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March/April 2021

The Journal

of the Pharmacy Society of Wisconsin

MONTH OF ADVOCACY

One Voice. Together While Apart.

Medication Safety and Quality

2021 PSW Virtual Educational Conference

Wednesday - Thursday
April 14 - 15, 2021

Working Together While Apart

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March/April 2021

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

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Advocating with One Voice - Together While Apart

CLICK HERE TO VIEW THE FULL SCHEDULE

by Danielle Womack, MPH

Elections and new legislative sessions provide a unique opportunity to foster relationships with policymakers across the state. With the Wisconsin State Legislature beginning its work in early January, now is the perfect time to reach out to your elected officials and establish yourself as a pharmacy resource.

If you have ever attended PSW's annual Legislative Day, held annually in February or March, you know that this conference is an opportunity to hear about the latest news in pharmacy and healthcare policy, as well as meet with your legislators and advocate for pro-pharmacy legislation.

Due to the COVID-19 pandemic, we cannot host our traditional Legislative Day this year – but that doesn't mean our advocacy efforts have waned! Instead, we are focusing on advocacy efforts throughout March and hosting the first PSW Month of Advocacy!

PSW's Month of Advocacy will include a series of events held a few times per week, focusing on hot topics in pharmacy policy – PBM reform, compounding regulations, COVID-19, provider status, recent law updates, and more. You'll have the chance to hear from elected officials, Pharmacy Examining Board members, and national experts on pharmacy policy. And, of course, we'll provide opportunities to connect with your legislative leaders through virtual communications and our Pharmacy Legislative Action Network (PLAN).

We ask that you pre-register for all events you plan to attend by visiting pswi.org/moa. The Month of Advocacy is free to all PSW members. Still, you may consider contributing to our Legislative Defense Fund or the PSW Friends of Pharmacy Fund to support our advocacy efforts. The PSW Friends of Pharmacy Fund contributes funds to pro-pharmacy candidates for elected office. Unlike the Friends of Pharmacy Fund, donations to the Legislative Defense Fund are not political contributions and are not given to any political candidates. Instead, these funds are used to support PSW's advocacy efforts, including lobbyist staff and grassroots advocacy software. For more information or to contribute, visit pswi.org.

PSW's top priorities for the 2021-2022 legislative session include expanding immunization authorities, pharmacy benefit manager reform, provider status, and matters surrounding technician roles. As legislation is introduced, all members will be updated through FastFacts. PLAN members will also receive additional communications relating to our legislative work and priorities – be sure to register if you are not yet a PLAN member by visiting www.pswi.org/plan.

With the new year and new legislative session, now is the best time to connect with both new and returning policymakers in Wisconsin – health care is a top issue for elected officials, and they want to hear from you! As we seek to make policy changes that better allow you to serve your patients, pharmacy professionals must be their own advocates and be at the table. I can't wait to see you all during our Month of Advocacy – **advocating with one voice, together while apart.**

- Danielle Womack, MPH
Vice President, Public Affairs

MONTH OF ADVOCACY

One Voice. Together While Apart.

I am a Pharmacy Professional and I... am a Vaccinator

May/June 2021
Theme: I am a Pharmacy Professional and I... Learned a New Skill

Email your response to mgrant@pswi.org by April 1.

Responses should be <100 words and include a photo.

Gretchen Kunze, PharmD, BCPS
Pharmacy Manager
Gundersen Pharmacy- Cass St., La Crosse

Patients that have undergone hematopoietic stem-cell transplantation require re-vaccination against pathogens they previously had immunity to. Many of these vaccines are covered under prescription drug benefits, therefore, it is more cost effective for the patients to receive them in the pharmacy setting rather than the clinic. This has led to a partnership with the hematology and oncology department at Gundersen Health System. We have worked together and developed a process to coordinate the prescribing, billing, ordering, and administration of these vaccines. The protocols being used fall outside of typical ACIP guidelines, therefore, we still require providers to drive the prescribing of these vaccines. However, as we become more familiar with the protocols and vaccines themselves, pharmacy staff is being more proactive in our efforts to initiate vaccine needs and resolve errors or gaps in vaccine therapy. This collaboration has been a great learning experience and is an example of how pharmacies can support the needs of other departments within the health system.

Riley Poe, PharmD
ICU Pharmacist
Aurora Health Care, Milwaukee

Being an ICU pharmacist, I have seen firsthand the difficult challenges COVID19 poses on patients, healthcare workers and the entire healthcare system. We have faced busy ICUs, unprecedented clinical scenarios with new medications and indications as well as feelings of helplessness and burnout. The COVID19 vaccine has provided us hope, not only to our fellow healthcare workers but to the patients we serve and the communities we live in. The opportunity to vaccinate colleagues, frontline workers and members of the community has been a rewarding experience. I will never forget the unending amount of joy and excitement from people who are getting their vaccine. Their smiles and positivity radiate and give hope to all of us in ending the COVID19 pandemic. I'm proud to be a healthcare worker during this time and work alongside such a resilient group of individuals.

Cassie Levetzow, PharmD, BCACP
Clinical Pharmacist, Outpatient Pharmacy & Pulmonary Clinic
St. Luke's Medical Center, Milwaukee

I have been helping with the COVID vaccine clinic at Aurora St. Luke's Medical Center since the first week we offered them. It has been an amazing experience to say the least. I have had many healthcare workers that have cried tears of joy or be silent and reflect on all the patients they have cared for during this pandemic. We typically vaccinate around 600 people a day and have recently hit 10,000 vaccines administered at our site. I'm excited for our first patients from the community to get their vaccine!

William Clark, RPh
Pharmacy Manager
Aurora Health Care, Lake Geneva

Just wanted to share my story. This is actually a story of two immunizers. I have been immunizing for more that 15 years working for Aurora Pharmacy. It is a part of my practice that I truly enjoy. Although we do influenza vaccines, I have concentrated mainly on the non-influenza vaccines mainly Shingrix, pneumonia, Tdap, Td providing a convenient way for our patients to receive these needed vaccines.

The other half of the story is my son, Tim Clark, a third year pharmacy student at UW-Madison and intern at Advocate-Aurora Lakeland Medical Center. He has spent his winter break giving COVID-19 vaccinations to healthcare professionals. The attached picture shows him giving me my first dose of vaccine.

Katherine Hartkopf, PharmD, BCACP
Pharmacy Manager, Ambulatory Care Services
UW Health, Madison

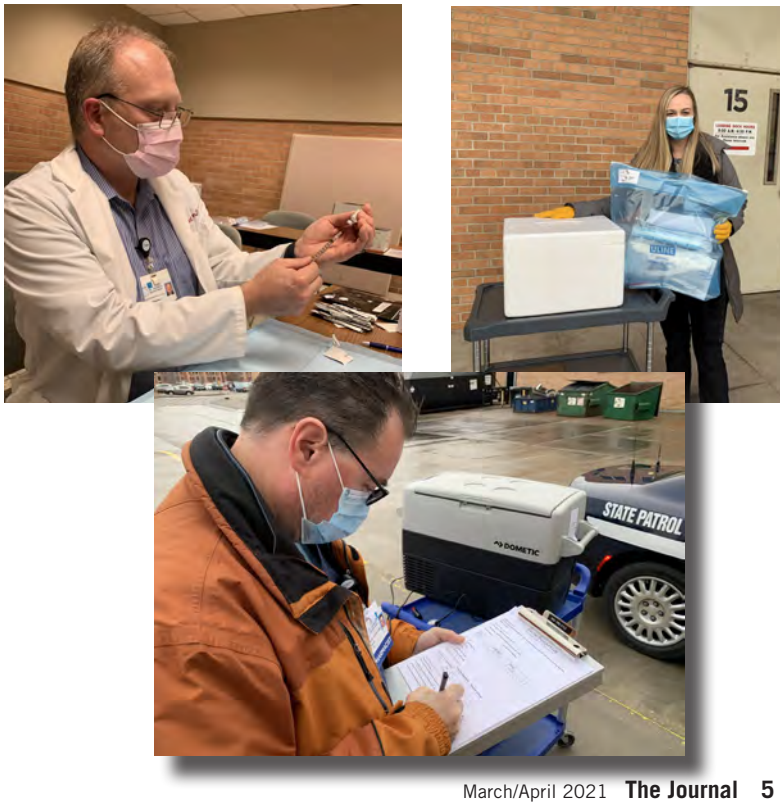
Samantha Lewiston
2021 Doctor of Pharmacy Candidate
University of Wisconsin-Madison School of Pharmacy, Madison

Emily Jaeger
2021 Doctor of Pharmacy Candidate
University of Wisconsin-Madison School of Pharmacy, Madison

This past fall, we collaborated to serve community members and UW Health employees while maintaining social distancing guidance through an innovative, pharmacy-led drive-thru influenza vaccine clinic. During respective APPE leadership rotations with Kate, Emily collaborated on the proposal and initial implementation and Samantha managed the ongoing service and daily operations. Community members and employees could schedule appointments or drop-in any time during operating hours. Patients age 6 and older were eligible for vaccination at this site, making it especially convenient for many families. Upon arrival, they were directed to remain in their vehicles and follow signage through the parking lot to a tent for screening and vaccination. The clinic was primarily supported by APPE and IPPE students certified in immunization delivery with pharmacist oversight. This clinic operated for 7 weeks during which 4,673 influenza vaccines were administered. We could not have provided this innovative and necessary service without the support and dedication of many excellent students, pharmacists, and the UW Health pharmacy department!

Mandy Kvam, PharmD
Pharmacist
HSHS Sacred Heart Hospital, Chippewa Falls

The pharmacy departments of the Health Sister's Hospital System of Western Wisconsin is honored to take part in COVID-19 vaccination efforts in our area. Months of planning with a multi-disciplinary team helped us hit the ground running and have vaccines in arms just hours after our first shipment arrived. Our pharmacists worked side by side with nurses, hospital leadership, and providers to take an active role in our vaccination clinics, including administering vaccine. We have a long way to go, but we are thankful for the stressful weeks of planning, the happy tears as we witnessed the first vaccinations, and the hope for a healthier future. Today and every day we are proud to be pharmacists. -Sacred Heart Eau Claire and St. Joseph's Chippewa Falls Pharmacy Departments.



PHARMACIST CE:

The Joint Commission's Requirements for Antimicrobial Stewardship in the Ambulatory Practice Setting: An Opportunity to Optimize Patient Care

by Sara Revolinski, PharmD, BCPS, Maxx Enzmann, PharmD, BCPS, John Tierney, 2021 PharmD Candidate

CE FOR **PHARMACISTS**

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

Learning Objectives

- State the rationale for ambulatory antimicrobial stewardship.
- Recognize how antimicrobial stewardship efforts affect medication safety and quality.
- Describe the rationale for each antimicrobial stewardship requirement as determined by the Joint Commission.
- List examples of actions ambulatory clinics can implement to promote antimicrobial stewardship efforts.
- Identify resources that can be used to assist with implementation of antimicrobial stewardship within an ambulatory care setting.

Up to 56% of outpatient antibiotics in the United States are inappropriately prescribed, with 30% of antibiotic prescriptions deemed unnecessary.[1,2] The over-prescribing of antibiotics can be harmful to patients, because these medications have the potential to cause adverse effects and toxicities. These range from common adverse effects, such as rash and diarrhea, to less common adverse events, such as severe allergic reactions.[3] Furthermore, antibiotic use has been identified as the most important risk factor for *Clostridioides difficile* infection.[4]

In addition to increasing the risk of adverse effects and toxicities, overuse of antimicrobials can also drive antimicrobial resistance and select for resistant pathogens, which is a global public health issue. According to the World Health Organization, antimicrobial-resistant infections contribute to over 500,000 deaths each year and are projected to increase to 10 million deaths per year by 2050.[5] Resistance to first-line antibiotics can also lead to the increased use of unfavorable treatment options, an increase in health care costs, and poorer patient health outcomes.[6]

Antimicrobial stewardship (AMS) functions to maximize the benefit of antimicrobial treatment while minimizing harm to individual patients and communities.[7] AMS helps ensure both the quality and safety of antibiotic treatment by determining whether antibiotic therapy is warranted; helping to ensure the most effective antibiotic is selected at the optimal dose, route, frequency, and duration; and minimizing adverse effects and other collateral damage.[8]

A recent study conducting a cross-sectional, multi-center survey describing the current state of ambulatory AMS programs in a national cohort of hospitals with ambulatory health care settings found only 7% of institutions reported having a fully functioning AMS program in the ambulatory care setting.[9] While AMS programs can be created in all health care settings in which antimicrobials are prescribed, the most common area where AMS programs currently exist is the inpatient hospital setting. This is due in part to the fact that every acute

care hospital in the United States that participates in Medicare or Medicaid is required by the Centers for Medicare and Medicaid Services to have an AMS program.[10] In addition, many AMS programs in acute care settings are driven by pharmacists, as the majority of hospital systems employ pharmacists in a variety of roles. While pharmacists are integral members of the health care team in an ambulatory setting, pharmacist roles are not as prevalent in the ambulatory care setting.

Based on this, regulatory agencies have recently worked to optimize ambulatory antimicrobial stewardship. The Joint Commission (JC) is an independent, non-profit governing body designed to ensure that health care organizations deliver high-quality care to patients through the development of practice standards designed to maximize patient safety and quality.[11] JC-accredited health care organizations must demonstrate effective implementation and maintenance of JC standards. While participation with the JC is voluntary, more than 22,000 health care organizations in the United States maintain accreditation. The JC has implemented an AMS standard for hospitals and nursing care centers since January 1, 2017, and established a similar standard for JC-accredited ambulatory care centers on January 1, 2020.[12,13] JC-accredited ambulatory care centers include organizations providing medical or dental care, urgent care facilities, occupational health centers, episodic care, or convenient care; ambulatory surgery centers are not included in this definition. The standard requires AMS to be an organizational priority, and defines five requirements that must be met by the organization. These requirements include designating a leader to establish and maintain appropriate antibiotic prescribing practices; implementing an annual goal to reduce the use of unnecessary antimicrobials; using current evidence-based guidelines to support antimicrobial prescribing; educating health professionals on AMS practices; and collecting and analyzing data pertaining to the stewardship.

This article will describe these five requirements in detail and contain recommendations for health care organizations that are looking to enhance patient safety and quality in the ambulatory environment by implementing or building on an ambulatory antimicrobial stewardship program.

Requirement #1

The organization identifies individual(s) responsible for developing, implementing and monitoring activities to promote appropriate antimicrobial medication prescribing practices

Identifying leaders for an AMS program establishes ownership and accountability for antibiotic use.[12] While the Infectious Diseases Society of America (IDSA) guidelines for implementing AMS programs in hospitals have suggested that leadership should belong to an infectious diseases-trained physician or pharmacist, this might not be practical in all settings.[8] Effective leadership, regardless of training specific to infectious diseases, increases the likelihood of optimizing antibiotic use through communication, and empowerment and accountability of practitioners.[12] A White Paper published by the Society for Healthcare Epidemiology of America outlines the desired knowledge and skills for an AMS leader, noting that successful AMS leaders demonstrate expertise in change management, project management, and measurement and analysis of project outcomes in addition to clinical expertise.[14]

Leadership plays a key role in ensuring clinical practice aligns with guideline recommendations. A study by Ashiru-Oredope and colleagues surveyed clinical practices in England to look at the review and implementation of AMS techniques found within national AMS toolkits.[15] While 60% of ambulatory practices reported reviewing the toolkits, only 13% created an action plan for implementing the techniques. This is in contrast to 87% of hospitals reviewing the toolkits with 46% implementing the recommendations. Implementation in the hospital setting was largely driven by infectious diseases-trained pharmacists, who are only present in 5% of ambulatory practices. This study suggests effective leadership increases implementation of AMS guidelines in practice.

Previous guidelines have established that pharmacists are critical leaders for antimicrobial stewardship.[16] Pharmacists often have additional time and resources to devote to AMS activities and partner well with other expert practitioners. As pharmacist roles in ambulatory care continue to expand, pharmacists will likely be increasingly involved with outpatient AMS. In addition, community pharmacists who process prescriptions from nearby clinics can begin to implement and lead AMS efforts in their area by assessing prescriptions for appropriateness, providing education to providers and patients, and providing data to prescribers.

A single-center cohort study published in 2018 explored how empowering leadership affected AMS.[17] This study was completed after a children's hospital in Switzerland underwent a leadership change from control-based to empowerment-based, allowing providers the ability to determine antibiotic de-escalation and duration of therapy for patients. Organizational guidelines directed clinical practice under the empowering leadership model, as opposed to laboratory values, which dictated decisions under the previous control-based leadership structure. With empowering leadership, antibiotic days per 1000 patient days decreased significantly over the course of two years, from 474.1 to 403.9. Furthermore, days of therapy for prophylaxis and suspected infection also decreased significantly, as did use of the broad-spectrum antibiotics meropenem or vancomycin.

Literature demonstrates that effective leadership promotes AMS, and can be effective even in the absence of formal training in infectious diseases.

Requirement #2

The organization sets at least one annual antimicrobial stewardship goal

The second requirement set forth by the JC is for the organization to set at least one annual ambulatory antimicrobial stewardship goal.[12] Establishing a goal allows for efforts to be targeted to the area of focus, so all stakeholders are working together to optimize antimicrobial stewardship. Ideally, the annual goal would be based on data from the health care organization that identifies areas of opportunity for antibiotic prescribing. Knowing where antimicrobial overuse

TABLE 1. Ambulatory Antimicrobial Stewardship Interventions Identified in the Literature

Study	*Study Design and Setting*	*Population and Intervention (if applicable)*	*Outcomes and Results*	*Notes and Conclusions*
Studies Identifying Areas where Antibiotic Prescribing is Suboptimal				
Havers, Outpatient Antibiotic Prescribing for ARI during Influenza Season, 2018[29]	Retrospective multicenter cohort study analyzing antibiotic use in patients presenting with an acute respiratory infection during influenza season. 123 outpatient clinics associated with US Influenza Vaccine Effectiveness Network Sites.	14,987 patients analyzed over 2 years: 2013-14 and 2014-15 influenza seasons.	41% of patients received an antibiotic. 41% of those antibiotics were not indicated based on diagnosis (viral URI was 84% of those diagnoses). 29% of patients with influenza but not pneumonia received antibiotics. 35% of patients received antibiotics for group A streptococcus pharyngitis (strep throat), but 38% of those tested negative for group A streptococcus. 38% of patients received antibiotics for sinusitis and only had symptoms for 3 days or less, indicating viral etiology.	Acute URIs are often viral in etiology, but still receive inappropriate antibiotic treatment. Targeting URIs such as viral URI/acute bronchitis, influenza, pharyngitis and group A streptococcus pharyngitis, and sinusitis could optimize ambulatory antibiotic use in outpatient clinics.
Palms, First-Line Antibiotic Selection in Outpatient Settings, 2019[30]	Retrospective cohort study utilizing the IBM MarketScan database for antibiotics prescribed in 2014.	Antibiotic prescriptions for pharyngitis, sinusitis, and AOM prescribed from retail clinics, EDs, urgent care centers, and provider offices were analyzed for place in therapy. First line therapies are amoxicillin or penicillin for streptococcal pharyngitis and amoxicillin or amoxicillin/clavulanate for sinusitis and AOM.	50% of antibiotics prescribed were considered first-line overall. First-line antibiotics based on practice site: Retail clinics: 70% EDs: 57% Urgent care: 49% Prescriber offices: 50% The most common non-first line antibiotics were macrolides.	Antibiotic selection may be a target for antimicrobial stewardship programs. This study did not assess clinical decision making for allergies or other compelling indications for second-line therapies, which may be relevant for different ambulatory care settings.
Jaggi, Outpatient AMS Targets for Treatment of SSTIs, 2018[31]	Retrospective cohort study of ambulatory encounter claims for SSTI or animal bites placed with Medicare in Ohio. Appropriate antibiotic selection (guideline-defined, single antibiotic) and appropriate treatment duration (7 days or less) was analyzed.	10,310 Medicare encounters were analyzed.	77.3% of patients received a duration of antibiotics over 7 days. 10% of patients received inappropriate antibiotics for SSTI. Patients seen by non-pediatricians (e.g., family practice, emergency department) were more likely to prescribe non-recommended antibiotics.	Duration of therapy may be an appropriate target for optimizing antibiotic use in pediatrics with an SSTI. Identifying which provider types are non-adherent can help target which provider groups would benefit from education.
Interventional Studies Analyzing Interventions Designed to Improve Antibiotic Use				
Yadav, A Multifaceted Intervention Improves Prescribing for ARI in ED and Urgent Care Settings, 2019[32]	Cluster randomized clinical trial. Three academic health centers participated with 5 EDs serving adults and pediatrics and 4 urgent care centers.	Adult and pediatric patients presenting with acute viral URI. Intervention included: provider and patient education, naming a physician champion, and providing feedback. Peer comparison was also added at some sites.	Antibiotic prescribing for viral URI reduced from 6.2% to 2.4%. Inappropriate antibiotic prescribing decreased from 2.2% to 1.5%. There was no difference between sites that used peer comparison and those that did not.	A multifaceted intervention reduces inappropriate antibiotic use in viral URI.

TABLE 1. Ambulatory Antimicrobial Stewardship Interventions Identified in the Literature (Continued)

Study	Study Design and Setting	Population and Intervention (if applicable)	Outcomes and Results	Notes and Conclusions
Interventional Studies Analyzing Interventions Designed to Improve Antibiotic Use				
Burns, Implementing Outpatient AMS in a Primary Care Office Through Ambulatory Care Pharmacist-led Audit and Feedback, 2020[33]	Pre-post interventional pilot study. Single-center primary care office.	Biweekly written feedback on antibiotics for UTI and URI given to prescribers (positive and negative feedback). Education and guidelines were provided prior to antibiotic review and feedback.	Guideline concordant antibiotics increased: UTI: 20% to 69.2% URI: 43.3% to 86.8%. Guideline concordant duration of therapy increased from 55% to 70.4%.	A feedback process incorporating both positive and negative feedback improved antibiotic selection and duration of therapy. Pilot studies may support incorporation of stewardship personnel in ambulatory clinics.
Eudaley, Development and Implementation of a Clinical Decision Support Tool for UTIs in a Family Medicine Resident Clinic, 2019[34]	Pre-post interventional study. Single-center family medicine outpatient clinic.	EHR tool to assist with the diagnosis, treatment, and documentation of UTIs. Development of a clinic-specific antibiogram to guide antibiotic use.	EHR utilization occurred 29% of the time. Significant decreases in antibiotic use: FQ: 27% (p<0.001). SMX/TMP: 20% (p=0.003). Significant increase in nitrofurantoin use (first line therapy): 31% (p=0.01). Significant increase in guideline concordance by 32% (p=0.010).	Despite low utilization of the EHR tool, improved antibiotic use was seen for the management of UTI. Sustained impact of the EHR tool was not assessed. Plan to assess impact of reduced FQ use on resistance.
Walters, An Ambulatory AMS Initiative to Improve Diagnosis and Treatment of UTIs in Children, 2019[35]	Pre-post interventional study. Single-center pediatric ED.	Development of a UTI algorithm for pediatric patients. 5 PDSA cycles used during implementation. Each PDSA cycle identified the goal measure, provided multidisciplinary education, provided feedback twice a week on data collected to date, provided positive reinforcement, and answered staff questions on the units.	Guideline concordance increased post-intervention: Urine collection: 54.7% to 96.2%. Antibiotic use: 23.1% to 96.6% (p<0.001). Improvements were sustained for 19 months. No change in ED length of stay or ED readmissions.	Utilization of PDSA techniques, a quality-based improvement method, resulted in sustained improvement in UTI management in pediatric ED patients. This study also ensured the changes did not adversely impact patients by measuring ED length of stay and readmissions.
Jindai, Improving FQ Use in the Outpatient Setting Using a Patient Safety Initiative, 2018[36]	Pre-post interventional study with interrupted time-series analysis. 10 Veterans Affairs community-based outpatient clinics in Oregon and Washington.	Mandated patient safety initiative with multiple interventions: 1. New order in EHR requiring indication for FQs, documentation of education on adverse effects and of medication reconciliation to look for drug interactions 2. Education provided to prescribers.	62% weekly reduction in FQ use upon implementation of the intervention (p<0.001). 2% increase in weekly FQ use after initial reduction. No change observed in rate of non-FQ prescribing	Targeting specific antibiotics can decrease utilization without increasing utilization of other antibiotics. Electronic health record interventions may not provide sustained results; feedback to providers on utilization of the tool may be needed.

AMS: antimicrobial stewardship; AOM: acute otitis media; ARI: acute respiratory infection; ED: emergency department; EHR: electronic health record; FQ: fluoroquinolone; PDSA: plan, do, study, act; SMX/TMP: sulfamethoxazole/trimethoprim; SSTI: skin and soft tissue infection; URI: upper respiratory infection; US: United States; UTI: urinary tract infection

exists, what local resistance patterns are, and what collateral damage is seen in the local population can help determine a goal.

As organizations are only starting to implement ambulatory AMS practices and might not have readily available data to drive goal setting, the first goal could be as simple as identifying antibiotic prescribing patterns in the ambulatory care environment, or establishing an antibiogram for ambulatory care. Considerations for collecting data can be found later in this paper, included in the description of the fifth requirement. Once prescribing patterns, resistance patterns, or other data is readily available, areas of opportunity can be identified that can serve as future goals.

TABLE 2. Resources for Ambulatory Antimicrobial Stewardship

Resource Name	*Description*	*Link to Access*
Centers for Disease Control and Prevention: Core Elements of Outpatient Antibiotic Stewardship	Multiple documents exist including literature supporting AMS, clinician and facility checklists to assess current AMS practice, action plans for practice and more.	https://www.cdc.gov/antibiotic-use/core-elements/outpatient.html
Centers for Disease Control and Prevention: Be Antibiotics Aware Partner Toolkit	Includes patient education documents, infographics, social media content, and public service announcements that can be used to educate patients on appropriate antibiotic use.	https://www.cdc.gov/antibiotic-use/week/toolkit.html
Centers for Disease Control and Prevention: Antimicrobial Resistance	Contains information on antibiotic resistant infection rates and mortality.	https://www.cdc.gov/drugresistance/index.html
Centers for Disease Control and Prevention: Antibiotic Use & Patient Safety Portal	Interactive map to compare outpatient prescriptions by state to determine what antibiotics are most often used in your state.	https://arpsp.cdc.gov/profile/antibiotic-use/208
Infectious Diseases Society of America (IDSA)	Clinical practice guidelines for multiple infectious syndromes. Guidelines for implementation of an antibiotic stewardship program.	www.idsociety.org

AMS: antimicrobial stewardship.

Publicly reported data can also be used to identify opportunities for improvement. The Centers for Disease Control and Prevention (CDC) reports data on antibiotic resistance patterns and outpatient antibiotic prescription rates by state through the Antibiotic Resistance & Patient Safety Portal and compares rates to those seen on a national level.[18] Identifying resistant pathogens or antibiotic overuse can help determine targets for improvement based on location. The healthcare effectiveness data and information set (HEDIS), is a performance improvement tool using data reported via insurance plans.[19] HEDIS contains over 90 different measures, several of which pertain to ambulatory antibiotic use, including appropriate treatment for children with upper respiratory infection and avoidance of antibiotic treatment in adults with acute bronchitis. Organizations can select one of these measures as a goal as well.

Additionally, it would be reasonable for sites to start with some of the areas of inappropriate prescribing or AMS interventions published to date. A study by Shively and colleagues analyzed outpatient prescribing patterns of primary care providers within the Veterans Affairs Pittsburgh Healthcare System over one year.[20] The authors determined the antibiotic index for each prescriber, defined as the number of antibiotic prescriptions per 1,000 patients per year, to identify which practitioners prescribe the most antibiotics. Identifying these prescriber trends at other sites would allow for targeted education to specific providers, which could serve as an AMS goal. The study also evaluated 5% of antibiotic prescriptions for guideline concordance, finding that antibiotics for the treatment of acute respiratory tract infection; skin and soft tissue infection; and urinary tract infections were concordant with guideline recommendations only 11%, 11%, and 29% of the time, respectively. Optimizing prescribing for these indications could also be a future goal. Finally, the authors identified which antibiotics were prescribed inappropriately, finding 84.0% and 78.4% of ciprofloxacin and azithromycin prescriptions, respectively, were inappropriately prescribed. Targeting improved prescribing for one of these antibiotics could also serve as a goal. Developing a goal based on local data can also increase engagement from practitioners and provide a starting point for further AMS initiatives.

A literature summary of relevant ambulatory AMS initiatives through 2016 has been published in the CDC's Core Elements of Outpatient Antibiotic Stewardship Appendix.[21] Further examples of studies that have identified areas of opportunity for ambulatory antibiotic prescribing since 2016 are described in Table 1.

Once the goal is determined, it is important for the AMS leader to communicate the goal to the stakeholders, including prescribers and other administrative leaders, to provide a cohesive approach to AMS. Further education might also be required to help providers reach their goals. Education is the fourth JC requirement and will be addressed later in this paper. Additionally, data demonstrating progress on the AMS goal should be shared with stakeholders and can be used as an educational tool as well.

Requirement #3

The organization uses evidence-based practice guidelines related to its annual antimicrobial stewardship goal(s)

The third requirement from the JC is for the organization to use evidence-based practice guidelines related to its annual AMS goals.[12] Evidence-based practice guidelines can influence appropriate antibiotic prescribing by ensuring patients only receive antibiotics when clinically indicated.[12] Furthermore, when patients do require antibiotic treatment, guidelines assist with antibiotic selection, dosing, and duration. It is appropriate to use nationally recognized guidelines, or to create organizational-specific guidelines from evidence-based literature and local resistance patterns, if known.[8] Some of the studies described in Table 1 have implemented treatment algorithms to optimize AMS.

Organizational guidelines and prescriber education can also be integrated

into the electronic health record (EHR). In a quasi-experimental study by Shoff and colleagues at the Durham Veterans Affairs Health Care System, an institutional guideline was developed based on a local urinary antibiogram and incorporated into the EHR via an order set to encourage guideline-concordant prescribing for outpatient urinary tract infections (UTIs).[22] After guideline implementation, monthly fluoroquinolone prescriptions for acute cystitis decreased from 45% to 32%, in alignment with the local urinary antibiogram which demonstrated fluoroquinolone resistance.

In another study developed to assess the impact of a protocol developed for the treatment of UTIs in patients with spinal cord injuries (SCIs), Patros and colleagues developed an algorithm-based order set using SCI-specific antibiogram data at the Clement J. Zablocki Veterans Affairs Medical Center, and conducted a pre/post interventional study to analyze impact.[23] The authors found that appropriate antimicrobial prescribing increased from 48% to 72% from pre- to post-protocol implementation, conveying that organizational guidelines based on local data can improve the appropriateness of antimicrobial prescribing.

Evidence-based guidelines are useful in the practice of AMS, as they assist with defining goals and implementing strategies for improvement of antibiotic use. They can also serve as educational material for prescribers.

Requirement #4

The organization provides all clinical staff and licensed independent practitioners with educational resources related to its antimicrobial stewardship goal(s) and strategies that promote appropriate antimicrobial medication prescribing practices

The fourth requirement set forth by the JC is for the organization to provide all clinical staff and licensed independent practitioners with educational resources related to its AMS goal(s) and strategies promoting appropriate antimicrobial prescribing.[12] Education of clinicians can be done actively, passively, or with a combination of the two. Passive education involves a one-way method of information being presented to an audience, such as a non-interactive lecture, while active education involves audience participation, such as group discussions or hands-on workshops. Active education has been shown to be more successful than passive education because it involves a more engaged audience, which leads to higher retention of content.[8]

Educational resources that can be provided to clinical staff include recommended prescribing practices and guidelines, such as guidance on medication selection or dosing, as well as strategies for addressing patient expectations and possible adverse effects when antibiotics are

not indicated in a particular patient. The CDC houses a plethora of resources for outpatient antimicrobial prescribing, which are described in Table 2.

In addition to providing resources to clinical staff, direct education of providers, either alone or as part of a multimodal intervention, has been used to implement AMS in the ambulatory care setting.[7] Education of clinical staff can take many forms, including, but not limited to, providing live education at staff meetings, sharing interactive data about AMS on the organization's website, and implementing clinical decision support in the EHR. As part of a multifaceted approach to decreasing inappropriate antibiotic prescribing for acute respiratory tract infections (ARTIs) at three high-volume urgent care clinics, Cummings and colleagues conducted a quasi-experimental study that used patient and staff education in addition to public commitment and peer comparison.[24] Provider education consisted of presentations at several physician staff meetings on the importance of appropriate, guideline-concordant antimicrobial prescribing; sharing an interactive infographic on US Antibiotics Awareness Week that included information about antimicrobial stewardship; and grand rounds presentations on AMS by infectious diseases physicians to medical residents and primary care providers. Patient education consisted of describing antibiotic resistance and antibiotic overuse/misuse via an interview with a local news station during US Antibiotic Awareness Week that was also shared on social media, and placing different print materials from the CDC's Be Antibiotics Aware campaign throughout waiting rooms and patient rooms. Public commitment was demonstrated by the medical director of urgent care signing the CDC's "Commitment Letter to Our Patients" for each respective location. These letters were placed alongside the patient education materials. To implement peer comparison, providers were sent feedback emails categorizing their inappropriate antibiotic use as low (23% or fewer inappropriate prescriptions based on the US National Action Plan for Combating Antibiotic Resistant Bacteria 2020 goal) or high (45% or more inappropriate prescriptions). In addition, emails containing blinded rankings of providers and their peers based on inappropriate antibiotic prescriptions for ARTIs were distributed. The authors found that fewer inappropriate antibiotic prescriptions for ARTIs were written during the intervention period (57.7%) compared with the pre-intervention period (72.6%). This study conveys that education as a part of a multimodal intervention was successful in optimizing antibiotic use.

Education of clinical staff can also be medication-focused, rather than disease-state-oriented. Another study implemented a multimodal AMS approach to specifically decrease the inappropriate outpatient use of fluoroquinolones within Parkland Health & Hospital system.[25] In addition to creating an outpatient protocol for management of cystitis and suppressing fluoroquinolone susceptibilities when appropriate, ambulatory care providers were educated on the risks of using fluoroquinolones via various forums. The authors found that after the intervention period, total fluoroquinolone prescriptions per 1000 patient visits decreased by 39%, and inappropriate fluoroquinolone use decreased from 53% to 34% across all primary care clinics, urgent care clinics, and emergency departments, once again demonstrating that multifaceted interventions that include education can optimize antibiotic use.

Education is an important component of an AMS program, because it helps ensure that prescribers are aware of AMS goals and current antibiotic use recommendations, which ultimately leads to optimized antibiotic use within an organization.

Requirement #5

The organization collects, analyzes, and reports data pertaining to the antimicrobial stewardship goal(s) to organizational leadership and prescribers

The last requirement for ambulatory AMS ties together many of the earlier requirements by helping to ensure that goals and processes such as guidelines and education are monitored to ensure effectiveness.[12] The data obtained can also then be used to inform leaders on AMS progress and serve as the basis for further education to practitioners and development of subsequent annual goals.[21]

Data can be analyzed on a population or individual level and can be broad or narrow in scope. Potential data could include antibiotic prescription rates; resistance trends or antibiograms; or clinical and process outcomes after implementation of an antimicrobial stewardship intervention.[12] Ideally, data should be easy to obtain on demand, sustainable, and gathered from an EHR or other database used by the health care system. Knowing this might not be feasible, manual chart review could also be employed, but this can be time-consuming, could lead to delayed sharing of data, and is difficult to sustain.

A variety of papers have described methods to report on and disseminate antibiotic prescribing data. Meeker and colleagues analyzed the impact of up to 3 interventions on antibiotic prescribing by 248 primary care clinicians for acute, viral upper respiratory infections (URIs).[26] One of the interventions included monthly peer comparison emails sent to each provider comparing his or her individual prescribing to that of prescribers with the lowest rate of inappropriate antibiotic prescribing. Antibiotic prescription data was obtained from the EHR. Emails either identified the prescriber as a top performer (top-performing decile for the lowest inappropriate antibiotic prescriptions) or not a top performer where individual antibiotic prescription rates were shared in addition to rates by top performers. In addition, prescribers also were educated on appropriate antibiotic prescribing for URIs. Prescribing rates significantly decreased to 3.7% from 19.9%. This study demonstrated that timely sharing of antibiotic prescribing, and the use of peer comparison data, decreased inappropriate use. The same authors analyzed prescription rates 12 months after the intervention was complete and found that antibiotic use increased, suggesting that sustained intervention and data sharing might be required to maintain appropriate prescribing.[27]

A similar study conducted in 2019 by Shively, et al. shared monthly e-mails describing individual, peer, and goal antibiotic prescription rates with primary care providers.[28] Compared to baseline,

monthly antibiotic prescribing decreased from 76.9 to 49.5 prescriptions per 1,000 office visits, as did unnecessary antibiotic prescribing (58.8% versus 38.9%).

Additionally, all studies in Table 1 demonstrate the use of data to describe outcomes related to antimicrobial stewardship goals. The majority of these studies demonstrate positive outcomes; however, not every intervention will be successful. When interventions are not successful, it is important to determine why, to modify or change the goal in the future.

Data is a necessary for implementing an effective AMS program, as it serves as evidence of goal attainment as well as education for practitioners.

Resources for Practitioners

Various publicly available resources exist to assist with the implementation of ambulatory antimicrobial stewardship and are described in Table 2. Any resources available from the CDC can be reproduced and posted within ambulatory clinics or provided to patients as educational materials.

Conclusion

AMS is an important patient safety and quality initiative, because it functions to optimize antibiotic use by helping ensure treatment effectiveness while minimizing collateral damage from antibiotic use, including adverse effects, resistance, and selection for resistant pathogens such as *C. difficile*. While AMS has been minimally employed in ambulatory settings, the ambulatory setting accounts for the majority of antibiotic use. The JC developed an ambulatory AMS standard with five individual requirements to promote evidence-based antibiotic use and to promote patient safety and quality. These requirements can assist any ambulatory setting with AMS implementation.

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

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Assessment Questions

1. All of the following are reasons supporting why antimicrobial stewardship (AMS) is a patient quality and safety initiative, EXCEPT:
   a. Up to 50% of antibiotics in the ambulatory environment are inappropriate
   b. Antibiotics have been associated with adverse effects and other collateral damage, like C. difficile
   c. Antibiotics are a significant financial burden on health care organizations
   d. Antimicrobial resistance is a significant health risk and resistance is propagated by antibiotic use

2. Which practice setting must meet the Joint Commission's Ambulatory Antimicrobial Stewardship standard?
   a. All dental clinics where antibiotics are prescribed
   b. Ambulatory surgical centers
   c. Urgent care facilities currently accredited by the Joint Commission
   d. Only ambulatory care facilities that have an outpatient pharmacy within its building

3. Which of the following reasons supports the need to identify a leader for ambulatory antimicrobial stewardship?
   a. Establishing a leader ensures accountability and communication for antimicrobial stewardship
   b. There is an abundance of infectious diseases-trained practitioners in the ambulatory environment who could serve as leaders
   c. The leader will be the sole person responsible for conducting antimicrobial stewardship interventions
   d. All of the above

4. Which of the following data could be used to monitor the impact of the ambulatory antimicrobial stewardship program?
   a. Antibiotic utilization
   b. Guideline adherence
   c. Resistance development
   d. All of the above

5. Education is an important requirement for ambulatory antimicrobial stewardship. Which of the following statements about education is TRUE?
   a. Passive education is more effective than active education
   b. Education allows for consistent antibiotic use among prescribers
   c. Education is ineffective when paired with another intervention
   d. Education must be developed by the organization; external resources cannot be used

6. Which of the following national organizations have publicly-available stewardship resources available for ambulatory antimicrobial stewardship?
   a. Centers for Disease Control and Prevention
   b. Society for Healthcare Epidemiology of America
   c. National Antibiotics Society
   d. Antimicrobial Stewardship Taskforce

7. Based on published literature, what disease states could be targets for ambulatory antimicrobial stewardship interventions?
   a. Upper respiratory infections
   b. Urinary tract infections
   c. Skin and soft tissue infections
   d. All of the above

8. Which of the following is an example of how AMS can optimize quality of care?
   a. Ensuring antibiotics are prescribed according to guidelines
   b. Monitoring antibiotic costs
   c. Recommending the newest antibiotics for treatment
   d. Requiring leader approval of antibiotic use

9. **True or False:** AMS functions to optimize patient safety by ensuring appropriate antibiotic use when necessary to minimize adverse effects
   a. True
   b. False

10. All of the following resources can be used to develop an ambulatory antimicrobial stewardship goal EXCEPT:
    a. Internal organizational data
    b. Leader preference
    c. Antibiogram data
    d. Published literature

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.

14. 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.

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

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

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

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

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

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

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Original Work

Pharmacist-Led Inhaler Training for Nurses

by Shih-Ting (Tina) Cheng, PharmD, Andy Starzinski, PharmD, BCACP, Emma Stoflet, PharmD, BCPS, Melissa Mikelson, RN, Sara Griesbach, PharmD, BCPS, BCACP

Abstract

Objective: To evaluate inhaler technique and confidence level in registered nurses educating patients on inhaler use after a pharmacist-led training session.

Methods: Educational handouts for nurses were developed and reviewed for the 13 types of inhaler devices currently prescribed within the Marshfield Clinic Health System (MCHS). After assessing baseline inhaler technique and confidence via scoring rubric and questionnaire, respectively, for four of the most prescribed devices out of 13, a live, pharmacist-led inhaler training session with PowerPoint slides and demonstrations was offered to the nurses with the option to listen online concurrently. Inhaler technique and confidence level were re-assessed after the training session. The confidence level and average scores of techniques among participants were compared before and after training to determine whether the training session was beneficial.

Results: A total of six nurses participated in this project. The percentages of inhaler steps correctly performed prior to the training session ranged from 30%–50% at baseline and increased to over 90% for all four devices after training. Nurses who attended the session online concurrently due to scheduling conflicts had slightly lower post-training scores compared to nurses who attended in person. Confidence level ranged from "not confident" to "extremely confident" before training and from "very confident" to "extremely confident" after training.

Conclusions: A pharmacist-led training session focused on four common inhaler devices enhanced nurses' inhaler technique and increased their confidence level in using and training patients on these devices. Possible clinical implications include increased quality of care delivery to patients and subsequently decreased disease burden on patients with chronic respiratory conditions requiring inhaled medications.

Inhaled medications for acute episodes and chronic symptom management are common regimens for respiratory diseases. However, because of their various delivery mechanisms, inhalers can be challenging to use. Many inhaler designs have different methods of priming, dose preparation, inhalation instructions, and maintenance. This makes inhaler technique potentially challenging for patients. According to the 2020 Global Initiative for Chronic Lung Disease (GOLD) guidelines, greater than two-thirds of patients diagnosed with chronic obstructive pulmonary disease (COPD) make at least one mistake while using their inhalers.[1] Lavorini and colleagues also found that up to 94% of patients diagnosed with asthma and COPD do not use inhalers correctly, leading to decreased medication efficacy.[2] Furthermore, Vanoverschelde and colleagues determined there is a four-fold increase in exacerbation risk if inhalers are not used correctly.[3] In order to maximize the benefits of these medications and decrease the risk of future exacerbations, proper inhaler technique is crucial.

Patient education on inhaler use has demonstrable benefits in reducing exacerbation rate. According to a meta-analysis by Maricoto et al., a statistically significant decrease in exacerbation risk was noted in elderly patients after they received a patient education intervention (risk ratio = 0.71).[4] Nurse-driven education has been proven to increase patients' knowledge of and adherence to inhalers, and in-person training has been shown to be the most effective way of improving inhaler techniques compared to watching videos or reading pamphlets.[5,6] Unfortunately, not all health care professionals are familiar with proper inhaler technique for the various devices currently on the market. Self and colleagues evaluated nurses' use of a metered-dose inhaler plus spacer and found that only 66% of participants performed the steps correctly which increased to 88% correct after a pharmacist demonstration.[7] Similarly, assessment of health care professionals' inhaler technique revealed that only half of the administration steps for dry power inhalers were performed correctly.[8] Furthermore, health care professionals who attended training sessions on inhaler use had consistently better performance with these devices compared to non-participants. These results demonstrate a need for inhaler technique education for practitioners as well as patients.

At Marshfield Clinic Health System (MCHS), transition-of-care registered nurses visit patients admitted for disease states associated with high readmission rates (e.g., COPD exacerbation) in person

TABLE 1. Average Percentage of Steps Correctly Completed Pre- and Post-Training (N = 6)

	Metered-Dose Inhaler (MDI)	*Diskus®*	*Handihaler®*	*Respimat®*
Total Number of Steps for Each Inhaler	**8**	**7**	**9**	**7**
Steps Completed Correctly				
Pre-training (%)	54.2	50	48.1	31
Post-training (%)	93.8	95.2	96.3	92.9
Post-training score for participants attending session in-person (n=4)	97	100	100	100
Post-training score for participants attending session online (n=2)	87.5	85.7	88.9	78.6

prior to discharge and via phone a few days after discharge. These nurses are the first line of contact for these patients after discharge and provide education to prevent 30-day readmissions. To enhance nurse education of patients with COPD, asthma, and other chronic respiratory conditions, the authors developed and implemented a pharmacist-led staff training session focused on inhaler techniques.

Methods

Design

This project was designed as a before-and-after in-person evaluation of inhaler techniques and confidence of nurses after a live, pharmacist-led training session. Outcomes were the percentages of inhaler steps correctly performed and the confidence level of nurses in using the devices and training patients to use the different devices. The project was deemed exempt from review by the Institutional Review Board.

Development of Training Materials for Nurses

Educational handouts intended to aid in the training session for nurses were developed for the 13 devices currently used by MCHS. Information sources for the handouts included inhaler package inserts and patient education leaflets developed by MCHS respiratory therapists. Each handout included the device name, brand names, priming techniques, steps for inhalation technique, cleaning recommendations, storage requirements, device expiration, and reminder tips. Assessment questions were also provided for each step of the inhalation process for ease of discussing technique over the phone with patients if needed. The handouts were reviewed by two co-investigators and given to the nurses during the training session.

Development of Assessments

Out of the 13 inhalers mentioned above, the top four devices used at MCHS were selected for in-depth teaching and assessment. They were the metered-dose inhaler (MDI), Diskus®, Handihaler®, and Respimat®.

To evaluate nurse confidence level in using inhalers and training patients on device use, a 5-point Likert scale questionnaire, which ranges from 1 ("not confident") to 5 ("extremely confident"), was created for each inhaler type. Because understanding the educational material does not necessarily reflect an individual's ability to teach others the same material, the questionnaire was designed for self-assessment as well as for patient assessment.

To facilitate technique scoring, the administration steps from the educational handouts mentioned previously were taken directly to make a scoring rubric (Supplement 1).[9] If one step was performed completely correctly, 1 point was given. If anything was missed in a step, 0 points were given without the option of a partial point. The total score received for each inhaler type was then divided by the total number of steps to get the percentage of steps correctly performed.

To ensure scoring accuracy, a mock technique walk-through was conducted with a pharmacist (who was independent from the project) prior to nurse assessment. During this mock assessment, the independent pharmacist demonstrated the inhaler techniques while both the lead investigator and co-investigator scored the demonstration and noted any omissions or points for clarification in the training materials and corresponding assessment. The pharmacists then compared their assessments and notes. Variability in scoring was minimized by identifying and addressing different scenarios that could occur and determining how these scenarios would be scored according to the rubric.

Baseline Assessment

One week before the training session, baseline confidence level and inhaler technique for the four most common inhaler devices were assessed in person for all six nurse participants. The nurses were first asked to fill out the questionnaires. Then, the primary investigator evaluated inhaler technique for the four main types of inhaler devices prescribed by providers by watching the nurses use the demonstration inhalers in person and scoring those demonstrations against the scoring rubric. The co-investigator was also present for observation.

Nurse Training Session

A live, pharmacist-led inhaler training session was offered to the nurses with the option to listen online at the same time. PowerPoint slides, handouts, and inhaler demonstrations were used throughout the training. The session started with a

TABLE 2. Confidence Level of Nurses in Using Inhalers Pre- and Post-Training (N=6)

Pre-training Confidence Level Per Inhaler Type				
	Metered Dose Inhaler n (%)	*Diskus® n (%)*	*Handihaler® n (%)*	*Respimat® n (%)*
Extremely confident	1 (16.7)	1 (16.7)	1 (16.7)	0 (0.0)
Very confident	3 (50.0)	4 (66.7)	3 (50.0)	2 (33.3)
Somewhat confident	1 (16.7)	0 (0.0)	1 (16.7)	1 (16.7)
Slightly confident	1 (16.7)	0 (0.0)	0 (0.0)	1 (16.7)
Not confident	0 (0.0)	1 (16.7)	1 (16.7)	2 (33.3)
Post-training Confidence Level Per Inhaler Type				
	Metered Dose Inhaler n (%)	*Diskus® n (%)*	*Handihaler® n (%)*	*Respimat® n (%)*
Extremely confident	4 (66.7)	4 (66.7)	4 (66.7)	2 (33.3)
Very confident	2 (33.3)	2 (33.3)	2 (33.3)	4 (66.7)
Somewhat confident	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Slightly confident	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Not confident	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)

Note: Percentages do not add up to 100% due to rounding error.

brief overview of COPD disease state, pharmacotherapy categories, and device options. Following this review, an in-depth 15-minute presentation was given on the four devices, which included a comparison of the individual devices and demonstration of administration steps with placebo devices. All participants who attended in person were also given demonstration inhalers to follow along. The total training lasted approximately 40 minutes.

Post-Assessment

Nurse confidence levels and inhaler technique were reassessed in person immediately after the training session for participants who attended in person. Participants who listened online were assessed a week after the training due to scheduling conflicts. Nurses who did not reach 100% competence on inhaler technique were re-educated on the steps missed right after the first attempt and immediately reassessed until 100% was achieved. The confidence levels and average score of technique from the first attempt were compared to the ones before training to determine whether the training session was beneficial. The scores of subsequent technique reassessments were not compared nor reported.

Results

Six transition-of-care nurses participated in the training session. Due to scheduling conflicts, two of the six participants attended the training session online without access to demonstration inhalers.

For each inhaler device, the average of the six nurses' scores was calculated for both the pre- and post-assessment. The average percentages of inhaler steps correctly performed among nurses prior to the training session ranged from 30% to 50% at baseline and increased to over 90% for all four devices after training (Table 1). Nurses who attended the session online had slightly lower post-training scores on average compared to nurses who attended in person. All four nurses who did not get 100% during the first post-training assessment were able to reach 100% on the second attempt after re-education. The most commonly missed steps for each device during the post-assessment were "sit up straight or stand up" for MDI, "hold the device in a level, horizontal position" for Diskus®, "listening for the capsule to vibrate or rattle" for Handihaler®, and "point inhaler towards the back of your throat" for Respimat®.

The confidence level of using and teaching inhaler technique pre- versus post-training in nurses is shown in Tables 2 and 3. Prior to training, answers ranged from "not confident" to "extremely confident." After training, responses ranged from "very confident" to "extremely confident." Though confidence level improved for all inhaler classes post-training, nurses were not as confident using or educating patients on the Handihaler® and Respimat® inhalers versus the MDI and Diskus® inhalers.

Discussion

Although it is known that technique is crucial in using inhalers, most studies to date have focused on evaluating patients' skills and describing how inhaler technique influences medication adherence and readmission rates.[2-4] There is currently limited literature describing health care professionals' inhaler techniques

and determining how this knowledge may impact patient care.[7,8] This study demonstrated that providing an in-person, pharmacist-led training session to transition-of-care nurses improved their inhaler technique and enhanced their confidence level in educating patients on the proper use of inhaler devices and medications. These results correspond to the findings of Self et al. and Basheti et al. and support the provision of in-person inhaler training sessions for health care professionals who provide care to patients with respiratory conditions.[7,8]

Review of post-assessment scores indicated that the most missed steps for each inhaler were actions that do not require direct manipulation of the devices. Rather, these were steps involving positioning the inhaler or body for the MDI, Diskus®, and Respimat® devices or listening for sounds for the Handihaler® device. These steps could be easily missed by users if they are not verbally emphasized by the demonstrator. Re-educating health care professionals may remind them to highlight these steps to patients.

We speculate the slightly lower confidence level of nurses in using and training patients on the Handihaler® and Respimat® devices after training may be due to these being newer devices or having more complicated steps, or that using the device itself is not as self-explanatory as other inhaler devices. Some nurses commented that they had never seen a Respimat® device before. However, overall, the nurses' technique and confidence level increased for all devices after the training session. This finding reinforces the importance of educating health care professionals on inhaler technique, especially for newer devices.

Though the average of first attempt post-training scores was slightly lower for participants who attended the online session, improvements were seen in the percentage of steps completed successfully, regardless of training format. Due to small sample size, it is unclear whether this difference was caused by a lack of access to demonstration inhalers for the online attendees. Since there was a delay in the post-training assessment of online trainees, it is also possible the scores differed due to recall bias and skills attrition. Nevertheless, there was no difference between the two groups in their confidence level in using and training patients on these devices.

TABLE 3. Confidence Level of Nurses in Teaching Patients to Use Inhalers Pre- and Post-Training

Pre-training				
	Metered-Dose Inhaler	*Diskus®*	*Handihaler®*	*Respimat®*
Extremely confident	1	1	1	0
Very confident	3	4	3	2
Somewhat confident	1	0	1	1
Slightly confident	1	0	0	1
Not confident	0	1	1	2
Post-training				
	Metered-Dose Inhaler	*Diskus®*	*Handihaler®*	*Respimat®*
Extremely confident	4	4	3	2
Very confident	2	2	3	4
Somewhat confident	0	0	0	0
Slightly confident	0	0	0	0
Not confident	0	0	0	0

Aside from differences in post-training assessments for in-person and online participants, a major limitation of this project is its small sample size. By providing this training to transition-of-care nurses only, our pre- and post-training dataset is limited to six nurses. This approach limits the generalizability of our findings and could lead to potential bias due to the Hawthorne effect. Further bias might have been introduced by the limited number of evaluators.

Due to time constraints, one co-investigator, who was present at the mock technique walk-through, also helped evaluate two nurses for the post-training assessments. Although this might cause slight variation in scoring, variability was minimized by discussing the rubric during the mock assessment walk-through and reviewing the results of the post-training assessments immediately after the assessment. Using a standardized scoring metric for pre- and post-training assessments ensured consistency among evaluators and assessments performed at different times. Future directions for this project might include re-educating and reassessing the participants' technique and confidence level at least one year post-training to evaluate skill retention. Providing additional training may help reinforce the commonly missed steps in administration, introduce nurses to new devices on the market, and facilitate skill retention. Expanding the training session to include other health care professionals would further increase our sample size and permit adequately powered statistical comparisons of pre- and post-training datasets and identify differences in pre- and post-training performance between in-person and online participants to determine which setting maximizes knowledge acquisition.

Conclusion

Pharmacist-led training sessions for nurses improves nurses' inhaler technique and enhances their knowledge and confidence level with using and educating patients about these devices. Improved nurse knowledge of inhaler use may in turn lead to improvements in patient education, inhaler technique, and medication adherence with the goal of reducing respiratory exacerbations and improving

patient quality of life.

Shih-Ting (Tina) Cheng has completed her PGY1 pharmacy residency. Andy Starzinski and Emma Stoflet are Clinical Pharmacists at Marshfield Clinic Health System in Marshfield, WI. Melissa Mikelson is the Director of Care Management for the Institute for Quality, Innovation, and Patient Safety at Marshfield Clinic Health System in Marshfield, WI. Sara Griesbach is the PGY1 Pharmacy Residency Program Director and Director of Clinical Pharmacy Services at Marshfield Clinic Health System in Marshfield, WI.

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Shih-Ting Cheng 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.

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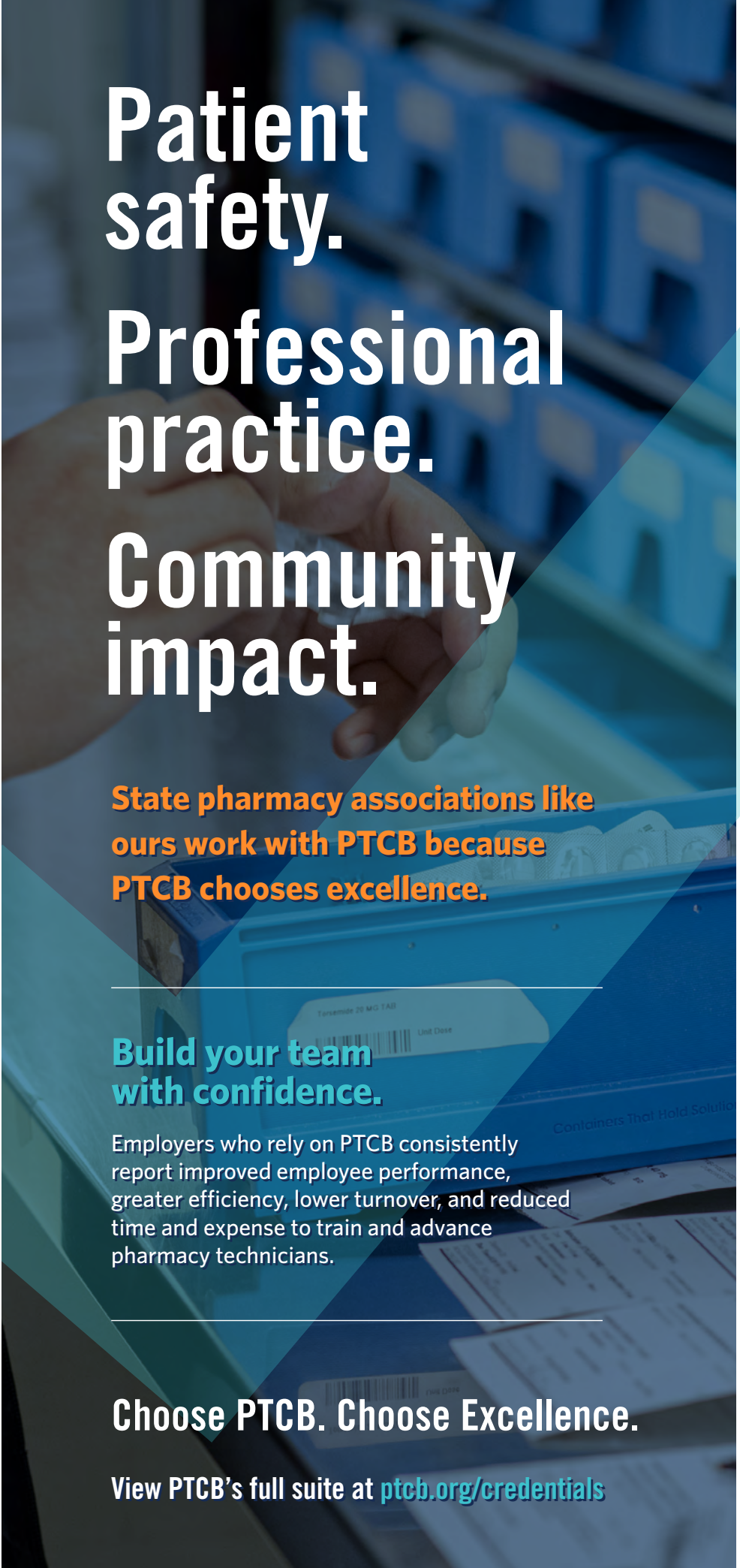
Supplement 1

Inhaler Technique Scoring Rubric

Metered-Dose Inhaler (MDI)	*Score (0 for a step performed incorrectly and 1 for a step performed correctly)*
1. Remove the cap from the inhaler mouthpiece. (Steps 1 & 2 can be switched.)	
2. Shake the canister well before each use.	
3. Sit up straight or stand up.	
4. Hold the inhaler upright, and exhale normally.	
5. Place the mouthpiece between your lips with lips sealed.	
6. Begin to inhale slowly. While breathing in **slowly and deeply** through your mouth, discharge one puff from the inhaler. Continue to inhale slowly for 3 to 5 seconds.	
7. Hold your breath for 10 seconds.	
8. Exhale slowly, away from the inhaler.	



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Original Work

The Impact of a Pharmacist Driven Intervention on Appropriate Statin Prescribing in Patients Living with HIV: A Population Health Perspective

by Kelsey K Phipps, PharmD, AAHIVP, Nicholas Olson, PharmD, AAHIVP, BCACP, Nicole Lentz, PharmD, BCACP, AAHIVP

The AIDS Resource Center of Wisconsin (ARCW), re-branded as Vivent Health, is a National Committee for Quality Assurance (NCQA) level 3-recognized patient-centered medical home. The patient-centered medical home is a model of care that encompasses five functions and attributes: comprehensive care; patient-centered care; coordinated care; accessible services; and quality and safety. Within Vivent Health, the clinical pharmacy team manages chronic diseases for patients living with HIV under collaborative practice agreements in a primary care clinic-based setting. These services currently include the management of hypertension, diabetes mellitus type 2, anticoagulation, and tobacco cessation. Notably, at the time of this study, initiation and management of HMG-CoA reductase inhibitor (statin therapy) was not currently included in the pharmacist scope of practice at Vivent Health.

Pharmacist participation in the multidisciplinary team has led to improved adherence and medical outcomes for patients.[1] Additionally, there is data to support a pharmacist's role in improving statin prescribing patterns in the outpatient setting. One study demonstrated a significant gap closure in statin therapy in patients with diabetes after community pharmacist-to-prescriber intervention.[2]

Abstract

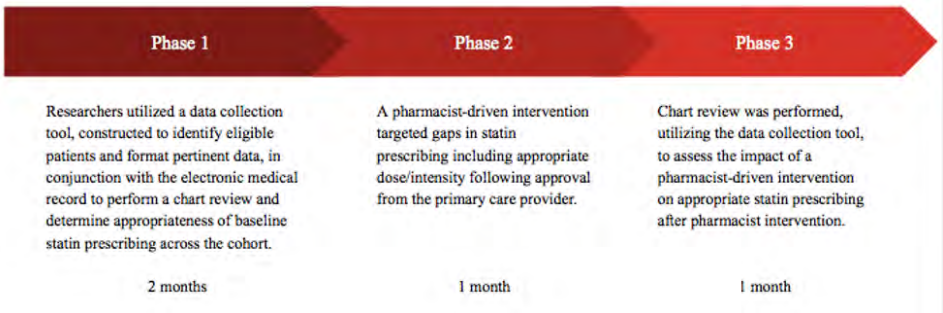
Background: Within ARCW (re-branded as Vivent Health), the pharmacy team manages conditions for patients via collaborative practice agreements. The aim of this study is to evaluate the impact of a pharmacist-driven statin management protocol for patients living with HIV.

Methods: This study occurred over 5 months across Vivent Health's four Wisconsin-based medical clinics. Eligible patients were > 21 years old, HIV+, and eligible for statin therapy based on 2013 ACC/AHA guidelines. In phase one, researchers used a data collection tool in conjunction with the electronic medical record (Epic) to perform a chart review and determine appropriateness of baseline statin prescribing. In phase two, a pharmacist-driven intervention targeted gaps in statin prescribing. Finally, chart review was performed to assess the impact of a pharmacist-driven intervention on appropriate statin prescribing.

Results: Of the 1,600 patients considered, 554 individuals met inclusion criteria. Only 66% of patients eligible for statin therapy were prescribed a statin at baseline (349/554). Twenty-seven (7.7%) of the patients receiving statin therapy were flagged for recommendation of a dose adjustment. Providers were agreeable to initiate or adjust therapy in 111 of the 214 eligible patients. Following the intervention, 72% of patients were prescribed guideline-recommended statin therapy (401/554) ($p < 0.05$).

Conclusion: Improvement in rates of appropriate statin prescribing in patients living with HIV was demonstrated via a pharmacist-driven intervention. The results of this study could be used to further support pharmacist involvement on multidisciplinary teams by demonstrating improvement in quality and clinical outcomes with pharmacist intervention.

FIGURE 1. Description of Phases and Study Progression



In this randomized control trial, patients who received medications from a large retail chain and had > 2 prescription fills for antidiabetic agents were identified within the Electronic Quality Improvement Platform for Plans and Pharmacies (EQuIPP). Primary care prescribers of patients were contacted by pharmacist via phone and fax to obtain a prescription for an appropriate statin. The number of statins prescribed was statistically significant between the intervention and control groups.[2]

Due to the advancement of effective antiretroviral treatment regimens (ART), the population of people living with HIV is aging and subsequently requires more ongoing management of chronic diseases. In 2017, the majority of people living with HIV in Wisconsin were over 50 years old.[3] Additionally, people living with HIV are twice as likely to develop cardiovascular disease (CVD) as their HIV-negative counterparts, underscoring the importance of cardiovascular prevention strategies. The underlying mechanism driving increased CVD risk is not clear, but likely involves a combination of factors, including the proinflammatory effects of the virus itself; side effects of ART including progressive atherosclerosis and elevated triglycerides; and the burden of traditional risk factors for cardiovascular disease, such as smoking, gender, and age.[4,5] Furthermore, HIV infection is being studied as an independent risk factor for CVD that might require earlier and more aggressive prevention interventions. There is a trial underway, titled "Evaluating the Use of Pitavastatin to Reduce the Risk of Cardiovascular Disease in HIV-Infected Adults (REPRIEVE)," to assess the impact of pitavastatin use on coronary outcomes in patients with HIV.[6]

Based on the 2013 ACC/AHA guidelines, patients with a history of clinical atherosclerotic cardiovascular disease (ASCVD); those diagnosed with diabetes mellitus type 2 (DMII); those with an LDL > 190; and/or those with a 10-year calculated ASCVD risk of > 7.5% should be prescribed statin therapy.[7] The 2019 update to the ACC/AHA Primary Prevention of CVD Guideline identified these same benefit groups, but described HIV diagnosis as an additional risk factor for statin initiation.[8,9]

A statin management protocol implemented by a pharmacist as a population health measure in a clinic-based setting is a novel idea published in the literature. The aim of this study was to evaluate the impact of a pharmacist-driven statin management intervention in people living with HIV. It was hypothesized that a higher proportion of patients would be prescribed appropriate statin therapy after pharmacist intervention.

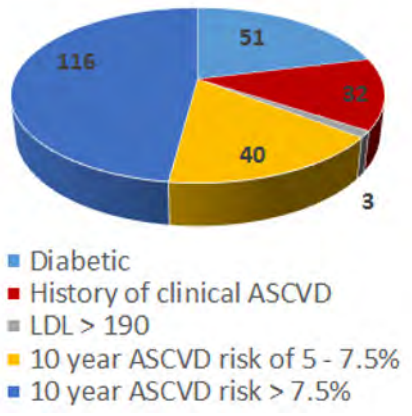
Methods

This self-control, single centered study occurred over four months, January through April 2019, across Vivent Health's four Wisconsin-based medical clinics. A data collection tool was created in conjunction with the electronic health record (Epic) to identify patients eligible for statin initiation. Data collected included the presence of statin indication, statin prescribed, and potential interacting agents (Supplement, Table 1).

Eligible patients were those over 21 years of age, living with HIV, and with an indication for statin therapy based on 2013 ACC/AHA guidelines. Patients were included in the cohort based on at least one of the following: calculated 10-year ASCVD risk > 5%, history of clinical ASCVD based on ICD-10 codes documented in the electronic health record, DMII documented in problem list, or most recent LDL > 190 based on most recent date of collection (Supplement, Table 2). At the time of project protocol and data collection tool creation (October 2018), 2013 guidelines were the newest and most widely accepted update in the literature. An ASCVD risk of > 5% was chosen based on a risk-benefit discussion recommended at this threshold, outlined in the ACC/AHA guidelines in addition to HIV infection identified as a complicating risk factor. Patients were excluded if they were being seen for pre-exposure prophylaxis (PrEP); had a contraindication to statin therapy, including history of rhabdomyolysis; or had advanced renal failure (Supplement, Table 3). The Institutional Review Board approved the study for exemption via Concordia University Wisconsin and required no oversight.

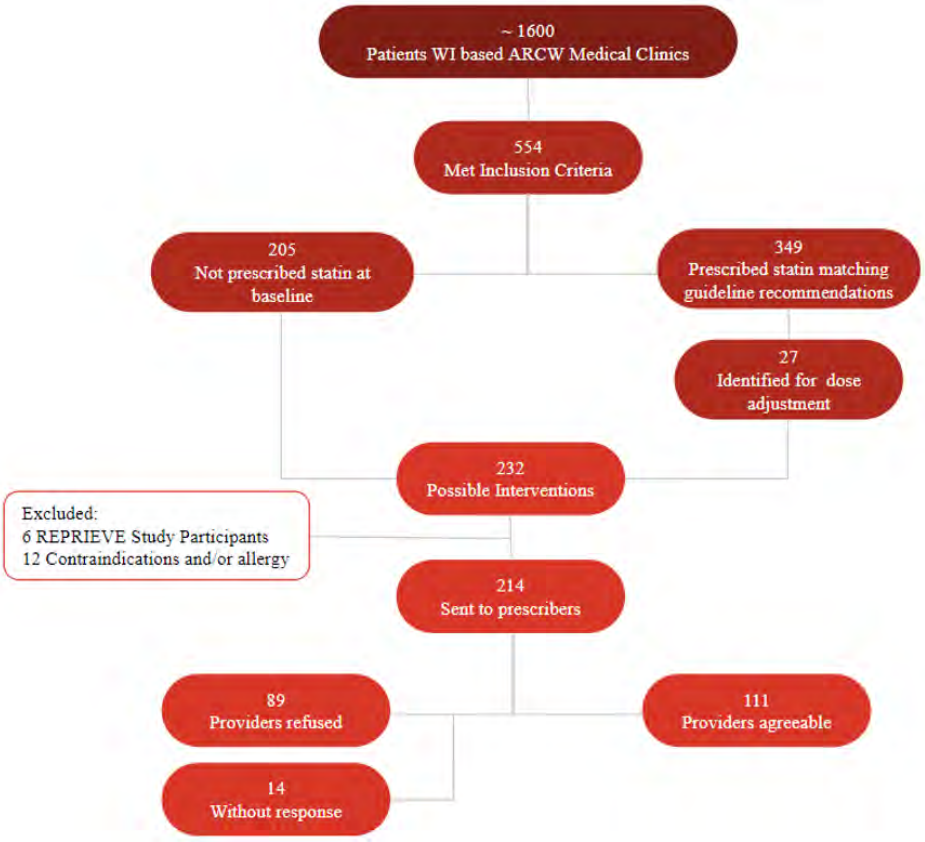
In phase one, researchers used the data collection tool to perform a chart review and determine the appropriateness of statin prescribing at baseline. In phase two, a pharmacist-driven intervention targeted gaps in statin prescribing following approval of the primary care providers. Researchers contacted primary care providers electronically with the pre-approved protocol and a corresponding list of patients under their care who could benefit from initiation or adjustment of statin therapy (Supplement, Figure 1). In phase three, researchers performed chart

FIGURE 2. Indication for Initiation of Statin Therapy for Eligible Patients not Prescribed a Statin at Baseline



ASCVD = Atherosclerotic Cardiovascular Disease

FIGURE 3. Patient Flow Diagram



REPRIEVE = Randomized Trial to Prevent Vascular Events in HIV

review to assess the impact of a pharmacist-driven intervention on appropriate statin prescribing compared to baseline (Figure 1). The baseline cohort was frozen at the beginning of the study to reflect the same group patients following the targeted intervention for a per protocol analysis. A chi-squared test was used.

The primary objective of this study was to determine the impact on the number of patients prescribed guideline-recommended statin therapy after pharmacist intervention. The secondary objective was to determine whether there was a cost benefit to Vivent Health, based on script capture in the dispensing outpatient pharmacy and improvement in Star Ratings, a Medicare assessment of performance and quality that impacts reimbursement.

Results

Of the 1,600 patients reviewed, 554 were eligible for statin therapy. Sixty-three percent were prescribed a statin at baseline (349/554). Patients with a calculated 10-year ASCVD risk score of > 7.5% made up the largest cohort of patients not prescribed a statin at baseline; patients with an LDL > 190 accounted for the smallest cohort (Figure 2). Twenty-seven patients already prescribed statin therapy were identified as potentially benefiting from a dose adjustment (7.7%). All medication dose changes were associated with a drug-drug interaction between statins and ART.[9] Of the 232 possible interventions (205 not on a statin and 27 dose adjustments), 214 advanced to phase two of the study. There were six exclusions for trial enrollment (REPRIEVE) and 12 subjects with allergy and/or contraindication (Figure 3).

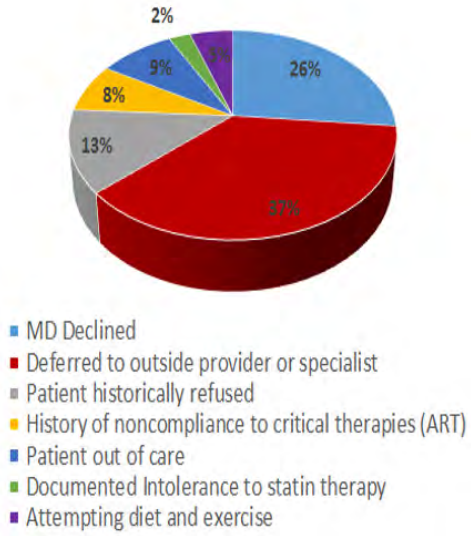
Providers were agreeable to initiate or adjust statin therapy in 111/214 patients (52%); 14 did not respond. The major reasons for refusal were most often a lack of provider-pharmacist relationship, and the patient receiving primary care and/or being seen by a specialist at an outside institution (Figure 4). After pharmacist intervention, 401/554 (72%) of eligible patients were prescribed statin therapy, a 9% increase from baseline accounting for 52 additional patients ($p < 0.05$).

Star Ratings associated with Vivent Health's outpatient pharmacy also showed improvement. Data collected from Prescribe Wellness showed that 89.6% of patients were 80% or more adherent to their statins at baseline. (Prescribe Wellness is a cooperation with over 10,000 community pharmacies whose role is to enhance patient medication adherence and outcomes through payor and refill data monitoring.) Following pharmacist-led intervention, 91% of patients were 80% or more adherent to their statins, suggesting that the majority of patients prescribed statin therapy had received the original prescription. The overall star rating improved from 3.2 to 5.0 over 5 months during the study interval.

Discussion

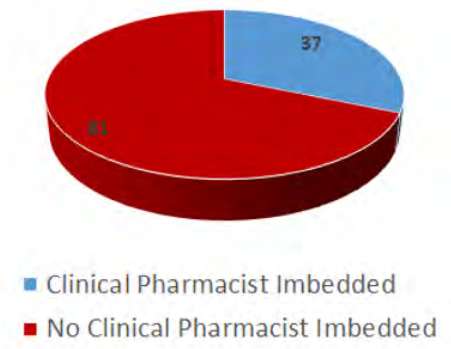
Improvement in rates of appropriate statin prescribing in patients living with HIV is possible via a pharmacist-driven statin management protocol. Patients receiving primary care management from an outside provider or cardiologist was the most common documented reason for refusal of statin initiation by providers. Patients at Vivent Health have the option to be seen for HIV care only, or HIV in

FIGURE 4. Documented Reason for Refusal of Statin therapy Initiation in Eligible Patients Provided by Primary Care Provider



ART = Antiretroviral therapy

FIGURE 5. Proportion of Provider Responses That Were Refused or Without Response Based on Presence of Clinical Pharmacist



addition to primary care management. For those being seen for HIV care only, there is a need for improved medication reconciliation and/or communication for best practice recommendations with outside providers and specialists moving forward.

Another large barrier to statin initiation was lack of routine pharmacist-provider relationship. Two of Vivent Health's campuses have a clinical pharmacist team imbedded in the care team, who has direct interaction with primary care and infectious disease providers on a regular basis. Two clinics do not have a pharmacist who has regular, in-person engagement with the clinical pharmacy team. Proportionally, the majority of refusals came from sites without a clinical pharmacist imbedded (Figure 5). This discrepancy demonstrates that a multidisciplinary team approach can improve patient outcomes and access to care.

Limitations of this analysis include the electronic health record-generated 10-year ASCVD risk score. An under-reported risk is possible due to missing components in the electronic health record, such as LDL. In addition, scores could change over the course of the study, with fluctuations in metrics like blood pressure control and smoking status.

The results of this study could be used to support pharmacists in other ambulatory care and population health settings, increasing their utility and promoting collaborative care by demonstrating improvement in outcomes with pharmacist intervention, including quality metrics.

Population health is an emerging role for clinical pharmacists, in addition to the more prevalent face-to-face ambulatory care services.

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

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Supplemental

TABLE 1. Data Included in Data Collection Tool and Retrieved from Electronic Health Record

Medical Record Number	Patient name	Date of Birth	Age
Gender	Race	Y/N clinical ASCVD	LDL for those > 190
Y/N diagnosis of diabetes	ASCVD Risk for those > 5%	Statin currently active in medication list*	Kinetic booster currently active in medication list**
Y/N allergy documented	Y/N contraindication documented	Smoking status	Most recent blood pressure
Vivent Health clinic location	Name of primary care provider	Name of preferred pharmacy	

Medication codes identified in the electronic health record:
**Statins: 1153*
***Kinetic boosters: 574877, 582702, 583084, 583821, 588222, 596867, 166359, 164471, 583457, 586387, 593789, 176935, 225256, 475556, 553459, 560479, 591300*
ASCVD: atherosclerotic cardiovascular disease; LDL: low-density lipoprotein

TABLE 2. ICD - 10 Codes for Clinical Atherosclerotic Cardiovascular Disease (ASCVD)

I20	Angina
I21.9	Acute MI, unspecified
I24.8-9	Acute IHD, unspecified
I25.10	Chronic IHD, unspecified
I25.2	Old MI
I25.8	Other forms of chronic IHD
I25.82	Chronic total occlusion of coronary artery
I25.84	Coronary atherosclerosis
I65.xx	Precerebral artery stenosis or occlusion (includes CA stenosis)
I66.xx	Cerebral artery stenosis or occlusion (includes strokes)
I67.89	Other cerebrovascular disease
I70.xx	Atherosclerotic PAD
I71	Peripheral aortic aneurysm and dissection
I73.9	Other PVD, unspecified
I74.x	Arterial embolism/thrombosis
I75	Atheroembolism
Z95.1, Z98.61	S/PCABGand S/PPTCA/PCI

CA = Carotid Artery; IHD = Ischemic heart disease; MI = Myocardial infarction; PAD = Peripheral artery disease; PVD = Peripheral vascular disease;

TABLE 3. Exclusions for statin initiation ICD-10 Codes

M62.82	Rhabdomyolysis
N17	Acute renal failure
N18.5	End stage renal disease (CKD stage V)
N19	Renal failure unspecified

CKD = Chronic Kidney Diseases

Supplemental Cont.

FIGURE 1. Communication/Protocol Electronically Sent to Providers

"Good Afternoon (Medical Provider),

With much time and assistance, I am excited to have designed a tool to help identify patients eligible for statin therapy based on ACC/AHA guidelines. We pulled data from EPIC to determine patients who may be eligible for statin initiation or adjustment. The patient's charts were then reviewed for appropriateness of therapy including dose/intensity.

1. A list of patients that could benefit from statin initiation or dose adjustment will be provided directly to the documented primary care physician (PCP) for the opportunity to review.
2. Following PCP review, the clinical pharmacy team will reach out to approved patients to discuss risk vs benefit of statin initiation or adjustment.
   a. Patient education to include:
      i. Indication: cardiovascular protection
      ii. Administration: once at same time each day, with or without food, etc
      iii. Adverse effects -
         1. Common: diarrhea, stomach upset, cold symptoms
         2. Serious: muscle/joint pain; contact doctor
         3. Review s/sx of allergy; seek emergency attention
      iv. Interactions:
         1. avoid grapefruit juice
         2. make ARCW provider aware of any new or change to medication
3. If agreed upon by the patient, a prescription order will be placed with the patients preferred pharmacy for a 90-day supply. Education will be provided and documented.
4. Ongoing fills will be managed and approved at the discretion of the PCP.
   The provider could consider assessing a fasting lipid panel (FLP) 3 months after initiation or adjustment, then once every 3 - 12 months thereafter.

I am hopeful this collaboration will aid in our joint effort to provide our patients with continued increased quality and access to care.

Please see the list of patients under your care who may benefit from statin initiation or dose adjustment attached."

Review Article

The Impacts of Pharmacist-Prescribed Hormonal Contraception in the Medicaid Population

by Amanda Yang, 2021 Doctor of Pharmacy and MPH Candidate

Question:

What is the impact of policy allowing pharmacists to independently prescribe hormonal contraception in the Medicaid population?

In 2016, Oregon became the first state to pass legislation allowing pharmacists to prescribe hormonal contraception without a collaborative practice agreement, opening the door to increased access of hormonal contraception.[1] While there are many reasons to use hormonal contraception, decreasing unintended pregnancies by increasing access to contraception is a cost-effective priority for Medicaid.[2] With Medicaid policies differing between states, there is not a lot of information on the impacts of pharmacist-prescribed hormonal contraception in Medicaid populations. Currently, Oregon is the only state with studies that discuss the impacts of pharmacist-prescribed hormonal contraception on reducing unintended pregnancies and cost savings in the Medicaid population.

Across the United States, approximately 90% of individuals live within five miles of a community pharmacy.[3] Community pharmacies are often among the most accessible places for health care, because they have more locations available, have extended hours in the evening and on weekends, and in many cases do not require an appointment for a pharmacist-provided service.[4] Preliminary data from the Oregon Medicaid population during the first two years of implementation has shown that 10% of new prescriptions for hormonal contraception were prescribed by pharmacists. Since 2016, 12 states and the District of Columbia have passed legislation that allows pharmacists to independently prescribe hormonal contraception.[5] In Wisconsin, AB304/SB286 was introduced in the 2019-2020 legislative session to expand access to hormonal contraception. Passage of this bill would allow Wisconsin pharmacists to prescribe hormonal contraception without a collaborative practice agreement.[6] During the Assembly session, legislators added an amendment to the bill that guaranteed Medicaid coverage and reimbursement for contraception prescribed by pharmacists.[7] While the bill has not been passed, guaranteed Medicaid coverage and reimbursement could incentivize pharmacists to provide the service, which would increase the number of locations where the Medicaid population could access hormonal contraception.

Pharmacists have a unique role where they have direct access to patients. In general, 65% of pharmacists have expressed interest in prescribing of hormonal contraception.[8] Pharmacists' stated reasons for wanting to prescribe hormonal contraception include: enjoying their one-on-one interactions with patients; expanding the scope of the pharmacist; providing a service for patients; assisting with public health efforts to improve reproductive health; and increasing patients' adherence to contraception use.[8,9] While many pharmacists would like to provide this service, the current lack of legislation is not the only barrier they might face. Lack of or low reimbursement rates for pharmacist-provided services continue to be a major barrier for implementing services across the United States. If pharmacist-prescribed hormonal contraception services are shown to be cost-effective in the Medicaid population, this could open the door for other payors and stakeholders to invest in further expansion of pharmacist-prescribed hormonal contraception.

Evidence Summary

A 2019 retrospective study used a decision-analytic model to review the effect of a new policy allowing pharmacists to prescribe hormonal contraception.[1] The primary outcome was unintended pregnancies, and secondary outcomes included costs and quality-adjusted life years (QALYs). There were 198,110 women included based on their risk of having an unintended pregnancy and their need to use Medicaid for family planning services. Data on women who were prescribed hormonal contraception were obtained from Oregon Medicaid claims data over a 24-month period after the policy was implemented. In addition to Medicaid claims data, data from literature was used to provide variables for multiple analyses with univariate and bivariate sensitivities and entered in a Monte Carlo simulation. The Monte Carlo simulation generated the probability of different outcomes based on the variables that were inputted. This allowed for simultaneous probability estimates. Univariate and multivariate sensitivity analyses were used to assess how the variation of one or more variables would impact the result.

The analysis found that 367 women out of 3,614 women who received hormonal contraception received it from a pharmacist.[1] The analysis estimated that having a pharmacist-prescribing policy prevented 51 unintended pregnancies, compared to if the policy had not been implemented. During the first two years, the Medicaid cost savings were estimated to be $1.6 million, and the quality of life for women would be 158 QALYs gained per 198,110 women. These results represent an economically dominant strategy indicating

that the intervention improved health outcomes and reduced health costs. Within the Monte Carlo simulation, the univariate analysis demonstrated that pharmacist-prescribed hormonal contraception decreased unintended pregnancies and costs. The multivariate analysis found that pharmacist-prescribed hormonal contraception was the dominant result, indicating it was the preferred outcome even when variables changed.

A strength of the study was that the authors ran 10,000 trials, using multiple variables, through a Monte Carlo simulation.[1] These variables included contraceptive continuation rates, cost of the pharmacist's time for service, and the cost of a provider's visit. This is a strength because it allowed for 10,000 different scenarios to occur simultaneously and predict the probability of how the different variables would impact unintended pregnancies, healthcare costs, and quality of life. The results suggest that pharmacist-prescribed hormonal contraception is a service being used by the Medicaid population, and is contributing to increased access to hormonal contraception and prevention of unintended pregnancies.

A weakness of the study is that the data was limited to the Oregon Medicaid population and only the first 24 months after the legislation was implemented.[1] Medicaid reimbursement varies from state to state, which limits the generalizability of this study to other Medicaid populations. With time, more pharmacies might implement the service and more women might use the service. Data from an extended time frame would provide stronger long-term evidence as to whether pharmacist-prescribed hormonal contraception makes a difference in reducing healthcare costs and preventing unintended pregnancies within the Medicaid population.

Recommendations from Others

In 2019, the American College of Obstetricians and Gynecologists (ACOG) updated its Committee Opinion on increasing access to over-the-counter hormonal contraception.[10] ACOG's recommendations do not have a grading system and are based on the expert opinions of members of the Committee on Gynecologic Practice. ACOG recommends pharmacist-prescribed hormonal contraception as a strategy to increase access to hormonal contraception. To ultimately decrease unintended pregnancies, ACOG recommends that hormonal contraception be available over the counter without any prescriptions or restrictions.

Evidence-Based Answer

A policy allowing pharmacists to independently prescribe hormonal contraception may be a cost-effective strategy to reduce unintended pregnancies among the Medicaid population. (Strength of recommendation = B based on limited evidence from a retrospective study with patient-oriented outcomes).

Amanda Yang is a 4th Year dual-degree Doctor of Pharmacy Candidate and Master of Public Health Student at the University of Wisconsin-Madison in Madison, WI. This clinical inquiry was written during her fourth-year pharmacy rotation at the Pharmacy Society of Wisconsin.

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

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Review Article

Beyond Dopamine and Tablets: Investigational and Newly Approved Antipsychotics for Treating Schizophrenia

by Kevin M. Bozymski, PharmD, BCPS, BCPP, Asia I. Mian, 2021 PharmD Candidate, Thomas Ringsred, 2021 PharmD Candidate, Eric Ripley, 2021 PharmD Candidate, Isabelle M. Sviatoslavsky, 2021 PharmD Candidate

Abstract

Objectives: To review the pharmacology, dosing/administration, efficacy, safety, and applicable costs of novel antipsychotics and formulations approved since 2018 or currently under investigation for the treatment of schizophrenia.

Methods: A PubMed search (2010 to November 2020) was conducted using the search terms schizophrenia, asenapine, evenamide, lumateperone, olanzapine, paliperidone, risperidone, roluperidone, samidorphan, ALKS 3831, HP-3070, ISM, ITI-007, LY03004, MIN-101, NW-3509, and PP6M. Additional data were obtained from references of identified articles, drug information databases, manufacturer product labeling and websites, and Clinicaltrials.gov.

Results: Two novel antipsychotic formulations have been approved (risperidone extended-release [ER] subcutaneous injection in July 2018, and asenapine transdermal patch in October 2019), with 2 risperidone ER intramuscular injections and 1 paliperidone ER intramuscular injection under investigation. One novel antipsychotic has been approved (lumateperone tosylate oral capsule in December 2019), with 3 additional drugs at least nearing phase 3 clinical trials: samidorphan (in combination with olanzapine to mitigate weight gain), roluperidone (for negative symptoms of schizophrenia), and evenamide (as an adjunctive agent for positive symptoms of schizophrenia).

Conclusions: As antipsychotic non-adherence increases risk of schizophrenia relapse, investigators have continued developing several novel molecules and non-oral formulations over the past few years that aim to solve existing efficacy gaps and minimize adverse effects. Due to the significant costs associated with these new treatments, pharmacists should be prepared to guide mental health professionals and educate patients on their efficacy, safety, and administration concerns relative to established antipsychotic treatments for schizophrenia.

Schizophrenia is a mental health disorder most often characterized by positive symptoms (such as auditory hallucinations, delusions, and disorganized speech and behavior) and negative symptoms (such as blunted affect, avolition, and anhedonia). While the lifetime prevalence is only estimated to be 0.3-0.7%, it is one of the top 15 causes of worldwide disability and increases premature mortality risk due to concurrent cardiometabolic disease.[1,2] Individuals are usually diagnosed in the second or third decade of life, leading to many years of clinical impairment and distress.

According to the 2019 American Psychiatric Association (APA) schizophrenia treatment guidelines, individuals diagnosed with schizophrenia should be started on an antipsychotic medication and continued thereafter, if observed improvements, to decrease the risk of relapse and hospitalization (evidence grade 1A).[3] Unfortunately, many individuals have poor adherence to antipsychotic medications. The National Institute of Mental Health (NIMH) sponsored Clinical Antipsychotic Trials of Intervention Effectiveness (CATIE) trial found that 74% of subjects (N=1061/1432) had discontinued their antipsychotic at 18 months, with 32% (N=340/1061) due to inefficacy and 20% (N=213/1061) due to intolerability.[4] Likewise, the European First Episode Schizophrenia Trial (EUFEST) of first-episode schizophrenia found that 41.6% of subjects (N=207/498) had discontinued

their antipsychotic for any cause at 12 months.[5] A meta-analysis of 1,154 total subjects from these two landmark trials found a statistically significant decrease in adherence that was associated with poorer insight, higher hostility, and increased substance use at six months.[6]

Due to the physical and psychosocial consequences of low medication adherence, research on novel antipsychotic drugs and non-oral formulations has greatly expanded over the past several years. Whereas antipsychotics to date have focused on dopamine D2 and serotonin 5-HT2A receptor antagonism, some molecules currently under investigation are exploring the glutamate system due to NMDA receptor antagonists being observed to cause psychotic symptoms.[7] Other researchers have been reformulating existing options into long-acting injectable antipsychotics (LAIAs), removing the need for daily oral administration. The APA guidelines recommend patients with a history of poor or uncertain adherence receive an LAIA (evidence grade 2B), as recent meta-analyses have found that LAIAs may reduce treatment discontinuation and hospitalization rate versus oral antipsychotics (though not necessarily relapse rates).[3,8,9] This article will review schizophrenia pharmacotherapies approved by the Food and Drug Administration (FDA) since 2018, along with molecules and formulations under investigation, using data from primary literature, governmental sources, manufacturer product labeling and websites, and Clinicaltrials.gov.

Novel Formulations

Long-Acting Injectable Antipsychotics

In July 2018, Indivior announced the FDA approval of a once-monthly, long-acting subcutaneous risperidone injection (Perseris™) for schizophrenia in adults.[10] This product is the first subcutaneous LAIA formulation available on the US market. Subcutaneous injections use a shorter and wider needle than intramuscular injections, which patients have been shown to prefer due to ease of administration.[11] Perseris™ is intended for patients who tolerate an oral risperidone dose of 3 or 4 mg/day, corresponding to a dose of 90 or 120 mg once monthly into the abdomen. It does not require oral risperidone overlap upon initiation like the existing intramuscular risperidone LAI (Risperdal Consta®), nor a loading dose like other available LAIAs.[12] The average wholesale price (AWP) of each subcutaneous injection ranges from $2,154.60 (90 mg) to $2,872.80 (120 mg), which is approximately 1.6-1.8 times the monthly cost of intramuscular risperidone LAI and 2.7 times the monthly cost of comparable oral risperidone tablet dosing.[13]

Nasser et al. conducted a phase 3, randomized, double-blind, placebo-controlled trial regarding the efficacy and safety of 90-mg and 120-mg doses of Perseris™.[14] Included subjects had a schizophrenia diagnosis according to the *Diagnostic and Statistical Manual of Mental Disorders* (DSM-5), had a schizophrenia exacerbation within the past 8 weeks, and would benefit from hospitalization. The primary endpoint was change in the total Positive and Negative Syndrome Scale (PANSS) score from baseline to day 56. A statistically significant least-squares mean difference (LSMD) was observed versus placebo for both 90 mg (-6.148, 95% CI [-9.982 to -2.314]; P = 0.0004) and 120 mg (-7.237, 95% CI [-11.045 to -3.429]; P < 0.0001). The most common adverse effects were headache, injection site pain, and weight gain. There were also notable increases in mean prolactin levels for both the 90-mg and 120-mg doses compared to placebo, though this finding is consistent with other risperidone formulations.

Andorn et al. conducted a phase 3, open-label, outpatient trial including 92 rollover patients from the Nasser et al. study and 408 new patients clinically stable on Perseris™ 120 mg once monthly.[15] The primary objective was to assess long-term safety and tolerability over 52 weeks, with long-term effectiveness being a secondary objective. The most common adverse effect reported was injection site pain (13%), though more than 80% of subjects reported no injection site reactions. Weight increase was observed in 12.8% of subjects, with such increases stabilizing after the first 3 months. The mean change in total PANSS score was -0.4 for new patients and ranged from -10.9 to -20.2 for rollover patients. This long-term study demonstrates that extended-release subcutaneous risperidone remains well-tolerated and effective over a 1-year period.

Additional intramuscular risperidone LAIs avoiding oral overlap and loading doses are under investigation. In May 2019, the FDA accepted a new drug application (NDA) from Luye Pharma for a microsphere formulation known as LY03004 or Rykindo®. Proposed dosing from the manufacturer is 12.5-50 mg once every two weeks.[16] In November 2020, ROVI announced filing an NDA with the FDA for Doria® (Risperidone ISM®), an *in situ* microimplant suggested to have greater stability and easier administration than existing LAIAs.[17] Investigators of this formulation recently conducted a phase 3, randomized, double-blind, placebo-controlled trial of 437 subjects experiencing acute psychosis with schizophrenia. Subjects were randomized 1:1:1 once every 4 weeks to Risperidone ISM® 75 mg, Risperidone ISM® 100 mg, or placebo, with a primary endpoint of change in the total PANSS score from baseline to day 85. A statistically significant LSMD was found versus placebo for both the 75-mg dose (-13, 95% CI [-17.3 to -8.8]; P < 0.0001) and 100-mg dose (-13.3, 95% CI [-17.6 to -8.9]; P < 0.0001). The most common adverse effects—of hyperprolactinemia (5.6-8.9%), akathisia (3.5-7.5%), and headache (3.4-6.3%)—versus placebo were comparable to those found with other risperidone formulations.[18]

Risperidone's active metabolite is currently available on the US market as 2 paliperidone LAIs: Invega Sustenna® (once monthly) and Invega Trinza® (once every 3 months, the longest duration of current FDA-approved LAIAs). Patients must be effectively treated for 4 months with Invega Sustenna® before moving to Invega Trinza®.[19,20] In November 2017, Janssen began a phase 3, randomized, double-blind, active-controlled, non-inferiority trial comparing time to relapse on investigational paliperidone palmitate 6-month formulation (PP6M) versus Invega Trinza®. While no results have been posted, the primary study completion date was in May 2020.[21]

Transdermal Patch

In October 2019, Noven Pharmaceuticals' Secuado® (HP-3070, asenapine) became the first FDA-approved transdermal antipsychotic formulation.[22]

It is applied to the abdomen, upper arm, upper back, or hip and is dosed 3.8-7.6 mg once daily. Asenapine was already available in a sublingual tablet formulation (Saphris®), though Secuado® aims to overcome its notable adverse effects (e.g. dysgeusia and oral hypoesthesia) and administration concerns (e.g. twice-daily dosing and avoiding food/drinks within 10 minutes).[23] The AWP for a package of 30 patches, regardless of strength, is $1,440, which appears to be similar to the monthly cost of sublingual asenapine.[24]

In a phase 3, randomized, double-blind, placebo-controlled trial of transdermal asenapine, 617 subjects experiencing an acute schizophrenia exacerbation were randomized 1:1:1 to 3.8 mg, 7.6 mg, or placebo.[25] The primary endpoint was change in the total PANSS score from baseline to day 42. A statistically significant LSMD was observed versus placebo for both 3.8 mg (-6.6, 95% CI [-9.81 to -3.40]; P < 0.001) and 7.6 mg (-4.8, 95% CI [-8.06 to -1.64]; P = 0.003). The most common adverse effects were headache, extrapyramidal symptoms (EPS, notably akathisia), weight gain, and application site reaction, a similar profile to sublingual asenapine except for site reactions.[25]

Novel Molecules

Lumateperone tosylate (Caplyta™)

In December 2019, Intra-Cellular Therapies announced the FDA approval of lumateperone tosylate (ITI-007, Caplyta™) for the treatment of schizophrenia in adults.[26] The approved dosing is 42 mg by mouth once daily (active free base equivalent to 60 mg of available tosylate salt). Though primarily acting as a D2 and 5-HT2A antagonist, lumateperone also exerts indirect glutamate receptor activation, presynaptic D2 partial agonism, and a larger difference between D2 and 5-HT2A affinity; the latter two features might suggest a lower propensity for EPS.[27] The monthly AWP of lumateperone 42-mg capsules is $1,584, which is approximately 3-7 times the cost of usual dosing of oral risperidone tablets.[13,28]

Lieberman et al. conducted a phase 2, randomized, double-blind, placebo- and active-controlled trial of 335 subjects experiencing acute psychosis with schizophrenia.[29] These subjects were randomized 1:1:1:1 to lumateperone 42 mg or 84 mg, risperidone 4 mg, or placebo, with a primary endpoint of change in the total PANSS score from baseline to day 28. A statistically significant LSMD was observed versus placebo for both lumateperone 42 mg (-5.8, effect size 0.42; P = 0.017) and risperidone, but not for lumateperone 84 mg (-0.9, effect size 0.7; P = 0.44); the study was not powered to directly compare lumateperone with risperidone. Somnolence was the most common adverse effect of lumateperone (17% for 42 mg and 32.5% for 84 mg), which the investigators concluded was a hindrance of the 84-mg dose's efficacy. While akathisia occurred in 7% of subjects receiving risperidone, akathisia rates for lumateperone 42 mg (1.2%) and 84 mg (2.4%) did not differ from placebo (2.3%). No significant difference in other EPS types or metabolic parameters were found between lumateperone and placebo.[29]

Correll et al. then conducted a phase 3, randomized, double-blind, placebo-controlled trial of 449 subjects experiencing acute psychosis with schizophrenia.[30] These subjects were randomized 1:1:1 to lumateperone 28 mg, lumateperone 42 mg, or placebo, with a primary endpoint of change in the total PANSS score from baseline to day 28. A statistically significant LSMD was again observed versus placebo for the 42-mg dose (-4.2, 95% CI [-7.8 to -0.6]; P = 0.02) but not the lower 28-mg dose (-2.6, 95% CI [-6.2 to 1.1]; P = 0.16). Somnolence was once more the most common adverse effect (11.3% for 28 mg and 17.3% for 42 mg), with no significant increases in EPS or metabolic abnormalities compared to placebo.[30] An additional phase 3 trial did not find statistically significant improvements in total PANSS score after 6 weeks on lumateperone 14 mg or 42 mg versus placebo (unlike an active risperidone comparator), though detailed study results have not been published.[31]

Olanzapine/Samidorphan (OLZ/SAM, ALKS 3831)

OLZ/SAM (ALKS 3831) is a combination product under investigation by Alkermes to optimize tolerability of the FDA-approved antipsychotic olanzapine, which is associated with a higher risk of metabolic abnormalities comparable to clozapine. Unlike clozapine, however, olanzapine's utilization is not limited by a Risk Evaluation and Mitigation Strategy (REMS) program, leading to more ubiquitous utilization.[3] These metabolic abnormalities are believed to be associated with activity at 5-HT2C, histamine-1, and muscarinic-3 receptors, as well as due to increased leptin levels.[32] Preclinical evidence suggests modulating the opioid system may improve feeding behavior and metabolism as reduction in weight gain has been reported in genetically engineered mice with mu-opioid receptors removed despite no differences in caloric intake from wild-type mice.[33] Samidorphan is an investigational mu-opioid receptor antagonist, not binding to any receptors suspected to be responsible for olanzapine's efficacy.[34] In a phase 1 trial of healthy volunteers, weight gain was significantly lower in those treated with OLZ/SAM than those treated with olanzapine alone.[35]

ENLIGHTEN-1 was a phase 3, randomized, double-blind, placebo- and active-controlled trial of 401 subjects experiencing an acute schizophrenia exacerbation.[36] Subjects were randomized 1:1:1 to OLZ/SAM (10-20 mg/10 mg), olanzapine (10-20 mg), or placebo, with a primary endpoint of change in the total PANSS score from baseline to day 28. Metabolic monitoring was performed at baseline, day 28, and a safety follow-up visit on day 43. A statistically significant LSMD in the primary outcome was observed versus placebo for both olanzapine (-5.3 ± 1.8; P = 0.004) and OLZ/SAM (-6.4 ± 1.8; P < 0.001). Mean changes in weight from baseline to day 28 for olanzapine, OLZ/SAM, and placebo were 2.38 ± 3.65 kg, 3.02 ± 3.56 kg, and 0.24 ± 2.76 kg, respectively, suggesting that samidorphan did not mitigate weight gain. However, the investigators emphasized that the study was primarily powered to assess efficacy. No differences in other adverse effects (e.g. somnolence, dry mouth, headache) were found between the active groups.[36] An open-label, 52-week extension of ENLIGHTEN-1 was conducted in 277 subjects, with all maintained on or switched to OLZ/SAM (10-20 mg/10 mg). Metabolic changes appeared to stabilize in the 183 study completers by week 52, with a mean weight increase of 1.86 ± 6.69 kg, fasting LDL cholesterol of 5.7 ± 28.8 mg/dL, and fasting glucose of 6.0 ± 14.4 mg/dL.[37]

ENLIGHTEN-2 was a phase 3, double-blind, randomized trial designed to assess the safety of OLZ/SAM in 550 subjects with stable schizophrenia, randomized 1:1 to either OLZ/SAM (10-20 mg/10 mg) or olanzapine (10-20 mg).[38] The co-primary endpoints were percent change from baseline in body weight and proportion of patients with >10% weight gain at week 24. Statistically significantly lower weight changes were observed with OLZ/SAM versus olanzapine, both in terms of percent change (4.21% vs. 6.59%; P = 0.003) and proportion with >10% gain (17.8% vs. 29.8%; P = 0.003). An open-label, 52-week extension of ENLIGHTEN-2 demonstrated that weight and other metabolic parameters in 265 subjects remained stable over long-term treatment, showing its promise as a novel therapeutic.[38] The FDA accepted an NDA for OLZ/SAM in January 2020, with the Psychopharmacologic Drugs Advisory Committee and Drug Safety and Risk Management Advisory Committee jointly voting in its favor in October 2020.[39,40] While the target NDA action date was in November 2020, the FDA has since requested resolution of identified concerns with the tablet coating process before OLZ/SAM may be approved.[41]

Roluperidone (MIN-101)

Currently available antipsychotic medications have shown efficacy evidence for positive symptoms of schizophrenia, though they have mixed to no evidence in relieving negative symptoms and

mood alterations.[3] Roluperidone (MIN-101) is under investigation by Minerva Neurosciences as the first drug for treating negative symptoms of schizophrenia through its antagonism of both sigma-2 and 5-HT2A receptors; it has no direct affinity for dopamine receptors.[42]

Davidson et al. conducted a phase 2, randomized, double-blind, placebo-controlled trial of 244 subjects with controlled schizophrenia except for >3 months of negative symptoms according to the PANSS.[43] Subjects were randomized 1:1:1 to roluperidone 32 mg, roluperidone 64 mg, or placebo, with a primary endpoint of change in the PANSS negative symptom pentagonal structure factor score from baseline to week 12. No other psychiatric medications were allowed during the study except for as-needed options to treat agitation or insomnia. Compared to the placebo group's least squares mean change from baseline (-1.53 ± 0.47), statistically significant differences were observed for both the 32-mg (-3.07 ± 0.49; P = 0.024) and 64-mg (-3.5 ± 0.48; P = 0.004) groups; a post hoc analysis found a poor correlation between these changes and Calgary Depression Scale for Schizophrenia (CDSS) total scores (r = 0.26). No significant improvement of PANSS positive symptom scores were observed in any groups at week 12. The most common adverse effect was headache, with no significant changes in EPS, vital signs, or metabolic parameters.[43] Minerva Neurosciences reportedly met with the FDA in November 2020 to solicit recommendations regarding the NDA process.[44] A 12-week, phase 3 trial of roluperidone for negative symptoms in schizophrenia is ongoing, with an estimated study completion date of April 2021.[45]

Evenamide (NW-3509)

As discussed previously, FDA-approved antipsychotic medications have acted primarily through D2 and 5-HT2A antagonism.[3] Newron Pharmaceuticals has begun investigating evenamide (NW-3509) as the first adjunctive therapy for treating positive symptoms of schizophrenia. Evenamide is a voltage-gated sodium channel blocker, indirectly modulating glutamate release that is hypothesized to be dysfunctional in schizophrenia.[46]

While quantitative data is limited, evenamide has been studied in a proof-of-mechanism, randomized, double-blind, placebo-controlled study of 89 subjects with uncontrolled schizophrenia despite receiving previously effective risperidone (>2 mg/day) or aripiprazole (>10 mg/day).[47] Subjects were randomized 1.3:1 to evenamide (15-25 mg twice daily) or placebo as an add-on to their existing antipsychotic medication, with statistically significant improvements versus placebo in the PANSS positive symptom score at week 4 according to an available abstract. Common adverse effects included somnolence, insomnia, and headache.[47] The FDA delayed further progression of evenamide's clinical trials in May 2019, citing safety concerns in rat and dog models. Plans for short-term exploratory studies in humans were discussed in November 2020 by the FDA and Newron Pharmaceuticals, now aiming to have initial results in early 2021 to allow for phase 3 trials later this year.[46,48]

Conclusion

As antipsychotic non-adherence increases risk of schizophrenia relapse, investigators have continued developing novel formulations beyond the oral administration route over the past few years. Additionally, mechanisms of action beyond dopaminergic and serotonergic receptor antagonism continue to be explored through novel antipsychotic molecules to solve efficacy gaps (e.g. negative symptoms of schizophrenia) and minimize adverse effects (e.g. EPS, weight gain). Due to the significant costs associated with these new treatments, pharmacists should be prepared to guide mental health professionals and educate patients on their efficacy, safety, and administration concerns relative to established antipsychotic treatments for schizophrenia.

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Review Article

Can Wisconsin Pharmacists Repeatedly Partially Fill Schedule II Controlled Substance Prescriptions at the Patient's Request?

by Michael E. DeBisschop, PharmD, Katherine E. Rotzenberg, PharmD, M.B.A., BCPS

Imagine a scenario like this (invented) example: Esmay Taylor, a regular patient, approaches your pharmacy counter. She appears much older than her 46 years would indicate. Before you can say a word, she looks you in the eye and says, "I'm worried about Isaiah," her teenage son. "I don't want these pills in the house with him there, but I can't imagine continuing on with this pain. You know all the things you read in the news these days." You look at the prescription, and see that it is for oxycodone, quantity 40, for acute pain associated with arthritis of her knee. Taylor's jaw is set, but her eyes glisten with the sheen of unshed tears. "Is there a way I could have less of these pills in the house, but still have the rest available—you know, just in case I need them? I don't want to have to bother the doctor again."

Background

Although the COVID pandemic has occupied much attention and energy over the past year, the opioid epidemic has continued unabated in the U.S. and Wisconsin. The most recently available national data indicate that 14,975 Americans died from a drug overdose involving prescription opioids in 2018.[1] For the same year in Wisconsin, there were 1,076 drug overdose deaths; specific data on deaths involving a prescription opioid are not available.[2] At the national and state levels, the 2018 statistics were an improvement over the previous year, but we are not out of the woods yet, as shown by more recent data.[3]

Provisional counts of Wisconsin drug overdose deaths from the Center for Disease Control's (CDC) National Center for Health Statistics (NCHS) are shown in Table 1.[3] In the most recent 12-month period for which data are available (July 2019-June 2020), Wisconsin experienced a 46.2% increase in drug overdose deaths due to opioids compared to the previous 12-month period, and a 112% increase since the July 2015-June 2016 reporting period (data not shown). The rate of deaths due to opioid overdose in Wisconsin continues to climb alarmingly.

The COVID pandemic has exacerbated the opioid epidemic, both in Wisconsin and nationally. More than 40 states have reported an increase in opioid-related deaths during the pandemic.[4] From March to July 2020, 325 suspected overdoses were recorded in Wisconsin, compared to 150 during the same period in 2019. This might be caused by increased isolation, stress, anxiety, and behavioral issues leading to more opioid use.[5]

One potential contributor to prescription opioid overdose deaths is the volume of unused prescription opioids in patients' homes. In a systematic review of prescription opioid use after inpatient or outpatient surgery, 67 to 92 percent of patients had unused prescription opioids, with average amounts ranging from 5 to 20 tablets remaining for the studies reporting this information. This might be acceptable if patients disposed of their prescription opioids appropriately; however, only a small number of patients (between 4 and 30 percent) planned to dispose, or actually disposed, of their leftover opioids.[6]

The U.S. Drug Enforcement Administration (DEA) sponsors an annual National Take Back Day during which the public is invited to safely dispose of their unwanted prescription drugs at collection sites in the community. Although the effort is aimed at eliminating excess controlled substance prescription medication, all medications are accepted. In October 2020, the DEA sponsored its 19th National Take Back Day and in Wisconsin collected almost 90,000 pounds of prescriptions from the public at 290 community collection sites. Both numbers lead the country, well ahead of more populous states like California and Texas.[7] Clearly, Wisconsinites have prescriptions to dispose of.

With the COVID pandemic continuing and the opioid epidemic intensifying, any potential solution for decreasing the quantity of unused prescription opioids in circulation should be considered. Could Wisconsin pharmacists help achieve this goal through repeated, patient-requested partial filling of Schedule II (C-II) controlled substance prescriptions? Both federal and state laws govern the use and handling of controlled substances;

TABLE 1. Drug Overdose Deaths in Wisconsin

Time Period	Drug Overdose Deaths	
	All Drugs	Opioids*
July 2018-June 2019	1113	715
July 2019-June 2020	1404	1045
Increase	**26.1%**	**46.2%**

**This category includes "natural, semi-synthetic, and synthetic opioids, including methadone."[3]*

TABLE 2. Resources for Keeping Up-to-Date on State Pharmacy Advocacy Issues

Resources	*Website for Sign-up*	*Type of Notification*
Wisconsin State Legislature	https://notify.legis.wisconsin.gov	Legislative proposals (based on keywords); administrative rule proposals based on section (e.g. Phar)
Department of Safety and Professional Services, Pharmacy Examining Board Newsletter	https://public.govdelivery.com/accounts/WIDSPS/subscriber/new (sign in or create account, then select "Pharmacy Examining Board" under Newsletters)	Updates on actions of the Pharmacy Examining Board, including new and proposed rules as well as variances
Pharmacy Society of Wisconsin (PSW) Fast Facts weekly newsletter	https://www.pswi.org	Weekly newsletter on statewide and national pharmacy news, including legislative advocacy topics (included with PSW membership)

confusion can arise when these laws are not consistent with each other. This article will describe current federal and state laws and regulations governing partial filling of C-II prescriptions, how to reconcile differences between them, and offer recommendations for current practice.

The Comprehensive Addiction and Recovery Act of 2016

Many Wisconsin pharmacists might not know that there is a federal law in existence to help reduce the volume of unused prescription opioids in patients' homes. The Comprehensive Addiction and Recovery Act (CARA), signed into law in 2016, provides a coordinated federal response to the opioid epidemic.[8] CARA addresses prevention and education, law enforcement, treatment, recovery, and miscellaneous matters. Within those miscellaneous matters is section 702, of special interest to pharmacists because it amends the provisions regarding partial fills of C-IIs within the U.S. Controlled Substances Act. Specifically, this section allows partial fills of C-IIs to be requested by the patient or prescribing practitioner and allows the remaining portions of the prescription to be filled within 30 days of the date the prescription is written, up to the total quantity prescribed, if these practices are not prohibited by state law. In comparison, emergency oral C-II prescriptions may be partially filled with the remaining portion filled within 72 hours, which CARA did not affect.

For many years, pharmacists have recognized two instances when a partial fill of a C-II prescription is permissible, per DEA regulations and echoed in Wisconsin's regulations concerning controlled substances, Phar 8.[9,10] A pharmacy may be "unable to supply" the full quantity of a C-II prescription and a one-time partial fill may be dispensed, with the remainder required to be dispensed within 72 hours. In the past, DEA has permitted a broad interpretation of "unable to supply" including when the drug is not in stock (the traditional interpretation), when the drug is in stock but the pharmacy is waiting for verification or clarification, when the patient cannot afford to pay for the full amount, or when the patient did not want the full amount.[11] In addition, C-II prescriptions for patients in long-term care facilities or who are terminally ill may be repeatedly partially filled for up to 60 days.[9,10]

The CARA partial fill provisions were confusing to many. DEA regulations requiring C-II partial fills to be completed within 72 hours were still intact, and now CARA permitted 30-day partial fills. Were the laws compatible or contradictory? Lawmakers sent open letters to the DEA urging a revision of their regulations to be consistent with CARA.[12,13] However, the DEA did not revise their regulations, exacerbating the confusion.

In 2020, the DEA released a revision of their Pharmacist Manual, and finally provided some clarity around the situation. The DEA interprets CARA legislation and existing DEA regulation to be compatible and co-existing.[14] Per the updated Pharmacist Manual, the remaining portion of a C-II partial dispensing must be filled within 72 hours when the pharmacist is unable to supply (or for an emergency prescription). Partial quantities, up to the quantity specified on the prescription, may be filled within 30 days when requested by the patient or prescriber. The Pharmacist Manual goes on to indicate, however, that if state regulations have not changed, and they still only specify the 72-hour "unable to supply" provision for partial filling, then the stricter state law/regulation applies until the state makes a change. This is consistent with the general approach of adhering to the stricter law when federal and state law conflict. This principle ensures pharmacists are adhering to both sets of laws. As of the writing of this article, Wisconsin has not changed its statutes or regulations to parallel CARA.

How Wisconsin's Neighbors Have Incorporated CARA Provisions

Wisconsin's neighboring states—Minnesota, Michigan, Iowa, and Illinois—have implemented CARA's C-II partial fill language to varying degrees. CARA states that the 30-day partial fill may be implemented under the condition that it is not prohibited by state law. None of Wisconsin's neighbor states (nor Wisconsin itself) expressly prohibits this practice. Each of these states in some way incorporates DEA's long-standing 72-hour "unable to supply" partial fill regulation, as well as the 60-day partial fill allowance for terminally ill and long-term care facility patients. Michigan, through legislation passed in 2017, allows partial filling for C-IIs "consistent with federal law and regulations."[15] Specific situations

are not named. Iowa has promulgated regulations to expressly allow 30-day C-II partial fills "at the request of the patient or prescriber."[16] Minnesota and Illinois have not adopted any language in their statutes or regulations interpreting CARA, although neither state's laws expressly prohibit patient-requested partial dispensing of C-IIs. Minnesota's Board of Pharmacy issued a Frequently Asked Questions document in 2019 that confirmed that patient-requested partial fill of C-IIs for 30 days is allowable under federal law.[17] However, with the DEA's interpretation in the 2020 Pharmacist Manual that states should change laws or regulations to parallel CARA, additional action may be needed to implement these changes in Minnesota.

In summary, three of the four states that border Wisconsin have endorsed CARA in some way. Two states have passed regulations or statutes indicating that patient-requested repeated partial filling of C-IIs within 30 days is permitted in addition to existing DEA C-II partial fill regulations.

What Can Wisconsin Pharmacists Do?

In Wisconsin, there is currently no statute or regulation expressly permitting or prohibiting patient/prescriber-requested 30-day partial filling of C-II prescriptions per CARA. Wisconsin regulations reflect only the historical 72-hour "unable to supply" allowance for partially filling C-II prescriptions.[10] Given the DEA's interpretation in the new Pharmacist Manual that states should change their laws or regulations before implementing CARA, it must be interpreted that this practice is not yet legal in Wisconsin. As of the writing of this article, the Pharmacy Examining Board (PEB) is in the process of revising Phar 8. Revisions that include language specifically allowing the CARA provisions would help enable more flexible patient/prescriber-requested partial fills of C-II prescriptions. Pharmacists can advocate for this at the time when PEB invites comments on draft revisions of Phar 8, anticipated some time during the next 12 months (the current scope statement for this revision expires in February 2022).[18] Table 2 provides several resources that pharmacists can use to sign up for notifications of upcoming state legislation and rulemaking. The DEA has recently posted a notice of proposed rulemaking to clarify how partial fills may be requested and recorded under CARA, with public comments due February 2, 2021.[19] When the final DEA rules are published, they will further support state efforts to implement CARA partial fills.

In anticipation of this change, pharmacy computer systems may also need to be reviewed and potentially adjusted to permit and document partial fills for C-II prescriptions appropriately, ensuring they are recorded as partial fills and not documented as refills or assigned a new prescription number. Another challenge might be for prescription coverage providers to recognize this practice and cover partial fills and dispensing costs appropriately.

Until regulations implementing CARA are promulgated in Wisconsin, pharmacists will need to use other strategies to help patients limit unused opioids in circulation and combat the opioid epidemic. Pharmacists can work with prescribers to suggest appropriate prescription quantities for acute pain prescriptions. State regulations permit pharmacists to change the quantity prescribed for a C-II prescription; this must be done in consultation with the prescriber and should involve consultation with the patient.[20] Pharmacists can counsel patients on proper disposal options for unused prescriptions, including in-store medication disposal kiosks, prescription take-back days, or chemical and physical sequestrant options that render drugs irretrievable. Pharmacists can also educate patients about the ongoing opioid epidemic and the role that prescription opioids play in the epidemic. As a harm-reduction strategy, pharmacists can enroll with the Wisconsin Department of Health Services (DHS) to prescribe and dispense naloxone under the Statewide Standing Order,[21] or work with a local provider to dispense naloxone. The DHS website contains detailed information on naloxone dispensing by pharmacists, including patients who should be considered to receive it.

Conclusion

Given the severity and ongoing nature of both the opioid epidemic and the COVID pandemic, pharmacists should be considering every avenue to help decrease the risk of opioid overdose and unused prescription opioids in circulation. Pharmacists currently have several tools to help patients receive the appropriate quantity of opioids and dispose properly of unused prescriptions. Although not currently permitted in Wisconsin, in the future, pharmacists might be able to discuss with patients the possibility of repeatedly partially filling their opioid prescriptions at the patient's request. The opening case concerning Esmay Taylor highlights just one of many scenarios in which this approach could be a beneficial option. Pharmacists in Wisconsin should look for upcoming revisions to controlled substance regulations, and advocate for inclusion of language that parallels CARA.

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UNIVERSITY WISCONSIN-MADISON SCHOOL OF PHARMACY STUDENT WRITING CLUB:

Diversifying the Pain Management Toolbox: A Review of IV Lidocaine and Oral Mexiletine as Non-opioid Options

by Stephaney Cheng, 2022 PharmD Candidate, Katie M. Fermanich, 2022 PharmD Candidate, Sommer L. Gay, 2022 PharmD Candidate, Jillian M Kolasinski, 2022 PharmD Candidate

In 2017, the US Department of Health and Human Services declared the opioid epidemic a public health emergency.[1] The following year, approximately 10.3 million Americans misused prescription opioids, highlighting the need for safe and effective alternative pain management options.

One solution to the growing epidemic is the use of intravenous (IV) lidocaine for the management of both acute and chronic pain.[2,3] Lidocaine is a class 1B sodium channel blocker and produces analgesia and anti-inflammatory effects at low doses.[3] Lidocaine is commonly used as a local injection, and increasingly used via IV to manage perioperative pain.[2] Intravenous lidocaine has additionally been used in the management of neuropathic pain, fibromyalgia, burns and other pain conditions, and may reduce or even eliminate the need for opioids in both acute and chronic pain management.[3,4]

Another pain management alternative is mexiletine, the oral analogue of lidocaine. Similar to lidocaine, mexiletine is a class 1B sodium channel blocker with analgesic properties useful in the treatment of neuropathic pain.[5] Currently, mexiletine usage in chronic pain therapy is limited due to a perceived lack of efficacy and tolerability.[4] One study demonstrated that a stronger response to IV lidocaine was predictive of patient acceptance of mexiletine.[5] Additionally, mexiletine provides unique benefits as an oral therapy in comparison to lidocaine, which may not be delivered orally due to high first-pass metabolism.[4] Although it is not commonly used as a first-line option, mexiletine can be considered as a safe alternative to opioids for chronic pain management.

The purpose of this article is to raise pharmacists' awareness of the use and benefits of two non-opioid pain management medications, IV lidocaine and oral mexiletine.

Clinical Indications and Administration

Currently, intravenous lidocaine is clinically indicated for local or regional anesthesia as well as treatment of ventricular arrythmias.[6] However, its potential off-label uses show promise in the world of refractory pain conditions. Sodium channel blockers, such as lidocaine, are commonly used to interrupt pain signal transmission. Through this mechanism, lidocaine therapy can have an impact on refractory neuropathic pain,[7] diabetic neuropathy, post-operative pain,[8] and migraine.[9] A meta-analysis of IV lidocaine for neuropathic pain by Tremont-Lukats et al. demonstrated modest benefits over placebo, which were more apparent at doses of 5mg/kg and above.

Despite its beneficial effects, IV lidocaine is not an appropriate option for every patient. The analgesic is not advised to be used in patients with underlying heart conditions due to QT prolongation.[9] Lidocaine is hepatically metabolized primarily by CYP1A2 and partially by CYP3A4, and thus should be used cautiously with other drugs that might induce or inhibit these same enzymes. For this same reason, the healthcare team should take precautions when dosing patients with liver dysfunction. Serum concentrations above 5 mg/ml lower the seizure threshold and should also be avoided in patients at risk of seizure or with a history of epilepsy.[10] Additionally, patients often must fail other first- or second-line pain relief options, such as antidepressants, gabapentin, tramadol, topical agents, and other anticonvulsants before lidocaine infusion can be considered.[9]

One limiting factor in the availability of IV lidocaine for patients are the complexities associated with its administration. Lidocaine infusions or injections must be administered in a clinic setting to provide appropriate patient monitoring. Prior to therapy, a patient's reaction to lidocaine is measured with a test to rule out any allergic reactions or adverse effects. On the initial visit, a test dose of 5 mg/kg is infused over one hour followed by a 30-minute monitoring period.[9] While the patient is in clinic, it is appropriate to measure their vitals, conduct an assessment of their current pain, and note any adverse effects they might experience. The cost of lab testing and availability of chairs in the pain clinic are barriers to patients receiving this care. Often, insurance companies will not cover the cost of lidocaine infusion. When making a therapeutic decision, the cost of the procedure should be weighed against the quality-of-life improvements that stand to be gained from this non-opioid option.

Mexiletine provides an alternative therapy for refractory pain, especially in patients who benefit from IV lidocaine, although its tolerability limits its use. Studies of neuropathic pain show a median dose of 600mg of mexiletine delivers a marginal improvement in pain intensity visual analog scale over placebo.[7] One prospective and one retrospective cohort study indicate that response to lidocaine

therapy can predict mexiletine's usefulness in that patient.[4,11] This correlation can help maximize the benefit of this medication by choosing the patient population for whom it is most likely to work. However, its practicality as an off-label pain reliever is limited by adverse events. Its side-effect profile includes nausea and vomiting with a reported incidence of up to 40% as well as dizziness, drowsiness, and anxiety but at lower rates.[12] Potential candidates for mexiletine include patients whose pain responds well to lidocaine therapy and can tolerate the drug. While this option might not work for all patients, the ability to manage the medication from home lessens the burden on the healthcare system.

Benefits of Opioid Alternatives

The Centers for Disease Control and Prevention (CDC) states that between the years of 1999 and 2017 almost 400,000 people died from an overdose involving opioids. Considering the high-stakes consequences associated with opioids, opioid therapy is an important issue for the healthcare system in the United States.[13] The use of non-opioid medications has the potential to demonstrate statistically significant pain improvement compared to pain management with opioids, without the consequences associated with opioids, such as addiction, tolerance, and even death. Thus, opioid pain management should be used as a last-line treatment plan for refractory pain.[14] Pharmacists can further support healthcare providers with evidence-based guidelines outlining the benefits of non-opioid therapies including IV lidocaine and oral mexiletine.

Intravenous lidocaine is considered a relatively safe drug that acts as an analgesic and an anti-inflammatory agent that might have a role in pain relief after trauma or surgery by decreasing the need for other opioid medications. Forouzan and colleagues studied the use of IV lidocaine compared to morphine sulfate in pain management in bone fractures.[3] The subjects' pain was scored from 1 to 10 using a visual analog scale (VAS). A pain score reduction of at least 3 points was required for the treatment to be considered successful. Success in decreasing pain severity 12 minutes after injection was 49.28% in the lidocaine group and 33.57% in the morphine sulfate group. Similar results were also found when comparing the level of decreased pain 30 minutes post injection.[3] The physiologic risks associated with lidocaine therapy are relatively low, in comparison to morphine sulfate. Lidocaine toxicity can produce bradycardia, hypotension, headache, nausea, and muscle weakness. Mexiletine, as previously stated, is an oral analogue of lidocaine and has been shown to be relatively safe and effective in treatment of pain associated with fibromyalgia, erythromelalgia, postoperative pain, and other chronic disease states.[15] Wu et. al, conducted a study to evaluate the change in pain intensity while using mexiletine compared to both morphine and placebo in patients with post-amputation pain. The study found that patients' self-reported pain relief during treatment was, on average, 53% with morphine, 30% with mexiletine, and 19% with placebo.[16] This shows that mexiletine was more effective in reducing pain scores than placebo, yet not as effective as morphine. While morphine should be reserved for patients with refractory pain, mexiletine would be sufficient for non-refractory pain.

Pharmacist Role

The CDC developed guidelines aimed at primary-care clinicians who are prescribing opioids for chronic pain. The recommendations address appropriate initiation of therapy, decisions about dosing regimens, discontinuing therapy, and proper assessment of the risk-to-benefit ratio of continued opioid use.[17] As front-line healthcare providers, pharmacists have a role in both the inpatient and outpatient setting for assessing and managing pain. Within healthcare teams, pharmacists can recommend other analgesics over opioids to help ensure a decrease in use of opioids. Implementing organizational guidelines targeted to reducing opioid use has been effective in reducing emergency department and discharge opioid use and reducing the length of stay.[18] With access to inpatient records, pharmacists can monitor patients for recommendations to switch to non-opioid therapies, such as IV lidocaine, to decrease the use of opioids. Upon initiation, pharmacists can play an important role in the monitoring of patients in clinic for their first dose and addressing adverse events immediately. Another area to be further studied involves the transition of lidocaine infusions to home administration, expanding the use of non-opioid therapies for pain management. With expanding roles in home healthcare, this could be a new service for pharmacists to help with pain management.

Therapeutic interchange from IV lidocaine to oral mexiletine further involves pharmacists in the monitoring of patients upon initiation and with continued use for adverse events. As an oral analgesic alternative, mexiletine can offer benefits patients perceive as valuable, such as ease of administration and reduced costs associated with returning to the clinic for lidocaine infusions. Although not a first-line therapy, its safety profile and ease of use should prompt its clinical use before opioid therapy.

Use of non-opioid therapies over opioid counterparts is an important shift that healthcare providers need to take advantage of to combat the opioid crisis and associated consequences. There needs to be a balance between reasonable pain management and the risks of opioid abuse when evaluating patients for alternative therapies.[19] There is a significant deficiency in services for community pharmacists in chronic pain management, but with increasing demand for non-opioid therapy, it creates an opportunity for pharmacists to take advantage of and help optimize patient quality of life.

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

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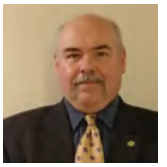
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UNIVERSITY WISCONSIN-MADISON SCHOOL OF PHARMACY STUDENT WRITING CLUB:

The Frontiers of Cannabidiol: Exploring Future Therapeutic Uses

by Nicole Donovan, 2022 PharmD Candidate, Tuyet Nguyen, 2022 PharmD Candidate, Kenton Cooksey, 2022 PharmD Candidate, Marcus Pribyl, 2022 PharmD Candidate, Fitim Useini, 2022 PharmD Candidate

When many people think about cannabidiol (CBD), they think about marijuana. They might be surprised to learn that we humans have our own regulatory system related to these chemicals. The endocannabinoid system (ECS) consists of receptors, neurotransmitters called cannabinoids, and enzymes for degradation, all used to regulate homeostasis of the immune system and nervous system within the human body.[1] One thing this system does is to treat inflammatory processes, which helps explain why tetrahydrocannabinol (THC) and CBD might be useful to treat processes like headache, cancer pain, neuropathic pain, and sleep. This article focuses on two main cannabinoids: THC and CBD. THC works as a cannabinoid[1] (CB1) and cannabinoid 2 (CB2) agonist.[2,3] Action on the CB1 receptor leads to the "high" that people can experience when using THC (as in marijuana), and can lead to psychoactive effects. Activation of the CB2 receptor has a major role in the immune system, by mediating cellular immune responses. CBD, in contrast, has less effect on both CB receptors; thus, it has less of an intoxicating effect on the brain.[2,4] Additionally, CBD does not cause euphoric effects in the brain like THC.[5] CBD is an expanding topic in current therapeutic research, as it has the potential to be used in treatment of numerous disease states.

As we learn more about CBD and it has become more available, there has been a recent market boom: CBD is sold at gas stations, grocery stores, convenience stores, and restaurants.[6] The only Food and Drug Administration (FDA) approved cannabinoid substance is Epidiolex. All other forms of CBD and THC are currently unregulated and can vary in strength and content, no matter where they are sold. Given the prevalence of CBD in the marketplace, pharmacists need to know more about it. The objective of this review article is to present current research involving novel CBD/THC use in various disease states.

Antimicrobial

Antimicrobial resistance has become a major threat in healthcare. For example, *Staphylococcus aureus* (*S. aureus*) is the second most frequent hospital-acquired infection and there are a decreasing number of drugs available that are still effective to fight this infection.[7] In addition, there has been a decline in the development and research of new antimicrobials, which makes the new climate of "super bugs" even more dangerous.[8] Cannabis is a common agent for antimicrobials, and is the drug extracted from the cannabis plant that contains both THC and CBD.[2]

Van Klingeren and Ten Ham conducted an in vitro study that tested the effectiveness of THC and CBD at killing bacteria.[9] The results showed that the minimum inhibitory concentration (MIC) was 1-5 µg/mL, meaning fairly low concentrations were required to stop the growth of the tested gram-positive bacteria. However, the cannabinoid's success was greatly reduced in 4% or 5% horse serum. This suggests that THC and CBD might be inactive in horse blood and have no place in therapy regarding systemic antibacterial action, but could be used in a topical formulation. THC and CBD were also investigated against gram-negative bacteria, but they were found to be less effective with a MIC of 20-50 µg/mL. A limitation of this study is that these findings were gathered from crude extracts and not pure samples of THC or CBD. In addition, there was no statistical analysis reported.

Nissen et al. analyzed the effects of essential oils extracted from hemp. Hemp is a form of the cannabis plant that has less than 0.2% THC.[10] The study found that the concentration of different essential oils in each of the hemp varieties is dependent on when the cannabis strains are planted and the plant age. This provides an opportunity to optimize antimicrobial activity of hemp use going forward. The results were promising and showed that hemp from Carmagnola, Fibranova, and Futura plants were able to inhibit bacteria growth in vitro at concentrations ranging from 0.7-2.0 (%v/v). Again, the authors see potential use as an antiseptic topical treatment for wounds and skin scrapes, and as a new treatment agent for antibiotic-resistant strains of bacteria like MRSA and Clostridium difficile.

Furthermore, Appendino et al. confirmed the results that both THC and CBD show potent antimicrobial activity in vitro (MIC values in the 0.5-2 µg/

mL range).[11] The results were impressive and showed that there was antimicrobial activity against SA-1199B, EMRSA-15 and EMRSA-16. This could lead to major breakthroughs in drug resistance, because EMRSA-15 and EMRSA-16 are currently the top methicillin-resistant S. aureus strains spreading through U.K. hospitals. The antimicrobial mechanism of cannabinoids is not fully known; however, Appendino et al. suggest that these compounds are not substrates for the leading resistance mechanism in bacteria. Another avenue of research is on the topical use of cannabinoids against MRSA skin colonization, which is starting to become resistant to mupirocin, the standard of care for this condition. This study did not address the activity of cannabinoids in any kind of serum or blood, which would give further insight into cannabinoid effectiveness as systemic antibiotics. Once again no statistical analysis was reported.

Overall, there is some evidence supporting the use of cannabis as an antimicrobial agent. However, there is limited high-quality research available into its effectiveness in systemic circulation. It seems as if CBD and THC may be useful as a topical antimicrobial. Going forward, more studies will be needed to confirm CBD's effectiveness as an antibiotic. We will want to investigate further as resistant microorganisms become a bigger problem in hospitals around the world.

Autism Spectrum Disorder

According to the United States Centers for Disease Control (CDC), Autism Spectrum Disorder (ASD) occurred in 1 of every 59 children in 2014.[12] The prevalence of ASD and lack of treatment has made it a prime candidate for possible treatment with CBD. Research into CBD use in this patient population is young and hasn't made strong conclusions yet, but the possibilities are exciting.

Previous studies on ASD have suggested that an imbalance of the neurotransmitters glutamate and gamma-Aminobutyric acid (GABA) in certain areas of the brain could result in symptoms of ASD.[13] Glutamate normally serves as an excitatory neurotransmitter in the brain, and GABA is normally inhibitory, with imbalances in the two resulting in neurological conditions. The locations of these imbalances in the brains of ASD patients are specific and have been studied to find potential therapeutic agents.

In a 2017 study, Ajram et al. set out to determine whether the drug riluzole, a glutamate blocker, could be a pharmacologic agent that could help to balance glutamate and GABA.[14] In a placebo-controlled, double-blind, randomized study of 37 men (17 with ASD, 20 control), a significant difference ($p < 0.05$) in neurotransmitter balance was found in patients with ASD. More specifically, riluzole increased the proportion of GABA in patients with ASD in specific brain regions. In the control patient group, riluzole decreased the proportion of GABA, indicating an opposing effect in patients with ASD versus control patients.

Ajram et al.'s study proved that pharmacologic agents could be used to help this neurotransmitter difference in patients with ASD, and paved the way for exploring other options, such as CBD. In a similar test to explore the efficacy of CBD to restore neurotransmitter balance, Pretzsch et al. conducted a placebo-controlled, randomized, double-blind crossover study of 34 men (17 with ASD and 17 control) looking for effects on glutamate and GABA balance.[15] While limited, preliminary results suggested that CBD helped balance the neurotransmitters in patients with ASD (puncorr= 0.001 when measuring GABA+ in both the basal ganglia and the dorsomedial prefrontal cortex).

Neurotransmitter balance is an area of focus in treating ASD but is not the only frontier where CBD is being explored. In another double-blind, placebo-controlled study conducted by Pretzsch et al., 30 male patients (13 with ASD and 17 control) were randomized and dosed with CBD or placebo and then administered a functional magnetic resonance imaging (fMRI) test.[16] The results of this study showed that patients with ASD showed a significant shift (pFWE=0.045) in the fractional amplitude of low-frequency fluctuations (fALFF), especially in key ASD-related areas, when administered effective doses of CBD. The fALFF test is a similar measure to the Amplitude of Low-Frequency Fluctuation (ALFF) test, both of which measure and quantify slow fluctuations of brain activity that are seen in the resting brain.[17,18] By administering CBD to patients with ASD, brain activity in these key areas was increased, which could correlate with benefit in ASD.

Symptomatic treatment for ASD is also a growing area of research with CBD. Symptoms of ASD include hyperactivity, aggression, sleep disturbances, anxiety, and self-injury.[19] These symptoms were observed in an open-label 2019 study performed by Barchel et al. on the effects of a premade oral CBD solution, containing some THC at a 1:20 ratio with CBD, on symptoms and co-morbidities of children with ASD.[20] The study asked parents of 53 children with ASD (45 male, 8 female; ages 4-22) to subjectively measure improvement in symptoms following the administration of the CBD premade solution for 30 days. Although the study was subjective and relatively small, the results pointed towards the improvement of symptoms (established non-inferiority compared to standard of care in all studied symptoms, and an overall improvement in 74.5% of participants) following the 30-day course of CBD solution.

While none of these current studies claim to prove CBD's efficacy in treating ASD, they pave the way forward. These studies are all within the last decade, and as understanding of both ASD and of CBD grows, these areas could continue to expand.

Smoking Cessation

Worldwide, 1.1 billion people smoke; in the United States, 17% of adults smoke. With that large population, CBD might provide helpful therapy for smoking cessation.[21,22] There is currently limited evidence for using CBD for smoking cessation, but it is an area of growing research. Hindocha and colleagues used CBD and measured the patient's desire to smoke when they saw cigarettes (also known as "attentional bias to cigarette cues").[21] This was done by showing the patient different stimuli and measuring their desire to smoke a cigarette after each cue. The major mechanism that CBD is thought to affect for smoking cessation is the inhibition of fatty acid amide hydrolase (FAAH), which is

involved in the breakdown of endogenous cannabinoids.[21,23] Patients took an 800 mg oral dose of CBD, and it was found that the attentional bias was similar to that of a patient who had recently smoked a cigarette or no longer desired one. When comparing CBD to placebo, the researchers found CBD reduced attentional bias by a statistically significant level for both a patient who had recently smoked (p-value 0.007) or did not smoke before testing (p-value 0.004).[21] Levels of cravings and withdrawals were also not impacted by the use of CBD. However, CBD might be beneficial in reducing the pleasant feelings of cigarettes.

Another study done by Morgan et al. found that CBD reduced cigarette consumption.[23] Here, a CBD inhaler was used at 400 micrograms/dose, and patients used the inhaler any time they had the urge to smoke a cigarette. Over a two-week period, patients saw reduced total cigarette consumption. The results were found to be statistically significant with a p-value of 0.002. Patient anxiety was also lowered (p-value 0.04), which could play a role in helping with the cravings of cigarette smoking. People who smoked more cigarettes going into the study saw the greatest reductions in usage while using the CBD inhaler. Furthermore, there was a correlation between increased benefit and more uses of the inhaler; however, no statistical significance was found with the correlation.

Overall, CBD might be useful in the future as an adjunct therapy for smoking cessation. There is a growing body of evidence being gathered that will help to clarify CBD's potential use in smoking cessation. Current research is focused mainly in the UK and is currently working to establish whether CBD is a valid option for smoking cessation, along with its optimal route of administration. Researchers propose that CBD disturbs memory consolidation, which is one way it might work with smoking cessation. This could mean that CBD may be beneficial in other addictive drug treatment in the future, but more evidence is needed.

Parkinson's Disease

Over 10 million people worldwide live with Parkinson's disease (PD).[24] It is a central nervous system disorder characterized by the loss of dopaminergic neurons.[25] Reduced levels of dopamine cause various motor and non-motor complications in the human body. Motor impairments include resting tremors, bradykinesia, muscle rigidity, and postural disturbances; non-motor symptoms present as cognitive deficits; sleep disturbances; and psychiatric disorders such as anxiety, psychosis, and depression. The most common drug therapy for managing PD is carbidopa/levodopa, yet this medication only improves motor function.[25,26] Therefore, current pharmacologic intervention for PD is limited, due to side effects and lack of efficacy for long-term use of these medications. There is a need for better treatment options, and that potential could be found in CBD. CBD is found to provide anti-inflammatory, neuroprotective, anxiolytic, and antipsychotic effects—all of which could help in the treatment for PD.

One of the very first human studies comes from Zuardi and colleagues, wherein they analyzed the effects of CBD on psychotic symptoms of PD patients.[27] This was an open-label pilot study where both the researchers and participants knew the treatment that the participant was receiving. Here, 6 PD patients (2 women and 4 men) who all had psychosis for at least 3 months received flexible oral dosing of 150mg/day of CBD for 4 weeks. Doses increased weekly from 150mg to 400mg depending on the tolerability of each subject. CBD was given in adjunct with their regular therapy. Different scales were used to evaluate psychotic symptoms: the Brief Psychiatric Rating Scale (BPRS); the Parkinson Psychosis Questionnaire (PPQ); and the Unified Parkinson's Disease Rating Scale (UPDRS). Use of CBD was correlated with a decrease in frequency and severity of sleep disturbances, in addition to hallucinations and delusions, evidenced by a significant decrease in all test scores listed above. Furthermore, motor and cognitive functions were not affected by CBD. No adverse reactions were observed during the course of treatment.

Later, in a double-blind clinical trial, Chagas and colleagues treated 21 PD patients (6 women and 15 men).[28] Patients were free from dementia and psychiatric disorders. They were divided evenly into three groups who received placebo, CBD 75 mg/day, or CBD 300 mg/day for a duration of 6 weeks. Measurements were performed at baseline and in the last week of the trial. Rating scales (UPDRS, Parkinson's Disease Questionnaire–39, and Udvalg for kliniske undersogelser-UKU) were used to assess the overall quality of life. Results showed no differences between motor scores on the UPDRS (p=0.544). Additionally, no significant adverse effects were reported when assessed with the UKU. However, the Parkinson's Disease Questionnaire–39 provided a more hopeful conclusion with statistically significant differences between the placebo group and the CBD 300 mg/day group (p=0.034). Greater improvements were identified in emotional well-being, mobility, cognition, communication, and body discomfort of PD patients in the CBD group.

A further case series from Chagas and colleagues revealed that CBD was helpful in the treatment of rapid eye movement sleep behavior disorder (RBD) in PD patients.[29] This disorder usually presents early on in PD, occurring years before motor symptoms. Patients who have RBD tend to act out their dreams due to loss of muscle tone. Dreams can be vivid, intense, or violent and cause harm to the patient or their bed partner. In this study, the four patients (all men) were administered 75 mg/day (three patients) or 300 mg/day (one patient) of CBD taken orally.[30] Patients reported a significant reduction in the frequency of RBD events with minimal side effects.

Generally, findings conclude that CBD seems to be well tolerated and provides therapeutic effects in non-motor symptoms. However, there are many limitations with these studies. The sample sizes were very small, and the duration of treatment was short, making it difficult to correlate the possible effectiveness involved in CBD's therapeutic properties. Moreover, neuroprotective effects are not easily measured in humans. One last aspect that was not touched upon was CBD's possible interactions with PD medications. There is a need for large-scale randomized controlled trials, ones to mimic and assess the long-term efficacy of CBD. Although there are few human studies out there, results from these early CBD trials offer a

FIGURE 1. Current CBD/THC Research Studies and the Disease States Used in Creating this Article

	Citations	Type of Study	Number of Participants	Control	Intervention	# evidence with confidence interval
Antimicrobial	Van Klingeren B, Ten Ham M. 1976	In vitro studies	N/A	N/A	THC 2mg/mL or CBD 2mg/mL	MIC for S. aureus: CBD: 1-5 µg/mL in agar broth and CBD: 20-50 µg/mL
	Nissen L, Zatta A, Stefanini I, Grandi S, Sgorbati B. 2010	In vitro studies	N/A	N/A	Hemp varieties: 0.7-2.0 (%v/v)	MIC for Clostridium difermentas: Futura hemp: 1.41 µg/mL (P<0.05)
	Appendino G, et al. 2008	In vitro studies	N/A	DMSO (3.125%)	CBD 125 µL or erythromycin 125 µL or tetracycline 125 µL	MIC for S. aureus (SA-1199B): CBD: 1 µg/mL, Erythromycin: 0.25 µg/mL, and tetracycline 0.25 µg/mL
Autism Spectrum Disorder	Ajram, et al. 2017	Double-blind RCT	37 subjects (17 w/ASD, 20 Control)	Placebo (n=20)	Riluzole 50 mg	Riluzole increased the proportion of GABA in the prefrontal cortex of the ASD group but decreased the proportion of GABA in controls (group × drug interaction; F(1, 24)=4.288, P<0.05)
	Pretzsch, et al. 2019	Double-blind RCT	34 subjects (17 w/ASD, 17 Control)	Placebo (n=17)	CBD 600 mg/day	CBD decreased GABA levels in patients with ASD, while decreasing levels in Control patients when looking at the basal ganglia and dorsomedial prefrontal cortex (F(1,22) = 13.506, puncorr = 0.001, η2 = 0.380)
	Pretzsch, et al. 2019	Double-blind RCT	30 subjects (13 w/ASD, 17 Control)	Placebo (n=17)	CBD 600 mg/day	CBD showed a significant change in patient fALFF scores for patients with ASD, but not in neurotypical control patients (vermis V1: TFCE, pFWE = 0.045, k = 7, CoG: x = 21.1, y = −55.7, z = −14; fusiform: TFCE, pFWE = 0.029, k = 19, CoG: x = 28.3, y = −51.8, z = −9.58)
	Barchel, et al. 2019	Open label cohort study	53 subjects	Symptoms prior to CBD therapy	CBD 16mg/kg, max 600 mg and THC 0.8mg/kg, max 40mg	74.5% of participants had improved symptoms (p values reported for individual symptoms, with no symptom showing a p value of <0.05).
Smoking Cessation	Hindocha C, et al. 2018	Randomized, double-blind crossover RCT	30 subjects	Placebo	CBD 800 mg capsule	Reduced attention bias if recently smoked (p=0.007)
	Morgan CJA, Das RK, Joye A, Curran HV, Kamboj SK. 2013	Double-blind RCT	24 subjects	Placebo	CBD 400 mcg/dose inhaler	Reduced cigarette consumption (p=0.002), reduced anxiety levels (p=0.04), no statistically significant reduction in cravings
Parkinson's Disease	Zuardi, et al. 2009	Open-label pilot study	6 subjects	N/A	CBD 150mg/day, increased weekly to max dose 400 mg/day	BPRS total scores improved (p<0.001), PPQ scores decreased (p=0.001), UPDRS decreased (p=0.046), CGI-I improved (p=0.001), MMSE and FAB scores no statistically significant change
	Chagas, et al. 2014	Double-blind RCT	21 subjects	Placebo (n=7)	CBD 75mg/day (N=7) or CBD 300mg/day (N=7)	UPDRS, BDNF levels, and H1-MRS no statistically significant change, PDQ-39 total score differences (p=0.034)
	Chagas, et al. 2014	Case series	4 subjects	N/A	CBD 75mg/day pr CBD 300mg/day	Case 1, 2, 3: no episodes of agitation, aggressive behavior or nightmares, Case 4: behavior and dream improvement, reduction in episodes of complex movement (laughing, kicking, pushing, punching)
Multiple Sclerosis	Novotna A, et al. 2011	Double-blind parallel group study	241 subjects	Placebo	Nabiximols: THC 2.7mg and CBD 2.5mg (max 12 sprays per day)	Highly significant difference in favor of nabiximols (P = 0.0002).
	Koehler J, et al. 2014	Medical Chart Review	166 subjects	N/A	1:1 ratio THC: CBD spray (mean dose 4 sprays)	Response rate of 72%, mean NRS score decreased by 57% in the first 10 days of treatment
	Paolicelli D, et al. 2016	Observational study	102 subjects	N/A	Nabiximols: THC 2.7mg and CBD 2.5mg (mean 6.5 sprays/day)	Mean reduction to the NRS spasticity score was 2.5 ± 1.2 points (P < .0001)
	Akgün K, .Akgün K, Essner U, Seydel C, Ziemssen T. 2019	Systemic Review	14 studies (n=7440)	N/A	Nabiximols: THC 2.7mg and CBD 2.5mg	Percentage of patients that reached MCID with at least a 20% reduction in NRS ranged from 41.9% to 82.9%.

ASD: ; CBD: ; GABA: ; MIC: ; RCT: ;

promising view of treatment for the future of Parkinson's disease patients.

Multiple Sclerosis

Multiple Sclerosis (MS) is a chronic autoimmune disease of the central nervous system (CNS) that was reported to affect 2.3 million individuals around the globe in 2018.[31] It is one of the most common causes of neurological disability in younger adults that leads to symptoms of pain, muscle spasticity, spasms, and bladder dysfunction.[32,33] As treatment of MS continues to be studied and developed, the management of the associated symptoms is important for patient compliance. Spasticity associated with the disease is present in 80% of patients and often leads to the symptoms of pain, spasms, and decreased function.[34] Current research has shown the effectiveness and safety of THC/CBD for this disease state, and might signal advancements in therapy in the United States.

Current medications being used for the indication of spasticity related to MS are baclofen, tizanidine, gabapentin, and dantrolene, but many patients fail to respond to these treatments or might suffer intolerable side effects with continuous usage.[35] Along with these more traditional treatments, nabiximols (Sativex®), a cannabis-based medication, has been approved for the same indication in Canada and some European countries, but has not yet been approved in the United States. It consists of a 1:1 ratio of delta-9-tetrahydrocannabinol (THC) and cannabidiol (CBD). It has been approved in other countries as an add-on therapy for symptom improvement in MS or as an alternative therapy in adults who have tried and failed other therapies.[35] Many of the studies on CBD use in MS address this medication's safety and efficacy in specific trials and a collective review.

In 2011, Novotna et al. created a randomized, double-blind, placebo-controlled, parallel-group study to assess the efficacy of nabiximols.[33] This was a 51-site study conducted throughout Europe for subjects who had MS and spasticity not relieved by another current antispastic drug. Nabiximols is formulated as an oromucosal spray. A spray containing 2.7 mg THC and 2.5 mg CBD was used in the study, where patients could administer 12 sprays in any 24-hour period. After four weeks of treatment in a single-blind preliminary study, only individuals who saw an improvement were continued on to a 12-week double-blind, randomized study. The primary end points evaluated were the

Numerical Rating Scale (NRS) for efficacy and safety and tolerability, while secondary end points included spasm frequency, sleep disruption, and Barthel Activities of Daily Living scores. The study showed nabiximols to improve spasticity in patients, but only among patients who had a successful four-week trial of therapy in the first phase of the study. Again, there appears to be efficacy of the medication, but further trials need to be conducted.

Similarly, in a 2014 study by Koehler et al., results showed benefits in spasticity in MS patients, but this time also demonstrated nabiximols being effective as monotherapy rather than as an add-on therapy.[36] Data was collected through medical charts at an MS clinic in Germany, which followed 166 patients over a 15-month timeframe who were initiated on the THC/CBD oromucosal spray. The study also included data on patients who had different forms of MS that included relapse-remitting, secondary progressive, and primary progressive forms. In all, 120 patients remained on the treatment and overall spasticity scores decreased with a mean dosage of 4 sprays per day. Those who discontinued use cited adverse effects of dizziness, fatigue, and oral discomfort.

In a 2015 study, Paolicelli et al. provided data regarding the post-marketing efficacy and safety of the THC/CBD medication in 102 MS patients.[37] They conducted a 40-week study where patients were assessed through the Expanded Disability Status Scale (EDSS), the NRS for spasticity, the Ambulation Index (AI), and a Timed 25-Foot Walk (T25-FW) at the beginning of treatment and then every 3 months after. The average dose in this cohort was 6.5 sprays per day, which reduced NRS spasticity scores by 2.5±1.2 points ($p<0.0001$). Yet, this data excluded patients who did not show significant improvement in spasticity scores after the first 4 weeks of the study. Researchers were able to determine the efficacy and safety of this medication but still needed additional structural evidence supporting the use due to data being self-reported by patients and excluding patients.

A recent meta-analysis in 2019 by Akgün et al. compiled 14 publications, including observational studies and treatment registries, that assessed patient characteristics, effectiveness, and safety outcomes.[35] They chose to look at studies outside of randomized controlled studies (RCTs) in order to confirm that what was reported in practice matched the results of RCTs. The mean dosage in the 14 publications reviewed was 5 to 6 sprays per day, and no new adverse events or reactions were noticed in practice. The selected reviews in this meta-analysis supported long-term THC:CBD spray use and noted the benefit of this medication as responders can be recognized within the first 4 weeks of treatment. The review provided evidence for the efficacy and safety of THC:CBD in clinical practice.

While some of the studies had limitations proving objective data, due to patients providing their own feedback and results, there does appear to be effective management of MS symptoms of spasticity with the combination medication. The safety and efficacy is continuously shown as similar to those of other medications with the same indication approved in the United States, which might signal another way to manage MS symptoms in the future.

Conclusion

Cannabidiol provides a frontier that still requires more research. Epidiolex® is the only form of CBD with FDA approval, but with more research, other cannabidiol forms could be approved in the future. As of October 2020, clinicaltrials.gov shows trials centered around conditions not mentioned in this article, like pain, epilepsy, alcohol use, PTSD, and heart failure.[38] Some of the current evidence, or lack thereof, should be considered when pharmacists and consumers approach these novel treatment options.

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ROSALIND FRANKLIN UNIVERSITY OF MEDICINE AND SCIENCE SCHOOL OF PHARMACY STUDENT WRITING CLUB:

Business Member Spotlight: Stacy Doyle, PharmD - Roundy's Pharmacies

by Dagmara Zajac, 2023 PharmD Candidate, Angelo Strappelli, 2024 PharmD Candidate

Stacy A. Doyle, PharmD, has been the Vice President of Pharmacy at Roundy's Supermarkets since 2017. The Roundy's Supermarket division, spanning Wisconsin and the Chicagoland area, is one of the 21 divisions of Kroger Health, the healthcare arm of The Kroger Company. Dr. Doyle received her Doctor of Pharmacy degree from Ohio Northern University in 2003. She started her career with the Kroger Company 24 years ago as a pharmacy technician. Since graduation, she has held a variety of positions: pharmacist, district pharmacist coordinator, division pharmacy sales manager, and her newest role as of 2017, Vice President of Pharmacy at Roundy's Supermarkets. Dr. Doyle stated, "I started my career in community pharmacy because I wanted to make a difference and to help people. As I move into new roles in the company, where there may be less patient interaction, I feel like I can make a difference more globally. I strive to impact patient care by supporting our pharmacists and give them the tools they need to take care of their patients. I share the vision of our entire company of helping people live healthier lives."

Day to Day Practice

The Roundy's Supermarkets division has 107 pharmacies: 67 in Wisconsin and 40 in the Chicagoland area. As the vice president, Dr. Doyle oversees the operations of all 107 pharmacies. Naturally, her days are very busy. Dr. Doyle's team consists of pharmacy practice coordinators focusing on the clinical and compliance elements, and an operations team focusing on the inventory and business side. The work environment is fast paced; she collaborates with different departments, sits in on various meetings, and does a lot of long-term planning. Dr. Doyle spends some of her time at her Milwaukee office. The rest of the time is spent doing site visits. During her pharmacy site visits, she seeks feedback to see how things are going and to find out whether there is anything that needs to be implemented, improved, or changed.

One of Roundy's Supermarket's pharmacy goals is to vaccinate patients in a timely and convenient manner. Recently, Dr. Doyle helped implement the changes made by the Wisconsin Health and Human Services (HHS) department to the immunization regulations. Doyle and her team updated the protocol and collaborative practice agreements. Pharmacists are able to immunize patients above 3 years of age with any vaccine, including any future coronavirus disease 2019 (COVID-19) vaccine. In addition to immunization services, additional pharmacy-based services, such as medication therapy management and health screenings, are offered.

Dr. Doyle and her team have worked with various local health departments to brainstorm projects, such as COVID-19 testing or flu shot clinics. Dr. Doyle is personally involved with the Kenosha County Health Department, where she sits on the Opioid Task Force. She has been an active member of PSW ever since she moved to Wisconsin in 2017. She has recently worked with PSW to determine how community pharmacies will have to change due to the COVID-19 pandemic. Also, Dr. Doyle's team represents Roundy's Supermarkets on different committees of PSW. Roundy's division pharmacists hold health fairs in nursing homes, and organize other festivals and health fairs in their communities.

Raising the Bar

Dr. Doyle believes that friendliness is one of the most important traits of a community pharmacist. During interviews, the Roundy's pharmacy team looks for this trait; it is indicative of how well the pharmacist will be able to provide excellent customer service and patient care, as well as being able to communicate effectively. Doyle also notes that pharmacists should be open to growth, approachable, and willing to try new things.

Dr. Doyle came into her current position soon after Roundy's merged with Kroger. As Roundy's adapted to new policies, procedures, workflows, and computer software, the pharmacists found it to be a welcomed change. The new workflow system improved task prioritization and patient communication, and thus improved patient outcomes.

One of the biggest innovations this year, out of necessity, was drive-thru COVID-19 testing at several Roundy's pharmacy sites across the country, including in Wisconsin (under the Pick 'n Save banner) and Illinois (as Mariano's). The pharmacies within the Kroger Health network worked to provide easy access and self-administered COVID-19 testing to many communities to help slow the spread of the virus with the result turnaround time of 72 hours. Additionally, Kroger Health was the first network of pharmacies to receive an FDA emergency use authorization for its COVID-19 test home collection kit. The testing kit was originally only available to frontline associates of The Kroger company, but it is now available to all patients. Kroger also partners with other businesses to provide COVID-19 tests. The COVID-19 at-home tests are mailed to the patient; they connect with a Kroger Health nurse practitioner via a Telehealth visit; and the nurse practitioner walks them through the administration procedure. They are instructed on packing and shipping the test and are notified of their results within 48 hours.

Roundy's pharmacies, as part of Kroger Health, have established many innovations

Above: *Roundy's Pharmacy, Milwaukee, WI.* ***Right:*** *Stacy Doyle, PharmD.*

to further differentiate themselves in the wide world of pharmacy. The pharmacists complete continuing education classes to maintain their licenses. They have taken focus-based training classes, on topics like health screenings, immunizations, and, with the Wisconsin HHS department, expanding access to childhood vaccines, a pediatric refresher class. They have been able to maintain a balance of both the clinical and dispensing sides of the pharmacy. Every February, they host heart-healthy screenings, and every June they host glucose screenings for their patients, in addition to conducting full biometric screenings year-round. They have also provided an online interface where customers can reorder and pay for medications, and arrange curbside pickup and delivery of medications and groceries, which is especially important during the pandemic. Additionally, as part of the COVID-19 protocols, the company has implemented many safeguards, including social distancing markers, plexiglass, mandatory masks, and enhanced cleaning and disinfecting procedures.

Bumps in the Road

One of the most recent challenges for Roundy's pharmacists is the COVID-19 pandemic. The shortages of and increased demand for medications was an issue at the beginning of the pandemic; pharmacies are also dealing with rapidly changing guidelines and processes from the Centers for Disease Control and Prevention and other federal and state agencies.

The pandemic has increased the importance of flu vaccination. To decrease the burden on our healthcare system from COVID-19 and influenza, it is important for pharmacy staff to encourage patients to get the flu vaccine.

A challenge that Dr. Doyle has seen throughout her career, one that pharmacists currently are trying to overcome, is helping patients and healthcare professionals understand what pharmacists are capable of doing for patients. Dr. Doyle believes it is very important to practice at the top of our licenses and to make sure that other healthcare professionals see the importance of pharmacists in the healthcare environment. She expresses that, with any new implementations or challenges, it is very important to be open to feedback and to be flexible.

Moving Forward

Dr. Doyle states that Roundy's Supermarket pharmacies are continually looking for opportunities to grow in the clinical and dispensing sides of pharmacy. They plan on continuing to attract potential customers and patients by promoting it as a one-stop place for prescriptions and grocery needs. They would like to incorporate other departments into the healthcare realm, to help provide healthy options. They would like to demonstrate that, in addition to caring for patients with chronic diseases, they are also helping to prevent them. Working with dietitians and nutritionists, they would like to provide food tours to promote healthier living among their customers.

Doyle's advice to pharmacists who are interested in the community/supermarket pharmacy area is to be flexible and willing to dive into unknown territory. She said, "The main responsibilities for a pharmacist are continuously changing, as is the profession. We must grow within our profession and be open and fluid to changes in our field. While dispensing is a part of our profession, it is no longer the focus. Using our clinical training and knowledge, we can provide patient care beyond dispensing a prescription."

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Spotlight

Leadership Spotlight: Melissa Theesfeld

by Hailey Thompson, 2022 PharmD Candidate, and Nicholas Olszewski, 2022 PharmD Candidate

Dr. Melissa Theesfeld is no stranger to forging her own path throughout her pharmacy experiences. As a student, she took a non-traditional path, pursuing a career as a study coordinator for two years at a contract research organization, prior to developing an interest in pharmacy. Following that spark, Theesfeld enrolled at the University of Wisconsin–Madison School of Pharmacy. Upon graduation, she completed her PGY-1 at Froedtert Hospital in Milwaukee, where she later became the program's first PGY-2 administrative resident. After practicing in a management role at Froedtert Hospital for a few years, Theesfeld decided to follow her passion for project management and to explore new opportunities. She continues to pursue roles that allow her to help others engage with their pharmacy pathways.

As current president of the Pharmacy Society of Wisconsin (PSW), Theesfeld sits on the board of directors and has played a crucial role in steering the organization through the uncertainty of a pandemic and a transition to new executive leadership. As PSW president, Theesfeld has prioritized the PSW membership to bolster the level of member engagement and provide opportunities for members to connect with one another. It is important to Theesfeld that pharmacists and pharmacy technicians see the value in their membership and use their experiences to shape the organization and the future of Wisconsin pharmacy practice.

Aside from her PSW presidency, Theesfeld has served in her current role as director of experiential education for Concordia University Wisconsin's (CUW) School of Pharmacy since 2011, having been a member of the experiential education team since the founding of the school in 2010. In this role, Theesfeld coordinates all IPPE and APPE rotations completed by the student pharmacists at CUW. She also connects with her students in the classroom as she coordinates pharmacy experience courses and guest-lectures in others. Her mission is to ensure that her students have access to quality experiences and can select where to complete their experiences. Having a varied offering of experiences for student pharmacists to choose from is important to Theesfeld. Combining this flexibility with different touchpoints throughout the curriculum provides extra guidance for students.

Opportunity Follows Challenge

Theesfeld's favorite aspect of her role as director of experiential education is her part in the creation of CUW's School of Pharmacy and determining how to structure and build the program into the success that it is now. Throughout this process, Theesfeld faced challenges that she had not had to ponder previously. For 127 years, until 2010, UW-Madison was the only pharmacy school in Wisconsin; nobody in the state had had to consider how to structure a new program for developing pharmacists. One of the largest hurdles that Theesfeld had to overcome was convincing multiple major health systems and their external partners of the benefits that CUW could bring to the profession. Showing these stakeholders how the school trains their pharmacy students, and highlighting their qualifications as future pharmacists, was a crucial step to establishing these partnerships. External stakeholders are essential in providing valuable experiential education to students.

Another difficulty in the creation of the experiential education program at CUW was proving to stakeholders that there are multiple ways to train pharmacists to become quality practitioners . Theesfeld continues to enrich stakeholder relationships in this role. She looks for ways to advise preceptors on how to avoid feeling burdened by optimizing the use of their student pharmacists. It is evident that pharmacies and other pharmacy sites are busy, so introducing the task of teaching a student has the potential to hinder a pharmacist's ability to complete responsibilities. To combat the burden of student presence, Theesfeld is continuously brainstorming and implementing ideas for how preceptors can direct their students' time and learning in ways that enhance engagement while also focusing efforts on the pharmacy's goals and responsibilities.

Advocacy for a Bright Future in Pharmacy

Pulling from her experience engaging stakeholders to establish a new pharmacy school, Theesfeld stresses the importance of securing external support and the broader impact it can have on the pharmacy profession. The future of pharmacy is in the hands of those willing to be champions for our profession, our abilities, and the crucial roles that we play in the provision of patient care. In recent years, Wisconsin pharmacists have enjoyed various expansions in the ability to offer care services due to the efforts of individuals who see the profession's value as well as the larger role that we can play in the prevention and treatment of diseases in our community.

One of the main challenges facing Wisconsin pharmacists is a lack of sustainable reimbursement for unique, pharmacist-provided patient care services. Wisconsin employs highly innovative pharmacists; however, patient access to their services and the expansion of these services are less robust than they could be. To continue these services effectively, pharmacists and pharmacy students must be prepared to advocate for our profession and articulate our essential roles to legislators, other healthcare team

members, and the public. Together we can demonstrate the abundance of care services pharmacists can provide in addition to the traditional dispensing role, and obtain the necessary external support needed to catalyze patient access.

Advocacy is a topic that Theesfeld is passionate about and has created ample opportunities for her students to be exposed to both in and out of the classroom. Throughout their time at CUW, pharmacy students participate in classes and simulations that address servant leadership and advocacy. Various student organizations also emphasize leadership and advocacy. Engagement of pharmacists, pharmacy students, and pharmacy technicians is crucial in the progression of the field of pharmacy. Advocating for our abilities, following our passions, and taking advantage of every opportunity facilitates the completion of our goals.

Advice for Future Leaders

Theesfeld's passion for developing well-versed pharmacists does not end with introducing advocacy; she also cares about other aspects of professional development. Theesfeld shared some words of wisdom that she received in her residency that helped shape her into the great leader that she is: "Why aren't you speaking up when you have an opinion?" This simple query inspired Theesfeld to reflect on her actions and fears, to challenge herself to make a constructive change. She now encourages her students and mentees that we, as leaders and pharmacy professionals, cannot be afraid of getting shut down for sharing our opinions. If we never share our thoughts, no one will know what we have to contribute, and further, nobody will benefit from the success that could come from a great idea that was hidden out of fear.

Additionally, Theesfeld encourages future leaders to take advantage of opportunities presented to them. As a part of a complex and varied profession, opportunities are always presenting themselves, and the future is unknown and full of possibility. Taking advantage of these opportunities connects people, facilitates learning moments, and provides moments to advocate for our profession and our patients. To grow as professionals, we must be open and willing to tackle new challenges. Theesfeld strongly believes that to become inspiring leaders, pharmacists must experience a wide array of opportunities, overcome their fears of rejection, and share their thoughts and ideas to experience personal and professional growth.

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Spotlight

Wisconsin Health Literacy

by Emily R Hoffman, 2021 Pharmacy Candidate, Logan M Wanca, 2021 Pharmacy Candidate

Wisconsin Health Literacy is an organization that focuses on improving health literacy throughout the state. It is a division of Wisconsin Literacy and it is headquartered in Madison, Wis. Its mission is "to promote clear communication between those who give and those who receive health care services." This year, it is celebrating 10 years as an organization. In 2010, Wisconsin Literacy staff and their partners across the state of Wisconsin gathered at a conference to discuss the future of health literacy efforts within the state and how to improve health outcomes through educational programming. Their goals were for all health care providers to be trained in health literacy concepts, for medication labels to follow universal design principles, and for health literacy efforts to have a sustainable infrastructure. From this gathering, Wisconsin Health Literacy was created, and there have been many successful projects since. One of the organization's earlier projects was Let's Talk About the Flu, which provided community education about the dangers of the flu and the safety and benefits of vaccines. This was the first project in the Let's Talk About series, and many others have followed this educational format aimed at improving health literacy for specific topics.

The term "health literacy" has many definitions. At Wisconsin Health Literacy, staff members believe that health literacy is two-sided. The patient side is typically described as having the ability to find, use, understand, and process information to make better healthcare decisions. The other side is that of the professionals. It is important for providers to be able to effectively communicate this health information to facilitate their patients' understanding. Health literacy goes beyond reading and writing. It extends to every aspect of healthcare, including listening, speaking, working with numbers, and then analyzing that information to improve patient health outcomes. Health literacy is fluid throughout life. It can change with age, education, and stressful situations, making everyone susceptible to having low health literacy at some point in their lives. This emphasizes the need for educational programming to encourage all patients to

Below: *Kari LaScala presenting a Let's Talk About Medicines workshop.*

be their own advocates.

Day to Day Practice

Wisconsin Health Literacy (WHL) works with people from every type of background. This includes health professionals and individuals within the community, including immigrants, refugees, and seniors. WHL staff have worked extensively with doctors, physician assistants, nurses, CNAs, social workers, pharmacists, insurance providers, caregivers, and others. Due to this diverse population, it was important to partner with various organizations to help facilitate connections. WHL has partnered with many organizations across the state, starting with the 70 coalition member literacy agencies of Wisconsin Literacy, Inc. Additional partners include organizations that serve seniors, as well as those connected with community centers, libraries, and housing units, to name a few. The goal is to be able to reach a large audience, and partnering with these organizations across the state helps with that goal. Since WHL is headquartered in Madison, Wis., these partnerships are essential in order to reach every region of the state, stretching as far as Ashland, Wis. They also thank many of their great volunteers across Wisconsin for making presentations possible. When volunteers are not local to a particular area that needs services, they will drive to wherever they are needed.

Additionally, WHL is partnered with the Pharmacy Society of Wisconsin (PSW) and the University of Wisconsin-Madison School of Pharmacy. Both organizations have been instrumental in providing guidance and insight for various projects relating to pharmacy, such as the Medication Label Project. Another advantage of the partnership is that it leads to increased participation among pharmacies. The connection with PSW makes it much easier to connect with pharmacies to discuss potential collaborations with WHL on various projects.

Raising the Bar

Over the past 10 years, there have been numerous projects initiated by WHL in an effort to increase health literacy across Wisconsin. Kari LaScala, associate director of WHL, recalls one of her favorite recent projects as the Medication Label Project, which aims to make sweeping changes to pharmacy labeling. Through a partnership with the University of Wisconsin-Madison School of Pharmacy, WHL is working to change how information is presented on medication labels. The goal of this project is to make it easier for patients to read, and ultimately understand, the information about their prescriptions. Instead, the directions for use are better written as, "Take 1 pill in the morning and 1 pill in the evening." Changing the presentation of this information should help decrease confusion and improve patient outcomes. This project has the potential to impact a large number of prescriptions. So far, over 4 million prescription labels per year have been improved thanks to this project. As more pharmacies adopt this label change, more prescriptions will be improved.

Above: *Some members from the Patient Advisory Group who helped guide the Medication Label Project from the patient perspective.*

Another recent favorite of LaScala's was the Let's Talk About Opioids program. Through this program, WHL partnered with prisons across the state to educate inmates on the risk of using opioids when they leave prison. They wanted to provide education about the risks of overdosing, and to discuss tolerance levels. Unfortunately, the team was only able to do a couple of in-person sessions before COVID-19 hit. Because of this, a lot of changes happened to the programming. Instead of having individuals from WHL come in and present in the prisons, they did a train-the-trainer webinar so staff in the prisons could give the presentations. They also reworked the materials that went with the presentation to allow for continued use. The workbooks were changed to be more self-guided and allow learners to read, answer questions, and learn more about opioids.

Measuring improvement is an important aspect of providing educational presentations. To do this, community-based projects utilize pre- and post- assessments. These can help assess what learners have gained from the presentation. If there appears to be a deficiency in the way information is taught, then WHL staff are very willing to make changes to improve future presentations. They can emphasize different areas, or try to clarify information. Additionally, they often do a 60- or 90-day follow-up survey. This survey not only tests for knowledge, but also for behavior change. Results can indicate whether the workshop had long-lasting impacts on how people act or use the techniques that were taught.

Bumps in the Road

All projects have occasional issues that need to be addressed. Projects initiated by WHL are not exempt from this. For pharmacy projects, time is a large factor. Community pharmacies are busy, and

adding additional projects can seem daunting. Many pharmacists might agree that a certain project is important and should be implemented, but they might not have the time or resources to participate. This is where student pharmacists become crucial. As avid learners, they are always looking for ways to move the profession forward. Because of this, they play an instrumental role in helping WHL complete these projects.

Another common challenge deals with initiating new projects. This makes having the necessary connections even more important for success. Wisconsin Health Literacy heavily relies on their partners to accomplish their goals. There is a mutual trust that must be built. This trust leads to continued partnerships and can even lead to growth through referrals. When it is important to reach many patients throughout the state, having trusted partners is essential.

Like many organizations, WHL has had to make changes due to the COVID-19 pandemic. In order to provide their workshops, they have had to transition to online video conferencing. This has been challenging, especially when it comes to creating rapport with learners. Participants are typically quieter and more nervous during these online workshops, compared to being in-person. Wisconsin Health Literacy hopes to transition back to their in-person workshops in the near future. For now, they will continue to provide their services in any way that they are able.

Moving Forward

Celebrating 10 years is quite the accomplishment. As a state, Wisconsin is always looking forward to what is next, and WHL follows this same motto, with several plans for growth. They have recently started to look at how health literacy impacts health equity and how the two relate. "Health equity" essentially means that all patients have the same fair and just opportunity to be healthy. Wisconsin Health Literacy wants to focus on how disparities in health equity can be remedied. Additionally, WHL plans to continue with its community-based projects. Staff believe that continuing to provide workshops and other educational materials is possibly more important now than ever before. WHL plans to create materials about COVID misinformation; communicating with patients with dementia; and finding health information online, just to name a few. They will also continue with the Medication Label Project, with the goal of expanding this to many more patients. There is always more work to be done. Health literacy will always need to be addressed, and the essential work of WHL will need to continue to help improve patients' lives.

If you would like to get involved with WHL and learn more about them, please visit their website at wisconsinliteracy.org/health-literacy, or reach out to them via email at healthliteracy@wisconsinliteracy.org. They are frequently looking for volunteers to help with their workshops, especially outside the Madison area; training is provided prior to presenting. For pharmacies interested in joining the Medication Label Project, please contact Kari LaScala at kari@wisconsinliteracy.org. The project is likely to end in the spring of 2021.

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