally resolve in 12 to 20 weeks.

Due to these serious adverse reactions, aducanumab therapy requires close monitoring.[19] Patients should receive a positron emission tomography scan or lumbar puncture to verify the presence of beta-amyloid plaques before initiating treatment. Patients should also receive a brain MRI before treatment and before infusions five, seven, nine, and twelve. Additional MRIs should be obtained if ARIA are suspected. Adjustments to dosing are made based on the severity of symptoms and the presence of ARIA on the MRI.

Clinical Trials

Aducanumab showed positive outcomes in transgenic mice when applied topically to beta-amyloid plaques, although systemic treatment did not show significant benefit.[20] The first human trial was a randomized, double-blind, placebo-controlled, single-dose escalation Phase I clinical trial (n = 53).[21] Patients received doses ranging from 0.3 to 60 mg/kg or placebo. Patients tolerated doses up to 30 mg/kg with some adverse effects, including headache, diarrhea, and upper respiratory infection. The most serious adverse effect was ARIA-E in patients receiving 60 mg/kg doses. Following this came a randomized, double-blind, placebo-controlled Phase Ib clinical trial, called PRIME (n = 125).[22] Patients received doses of 1 to 10 mg/kg or placebo intravenously every 4 weeks for 52 weeks. There was a decrease in beta-amyloid plaques and cognitive decline for individuals receiving 3 to 10 mg/kg doses; however, higher doses were also associated with greater instances of ARIA-E.

Two duplicate Phase III clinical trials to determine the safety and efficacy of aducanumab as treatment of mild AD started in 2015.[17] These trials were randomized, double-blind, placebo-controlled trials, called EMERGE (n = 1,643) and ENGAGE (n = 1,647). Participants received low or high target doses of 3 to 10 mg/kg or placebo intravenously every 4 weeks for 76 weeks. Primary endpoints were measured by changes in Clinical Dementia Rating Scale sum of boxes (CDR-SB), which measures cognitive decline in dementia. The EMERGE trial satisfied the primary endpoints, while ENGAGE did not. The CDR-SB results were in favor of the high-dose in EMERGE and in favor of the placebo in ENGAGE. In March 2019, the trials were discontinued after meeting their predetermined futility limits because of these discrepancies between the EMERGE and ENGAGE results.[17]

Approval and Controversy

Aducanumab was approved for the treatment of AD in patients with beta-amyloid plaques in June 2021.[19,23] This is the first new treatment for AD since 2003 and the first to directly target the pathophysiology of AD.

The medication was approved via the FDA's accelerated approval process, which is reserved for medications that treat serious or life-threatening illnesses and provide a meaningful therapeutic benefit over existing treatments.[23] Accelerated approval can be determined based on the medication's effect on a surrogate endpoint that is likely to lead to clinical benefit; however, a post-approval trial is required to verify that the medication is providing its expected benefit. For aducanumab, the surrogate marker is the beta-amyloid plaques present in AD patients.[24] This verification trial has not yet been completed.

Traditionally, the FDA has preferred two adequate and well-controlled trials to show clinical efficacy for any potential new approvals. However, in 1997, an amendment was introduced that allowed the FDA to use evidence from a single trial to approve a new medication.[25] In November 2020, an FDA statistician and an advisory committee concluded that aducanumab should not be approved, due to the contradicting trial results in the Phase III trials EMERGE and ENGAGE.[25,26]

Additionally, the sponsor and manufacturer of aducanumab worked closely with the FDA to further analyze these trials. This was seen as a highly unusual collaboration between the FDA and a sponsor and has been criticized as undermining the FDA's credibility and compromising their objectivity in approving the medication.[24] Despite these concerns, the FDA approved the medication, even

with ten of the eleven members of the FDA advisory committee advising against approval. In protest of its approval, three of the advisory committee members have since resigned, with one member calling this "probably the worst drug approval decision in recent US history."[27]

Effects on Patients

In addition to emotional stress of the disease, there are significant obstacles patients face with AD, including struggles with adherence due to increased forgetfulness, increased dependence on caregivers, and financial burdens associated with the medications and healthcare expenses.

As the disease progresses, the patient develops increased forgetfulness, which can lead to lower medication adherence, thereby creating a spiral of forgetting and disease progression. Normal techniques to increase adherence, such as bubble packs and strategic placement of medication, are not as effective in this population.[28] The biggest way healthcare providers can improve adherence in patients with AD is through family and caregivers, especially during the early onset of AD.[29]

A study looking at adherence and tolerability of AD medications found that cost, in conjunction with adverse effects, was responsible for almost 70% of patients discontinuing their medications.[30] Anticholinesterase inhibitors are $4 to $16 per pill, depending on dosage form, for an annual cost of up to $5,600.[11-14] A new medication like aducanumab is only available through IV and is roughly $340 per mL, which can cost $28,000 anuually.[19] Even if covered by insurance, any of these agents could be a financial burden.

Each medication used to treat AD has a variety of adverse effects, some of which may be serious. NMDA inhibitors can cause more confusion compared to acetylcholinesterase inhibitors, which is problematic in elderly patients.[14] Aducanumab has an increased risk for brain bleeds and swelling, resulting in a need for increased monitoring including MRIs, and potentially patient harm.[19]

Recent Updates in Therapy

Gantenerumab is a monoclonal antibody treatment similar to aducanumab in that it binds to the alpha-beta deposits and removes the beta-amyloid plaques. Like the trials for aducanumab, the study evaluating gantenerumab, SCarlet RoAD, was halted early for futility.[31] There were no observable differences between groups in this Phase III clinical trial as of November 2022. Researchers stated that gantenerumab achieved amyloid clearance in 28% and 25% of patients in the first and second Phase III trials respectively, half of what the manufacturer expected to see.[32,33]

Lecanemab (Leqembi®) is a monoclonal antibody similar to aducanumab and gantenerumab that was recently approved by the FDA through an accelerated approval process. Patients receiving treatment also showed statistically significant reductions in beta-amyloid plaques. Additionally, the rate of cognitive function decline slowed at 18 months with lecanemab versus placebo. While these results are statistically significant (p=0.00005), it is unclear whether this would be a clinically significant change in decline rate for patients.[34] These are promising results, yet the FDA only considered the phase II trials.[35] During the Phase III trial, 13% of patients developed mild to moderate brain swelling and about 17% of patients developed brain bleeding.[34]

Conclusion

Current guidelines for the treatment of AD involve the use of cholinesterase inhibitors and memantine to slow disease progression. Aducanumab is a new treatment for AD that was approved using the FDA's accelerated approval process. During this approval, the Phase III evidence was conflicting, and efficacy was focused mainly on the surrogate marker of beta-amyloid reduction versus clinical cognitive improvements. Despite the controversy of aducanumab, there continues to be heavy interest in developing new medications for AD.

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

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Acknowledgments: We would like to thank Dr. Rachel Kavanaugh, PharmD, BCACP for her mentorship and guidance throughout the review process, alongside Dr. Michael Nagy, PharmD, BCACP for his facilitation of the Medical College of Wisconsin School of Pharmacy Student Writing Club. Without their consistent, unwavering support this review article would not have been possible.

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.

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Join the Pharmacy Society of Wisconsin and the Wisconsin Pharmacy Foundation for a day of fun on the green at the second annual Christopher Decker Scholarship Golf Outing! This year's outing will be held on Monday, June 5 at the picturesque Wild Rock Golf Club in Wisconsin Dells. Not only will you enjoy a day of golfing with friends and colleagues, but you'll also be supporting the education of future pharmacists through the Christopher Decker Scholarship. Don't miss out on this exciting opportunity to network, have fun, and give back to the pharmacy community.

Legislative Day Recap

2023 PSW Legislative Day Recap

by Will Carns, 2023 PharmD Candidate

PSW's 2023 Legislative Day brought together more than 225 pharmacists, pharmacy technicians, and students from across the state of Wisconsin. This year marked the first time the event was held in-person since the beginning of the Covid-19 pandemic.

The morning opened with an address by PSW President Janet Fritsch, who offered a warm welcome to attendees and thanked members for their advocacy for the profession and their continued support of PSW. This year, PSW is highlighting the importance of storytelling. Fritsch spoke about how everyone's story is unique, and that telling your own story is key to influencing the future of pharmacy. Throughout the morning, attendees were encouraged to reflect on their own experiences in pharmacy in preparation for discussions with legislators.

Fritsch then presented the PSW Student Good Government Award, given to those who have shown significant advocacy for the profession. This year, the honor was awarded to three students: Kourtney Peterson (UW-Madison), Ryan Rypel (Concordia University), and Saba Tahir (Medical College of Wisconsin). The PSW Good Government Awards was then presented to Jake Olson, the 340b Pharmacy Manager at Froedtert Health, for his role as an educator to state and federal policymakers on the topics of pharmacy compounding, payment, and patient care. Olson shared a few anecdotes about how he leverages storytelling to effectively communicate his perspectives.

The morning continued with Danielle Womack, PSW Vice President of Public Affairs, introducing a lively bipartisan panel of legislative leaders. Panelists included State Senator Rachel Cabral-Guevara, State Representative Donna Rozar, State Senator Kelda Roys, and State Representative Lisa Subeck. Each member opened with a brief introduction and an overview of the current bills being worked on for the legislative session. Womack then asked each panelist about current pressing issues in pharmacy, including drug costs, support for medical marijuana, healthcare workforce issues, and Department of Safety and Professional Services (DSPS) licensing delays. The panelists offered insights into policy-making, debunked common misconceptions, and emphasized that, despite appearances, there is more bipartisan support for healthcare-related issues than is often recognized. The session concluded with a valuable piece of advice: to remain engaged with legislators of all political backgrounds, as these interactions will ultimately shape the future of pharmacy.

Following the panel discussion, Chairperson John Weitekamp and Vice Chairperson Tiffany O'Hagan gave an update on Pharmacy Examining Board (PEB) activities regarding Phar 1, 5, 7, 10, 18, and 19, which include technician registration, changes to the top 100 drugs list, and third-party logistics providers. PEB resources on applications and licensure dates were shared, and pharmacists were encouraged to stay up to date by registering for email updates on the DSPS website.

Next, Sarah Sorum, Executive Vice President and CEO of PSW, took the stage to moderate a panel focused on the status of the pharmacy workforce. Sorum began with a presentation on trauma-informed leadership and the risks trauma poses in the workplace. The increased trauma experienced over the last few years of the pandemic has been especially difficult and has led to issues in the pharmacy workforce. Despite these issues, PSW has remained dedicated to its mission of "One Voice, One Vision" by continuing to provide opportunities connecting the pharmacy community. Sorum then welcomed pharmacist panel members Rocky LaDien, Milwaukee Area Healthcare Supervisor at Walgreens; Chad Smith, Vice President of Pharmacy Operations at Advocate Aurora Health; and Hannet Tibagwa Ambord, Director of Pharmacy Services at Reedsburg Area Medical Center, to share examples of what they are seeing in their practices and strategies to manage challenges. One key takeaway from the discussion was the need for pharmacists to collaborate as a single profession, rather than operating under separate disciplines. The panelists emphasized that the success of one pharmacy is intimately tied to the success of others, and that a collaborative effort is necessary to address the challenges faced by the industry.

The day concluded with an overview by Womack of three bills that are currently being worked on to prepare for discussion at legislator office visits. The first bill involves

2023 PSW Legislative Awards

pharmacist prescribing of contraception in pharmacies. The second bill regards issues related to Pharmacy Benefit Manager (PBM) reform and patient choice in pharmacy. The bill is currently in the drafting phase. The third bill involves eliminating the Muiltistate Pharmacy Jurisprudence Examination (MPJE) for pharmacy graduates to help address issues in licensing delays. Following this overview, attendees walked to the Wisconsin State Capitol to discuss these bills with legislators.

Legislative Day 2023 was another successful opportunity to highlight the importance of PSW member advocacy. Following a successful virtual version of the event in 2021 and 2022, members of the pharmacy profession were once again able to show their support through in-person visits to the capitol. As the practice of pharmacy continues to advance, PSW encourages you to continue sharing your story to advocate for the profession. PSW offers a number of opportunities to get involved at https://www.pswi.org/Get-Involved.

Will Carns is a 2023 Doctor of Pharmacy Candidate at the University of Wisconsin-Madison School of Pharmacy in Madison, WI.

Left: *PSW President, Janet Fritsch (left), Michael Plautz (center), and award receipient Ryan Rypel (right).*

Below: *PSW President, Janet Fritsch (left), Michael Nome (center), and award receipient Kourtney Peterson (right).*

Left: *Award receipient Saba Tahir (left), Karen MacKinnon (center), and PSW President, Janet Fritsch (right).*

Below: *PSW President, Janet Fritsch (left), and Good Government award receipient Jake Olson.*

MEDICAL COLLEGE OF WISCONSIN SCHOOL OF PHARMACY STUDENT WRITING CLUB:

Leadership Spotlight: Megan Ose

by Jessica L Mickevicius, 2024 PharmD Candidate, Kaitlyn B Henderson, 2024 PharmD Candidate, Emma G Hilgendorf, 2024 PharmD Candidate, and Alexia C Monty, 2024 PharmD Candidate

Megan Ose, PharmD is the director of pharmacy services at Children's Wisconsin and recently joined the Pharmacy Society of Wisconsin (PSW) Board of Directors. After completing her Doctor of Pharmacy degree at the University of Wisconsin-Madison in 2008, she accepted a clinical staff pharmacist position at Marshfield's Saint Joseph Hospital. There she was able to work in varied areas including the emergency department, intensive care units, and pediatric units. Over six years, she gained a clinical foundation that was key to understanding the workflow within that specific hospital. This experience equipped her with the ability to adapt to new settings when she transferred to Children's Wisconsin in Milwaukee. After approximately a year and a half at Children's Wisconsin, she transitioned to a pharmacy operations manager role. During this time, she pursued additional education both online and in person, receiving her Master of Health Services Administration (MHSA) degree from the University of Michigan. Following that program, she completed the American Society of Health Systems Pharmacists (ASHP) Pharmacy Leadership Academy to gain additional pharmacy-focused leadership training. Currently, Ose is enrolled in the American College of Healthcare Executives (ACHE) Leadership Development Program, provided through the Wisconsin chapter.

Ose's current role as the director of pharmacy services gives her a variety of day-to-day experiences. A significant amount of her time is spent planning and working with other groups outside of the pharmacy field to incorporate pharmacists and technicians into workflows to encourage process improvements. Currently, Ose is focusing on a new ambulatory position and developing what the workflow could entail as the position is realized and then implemented. With this new position, Ose must communicate with the pharmacy team about how to find people who are interested, and plan how the department can staff the position. She also feels enthusiastic about working with key stakeholders within the pharmacy world to determine how to promote the pharmacist profession, promote pediatric care, address different opportunities for expanding roles of the pharmacist, and ensure that the patients get the best care possible.

Accomplishments

Throughout her fourteen years as a pharmacist, one of Ose's greatest professional achievements was playing a crucial role in the addition of three new retail pharmacies to Children's Wisconsin in 2019. She not only contributed valuable input on the project team, but she also gained invaluable knowledge about the intricacies of developing, designing, and implementing new pharmacies. Along with professional accomplishments, Ose expressed that her greatest personal achievement is her family. She values spending quality time with family and watching her young son grow and learn.

Ose is appreciative of all the opportunities she has been able to pursue to develop her leadership skills, including completing the ASHP Pharmacy Leadership Academy, receiving her MHSA, enrolling in the ACHE Leadership Development Program, and attending the PSW Leadership Conference. She states that the different opportunities built crucial connections and networks for her career, as well as provided her with the tools and knowledge to become a strong leader. Ose has reflected on what skills and traits make a leader multiple times in her career—most recently when reviewing the operations manager role at Children's. She explained that a leader takes advantage of opportunities to improve, in addition to implementing change and incorporating suggestions. Ose emphasized how pharmacy leaders (both informal and formal) use this skillset every day when they pursue opportunities to improve patient care and further clinical knowledge in the healthcare field.

Concerns Today

Ose is grateful for the opportunities given to her through her experiences during the last eight years at Children's Wisconsin, including the past year as a director of pharmacy services. Although her career has brought great reward in seeing the positive changes throughout the years, there are challenges that the pharmacy and health care fields are facing. One of the biggest challenges that Ose and many other executives are experiencing is staffing difficulties. She notes that they have been seeing greater shortages on the technician front, and she is concerned that this may expand more into the pharmacist realm, especially as a result of the pandemic. With this challenge, she expressed that many employees have been reevaluating how they use their time, looking to use their allotted time away from work. She thinks that this might change the job market from what we have been used to, and this shift in priorities is going to require leaders to envision new ways to accomplish pharmacist tasks to meet the needs of pharmacy staff, healthcare colleagues, and the patients. In her role as director, she has been able to come up with creative solutions during the pandemic with remote work positions. She expressed that these flexible positions have positively affected pharmacist efficiency by using available technology. Ose hopes that these changes will allow for pharmacists to meet more patients' needs while practicing in a sustainable manner that enhances well-being.

One of Ose's personal concerns, and an area she hopes to improve upon, is ensuring that as a pharmacy team leader she can collaborate with other administrators to mitigate workforce burnout for healthcare

professionals. She expressed this as a real concern that has come to the forefront of health care professionals' minds throughout the pandemic. There is an expectation for pharmacists to consistently perform at the top level to get daily tasks accomplished, which can become overwhelming quickly. Ose plans to evaluate processes to ensure that as a health care entity, Children's Wisconsin, and hopefully other health care systems, can support their teams and continue to invent new and creative ways to do so.

Advice for Future Leaders

As Ose reflects on her career as a pharmacist, her advice to future leaders is to take on challenges that expand your knowledge in your areas of interest and to take on projects, as each one is an opportunity for growth. She shares that working with a wide variety of individuals has been something she enjoys the most in her career. Ose also wants future leaders to understand that there are many routes into becoming a leader and many ways that one can choose to lead others. She wants to remind everyone not to be discouraged if their path is not the one others are pursuing, or if it is not the one that was originally planned. She encourages everyone to continue building their leadership skillsets by using the resources provided by programs in the field of pharmacy that support and cultivate leadership.

Ose highlighted the importance of establishing formal and informal mentors while developing herself within her career and encourages future leaders to find mentors early on. Ose explains that gaining multiple perspectives and maintaining relationships is crucial in leadership. She states that each mentor has played an influential role in shaping her into the leader she is today. Ose is a preceptor, which was her first formal leadership role, and encourages everyone to spend time teaching and learning from others in the profession.

Jessica Mickevicius, Kaitlyn Henderson, Emma Hilgendorf, and Alexia Monty are 2024 Doctor of Pharmacy Candidates at the Medical College of Wisconsin School of Pharmacy in Milwaukee, 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.

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Destiny Rogers Samford University
Caroline Eason Univ. of North Carolina at Chapel Hill
Casey Hourigan Univ. of the Incarnate Word
Diana Ghanimah Medical College of Wisconsin
Katelyn Sutton Duquesne University
Gunjan Patel University of Illinois at Chicago
Haley Weaver Harding University
Jackson Beach Southwestern Oklahoma State Univ.
Lauren Williams University of Kentucky
Mohit Kumar University of Georgia
Moriah Willis University of Oklahoma
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