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The Journal

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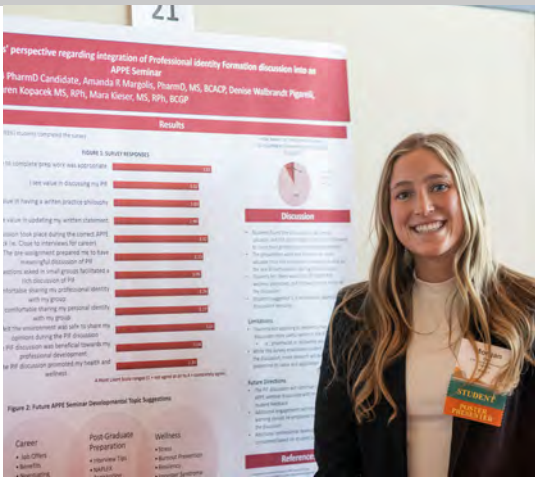

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The Journal
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The Journal of the Pharmacy Society of Wisconsin is a professional publication for original research, review, experience, and opinion articles that link science with contemporary pharmacy 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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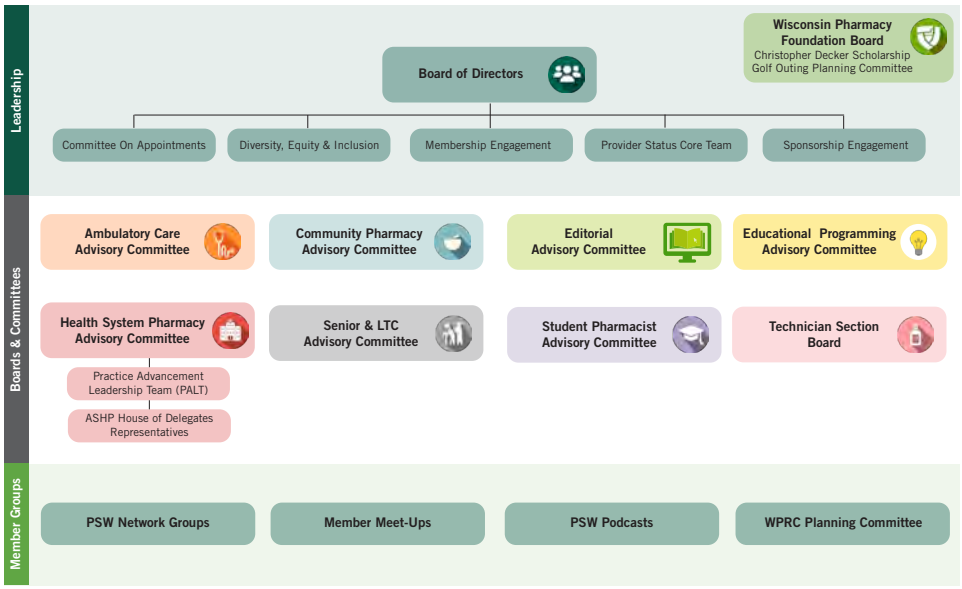
UpFront: One Voice, One Vision – The Pathway to Inclusion

by Sarah Pagenkopf, PharmD, BCPS,
Quinlan Alfredson, 2026 PharmD Candidate

The Pharmacy Society of Wisconsin was born to represent a unified voice of all Wisconsin pharmacy professionals. After two years exploring how that unified voice would be best represented, a strong foundation, with the aim of catalyzing connection between pharmacy professionals in all settings, was laid on January 1, 1998. Our work as a professional organization was set in motion, and the dedicated members of PSW have been actively working to ensure comprehensive representation for all. Their ongoing efforts continue to make a difference in identifying the path forward.

In early 2022, in an extension of PSW's original vision to collect the unified voice of Wisconsin pharmacy, the PSW Board of Directors developed a special committee, the PSW Committee on Appointments. This committee of past and current PSW Advisory Committee Chairs and a Diversity, Equity and Inclusion (DEI) leader was charged with the creation and development of a consistent and streamlined approach to appointing members to PSW Advisory Committees. The Committee was charged with developing and recommending a process that would facilitate the thoughtful inclusion of individuals who demonstrate commitment to PSW, as well as qualities befitting a pharmacy leader. Service on committees is a growth opportunity that builds future PSW Board leaders. Ultimately, the team was charged with developing a pathway towards inclusive representation by nominating deserving individuals from our membership to PSW Advisory Committees.

FIGURE 1. PSW Leadership Organization Chart



In order to embrace technology and engage with our members across various practice settings, the Committee on Appointments instituted an all-new online portal. The portal, which opened for nominations on January 1, 2023, allows members of PSW to conveniently submit their nominations for membership on specific PSW Advisory Committees through a web-based survey. Through the survey, members can easily explore multiple volunteer-based committee opportunities and request nomination in more than one committee of interest. In an effort to ensure inclusivity, the portal is available to all members more than 6 months each year. This initiative aims to provide all members with access and opportunity to participate in the nomination process.

Led by the past and current Chairs

of the PSW Advisory Committees, the Committee on Appointments completed a comprehensive review of the strong practices in developing and maintaining successful committee processes. Based upon their time volunteering, committee leaders also brought forth opportunities for improvement and areas for enhancement. These strong practices were summarized, and committees adopted uniform and specified roles (chair, chair-elect, past chair); more clearly defined terms of appointment (2 years for general members); parameters for re-appointment; a process for special circumstances; and recommendations for use of a standardized nomination evaluation tool.

Furthermore, the DEI leader emphasized the importance of adopting a redacted process for sharing nominations with committee leadership. This process involves removing the nominee's name and identifying information. This effort was approved by the Committee on Appointments as a strategy to remove unconscious or conscious biasing, which could impact the nominee selection process.

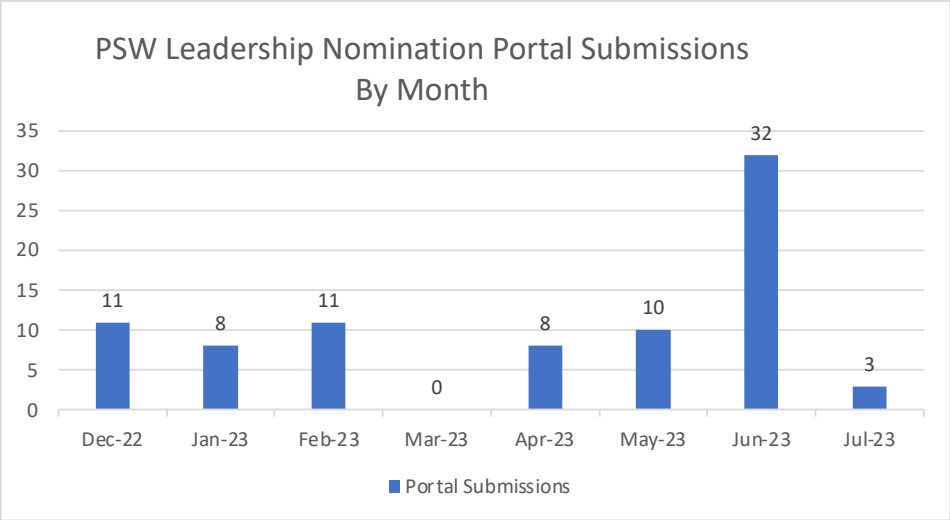
Additionally, a harmonized nomination cycle has been implemented across all PSW Advisory Committees. The cycle now begins in September and ends in August of the following year, mimicking the same term year used by the PSW Board of Directors. This harmonized nomination cycle was sought after feedback from members indicated that varied nomination cycles used by each committee were confusing to members, and members frequently missed the *FastFacts* posts outlining when a specific nomination cycle was open. The September to August term year also aligned well with the PSW Annual Meeting, a celebration of our membership and all the important work members do to support their communities, their teams, and PSW. At the 2023 Annual Meeting, incoming, current, and outgoing committee members will be invited to the first annual Advisory Committee Assembly, an opportunity to join in shared fellowship and to immediately begin building strong and lasting connections.

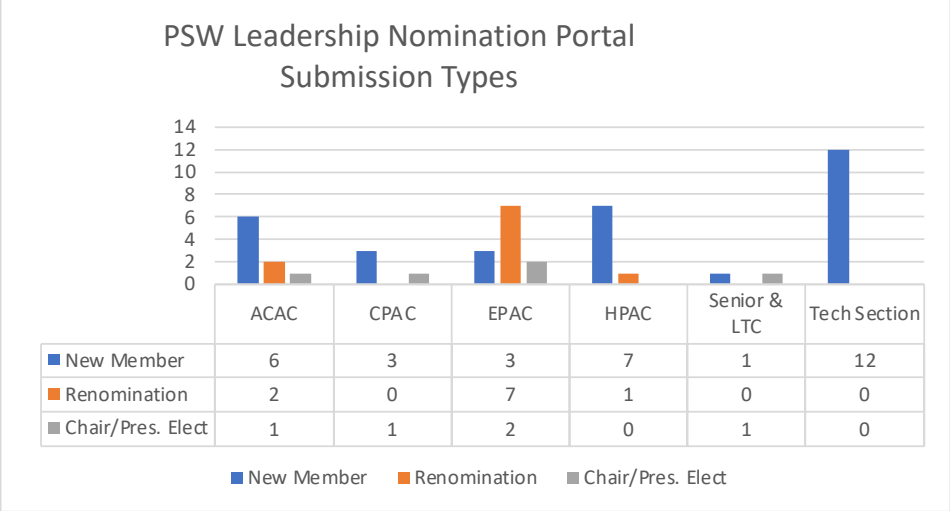
Focusing on the aim to create a unified voice to represent Wisconsin pharmacy professionals, the PSW committees began sharing Summary Reports with the Board of Directors in late 2022, based on the recommendation of the Committee on Appointments. The Summary Reports highlight the important elements, opportunities, and advocacy needs of each of the unique PSW Advisory Committees. Developed and prepared by the committee chairs, chair-elects, and Past chairs, this summary aims to help the PSW Board of Directors best formulate a narrative of critical needs, while fostering a reliable and transparent communication structure.

Ongoing and future endeavors of the PSW Board-appointed Committee on Appointments include ongoing process improvement and evaluation of the on-line self-nomination portal and nominee evaluation tool. Additionally, the Committee will continue to focus on strong practices in communicating the work of the Advisory Committees, the best ways to ensure members are aware of volunteer opportunities within PSW, and expansion of strong practices discovered by our Advisory Committees to other areas and practices within PSW.

A special thanks to those who were part of the Committee on Appointments work: Holly Altenberger, Julie Bartell, Janet Fritsch, Dave Hager, Lisa Imhoff, Katie Kuecker, Sarah Raether, Xin Ruppel, Nicole Schreiner, Ellina Seckel, Sarah Sorum, Miranda Wagner, and Maria Wopat.

FIGURE 2. Initial Data from the PSW Advisory Committee Nomination On-Line Portal





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PHARMACIST & TECHNICIAN CE:

Questioning Quasi-Experimental Research: An Overview of Quasi-Experimental Research Design

by Cassie Sedgwick, PharmD, Clara Nickel, 2024 PharmD Candidate, Anna Erickson, 2024 PharmD Candidate, Grayson Cooley, 2024 PharmD Candidate, John MacDonald, 2024 PharmD Candidate, Amanda Margolis, PharmD, MS, BCACP

CE FOR **PHARMACISTS & TECHNICIANS**

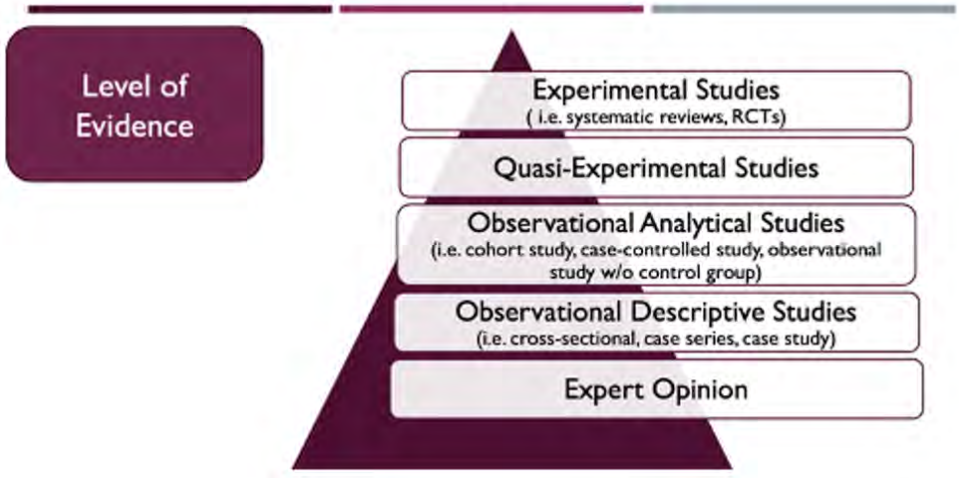
COMPLETE ARTICLE AND CE EXAM AVAILABLE ONLINE: **WWW.PSWI.ORG**

Learning Objectives

- Describe when quasi-experimental research design is used compared to traditional experimental research.
- Differentiate among the major types of quasi-experimental research design.
- Identify the strengths and limitations of propensity score matching and interrupted time series.
- Identify critical appraisal checklists that can be used to evaluate a quasi-experimental study.

Appropriately assessing and using literature is important for informed practice and clinical decision making.[1-3] Pharmacists are well trained in assessing true experimental research, such as systematic reviews, meta-analysis, and randomized controlled trials (RCTs); and observational studies, such as cohort and case-controlled studies. This information is then translated into practice and used to ensure patients are receiving high-quality, evidenced-based care.[4] Quasi-experimental research is being used more often in medical literature, though how to interpret these studies is not always covered in pharmacy curriculum. Quasi-experimental research is similar to traditional research (i.e. RCTs); however, it does not involve randomization. A quasi-experimental design can be used when randomization for an RCT is unethical, such as when the outcome in question may result in harm. It can also be used when a traditional experimental design may be cost- or time-prohibitive or to explore a causal relationship in the early stages of research. Quasi-experimental studies fall below traditional experimental research in level of evidence though are still higher than observational studies or expert opinions (Figure 1).

FIGURE 1. Level of Evidence Pyramid



As quasi-experimental research becomes increasingly prevalent in medical literature, it is important that pharmacists understand how to interpret this study design in order to translate it to clinical practice. A survey was administered to pharmacists across Wisconsin to assess understanding of quasi-experimental research design. The survey included four multiple choice questions and one short answer question to assess general knowledge of quasi-experimental design, including interrupted time series and propensity score matching, and three questions using a 5-point Likert scale (1=not confident at all to 5=very confident) to assess confidence in assessing different research methods including randomized controlled trials, interrupted time series, and propensity score matching. Fifteen pharmacists responded to the survey. Respondents scored between 0% and 40% on the multiple choice and short answer questions assessing knowledge. Mean confidence in assessing RCTs was 4.2 compared to 1.5 and 1.8 for interrupted time series and propensity score matching, respectively. This survey demonstrates that a gap in knowledge exists for pharmacists in how to interpret quasi-experimental design. The purpose of this article is to increase pharmacist knowledge and ability to assess studies using quasi-experimental research design.

When to Use Quasi-Experimental Research

As previously mentioned, quasi-experimental study design is becoming increasingly prevalent in medical literature; therefore, understanding and assessing these types of studies has become essential to clinical practice. The prefix "quasi" means "resembling."[5] Quasi-experimental research resembles experimental research without being truly experimental due to a lack of randomization.[5-7] Despite this difference, the goals of quasi-experimental research remain the same: to establish causal relationships between independent and dependent variables. In quasi-experimental research, the investigator directs the dependent variable and therefore it is a higher level of evidence than observational research.[5] However, quasi-experimental research is still at a higher risk for other limitations compared to RCTs, such as confounding variables.

Quasi-experimental design can be used in cases where it would be unethical to randomize.[5] An example of this would be if the outcome in question is centered around whether an intervention causes harm. In many cases, patients choose whether they receive a particular intervention, such as a treatment or procedure. Investigators can then follow patients or review the medical record retrospectively to see if a certain intervention caused harm. In these cases, quasi-experimental research may be able to fill gaps in knowledge or answer questions that would otherwise be unethical through an RCT. However, by applying quasi-experimental techniques to the traditional retrospective cohort design, it may produce similar distributions of baseline characteristics and minimize some aspects of selection bias.[7] Quasi-experimental design can also be used to reduce cost or resources to test a hypothesis. The cost of an RCT can be high, especially when considering many involve multi-center approaches. Quasi-experimental design is a less costly way to establish a causal relationship. Cancer screening and prevention trials are generally very long and would be costly to conduct as RCTs, so many of those studies use quasi-experimental approaches.[8-10]

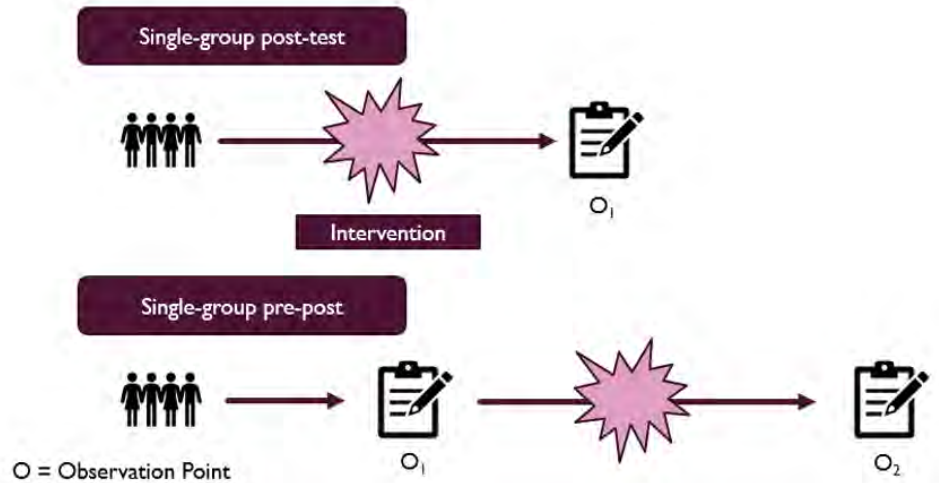
Quasi-experimental research is also used to evaluate new programs, services, educational materials, or workflows.[5,7,11] When a new service or workflow is implemented across a department, randomization, or even prospective data collection, is often not feasible.[11] Because of this, randomization is not possible and a quasi-experimental approach can be used. Additionally, whether a patient is enrolled in a program or receives a specific treatment is often dependent on patient specific factors and is chosen by the patient or clinician. Using quasi-experimental research designs can often include individuals who may be excluded from an RCT and are often considered more pragmatic.[11]

Though quasi-experimental designs are not considered the "gold standard" of research, these methods have many strengths. Since the study population tends to resemble the general population more closely, quasi-experimental studies have higher generalizability.[5,6,11] Additionally, interventions are often assessed in real-world settings rather than a controlled laboratory environment, leading to higher external validity.[6,11] Quasi-experimental research designs meet some criteria for causality which allows for some causal inferences when randomization is not possible.[11,12] A quasi-experimental study can lay the foundation to justify further research when implementing an experimental design may not be feasible due to cost or time constraints.[5,6] Quasi-experimental methods can also be used in the retrospective analysis of interventions that have occurred outside of the investigator's control and can use previously collected data.[5,6,11]

Conversely, quasi-experimental design has many limitations. As subjects are not randomly assigned within the quasi-experimental structure, these study designs have lower internal validity than RCTs.[5-7,11] Less control increases the risk of confounding variables and bias. An example of a potential bias is in the selection of subjects. Without a standard system for randomization, natural human bias can influence who is chosen to be included in the study population, and who may receive the intervention, leading to differences between the intervention and control groups. Additionally, other factors such as age and comorbidities may influence whether a subject receives the intervention. Another threat to the quasi-experimental methodology is historical bias, which occurs when events outside the intervention influence the measured outcomes.[5,11] These unrelated events may precede or coincide with the intervention and may misrepresent trial results. For example, suppose an investigator is evaluating patients seen in a new asthma clinic, but many of those patients are also enrolled in an asthma education course. In that case, it could be challenging to determine if their increase in proper inhaler use was due to the clinic or the education course. Finally, if subjects are followed for extended periods of time, methods of testing may change or evolve. Instrumentation bias, as this phenomenon is called, could complicate data comparisons over time.[11]

Additionally, some quasi-experimental studies may have ambiguous temporal precedence, as the timing of the intervention may not be defined.[6] A vague timeline makes distinguishing between

FIGURE 2. Pretest-Posttest Design



pre-intervention and post-intervention data difficult. For instance, if only a post-intervention test is performed, it can be unclear if the outcome was present before the intervention or if the measured effect was truly due to the intervention.

Variations of Quasi-Experimental Research

Though there are several variations of quasi-experimental research, some of the most common include the pretest-posttest, interrupted time series (ITS), and propensity score matching.[5,6,11] These methods can be used independently; however, many studies combine designs when analyzing casual relationships.

Pretest-Posttest Design

The pretest-posttest method may include a single group or use multiple groups, with both an intervention and control.[5,6,11] The factor that differentiates pretest-posttest from interrupted time series is that the dependent variable is only measured once before (unless the design is post-test only) and once after the intervention. Single group pretest-posttest designs (Figure 2) are considered to be the weakest form of quasi-experimental research. Due to lack of repeated testing, this type of design may be subject to the Hawthorne effect, where individuals act differently or modify their behavior in response to being observed. Also, since there is no control group, it can be difficult to determine if the impact on the dependent variable is due to the intervention, co-occurring events, or if the outcome would have occurred without the intervention.

Interrupted Time Series (ITS)

ITS are similar to the pretest-posttest design; however, with this design, multiple data points are collected before and after the intervention, creating a timeline of outcome measures (Figure 3).[5,6,11] This creates a stronger causal relationship between the independent and dependent variables. ITS can be single-group, or can include a comparator or control group. One example of when a single-group ITS may be used is when a policy or procedural change impacts an entire department or facility and there is not a group that was not impacted by the change. If an institution changes the way antibiotics are ordered in the emergency department to reduce inappropriate antibiotic prescribing, the desired outcome could only be measured prior to the intervention and after. There would not be patients who were not impacted by the change in procedure. In this case, if the number of documented errors or time from ordering to receive medication was previously measured on a consistent schedule, that could be compared to measurements taken post-change to determine the impact. In an ITS, the consistent frequency (i.e. monthly, quarterly, etc.) of observations or outcome measurement should have a clinical or practical significance.[11] Single-group ITS can also be conducted with multiple interventions.[5,6] This can be useful when trying to improve services or workflows with changes being made periodically. The impact of each change could be measured throughout time and each change would be a set timepoint where an intervention occurred.

Use of a comparator or control group (Figure 4) strengthens the design of an ITS. A main difference between an RCT and an ITS is that subjects are not randomized to the intervention and comparator groups.[5,6,11] In an ITS, the clinicians, patients, or other factor (e.g. time of process change, floor admitted to) determines whether a patient receives the intervention. However, the use of a control group in an ITS can help reduce historical and instrumentation bias and distinguish the intervention effect from co-occurring events.[6] Both single and multigroup ITS rely on extrapolation to estimate what the postintervention data would have been without the intervention.[6,11] This helps to determine the impact or the difference that the intervention had on the outcome in question. The difference between the outcome line postintervention and the extrapolated line shows the perceived impact of the intervention (Figure 5).

Figure 5 depicts an example of how data from a comparative ITS may be shown.[5-7,11] The extrapolated data is depicted by the dashed line while the solid line depicts the actual data collected. Use of a comparator group can help to distinguish the impact of the intervention from the impact of co-occurring events. The difference between the extrapolated line of the comparator, or control, group and the collected data postintervention can be considered to be the difference caused by co-occurring events. This difference can then be subtracted from the difference between the extrapolated

FIGURE 3. Single-group Interrupted Time Series

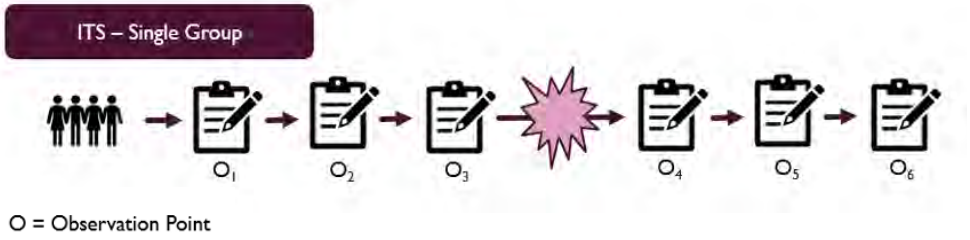
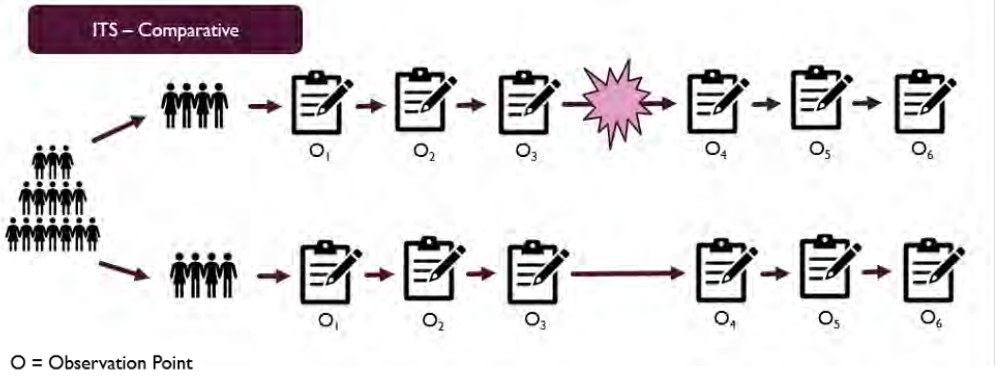


FIGURE 4. Comparative Interrupted Time Series



and collected data lines of the intervention group to determine the difference caused by the intervention. This is also referred to as a difference-in-differences approach.[6,7]

Though ITS have many strengths, there are still several limitations. Like pretest-posttest design, it can be difficult to determine if the impact on the dependent variable is due to the intervention, some co-occurring events, or if the outcome would have occurred without the intervention in a single-group ITS.[5,6,11] As previously mentioned, use of a comparator group can help to distinguish intervention effect from the effect of co-occurring events.[6] In ITS, the time point of an intervention can be unspecific or difficult to determine. Varied implementation of an intervention can also contribute to ambiguity of the start of the intervention. The impact on the dependent variables may have a delayed or weak impact, which may not be detected by the investigators depending on the length of the ITS. Lastly, given lack of randomization, there is also the risk for selection bias.

There are ways to strengthen an ITS and reduce the impact of bias and limitations. One way would be to control the time point of the intervention. This could involve choosing to intervene when threats to the intervention are less likely. Additionally, collecting more data points both pre- and post-intervention can help to strengthen the study design. Lastly, investigators can match subjects in the treatment and comparison group based on covariates and excluding some outliers to increase similarities between the two groups. This can be done through propensity score matching.

Propensity Score Matching

Propensity score matching can be used to help strengthen quasi-experimental research as it helps to better compare groups that were not established randomly.[5] A propensity score is the conditional probability that a subject belongs to the treatment group based on specified covariates.[6] The use of propensity score matching allows investigators to make the intervention and control groups more similar and improve internal validity of the study. In randomized controlled trials, subjects are assigned randomly to either the intervention or control group and are often stratified by characteristics specified ahead of time by the investigators. As shown in Figure 6, this creates groups that are similar at baseline. This increases the likelihood that any differences seen between groups is due to the intervention and not differing baseline characteristics.

Traditional cohort studies involve following subjects over time and measuring dependent variables in groups of people who were exposed to certain risk factors compared to those who were not exposed to determine the impact of the exposure.[6] However, without randomization, whether a subject receives an intervention depends on various factors. For example, certain subjects may be more or less likely to receive a certain pharmacologic treatment or procedure depending on age, comorbidities, geographic location, subject's ability to perform self-cares, support system, or socioeconomic status.[5,6] This often

FIGURE 5. Single-group Interrupted Time Series

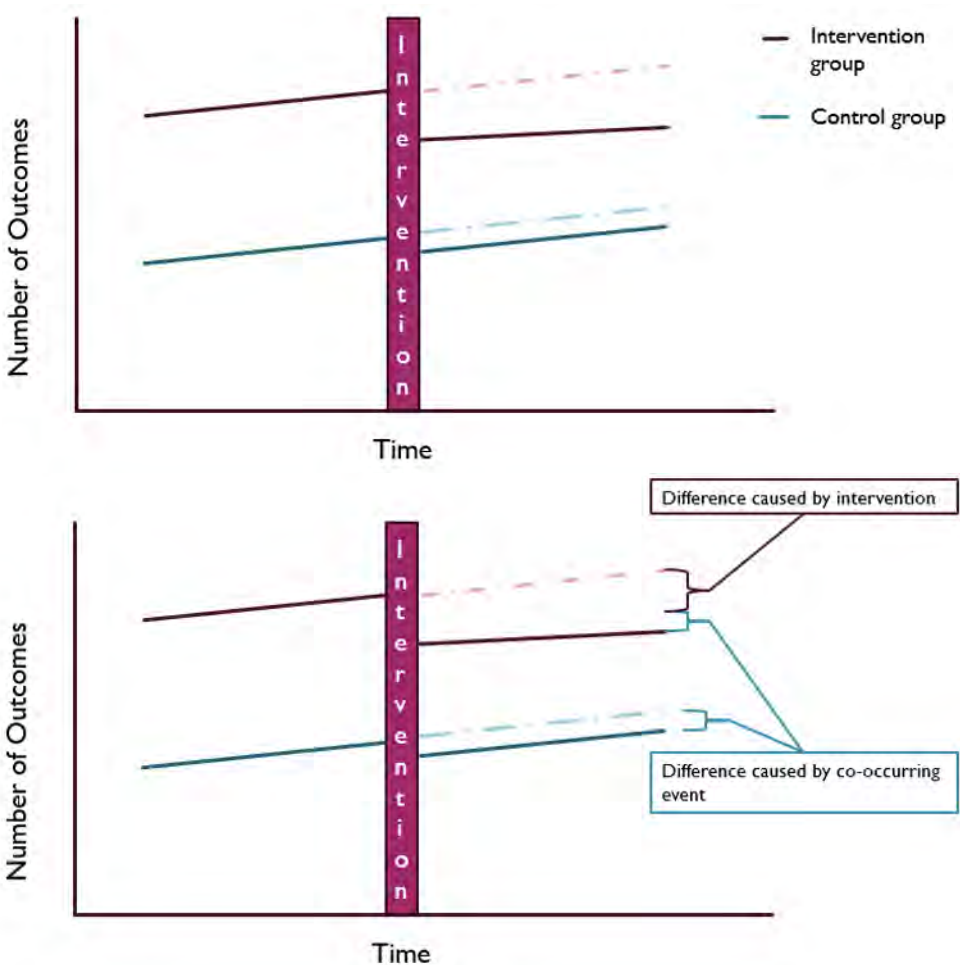
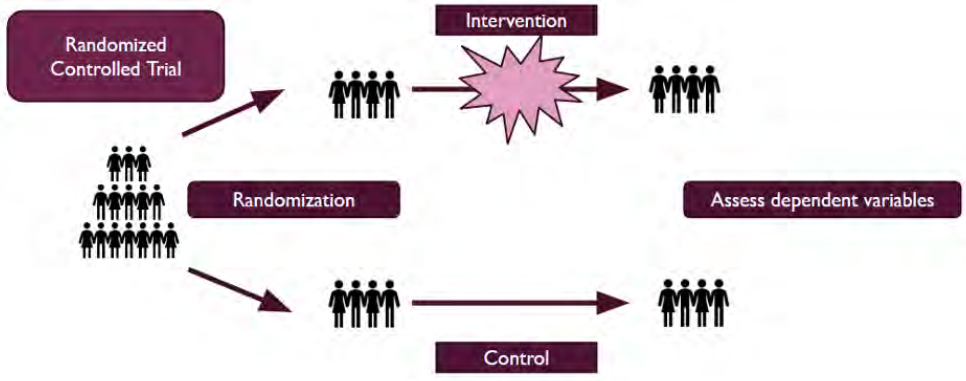


FIGURE 6. Randomized Controlled Trial Design



causes group to differ at baseline (Figure 7). This can confound the results and make it unclear whether the effect of the intervention is due to the intervention itself or the difference in baseline characteristics. Propensity score matching is one quasi-experimental technique that can be used to create more similar groups at baseline without the use of randomization.[6,7]

The first step to conducting a propensity score match is to determine the dependent variable. The dependent variable is selected by investigators and is the primary outcome of interest. Next, investigators select what covariates should be used to calculate the propensity score.[7] This includes anything that the investigator may suspect would impact whether a subject receives the intervention, as long as it was measured, but may also include factors that may impact the outcome of interest. These are often baseline characteristics seen in "Table 1" of research papers.

Next, a statistician builds a model to estimate a subject's likelihood, or propensity, to be in the intervention group.[6] This is the propensity score. Subjects in the intervention and control groups are then matched based on their propensity scores. The unmatched subjects tend to be excluded from the analysis if there is no one in the other group that has the same propensity to be in the intervention group as they do. For example, someone in the intervention group who has a very high propensity score may not have a match to a subject in the control group —there may not be someone in the control group who has that high a likelihood based on covariates that would have been in the intervention group. Figure 9 illustrates this with the size of the person correlating to a higher propensity score. The subjects who are excluded have a very high or very low propensity score. There are a number of techniques statisticians can use to match subjects by propensity. Once the propensity score matching has been completed, and baseline characteristics between groups are more similar, the treatment effect can be determined.

One limitation of propensity score matching is that, though it creates more similar groups, by removing subjects from the study, generalizability of the results decreases. Additionally, the best methods for balancing and matching based on propensity score are still being determined.

FIGURE 7. Traditional Cohort Design

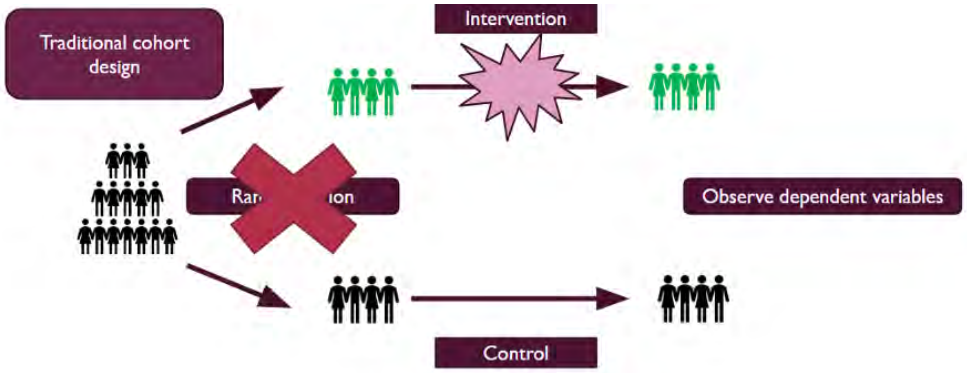


FIGURE 8. Propensity Score Matching

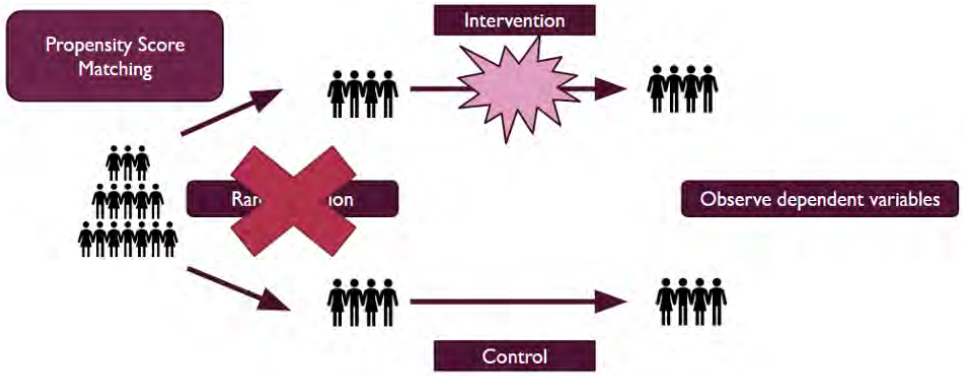
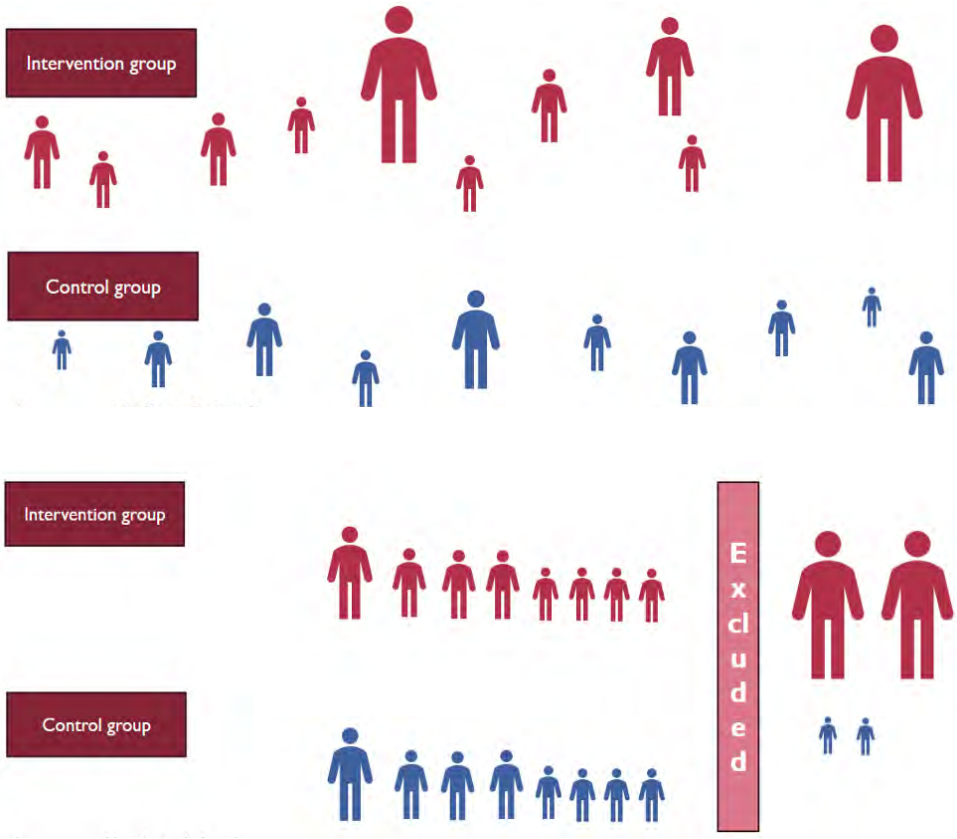


FIGURE 9. Propensity Score Matching Example



Overall, using propensity score matching in quasi-experimental research can help to minimize selection bias and improve the strength and quality of the study.

Critical Appraisal Tools

Being able to assess the quality of scientific literature is an important skill all healthcare professionals should have in order to provide optimal, evidence-based care to patients.[13] A critical appraisal tool is a checklist of prompts created to evaluate the quality of a study.[14,15] The prompts challenge the reader to question the study's design, conduct, and analysis to consider inconsistencies and potential biases thatmay result in misleading conclusions. Proven critical appraisal tools have been formulated for different types of study designs, as each has unique capacities for those inconsistencies and biases. There are critical appraisal tools specific for quasi-experimental design, which pharmacists are encouraged to seek out when reading quasi-experimental studies (Table 1).

Conclusion

Using literature is fundamental in informing evidence-based practice.[1-3] Meta-analyses and randomized controlled trials have the highest level of evidence and should be used whenever possible. However, a quasi-experimental study design is an alternative that can be used to evaluate potentially causal relationships in cases where traditional research design cannot be used. With this design becoming more and more common, it is necessary for healthcare providers to understand how to interpret these types of studies as well as recognize their strengths and limitations.

TABLE 1. Critical Appraisal Tools

Organization	Types of Critical Appraisal Tools	Website
Joanna Briggs Institute (JBI)[14]	Analytical Cross Sectional Studies Case Control Studies Case Reports Case Series Cohort Studies Diagnostic Test Accuracy Studies Economic Evaluations Prevalence Studies Qualitative Research Quasi-Experimental Studies Randomized Controlled Trials Systematic Reviews Text and Opinion	jbi.global/critical-appraisal-tools
Centre for Evidence-Based Medicine (CEBM)[15]	Systematic Reviews Diagnostics Prognosis Randomized Controlled Trials Critical Appraisal of Qualitative Studies IPD Review	https://www.cebm.ox.ac.uk/resources/ebm-tools/critical-appraisal-tools
Critical Appraisal Skills Programme (CASP)[16]	Randomized Controlled Trial Systematic Review Qualitative Studies Cohort Study Diagnostic Study Case Control Economic Evaluation Clinical Prediction Rule	casp-uk.net/casp-tools-checklists/

Cassie Sedgwick is a clinical pharmacy practitioner at the William S. Middleton Memorial Veterans Hospital in Madison, WI. Clara Nickel, Anna Erickson, Grayson Cooley, and John MacDonald are 2024 Doctor of Pharmacy Candidates at the University of Wisconsin-Madison School of Pharmacy in Madison Wisconsin. Amanda Margolis is an Associate Professor at the University of Wisconsin-Madison School of Pharmacy in Madison Wisconsin..

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Assessment Questions

1. Which study design has the highest internal validity?
   a. Cohort with propensity score matching
   b. Interrupted time series
   c. Randomized controlled trial
   d. Case-control study

2. Which of the following scenarios is most likely to require a quasi-experimenal approach as an RCT is less feasible?
   a. Determining efficacy and safety for a new medication for use in diabetes
   b. Evaluation of a new FDA approved antibiotic used to treat urinary tract infections compared to nitrofurantoin
   c. Determining the titers developed following a new vaccine for respiratory syncytial virus (RSV)
   d. Evaluation of the efficacy and safety of change in antibiotic order process in the emergency department

3. Which of the following study questions is most appropriate for the quasi-experimental design?
   a. Determining the efficacy and safety of a new anticoagulant compared to apixaban in patients with atrial fibrillation
   b. Determining the change in prescribing habits after implementation of a diabetes education program
   c. Evaluating the safety of a new SGLT1/SGLT2 inhibitor in patients with heart failure with midrange ejection fraction (HFmrEF)
   d. Assessing an association between physical activity and cognitive function in older adults

4. **True or False:** Quasi-experimental research design has a lower level of evidence than a case-controlled study.
   a. True
   b. False

5. Which study design does the following study describe?

   A checklist for checking chemotherapy infusions is implemented in an inpatient pharmacy. Error rates and near misses are reported monthly and data is available over the previous three years. One month after the implementation of the checklist, error rates and near misses are collected again and a month after implementation the effects of using the checklist are evaluated.
   a. Pretest-Posttest
   b. Randomized controlled trial
   c. Interrupted time series
   d. Cohort with propensity score matching

6. Which statement regarding bias is specific to an interrupted time series?
   a. The time point of the intervention is not always clear
   b. Interrupted time series have low generalizability as specific to time of intervention
   c. Interrupted time series have greater power than randomized controlled trials
   d. In an interrupted time series, investigators are unable to use a control arm, which reduces selection bias

7. What is an advantage of using propensity score matching?
   a. There are clear methods available for balancing propensity scores
   b. Propensity score matching increases generalizability of cohort studies
   c. Readers do not need to be concerned about other potential forms of bias such as historical bias or attrition
   d. Propensity score matching reduces selection bias

8. **True or False:** Critical appraisal checklists can be used to evaluate strength of a study using quasi-experimental design
   a. True
   b. False

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PRECEPTING SERIES:

Debating Debates: How to Incorporate Debates into Clinical Teaching

by Shivani Patel, PharmD, Amanda Margolis PharmD, MS, BCACP

Many pharmacy preceptors offer case discussions and journal clubs to their learners. Servais and Zook give suggestions for discussion preparation, learning styles, and facilitation.[1] However, when these discussions are offered routinely, it can be advantageous to vary the discussion style to maintain learner interest and motivation. One way to do this is through a debate. A debat is defined as "a formal discussion of an issue at a public meeting or in a parliament."[2] Early exposure to debate skills encourages evaluating evidence, formulating a recommendation or defense, or presenting to an audience and serves as preparation for controversial encounters throughout clinical rotations and future practice.[3] Furthermore, facilitating debate activities prepares learners to make concise, evidence-based recommendations. Topics to consider for a student or resident debates include healthcare ethics, guideline updates, and new medication approvals.

Preparation

Instructor preparation for a debate includes selecting the debate topic, choosing preparatory work that will result in strong foundational understanding upon completion, and establishing a debate format appropriate for the number of learners involved. It is also essential to determine who will be participating in the debate and whether the participants differ in rank (i.e., student, resident, practicing pharmacist/preceptor).

When selecting a topic, it is important to choose two arms that are controversial to encourage learners to use information collected in pre-discussion work to supplement their arguments. Ideal topics include new medication approvals with varying safety and efficacy profiles, or controversial topics in pharmacy. It is not necessary for the topic to have one clear, "correct" side. By choosing a topic that is not standardized in practice, participants are required to assess the available literature, interpret statistics, and approach the topic holistically to argue their side of the debate. If learners are not of the same rank (i.e., a resident pharmacist and a third-year pharmacy student), topic selection should be one that has been covered during didactic coursework for the student or one that pertains to the rotation they are currently on to ensure a baseline understanding.

Learner preparation for a debate should include a review of landmark trials and/or published literature pertinent to the debate topic. This review can range from reading a trial or publication to using a formal critical appraisal checklist to assess a trial. Preparatory work should be similar for each of the learners. When debating two therapeutic agents, landmark trials used in the approval of the agents would be beneficial. If debating ethics, published case reports may be reviewed. If debating guideline updates, reviewing both the new and old guidelines may promote a rich debate.

Preparation may look different if the debate is facilitated by individuals or in teams. For team debates, reviewing the assigned landmark trials may be sufficient, since the learners will be able to discuss their arguments as a team. If the debate is among individuals, it may be beneficial to assign additional preparatory assignments, such as review of pertinent disease states or additional literature, to better equip the learner to develop their own arguments.

Establishing the format of the debate will depend on the number and rank of the learners. A small group (10 or fewer learners) is advantageous for a debate compared to just two participants or larger groups (more than 10 learners).[4] Sharing the format of the debate in advance will create less confusion on the day of the debate. Small groups allow for more intimate discussion within the teams, fewer distractions, and more opportunities for participation for each learner.[4] For small groups, it is recommended to have sections for initial arguments, rebuttals, questions, discussions, and closing arguments.[3] When people with different levels of experience are debating, with varying baseline knowledge,, it would be beneficial to prepare probing questions and discussion points to ensure everyone has appropriate baseline knowledge prior to starting the formal debate.

FIGURE 1. Sample Debate Structure

-5 minutes for role assignments and team preparation-
Team 1-opening speaker (3 minutes)
Team 2-opening speaker (3 minutes)
-1 minute regroup-
Team 1-rebuttal speaker (3 minutes)
Team 2-rebuttal speaker (3 minutes)
-1 minute regroup-
Team 2-questions to opposition (3 minutes)
Team 1-questions to opposition (3 minutes)
-1 minute regroup-
Team 2-conclusion (2 minutes)
Team 1-conclusion (2 minutes)

Logistics and Facilitating the Debate

Debate activities are best facilitated in small group settings among learners of the same rank to promote diversity of thought and communication among peers. A sample debate structure, including timing, can be found in Figure 1. Timing intervals can be lengthened depending on the size of the teams and complexity of topic.[3]

The debate structure presented in Figure 1 was used during a learner debate activity facilitated at the University of Wisconsin-Madison School of Pharmacy among 7 third-year PharmD students (DPh3s). Overall, this debate structure was successful. Feedback from students indicated that more team preparation time before starting and in between sections would have been beneficial. Students also advocated for a discussion section to be added within the debate structure to allow for more conversation between the teams. Further elaboration on the activity can be found later in this article.

When facilitating the debate, it is best for the preceptor to allow learners to formulate their own stances prior to providing additional support. This allows for the learners to gather, interpret, and assess information to formulate an argument prior to preceptor input. If possible, the preceptor's sole function throughout the debate should be to facilitate. This includes giving feedback on both clinical knowledge and communication style. Preceptor presentation of clinical pearls should ideally be reserved for after the conclusion of the debate. This structure mimics various responsibilities learners will have while on rotation, such as answering drug information questions or providing recommendations on rounds.[5]

TABLE 1. Student Satisfaction with Debate Activity (n=7)

	Strongly Disagree	*Disagree*	*Agree*	*Strongly Agree*
The instructions for this activity were clear	0	0	1	6
The preparation work was helpful	0	0	1	6
Amount of time allotted for the debate during class was appropriate	0	0	3	4
Topic was appropriate for a classroom debate	0	0	0	7

TABLE 2. Student Suggestions for the Debate Activity

Question	*Student response (n=7)*
What other topics would be appropriate for a similar debate activity?	• Diabetes medications (Glucagon-like-Peptide-1 Receptor (GLP-1) agonists versus Sodium-glucose Cotransporter-2 Inhibitors (SGLT-2i) • Congestive Heart Failure (CHF)-should all medications be started at once and then titrate or should they be started one at a time • Efficacy of varying birth control agents • Warfarin versus direct oral anticoagulants (DOACs) • Comparing efficacy of any 2 drugs in the same class/indicated for the same disease state • Treatment options for disease states that were recently covered in therapeutics • Rheumatoid Arthritis (RA) • Chronic obstructive pulmonary disease (COPD) • Infectious Disease (ID) • Anything without a standardized treatment regimen
What changes would you have made to the activity?	• More preparation time in class with team (x3) • It would have been beneficial to have reviewed both articles prior to the debate instead of just the one assigned (x2) • Outline of debate format given prior to class • Add a discussion section to the debate format • Notice of debate activity prior to coming to class

Results of a Pilot Debate Activity

A debate activity was facilitated during a complex cases class at the University of Wisconsin-Madison School of Pharmacy among DPh3 students. Half of the class was assigned to complete a journal club handout for a trial publication of benralizumab (4 learners) and the other half was assigned a trial publication of tezepelumab. Learners were only required to review the agent that they were assigned but had access to the other should they have chosen to review it. Completed journal club handouts, which facilitated a detailed review and critical appraisal of the article, were due prior to the start of class. A complex patient case was posted on Canvas (the learning management system) prior to the start of class to facilitate the discussion.

Upon arrival to class, the students were separated into the two groups associated with the trial they were assigned to review. They were then introduced to the debate activity by the instructor. The purpose of the debate was to convince a physician to prescribe a patient with uncontrolled asthma their assigned biologic medication. Each team was given the debate structure in Figure 1 in the form of a handout and was told to assign each member of their team one of the following roles: opening speaker, rebuttal speaker, questioner, and closing speaker (Figure 2). Upon assigning roles, the two teams were given 5 minutes to formulate a plan for the debate. At the conclusion of the planning period, the order of speakers (Figure 1) was followed to proceed with the debate with teams being given 1 minute in between each speaker type to regroup and adjust their plans if needed. When each team had given their concluding statements, the debate had ended. The debate lasted for a total of 30 minutes, including the 5 minutes of preparation. At that time, students were given questions to help them reflect on the purpose of the debate activity and how they could apply the skills they used in future practice. Students were presented with a survey with the questions in Tables 1 and 2 at the conclusion of class. When asked, "I would have preferred to have a traditional case discussion," 6 students disagreed and 1 agreed.

Assessment of a Pilot Debate Activity

A total of seven DPh3 students from the University of Wisconsin-Madison School of Pharmacy participated in the pilot debate activity in a complex cases course. Most (6/7) students strongly agreed that the

in-class instructions of the activity were clear, and the preparation work (reviewing randomized controlled trials and completing journal club handouts) was appropriate for the activity. Three of the seven students agreed that the time allotted for the activity (30 minutes) was appropriate, while the rest strongly agreed. All students strongly agreed that the topic was appropriate for a debate activity. More preparation time within the teams, being informed of the debate occurring prior to class, and being instructed to review both pre-work trials were the most common improvements suggested for the activity. Most students (6/7) preferred the debate activity to a traditional case discussion. A wide variety of topics appropriate for debates were suggested. The most common suggested topics included comparing anticoagulants or antidiabetic agents. Unique recommendations included debating the efficacy of various contraceptive options and treatment regimens of congestive heart failure.

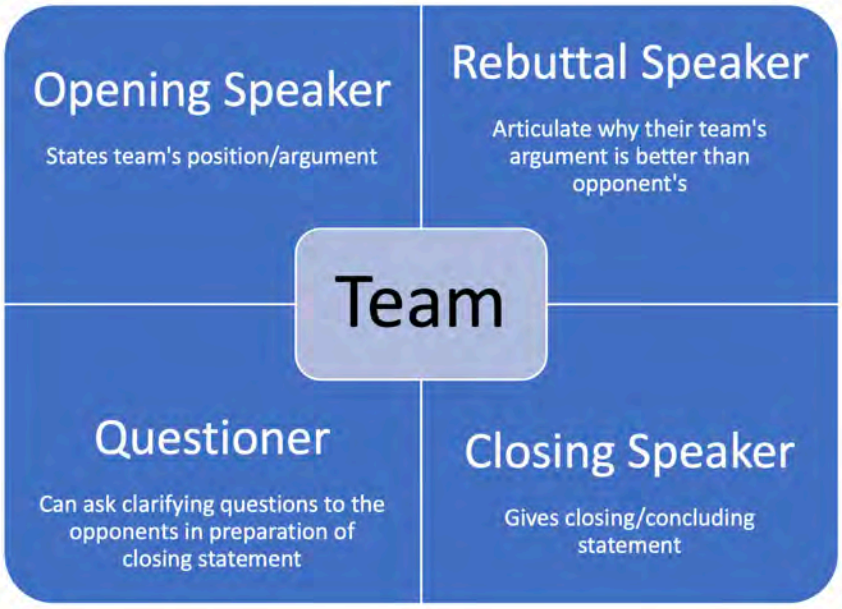
Discussion

Participating in a debate among peers can be uncomfortable for some learners; it may induce anxiety, exacerbate feelings of imposter syndrome, or lead to disengagement from the activity. This may be due to not participating in similar activities in the past, learners feeling as though they do not have the appropriate clinical knowledge to participate, or fear of letting their team members or preceptors down.

Facilitating a debate also comes with several moving parts that need to be executed well for a successful and meaningful activity for learners. This is a high-risk activity; it is dependent on learners actively participating and engaging with the content, as well as simply understanding the logistics of the activity. Should students not engage, or the activity is not executed as expected, the potential learning opportunity may be lost.

However, facilitating a debate among learners promotes critical thinking, is a challenge that may be an exciting way to engage in with the content, and can simply be more enjoyable than a traditional topic or case discussion. Variety in activities facilitated by preceptors offers learners the opportunity to reflect on the strengths and weaknesses in their knowledge base outside of being able to answer questions posed to them.

FIGURE 2. Debate Roles



As evidenced by the response from learners participating in the pilot debate activity at the University of Wisconsin-Madison School of Pharmacy, many learners prefer the debate style activity to traditional case discussions. Learners were engaged, felt comfortable among their peers, and left the activity with a better understanding of the debate topic. The overall response to this activity was positive.

Conclusion

Debates among learners simulate real-life scenarios requiring development of evidence-based recommendations in the setting of controversial issues. Practicing these skills in a controlled environment affords learners the opportunity to reflect on how they will apply the learned skills in practice. Emphasizing preparation, collaboration, and clear and concise communication will serve as foundation for learners establishing themselves as clinicians.

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Original Work

TL;DR – Insulin Pumps and A Case of Mistaken Insulin Identity

by Maija A. Anderson, PharmD, Jacob J. Keeffe, PharmD, BCACP

The pharmacotherapy department at SSM Health-Monroe Clinic Medical Group was established in 2007 and is an independent department of pharmacists, residents, and medical assistants working under a collaborative practice agreement to manage a wide range of chronic disease states including but not limited to: anticoagulation, diabetes, hypertension, lung disease, and pain management. Based in Monroe, Wis., they serve many patients living in rural areas in both Wisconsin and Illinois.

Overview of Insulin Pump Management and Definitions

Insulin pumps are one of many insulin delivery devices available for patients with diabetes mellitus. They are most often used by patients with type-1 diabetes but are also occasionally used by patients with type-2 diabetes. Insulin pumps provide a continuous delivery, or basal rate, of rapid-acting insulin such as insulin aspart (Novolog™ or Fiasp™) or insulin lispro (Humalog™). Additionally, they provide mealtime or prandial insulin in the form of bolus doses of the same type of insulin. Medtronic® and Tandem® are two of the most popular manufacturers of insulin pumps in the United States. Both have models that function as a pseudo-artificial pancreas when connected to a continuous glucose monitor (CGM). This means the insulin pump will adapt and predict the patient's insulin needs based on their sensor glucose readings provided by the CGM device. This technology has significantly advanced the field of insulin pump management and pharmacists are well-positioned to be able to manage these patients with their strong foundational knowledge of insulin pharmacokinetics and attention to detail. See Table 1 below for additional terminology that is used through the remainder of this case report.

Meet the Patient

A 73-year-old with type-1 diabetes and hypoglycemia unawareness was seen in office for routine follow-up. The patient uses a Medtronic MiniMed 770G™ insulin pump with a Medtronic Guardian™ continuous glucose monitor (CGM) and the Auto Mode feature to adjust basal rates.

TABLE 1. Terms and Definitions for Insulin Pump and Diabetes Management

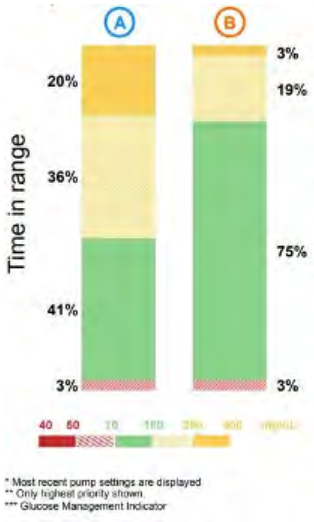
Term	*Definition*
Basal rate	Continuous insulin delivery of rapid-acting insulin via an insulin pump
Bolus dose	A programmed or scheduled dose of insulin administered immediately prior to mealtime (e.g., units/hour)
Continuous glucose monitor (CGM)	A sensor that inserts a small microfilament under the skin to measure glucose concentrations in the interstitial fluid. Readings are connected via Bluetooth to a device to collect and analyze trends.
Carbohydrate ratio	The grams of carbohydrate consumed that are treated by 1 unit of insulin
Correction factor	The amount of glucose (measured in mg/dL) corrected by 1 unit of insulin, sometimes referred to as insulin sensitivity
Active insulin	The amount of insulin presently at work in the body, often estimated using an assumed end point based on kinetics of the insulin (commonly 4 hours)
Manual insulin delivery	Basal insulin delivered at a pre-determined rate (units/hr) during specified periods of time (e.g., between 8 a.m. and 11 a.m). Referred to as Manual Mode by Medtronic.
Automated insulin delivery ("smart" basal)	An algorithm taking several variables into account (e.g., insulin sensitivity, active insulin time, current sensor glucose and rate of change, etc.) to establish or adjust basal insulin delivery. Referred to as Auto Mode in our case report.
Bolus calculator	A pump feature that supplies a bolus suggestion for patient-entered carbohydrate consumed, current sensor or blood glucose, and pump-estimated active insulin. Referred to as Bolus Wizard™ throughout our case report.
Glucose Management Indicator (GMI)	The A1c value associated with a given average sensor glucose. Analogous to A1c and estimated average glucose.
Time in Range (TIR)	A percentage of time spent within target range for sensor glucose (70-180 mg/dL); American Diabetes Association guidelines recommend a TIR > 70% for most patients.

Their pump is synced via cell phone to the clinic's CareLink™ account, which is a browser-based software for handling pump and sensor data. Historically, the patient has had a controlled A1c for their goal of less than 7.5% and spends over 70-80% of time in their target range (70-180 mg/dL). They also spend between 2% and 8% of time low (<70 mg/dL) and no time below 50 mg/dL. At this visit, the patient did note their glucose control had slightly worsened with no clear etiology. The patient felt their sugars were not responding adequately to bolus doses; therefore, insulin sensitivity and carbohydrate ratio pump settings were adjusted. A routine follow-up was scheduled months out, given the patient's history of good A1c control. Approximately two weeks later, however, the patient called to report ongoing elevations starting after breakfast. Available sensor data was reviewed online, and a trend of recurring early morning hypoglycemia is also noted. The patient was offered a telehealth appointment the next day to address these concerns.

Sensor Glucose Trends & Identifying the Culprit

To prepare for the telephone visit, the patient's chart, prescription fill history, and online CGM and pump report were reviewed (see Figure 1). According to CareLink™, the patient's total insulin requirements had increased over 50% from an average of 20.9 units per day to 36.8 units per day. Additionally, the patient's time in range had decreased from 75% to 41%, further supporting evidence of worsening sensor glucose control. The patient's lack of response to their bolus dose was apparent and worsening despite the adjustments that were made to the carbohydrate ratio and correction factor weeks prior. They were experiencing frequent overnight and early morning hypoglycemia in the preceding 14 days, which normally indicates heavy-handed basal rates; however, use of Auto

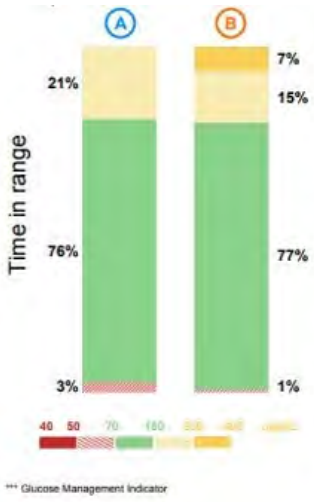
FIGURE 1. Initial Carelink Report
Time in Range, Auto Mode Summary, and Insulin Requirements from telemed visit. Blue (A) results are most recent, red (B) is his baseline (months prior).



Auto Mode Exits	A	B
No Calibration	• 1	0
High SG Auto Mode Exit	+ • • • • • 10	1 •
Auto Mode max delivery	• • • • 4	0
Auto Mode min delivery	• 1	1 •
BG required for Auto Mode	• 1	0
Sensor Algorithm Underread	• • • • 4	0
Sensor Updating	0	0
No SG values	• • 2	2 • •
Sensor Expired	0	0
Auto Mode disabled by user	0	0
Alarms	0	0
Pump Suspend by user	0	0
Auto Mode Warm Up	0	0
Unidentified	0	0

Statistics	A	B
Auto Mode (per week)	92% (6d 10h)	99% (6d 22h)
Manual Mode (per week)	8% (14h)	1% (02h)
Sensor Wear (per week)	96% (6d 17h)	98% (6d 20h)
Average SG ± SD	187 ± 66 mg/dL	146 ± 48 mg/dL
GMI***	7.8%	6.8%
Coefficient of Variation (%)	35.5%	33.2%
Low / High SG Alerts (per day)	3.1 / 6.5	3.4 / 1.7
Average BG	217 ± 69 mg/dL	181 ± 55 mg/dL
BG / Calibration (per day)	13.6 / 3.4	9.5 / 3.6
Total daily dose (per day)	36.8 units	20.9 units
Bolus amount (per day)	17.7U (48%)	11.4U (55%)
Auto Basal / Basal amount (per day)	19.1U (52%)	9.5U (45%)
Set Change	--	--
Reservoir Change	Every 2.2 days	Every 5.0 days
Meal (per day)	9.6	7.4
Carbs entered (per day)	214 ± 61 g	150 ± 42 g
Active Insulin time	4:00 hrs	4:00 hrs

FIGURE 2. Follow-up Carelink Report
After patient had resumed utilization of insulin aspart in their pump. Blue (A) results are most recent, red (B) is his baseline (months prior).



Auto Mode Exits	A	B
No Calibration	0	0
High SG Auto Mode Exit	0	3 • • •
Auto Mode max delivery	0	1 •
Auto Mode min delivery	0	0
BG required for Auto Mode	0	0
Sensor Algorithm Underread	0	0
Sensor Updating	0	0
No SG values	0	1 •
Sensor Expired	0	0
Auto Mode disabled by user	0	0
Alarms	0	0
Pump Suspend by user	• 1	0
Auto Mode Warm Up	0	0
Unidentified	0	0

Statistics	A	B
Auto Mode (per week)	10% (17h)	98% (6d 21h)
Manual Mode (per week)	90% (6d 07h)	2% (03h)
Sensor Wear (per week)	98% (6d 20h)	98% (6d 21h)
Average SG ± SD	139 ± 43 mg/dL	152 ± 49 mg/dL
GMI***	--	--
Coefficient of Variation (%)	--	--
Low / High SG Alerts (per day)	2.0 / 0.3	1.0 / 2.0
Average BG	161 ± 49 mg/dL	196 ± 74 mg/dL
BG / Calibration (per day)	6.9 / 3.0	8.9 / 4.0
Total daily dose (per day)	20.9 units	20.8 units
Bolus amount (per day)	11.4U (55%)	12.5U (60%)
Auto Basal / Basal amount (per day)	9.5U (45%)	8.3U (40%)
Set Change	--	--
Reservoir Change	Every 3.0 days	Every 5.0 days
Meal (per day)	5.3	7.9
Carbs entered (per day)	147 ± 30 g	168 ± 29 g
Active Insulin time	4:00 hrs	4:00 hrs

Mode typically prevents this by pausing administration of insulin.

The final piece of the puzzle fell into place upon review of their prescription fill history. The clinic uses Epic® electronic health record software, and data on fill history is available via Surescripts™. The patient's last refill for their pump insulin, insulin aspart (Novolog™), was almost six months prior. Interestingly, the patient's backup insulin, insulin detemir (Levemir™), had been filled twice in the past couple of months. This was immediately suspicious, as the patient had not reached out to the clinic to report any recent insulin pump failures. This information, along with the glucose trends, would seem to support the possibility that insulin detemir was being used in the insulin pump instead of insulin aspart.

During the telephone call, the patient was asked to read off the label of the insulin they used to fill their pump. They confirmed they had used insulin detemir and had no insulin aspart at home. Education was provided to the patient regarding the difference between the types of insulin and how this related to their current glucose readings. The pump manufacturer was contacted for advice on transitioning the patient's insulin safely back to insulin aspart and how to re-initiate Auto Mode.

The patient was advised to pick up a new prescription for insulin aspart and conduct a complete set change (tubing, reservoir, and infusion site). Next, the patient was instructed to suspend delivery of insulin until the following morning (about 24 hours) because they still had active basal insulin in their system in the form of insulin detemir. For mealtime bolus doses, the patient was instructed to resume insulin only while the bolus infused and then suspend again.

The patient was advised to wait until the next day to resume basal insulin delivery using manual mode for at least six days; this recommendation was provided by the Medtronic representative. This was to allow the pump time to re-learn the patient's basal insulin needs. As an additional safety measure to prevent hypoglycemia, the patient was instructed to turn on the "suspend before low" setting, which is normally deactivated while using Auto Mode. Teach-back was utilized to gauge patient understanding of these complicated instructions given via a telehealth visit.

The patient was contacted the next day to ensure they had successfully resumed delivery of basal insulin. By that time, sensor glucose trends had already significantly improved (see Figure 2). Daily insulin requirements had returned to baseline of 20.9 units/day, and time in range had improved from 41% the day prior to 76%. At the time of this writing, the patient has not contacted the department with any issues and is planning to follow up as previously scheduled.

Discussion and Recommendations

While working up the case, case reports or guidance on accidental use of long-acting insulin in an insulin pump were not readily found. This case offers good examples of the clinical features with which a patient using long-acting insulin in their insulin pump with "smart basal" may present. A patient with glucose readings slow to respond (or unresponsive) to boluses and recurring hypoglycemia despite pauses in basal insulin should prompt inquiry about the type of insulin they are putting into their pump.

This case also illustrates the importance of clear communication among providers, pharmacies, and patients. This patient has been managing their insulin with the same insulin pump for many years. This begs the question, "What went wrong in this case that can be prevented in the future?" It is important not to point the finger at any one person for this outcome. Instead, let us look at the layers of errors and anomalies that aligned to allow this to occur.

First, Levemir™ and Novolog™ are made by the same company, Novo Nordisk®, and have nearly the same packaging except for color-scheme, as seen in photos to the right and below. Unfortunately, color was not enough of a distinguishing factor for our patient to identify the difference in this case. Additionally, both of this patient's insulins were prescribed in vials. If insulin detemir pens had been utilized instead, the patient would have had to take additional steps to be able to put this insulin into his pump, and it would have provided a visual difference between the two types of insulin.

Right: *Novolog® vs. Levemir® Vials (Image source: Author)*

Below: *Novolog® vs. Levemir® Packaging (Image source: Author)*

Another consideration with this approach is the added benefit of providing five different back-up treatments per package, whereas a vial of insulin (even if only used once) should be discarded if the contents are not used within a month.

If cost is a limitation to prescribing insulin pens, clues can still be provided in prescription instructions and on the prescription label itself. Prescribers are encouraged to clearly indicate the rapid-acting insulin is "for use in insulin pump" to help pharmacies identify a pump patient. For long-acting insulins, including the phrases "In case of pump failure" and "Not for use in insulin pumps" on the label may also deter accidental use by this route. Technicians who have identified a pump user may wish to verify what type of insulin the patient is requesting when they ask for their generic "insulin" refill.

In conclusion, insulin pump management is very complex and requires careful coordination among providers, dispensing pharmacies, and patients to ensure safe and effective insulin therapy. The authors hope that through sharing their experiences, a future similar event may be prevented.

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Original Work

Design and Implementation of Student Pharmacist-Driven Assessment of Heart Failure Regimen Appropriateness in Skilled Nursing Facility Residents with Heart Failure: A Quality Assurance Project

by Judy Zheng, 2024 PharmD Candidate, Natalie McCourt, 2024 PharmD Candidate, Mara Kieser, MS, RPh, BCGP

Abstract

Objective: To provide a framework and evaluate the impact of student pharmacists in optimizing heart failure (HF) regimens in hospitalized patients discharged to skilled nursing facilities (SNF) through targeted disease state patient profile reviews.

Methods: Two student pharmacists performed patient profile reviews of residents with HF to assess for guideline-directed medical therapy (GDMT) at the recommended doses and identify medications that may worsen HF. Findings and recommendations were presented to a pharmacist, using evidence-based guidelines, who later presented them to the SNF providers during weekly huddles.

Results: Thirty patient profiles with a confirmed HF diagnosis (21 HFpEF, 6 HFrEF, 3 unclassified) were reviewed, and 21 were identified to be on GDMT with 3 patients at target doses. Of the 30 patients, 10 (33%) warranted no changes while 20 (67%) tallied 23 total recommendations. These included 6 suggestions to discontinue medications, 4 to decrease dose, 4 to increase dose, 8 to change regimen, and 1 to initiate a new GDMT medication. The most common medications that may worsen HF (5 or more occurrences) included albuterol (11), furosemide (11), ondansetron (8), pantoprazole (6), sertraline (5), and trazodone (5). Other less common medications were amiodarone, metformin, tamsulosin, and citalopram.

Conclusion: Student pharmacists completed patient chart reviews to optimize HF regimens. These assessments demonstrated a positive outcome of incorporating student pharmacists as pharmacy extenders and preventing HF readmission and hospitalization rates. Additionally, this quality assurance project adds to the growing body of evidence for student-led targeted disease state interventions and provides a framework for future work, particularly in SNFs.

Heart failure (HF) is a leading cause of morbidity, mortality, and hospitalization in adults over the age of 65.[1] The disease is characterized by structural and/or functional abnormalities of the cardiac hemodynamics, thereby impairing the heart's ability to sufficiently meet the body's oxygen demand. The disease state is predominantly divided into two classifications based on ejection fraction (EF), the percentage of blood volume pumped out of the heart to the rest of the body per heartbeat. These classifications include heart failure with reduced ejection fraction (HFrEF), in which the heart ejects 40% or less blood volume present in the left ventricle, or heart failure with preserved ejection fraction (HFpEF), in which the heart ejects 50% or more blood volume present in the left ventricle.[2] HFrEF and HFpEF determine which guideline-directed medical therapy (GDMT) pathway is utilized to assess gaps in HF medication management.

HF patients commonly present with cardinal symptoms of fatigue, dyspnea, and reduced exercise tolerance, with incidence being highest among older adults, a population often burdened with concomitant comorbidities, polypharmacy, and age-related pharmacokinetic and pharmacodynamic changes.[1] These, among other patient-specific factors, such as declining cognitive function, insurance coverage, and socioeconomic status, pose major and variable challenges to HF management. HF is a common cause of hospitalization in the United States. One strategy adopted by health systems to reduce the length of hospital stay and healthcare costs is to discharge older, frail adults to skilled nursing facilities (SNF) for recovery.[3] However, these patients, as well as long-term residents of SNFs, face substantial risks of adverse events. This includes increased mortality and hospital readmission rates, with SNF 30-day rehospitalization rates due to HF in 27-43% of HF patients.[1,3-4]

Current nursing home quality measures related to HF include the percentage of short-stay residents who are hospitalized after admission and percent of residents who make improvements in overall function. In addition, long-term quality measures consist of the number of hospitalizations per 1,000 long-stay residents, percent of residents experiencing one or more falls, and percent of residents with increased need for help with activities of daily living.[5] Notably, in the early month of the second quarter of 2023, the Center for Medicare and Medicaid Services proposed changes to the SNF payment rates for the fiscal year 2024. These proposals support the SNF Quality Reporting Program and the SNF Value-Based Purchasing Program.[6] As a nation, there has been a major shift in payment structures that prioritizes quality and outcome of care and, thus, there needs to be a change in the way health care providers deliver care. These modifications are essential for health systems to meet new reimbursement criteria and ensure adequate compensation to continue serving patients and their families.

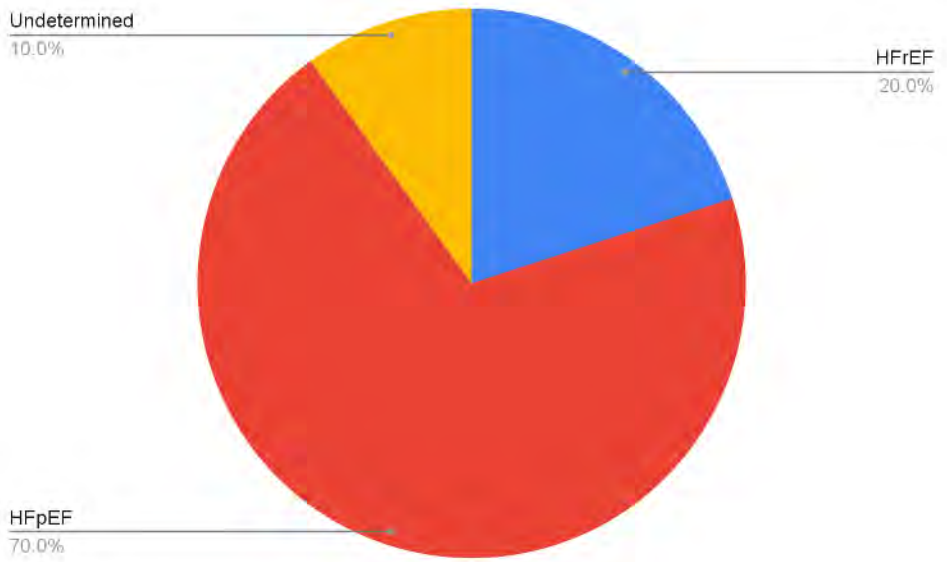
Of the various HF management strategies, conducting targeted disease state interventions with the goal of optimizing medication regimen for safety and efficacy is an integral component of pharmacy services. However, health systems are often limited in their ability to perform a comprehensive review of patient charts due to time, resources, and cost constraints. These limitations are further amplified post-COVID-19 pandemic due to high staff turnover and employee burnout rates. In an effort to combat these issues as well as enhance quality of care and cost efficiency, an interdisciplinary team leveraging student pharmacists was formed to develop a streamlined process for assessing medication therapy management for SNF residents. To date, there is no literature evaluating the impact of student-driven targeted interventions on HF residents in SNF.

The primary objective of the quality assurance project was to incorporate student pharmacists in the development and implementation of a framework assessing the appropriateness of HF medication regimens for hospitalized patients discharged to SNFs. Student pharmacists were tasked with reviewing HF patient charts weekly for GDMT at recommended doses as well as medications that may worsen HF, thus making appropriate recommendations using evidence-based guidelines.

Methods

A team of one consultant pharmacist/faculty member and two second-year student pharmacists from the University of Wisconsin-Madison School of Pharmacy collaborated with the Capitol Lakes Health Center (CLHC) medical director to develop a workflow for HF medication management for residents at the CLHC facility. The site is a 52-bed SNF consisting of rehabilitation and residential floors that provide care for patients with a wide range of diagnoses, including infections, HF, hypertension, diabetes, dementia, and falls.

FIGURE 1. Heart Failure Diagnosis
Proportion of residents with confirmed heart failure and classification



HFrEF, heart failure with reduced ejection fraction; HFpEF, heart failure with preserved ejection fraction

During the onboarding process, the second-year student pharmacists with no prior experience or knowledge of this clinical disease state underwent a detailed review of HF, including the pathophysiology, classifications, symptoms, risk factors, and guidelines. In addition, the learners were granted access to the SNF's electronic health records (EHR) and an electronic Box folder where all chart review documents were stored. To ensure compliance with the Health Insurance Portability and Accountability Act, all protected health information on the chart reviews was de-identified. For example, only patient initials were recorded, as opposed to their full name. Moreover, an initial chart review template was provided to the students, which was revised throughout the duration of the project to only collect pertinent patient health information. Electronic access to both the EHR and Box folder enabled the students to independently review patient profiles remotely. However, a weekly in-person meeting was held on-site at the SNF to review recommendations and rationales.

The original inclusion criteria were admitted HF patients on diuretics with an HFrEF diagnosis, which later expanded to also include those with HFpEF. Patient profiles were assessed for GDMT regimens using the 2021 Optimization of Heart Failure Treatment: Expert Consensus Decision Pathway guideline, which was replaced midway by the 2022 AHA/ACC/HFSA Guideline for the Management of Heart Failure update to keep current with the most recent clinical evidence.[2,7] Additionally, medications that may worsen HF were identified using the 2016 Scientific Statement: Drugs That May Cause or Exacerbate Heart Failure.[8]

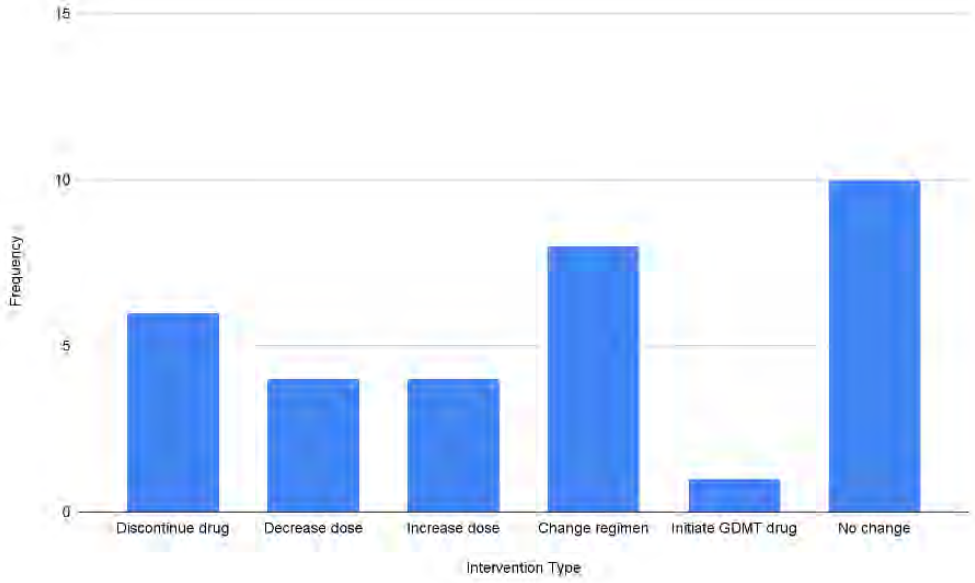
Each week, the consultant pharmacist identified two HF patients for review and notified the student pharmacists of their assigned patient. The student learners then individually conducted patient profile reviews using chart review documentation developed and revised by the team, as well as EHRs to survey for the primary objectives and make appropriate recommendations to optimize the resident's HF therapy. This was due prior to the weekly interdisciplinary patient review, also known as a "huddle." Students began by collecting pertinent patient information from the EHR by sifting through the records and documents, including discharge summaries. After data collection, students reviewed the information and made appropriate therapy recommendations, such as discontinuing medications, altering doses, switching regimens, and initiating a GDMT drug. These recommendations were then documented in a provider presentation format (discontinue, taper, start, monitor, etc.) prior to meeting with the consultant pharmacist.

After finalizing documentation, the student pharmacists and pharmacist reviewed the patient charts together and discussed recommendations including rationales. Finally, the pharmacist presented the recommendations to nurse practitioners and providers of the facility during Friday afternoon huddles at the SNF. Upon follow-up, the pharmacist shared treatment decisions made during the previous week's huddle with the learners.

Throughout the course of the project, the pharmacist tracked the assessments and recommendations made by the student learners. This included tallying the number of patients on GDMT, on a recommended GDMT dose, the type of HF, whether the patient was on medications that worsened their HF, and the name of the medication that worsened their HF. The information was recorded on an Excel spreadsheet that was updated weekly. The primary objective implemented by the student learners included utilizing a framework developed to assess information, such as whether the HF patients were on GDMT, whether the GDMT was at recommended doses, and whether the patient was on medications that may worsen their HF.

FIGURE 2. Frequency of Interventions

Frequency of types of interventions from 30 patient chart reviews



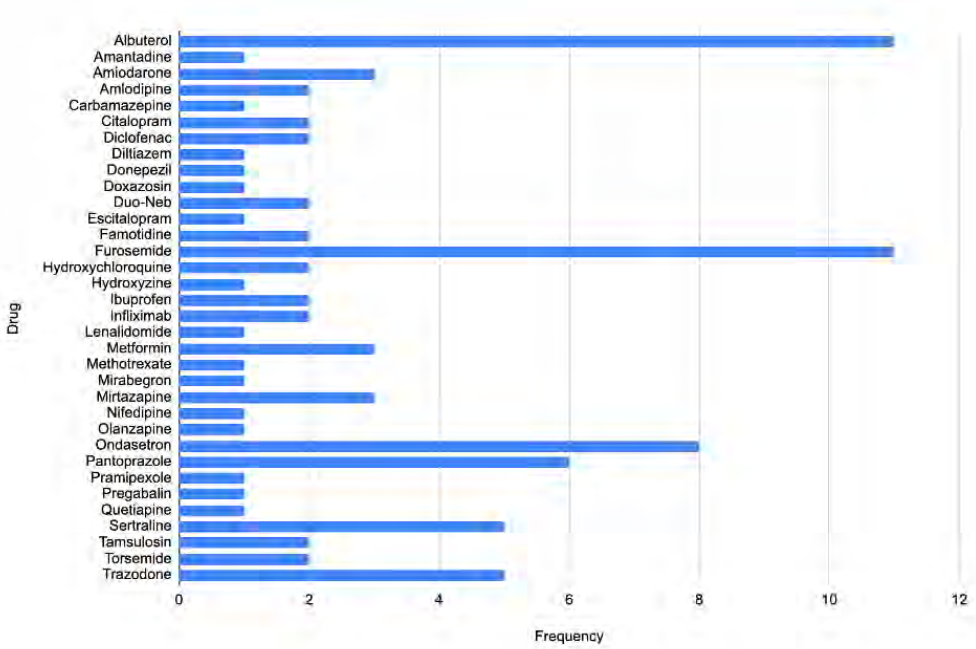
Results

Thirty (8 males, 22 females) patient chart reviews were completed between February 2022 and June 2022. The average resident age was 85 years old with a mean body mass index of 25.8 kg/m^2. Among the HF diagnosis, 21 were HFpEF and 6 were HFrEF with 3 undocumented EF values (Figure 1). The student learners identified that 21 patients were on at least one GDMT agent with 3 patients at target doses. Of those patients, 11 were on an angiotensin converting enzyme inhibitor (ACEi) or an angiotensin II receptor blocker (ARB); 20 were on beta blockers with metoprolol succinate and carvedilol being most common; 9 were on spironolactone; 2 were on empagliflozin; and 27 were taking diuretics, mostly furosemide with 2 prescribed torsemide.

Out of the 30 chart reviews, 10 (33%) warranted no change in recommendations at the time of assessment, while the remaining 20 (67%) tallied a total of 23 recommendations provided by the student learners. Recommendations included 6 suggestions to discontinue medications, 4 to decrease the dose, 4 to increase the dose, 8 to change the regimen, and 1 to initiate a new GDMT medication (Figure

2). The most common medications observed that may worsen HF, defined as 5 or more occurrences, included albuterol (11), furosemide (11), ondansetron (8), pantoprazole (6), sertraline (5), and trazodone (5). Examples of other less common medications were amiodarone, metformin, tamsulosin, and citalopram, among others (Figure 3).

FIGURE 3. Frequency of Drugs that May Worsen Heart Failure[8]
Prevalence and frequency of drugs used by residents that may worsen heart failure



Discussion

The primary purpose of this quality assurance project was to develop a framework for assessing whether HF patients at a SNF were on GDMT at the recommended doses, as well as whether they were prescribed medications that may potentially worsen their HF. The template utilized to assess HF regimen appropriateness initially entailed tallying the total number of patients based on whether those patients were or were not on GDMT, were or were not at the recommended doses, and were or were not on medications that worsened their HF. As the project progressed and the second-year student pharmacists gained in-depth knowledge of the disease state, the framework expanded to include medication recommendations made by the student pharmacists. These recommendations included initiation of medication, including starting doses, discontinuing a medication with a taper schedule, if necessary, as well as supportive care medication alternatives. At the beginning of the project, these frameworks were due one week prior to the weekly huddles to discuss the care of each SNF resident. Due to quick patient turnover and short time to discharge, this framework was transitioned to be completed one day prior to these meetings.

After assessing the appropriateness of medication regimens in HF patients in a SNF over five months, the majority of the patient population presented with preserved ejection fraction compared to reduced ejection fraction, with the remaining population being undetermined. When assessing the frequency of use of GDMT drug classes, diuretics were most commonly prescribed followed by beta blockers, as well as ACEis and ARBs. Achieving target doses of HF GDMT was often limited due to patient comorbidities, fragility, and vulnerability to adverse effects such as hypotension, bradycardia, and worsening kidney function. When monitoring medications that may worsen HF, literature is limited to medications that may worsen heart contractility for patients with HFrEF. The pathophysiology of these medications was defined as whether they prolong the time it takes for the heart's electrical system to recharge between heartbeats. The most frequently prescribed medications that worsened HFrEF included furosemide, albuterol, and ondansetron. The quality assurance project duration was concluded after five months due to the declining census of the CLHC, which limited the number of HF patients for review.

This project highlights the ability of student pharmacists to serve as extensions of pharmacy services. Previous studies have defined the role of student pharmacists in HF management, placing emphasis on the extent of knowledge they possess around pathophysiology and GDMT for HF. One retrospective study investigated the impact of student pharmacist-driven phone calls to HF patients post-hospital discharge to assess 30- and 90-day hospital readmission rates.[9] With the utilization of student pharmacists on their Advanced Pharmacy Practice Experiences for HF patient monitoring, a statistically significant decrease in hospital readmission rates was observed for both 30-day (-12.98%, p = 0.006) and 90-day (-15.27%, p = 0.007) readmission. Another publication evaluated the impact of home-based visits with HF patients that were conducted by a nurse and pharmacist to assess HF medication regimen appropriateness within one week of hospital discharge.[10] The study focused on comparison of in-home visits versus usual care to assess the intervention's impact on the rate of hospital readmission, death, and the cost of hospital readmission. The HF patients that received home-based visits had fewer unplanned readmissions (36 vs. 63, p = 0.03) and reduced mean cost of hospital-based care ($3,200 [95%CI $1,800-$4,600] vs. $5,400 [95%CI $3,200-$6,800]).

Both studies show that pharmacy involvement, including student pharmacists, provides valuable knowledge and skills that contribute to improving health outcomes and reducing healthcare costs. Our intervention further highlights that student pharmacists in the second year of their pharmacy curriculum are also capable of providing comprehensive HF medication reviews and establishing recommendations to optimize HF regimens. Additionally, this project focuses on the long-term care facility population, which currently lacks literature that utilizes interventions similar to this framework. Upon review of the results at the conclusion of the project, it was found that zero of the HF patients receiving this intervention were readmitted to a SNF or were rehospitalized for any cause. This further translates to a potential reduction

in healthcare costs for both the HF patients and the facilities.

Limitations

One limitation of this evaluation is the time lag between patient discharge and the scheduled weekly huddles at the SNF. Despite prompt completion of weekly patient chart reviews, resident discharge can be unpredictable in nature. As a result, recommendations lose feasibility for implementation after the patient leaves the facility. Although there were few unsuccessful attempts made to follow up with patient providers, efforts were shortly terminated.

Another limitation is the change in inclusion criteria to better adapt to HF diagnoses observed at the SNF. Shortly after piloting the project, it became apparent that HFpEF was the more common HF diagnosis; however, guidelines and resources were selected and tailored to those with HFrEF. With further research, it was evident that there lacked available clinical evidence and recommendations specific for HFpEF. Thus, the team agreed to use the best available alternative and adopted the HFrEF guidelines and resources for the HFpEF patients. Fortunately, the HF management guidelines were updated midway in April of 2022 and included evidence-based recommendations for those with HFpEF. The team quickly reacted and adapted to the most recent report. However, the resource used to screen for medications that may worsen HF continued to be applied throughout the project duration despite specifications for the HFrEF patient population.

Other limitations include the consistently low census at the SNF and the few patients admitted with HF, and the high cost of GDMT medications, such as valsartan/sacubitril and the SGLT2 inhibitors drug class.

Conclusion

Student-driven patient chart reviews for optimizing HF regimens demonstrated a positive outcome of incorporating student pharmacists as pharmacy extenders. Assessments were completed by identifying target doses of GDMT and medications that may worsen HF and subsequent evaluation of patient health information to make appropriate recommendations using evidence-based guidelines. This quality assurance project adds to the growing body of evidence that supports student-led targeted disease state intervention and provides a framework for future work, particularly in SNFs.

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

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MEDICAL COLLEGE OF WISCONSIN SCHOOL OF PHARMACY STUDENT WRITING CLUB:

Thrombolytics for Pulmonary Embolisms: A Narrative Review

by Sage L. Orlowski, 2025 PharmD Candidate, Soriene N. Ozcan, 2025 PharmD Candidate, Katherine M. Bush, 2024 PharmD Candidate

Abstract

Pulmonary embolism (PE) is a type of venous thromboembolism (VTE) where the pulmonary artery, or its smaller connecting arteries, are blocked, and can lead to significant morbidity and mortality. Thrombolytic therapy can be beneficial in treating pulmonary embolism. First generation thrombolytics include urokinase (Kinlytic®) and streptokinase (Streptase®); second generation thrombolytics include alteplase (Activase®) (tPA); and third generation thrombolytics are tenecteplese (TNKase®) and reteplase (Retavase®). The use of thrombolytics in patients with pulmonary embolisms is progressing rapidly and, in some cases, can be lifesaving, but there are several patient-specific factors and adverse effects that must be considered for each patient case, which may potentially lead to hesitancy when considering thrombolytic agents.

Approximately 60,000-100,000 deaths each year in the United States are caused by pulmonary embolisms.[1] Pulmonary embolism (PE) is a type of venous thromboembolism (VTE) where the pulmonary artery, or its smaller connecting arteries, is blocked.[2] The problematic blockage can be made up of air, fat, tumor, or thrombus. Many cases of PE are a severe development of deep vein thrombosis (DVT) where the pulmonary vein is blocked by a thrombus that detached from another area of the body.[2] There are various sub-types of PE based upon stability, risk, and/or location of the blockage.

Stability can be broken down into massive and sub-massive, with massive having the highest risk of mortality. Massive PE can be defined as PE resulting in a systolic blood pressure of <90 mmHg.[3] Only approximately 50% of patients with massive PE survive over 90 days despite treatment.[3]

Pulmonary embolisms are also classified as high risk, intermediate risk, or low risk. High-risk patients are hemodynamically unstable and have myocardial injury and right ventricular damage.[4] Intermediate-risk patients are hemodynamically stable but symptomatic and may have myocardial injury or right ventricular damage.[4] Treatment is based on which risk level the patient falls into.

Blockage(s) can occur in many different locations in pulmonary vessels. Saddle PE occurs as a PE that straddles a bifurcation, most commonly the main pulmonary trunk bifurcating to the left and right pulmonary arteries.[3,5] Lobar, segmental, and subsegmental PE occur in the branches of the main pulmonary artery, with lobar PE occurring in the larger branches directly bifurcating from the main pulmonary artery, and segmental and subsegmental PE in the increasingly smaller branches.[6] The occlusion of the arteries can cause impaired gas exchange and prevent circulation.[2] Clinical presentation of PE may include hypotension, dyspnea, syncope, hypoxemia, tachycardia, and sudden death. Without prompt detection and treatment, PE can significantly affect morbidity and mortality.

Prophylaxis

As with many diseases, the greatest hope of reducing morbidity and mortality is in preventing PE before it occurs. Since many PEs result from a thrombus detaching and embolizing in a patient with DVT, much of PE prophylaxis is centered on reducing this occurrence. In hospitalized patients with a low risk of thrombosis, the American College of Chest Physicians (CHEST)'s Evidence-Based Clinical Guidelines eighth edition recommends that acutely ill, hospitalized patients with an increased risk of thrombosis be administered anticoagulant thromboprophylaxis such as low-molecular weight heparin (LMWH), low-dose unfractionated heparin (UFH), or fondaparinux.[7] They also recommend that acutely ill or critically ill, hospitalized patients with an increased risk of bleeding or who are actively bleeding and have an increased risk of thrombosis should receive mechanical thromboprophylaxis such as graduated compression stockings or intermittent pneumatic compression as opposed to anticoagulant thromboprophylaxis. Once the risk of bleeding subsides, pharmacological thromboprophylaxis should then be used in place of the mechanical thromboprophylaxis. After the initial anticoagulant prophylaxis, the duration of pharmacological prophylaxis should be extended including when the patient leaves the hospital.

The risk of a DVT, PE, or VTE emergency can increase based on a variety of risk factors including recent surgery, advanced age, estrogen use, severe obesity, and pregnancy. Patients with risk factors should take additional precautions when traveling long distances or flying.

For an initial pulmonary embolism, prophylactic anticoagulation is chosen based on risk factors, in addition to respiratory and hemodynamic support. These risk factors include but are not limited to: age greater than 65, chronic

conditions, cancer, previous stroke, recent falls, recent surgery, and alcohol use.[8] Goals of pulmonary embolism therapy are to prevent the clot from becoming more prominent, prevent recurrent blood clot formation, and prevent long-term complications. Oral anticoagulants are used for prophylaxis in high-risk patients and for long-term management of pulmonary emboli. Commonly used anticoagulants in management of patients with a diagnosed pulmonary embolism are included as oral medications, low molecular heparin injections, fondaparinux, and heparin. An independent analysis of clinical trials in elective surgeries has shown a reduction of 60% to 70% in the incidence of fatal pulmonary embolisms in heparin-treated patients compared to placebo patients.[9]

Treatment

Management of an initial pulmonary embolism diagnosis may include respiratory support, hemodynamic support (including intravenous fluid administration), and use of vasopressors such as norepinephrine or dobutamine.[10] Current pulmonary embolism treatments include thrombolytic therapy, embolectomy, and placing a filter in one of the major blood vessels, such as the vena cava.[11]

In severe cases of life-threatening pulmonary embolisms, thrombolytic therapy may be suggested. Thrombolytic therapy is reserved for patients with severe complications due to pulmonary embolism and with minimal risk of serious bleeding as a side effect of the therapy.[12] Response to thrombolytic therapy is best when there is a short time between the diagnosis of pulmonary embolism and the start of the thrombolytic agents.[13] Thrombolytic agents activate plasminogen to form plasmin, which accelerates the breakdown of the emboli. First generation thrombolytics include urokinase and streptokinase; second generation thrombolytics include alteplase (tPA); and third generation thrombolytics include aretenecteplese and reteplase (Figure 2).

Another pulmonary embolism treatment option is embolectomy. Embolectomy is the removal of pulmonary embolism from the lungs. It may be performed using catheters placed in the blood vessels containing the clot. This procedure can be considered if the patient develops a massive pulmonary embolism within two months of having craniotomy or spinal surgery and for patients with intracranial hemorrhage.[14]

An inferior vena cava filter is a device that blocks the circulation of clots in the bloodstream, especially the movement from the legs to the lungs. It is placed in the inferior vena cava with a catheter inserted into a vein in the groin area and threaded throughout the blood vessels.[15] This treatment can be used for patients who cannot use anticoagulants due to recent surgery, stroke, or significant bleeding in any bodily area. However, when appropriate, an inferior vena cava filter is often used along with other prophylactic and management strategies, such as anticoagulation use, thrombolysis, and embolectomy.[16]

Tissue plasminogen activator (tPA) is a natural fibrinolytic agent found in endothelial cells that demonstrates fibrin affinity and specificity. The goal of thrombolytic therapy is to convert plasminogen into plasmin, via direct or indirect mechanisms, which results in clot dissolution.[16,17] The direct plasminogen activators (urokinase, tPA, reteplase, and tenecteplase) are serine proteases that have a direct action on plasminogen, which catalyzes its activation. On the other hand, indirect plasminogen activators (e.g., streptokinase), lack enzymatic activity on their own, and instead form a 1:1 complex with plasmin or plasminogen. This complex activates the plasminogen molecules present in circulation.[18,19] Adivitiya, Khasa YP offers more detail about the fibrin pathway.[19]

Thrombolytic therapy has been shown to improve oxygenation, perfusion, pulmonary artery pressure, and echocardiographic assessment. These improvements lead to a relief in symptoms, prevention of recurrent PE, and a reduction in mortality.[20] However, these benefits do not necessarily outweigh a patient's risk of bleeding, and, unfortunately, there is not a validated tool that can be used to predict the bleed risk in patients undergoing thrombolytic therapy; only to identify risk factors.[20] As a result, thrombolytic therapy choice depends on many factors, including but not limited to cost, stability, half-life, side effects or tolerability, specificity toward fibrin, and immunogenicity.[18] Consequently, there is a lasting push to develop innovative medications at a lower cost to address these factors.[17]

First-Generation Agents

The first-generation plasminogen activators, namely urokinase and streptokinase, work not only by activating free circulatory plasminogen to plasmin, but also by degrading fibrinogen and other clotting factors. The addition of plasminogen activators results in the degradation of the α2-antiplasmin, which under normal conditions would inhibit free plasmin, resulting in a systemic fibrinolytic state leading to bleeding complications.[18] Although streptokinase is typically preferred over other thrombolytic agents from a cost perspective, it unfortunately has more associated adverse effects, including allergic reactions and hypotension, and is no longer commercially available in the United States. Furthermore, streptokinase has an antigenic structure, meaning it is recognized by the immune system and can trigger an immune response leading to an allergic reaction, and it is not able to be safely re-administered for at least six months.[16]

Alteplase, a second-generation plasminogen activator, on the other hand, is not antigenic, and therefore is infrequently associated with any allergic manifestations.[16] Second-generation plasminogen activators also differ from the first-generation plasminogen activators via targeted thrombolysis opposed to non-specific fibrin degradation. Non-specific fibrin degradation causes systemic fibrinolysis and leads to hemorrhage.[17]

Third-generation plasminogen activators, such as tenecteplase and reteplase, have been engineered to improve some of the functional and structural properties, such as longer half-life, enhanced fibrin specificity, improved safety and efficacy, and resistance to inhibitors.[17]

Tenecteplase and reteplase are both approved for treatment of acute coronary syndromes but have ongoing trials evaluating their use in PE.[18,20]

Fibrin-specific agents require the presence of fibrin for the conversion of plasminogen into plasmin. Some agents, such as alteplase, reteplase, and tenecteplase, can convert plasminogen into plasmin in the absence of fibrin, but on a minimal scale. The fibrin-specific agents have longer half-lives, allowing for bolus administration, and do not hold the risk of allergic reactions commonly associated with first-generation

thrombolytic agents. Non-fibrin specific agents do not require fibrin presence for the conversion of plasminogen into plasmin.[16] Streptokinase, urokinase, and alteplase are the only thrombolytic agents that are FDA-approved for use in PE. Of these agents, alteplase is the only one commercially available in the United States (Figure 1). Fibrin specific thrombolytics are alteplase, reteplase, tenecteplase, and non-fibrin specific thrombolytics are streptokinase, antistreplase, and urokinase (Figure 2).

FIGURE 1. Therapeutic Agents for Thrombolytics

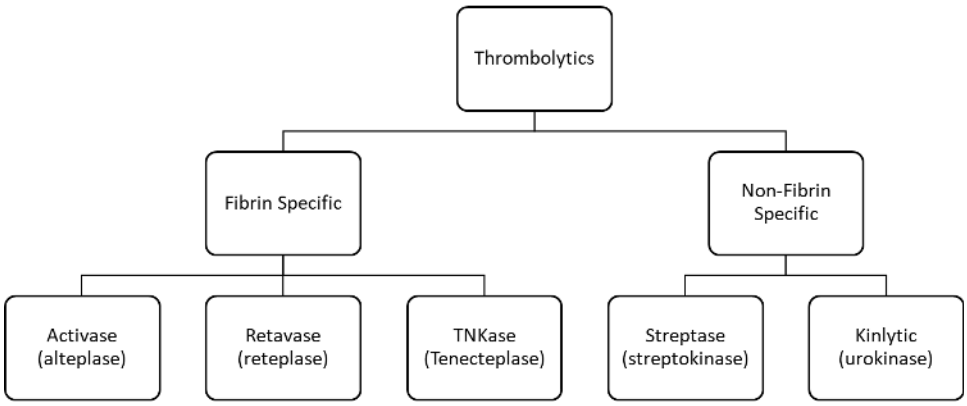
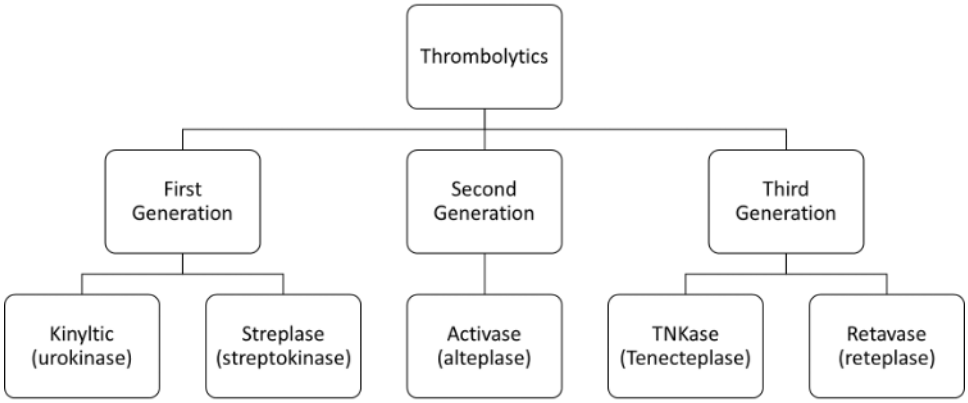


FIGURE 2. Different Generations of Thrombolytics



Alteplase

Alteplase is a tissue plasminogen activator indicated for use in pulmonary embolism. Alteplase is administered using intravenous infusion using a peripheral vein. The dose for acute massive pulmonary embolism is 100 mg administered intravenously for 2 hours once (Table 1). Bolus dosing of alteplase has been investigated in the setting of pulmonary embolism with cardiac arrest, but it is not considered an FDA-approved indication of use and is typically reserved for case-by-case assessment when PE is thought to be the cause of the arrest.[21] Side effects from alteplase are signs of bleeding like blood in vomit or vomit that looks like coffee grounds, skin discoloration, chest pain, severe dizziness, severe headache, vision changes, muscle pain, severe abdominal pain, back pain, nausea, dark urine, vomiting and catheter site pain or irritation. Adverse reactions of alteplase include primarily cardiovascular hemorrhages but are not limited to dermatologic, gastrointestinal, and genitourinary hemorrhages.[22]

Reteplase

Reteplase is a tissue plasminogen activator used off-label for treatment of pulmonary embolisms. Reteplase treatment is initially given as 10 units intravenously over 2 minutes, then followed by a second dose 30 minutes later of 10 units intravenously over 2 minutes (Table 1). Some of the side effects that can occur due to reteplase are vomiting, nausea, abdominal pain, dark urine, muscle pain, vision changes, chest pain, dizziness, severe headache, changes in urine output, skin discoloration, and weakness on one side of the body. Some of the adverse effects from reteplase are bleeding at injection site, and gastrointestinal, oncologic, and hematologic hemorrhage.[23]

Tenecteplase

Tenecteplase is a tissue plasminogen activator and used for pulmonary embolism off-label. Tenecteplase is dosed with weight-based dosing and administered as a bolus dose over five to ten seconds (Table 1). Some side effects with tenecteplase are vomiting, nausea, severe abdominal pain, dark urine, muscle pain, vision changes, chest pain, dizziness, severe headache, changes in urine output, skin discoloration, and weakness in one side of the body. Tenecteplase has possible adverse reactions of hematologic, oncologic, cardiovascular, dermatologic, gastrointestinal, genitourinary, respiratory, and local hemorrhages.[24]

Streptokinase

Streptokinase is a thrombolytic drug that is derived from various streptococci. Streptokinase is a fibrinolytic agent that has been used worldwide due to low cost and good efficacy and safety. Streptokinase is used in treating pulmonary embolism and initially given as 250,000 units intravenously infused over 30 minutes (Table 1).[25] This dose is followed by infusion of a maintenance dose of 100,000 units every hour for 24-72 hours. With this treatment, since thrombolytic activity rapidly fades when infusion has stopped, streptokinase treatment is generally followed by 3-4 hours of intravenous heparin treatment and then oral anticoagulants to prevent re-occlusion. The adverse effects of streptokinase are hemorrhage, rash, fever, nausea, vomiting, and abdominal and back pain.[26,27]

Urokinase

Urokinase is a thrombolytic agent that is produced by human neonatal kidney cells and is found in urine. It converts plasminogen into its active form, plasmin, which results in fibrinolysis. Kinlytic™ (urokinase for injection) is administered

intravenously with a loading dose of 4,400 international units per kilogram and given at the rate of 90 ml per hour over a period of 10 minutes. This loading dose is followed with continuous infusion of 4,400 units per kilogram at the rate of 15 mL for 12 hours (Table 1). The most common adverse reaction from Kinlytic™ (urokinase for injection) is bleeding. In a study, it was found that significant bleeding events requiring transfusion of greater than 2 units of blood were observed during the 14-day study period in 3 of 141 urokinase-treated patients with multiple bleeding events occurring in an individual patient. Most bleeding occurred at sites of external incisions and vascular puncture, with lesser frequency in gastrointestinal, genitourinary, intracranial, retroperitoneal, and intramuscular sites.[28] Other adverse reactions that can occur with Kinlytic™ (urokinase for injection) are myocardial infarction, recurrent pulmonary embolism, hemiplegia, stroke, decreased hematocrit, substernal pain, thrombocytopenia, and diaphoresis.[29,30]

Conclusion

Pulmonary embolisms can significantly affect morbidity and mortality. The use of anticoagulants, thrombolytics, as well as new pharmacological advances can significantly improve patients' chances of survival and quality of life. The use of thrombolytics in patients with pulmonary embolisms is rapidly advancing and, in some cases, can be lifesaving, but there are several patient-specific factors and adverse effects that must be considered with each case, which may potentially lead to hesitancy when considering thrombolytic agents. Adverse side effects of using any thrombolytic agent are similar across the board, which include but are not limited to bleeding and allergic reactions. In thrombolytic agents, streptokinase causes the most allergic reactions; therefore, efficacy may be limited for some patients. Urokinase causes more cases of increased bleeding than other agents. Future generations of thrombolytic agents hope to address many of the adverse effects along with an increase in the efficacy of the agents in the treatment of pulmonary embolisms.

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

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TABLE 1. Thrombolytic Treatments Used for Pulmonary Embolism

Medication	FDA Approval Status for Pulmonary Embolism	Dosage	How Medication Works	Teaching Points
alteplase	Approved	100 mg intravenously infused over 2 hours	Recombinant plasminogen activator.	Not antigenic therefore it is not associated with any allergic reactions
reteplase	Not Approved	10 units intravenously over 2 minutes, then followed by another10 unit dose over 2 minutes occuring30 minutes after the first dose	Recombinant plasminogen activator, and it catalyzes the cleavage of endogenous plasminogen to generate plasmin.	Can cause hypersensitivity and it can increase the risk of bleeding. Heparin and Retavase are incompatible and cannot be administer at the same time.
tenecteplase	Not Approved	Weight based dosing followed as: • Weight less then 60 kg: 30 mg single intravenous bolus • Weight between 60-70 kg: 35 mg single intravenous bolus • Weight between 70-80 kg: 40 mg single intravenous bolus • Weight between 80-90 kg: 45 mg single intravenous bolus dose • Weight over 90 kg: 50 mg single intravenous bolus	Recombinant plasminogen activator and has higher fibrin specificity with longer half-life with final clearance.	Lacks antigenicity and is more comfortable to administer compared to some other agents.
streptokinase	Approved	250,000 units intravenously over 30 minutes	When it binds to free floating plasminogen, it forms a complex that converts additional plasminogen to active plasmin.	Re-administration of streptokinase within 6 months is not considered safe due to high antigenicity and associated antistreptococcal antibody titer.
urokinase	Approved	Initial dose is 4,400 IU/kg intravenously 90 ml per hour rate for 10 minutes then followed by 4,400 IU/kg intravenously 15 ml per hour for 12 hours.	Physiologic thrombolytic produced by kidney and purified from human urine. Kinlytic directly converts plasminogen into plasmin.	Low antigenicity, and it can allow for more repeated dosing without any allergenic issues.

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"MORTAR & PENCIL" CONCORDIA UNIVERSITY WISCONSIN SCHOOL OF PHARMACY STUDENT WRITING CLUB:

The Hispanic Paradox and Implications for Pharmacy Practice

by Claudia D. Betancourt Perez, 2024 PharmD Candidate, Luis M. Marin, 2024 PharmD Candidate, Robert M. Mueller, PharmD, BCPS

Abstract

The Hispanic/Latino population is the largest racial and ethnic minority group in the United States, and has an immense impact on the cultural diversity, economy, and public health of the country. As a minority group, Hispanics often face several health disparities, such as low socioeconomic status, limited access to health services, low health literacy, and language barriers. Despite these disparities and the high prevalence of cardiovascular disease within the Hispanic population, studies have indicated that on average Hispanics have lower all-cause and cardiovascular mortality rates than non-Hispanic Whites. This phenomenon has been described as the "Hispanic Paradox." Various theories have been proposed to explain the paradox, including the healthy migrant hypothesis, the salmon bias, acculturation, and the dominant resilience hypothesis. Understanding the different aspects of the Hispanic Paradox can help provide pharmacists with an insight on how to provide patient-centered care and potentially improve outcomes by assessing nutritional quality, psychological and social factors, language, health literacy, socioeconomic status, and the use of complementary and alternative medicine.

The Hispanic population represented 18.9% (62.2 million) of the total population of the United States in 2022.[1] While some people and scholars make a distinction between the terms Hispanic and Latino, these terms are often used synonymously and interchangeably, especially within medical literature.[2] Therefore, for the rest of the article, the term Hispanic will be used. As the largest racial and ethnicity minority group, Hispanics have a large impact on the cultural diversity, economy, and public health of the United States.[1,3] The Hispanic population in the United States includes both foreign-born individuals from Latin American countries, Spain, and several Caribbean countries, and those born in the United States.[1,3] Although Hispanics are a very heterogenous population, which includes a variety of races, ancestries, cultural practices and beliefs, dietary habits, etc., many share a common feature in the use of the Spanish language.[4] Census data from 2019 demonstrated that 71.1% of Hispanics speak a language other than English at home.[5] Spanish is the preferred language among many Hispanics, especially in the home or in familiar environments.[4] Surveys have also shown that among the foreign-born Hispanics who have lived for fewer than three years in the United States, more than 80% report a limited English-speaking ability or no ability to speak English at all.[6] This language discordance (when a provider and patient do not share a common language or have limited proficiency in each other's language) has the potential to lead to negative health outcomes.[7]

Cancer and heart diseases are the leading causes of death in the Hispanic population in the United States.[3,6,8] However, several studies have indicated that Hispanics, a disproportionately low social economic status (SES) group, have lower overall mortality and cardiovascular mortality than non-Hispanic Whites (NHWs), despite the various disparities and the high prevalence of cardiovascular disease within the Hispanic population. This phenomenon is referred to as the Hispanic Paradox.[9] A number of theories been proposed to explain this phenomenon. Many of them suggest that sociodemographic variables, food, habits, cultural influences, and genetic predisposition could have be potential influential factors.[9,10] Like the French Paradox, where researchers discovered that the French population had a lower rate of coronary heart disease (CHD), which helped identify the beneficial role of the Mediterranean diet and wine consumption as protective factors for CHD, a better understanding of the Hispanic Paradox may help identify additional protective factors against cardiovascular disease that can be extended to all Americans.[11]

The purpose of this article is to review the literature on the Hispanic Paradox and outline several recommendations for pharmacists aimed at improving patient care for the Hispanic population in the United States based on challenges, cultural factors, and risk factors associated with the Hispanic Paradox phenomenon.

"The Hispanic Paradox"

Several studies have explained how social determinants of health influence the overall health outcomes of populations.[3,6] Socioeconomic factors including education level, employment status, cultural factors, and environmental factors strongly influence mortality and morbidity within the Hispanic population.[6] Several studies have also reported that financial, structural, and personal barriers influence patients' use of and access to health care services.[6] Low income and lack of health insurance are two of the financial barriers often present in the Hispanic population.[6] Environmental factors, such as poor geographic access to providers and limited transportation,

also influence use of health care services.[6] Moreover, cultural barriers (such as language discordance) and health-related behaviors (such as smoking, alcohol consumption, and sedentarism) negatively impact health outcomes.[6] Based on the potential impact of these health disparities, it would be expected that on average Hispanic patients would have a higher mortality rate compared to NHWs. However, literature suggests that this is not always the case, and that Hispanics actually exhibit lower or equal mortality rates to non-Hispanics, including lower infant mortality rates and lower prevalence for most major diseases.[3] This paradox was first identified based on mortality data in the United States from the National Death Index (NDI).[6,12,13] A cohort study analyzing data from the National Health Interview Survey (NHIS) and NDI from 1986 through 1991 suggested that the mortality rate is lower among Hispanics compared to NHWs, especially among adults 65 years old and older.[6,13] Another cohort study following the NHIS data from 1979 through 1987 concluded that, compared to non-Hispanics, Hispanics had lower mortality rates related to cancer, cardiovascular diseases, and overall. However, it concluded that Hispanics have higher mortality rates from diabetes and homicide compared to non-Hispanics.[6,14] Other studies have shown that Hispanics have lower CHD events and mortality related to CHD compared to NHWs.[9,14] One meta-analysis showed that there was a significant association between Hispanics and lower mortality rates due to cardiovascular events.[15] Additionally, results showed lower all-cause mortality rates among Hispanics, supporting the existence of the Hispanic Paradox.[15] Other studies have suggested that Hispanics generally have longer life expectancies compared to other ethnic groups. For example, according to data from the CDC in 2011, the average life expectancy from birth in the Hispanic population was 81.4 years, compared to 74.8 years in the non-Hispanic Black population and 78.8 in the non-Hispanic White population.[16] A study conducted in California analyzed the influence of clinical, individual, and environmental factors on non-small cell lung cancer survival in the Hispanic population. Results showed that foreign-born Hispanics had improved survival rates compared to NHWs.[17] This study also found that native-born Hispanics had equivalent survival rates to NHWs. These results further supported the health advantage paradox of the Hispanic population.[17] Additional literature suggests that the Hispanic health advantage is even present among Hispanic kidney transplant recipients.[18] Overall, the sum of data support the presence of the Hispanic Paradox phenomenon, highlighting the need to better understand it and potentially use it to further improve patient care and patient outcomes within and beyond the Hispanic population.

Although there are data and articles that support the phenomenon of the Hispanic Paradox, many still refute its existence. For example, a study analyzing Hispanic death and life expectancy estimates in the United States between 1990 and 2000 concluded that there is no Hispanic Paradox. Instead, the authors believed that the phenomenon could possibly be explained by inconsistencies in reporting of Hispanic deaths.[19] Even though some of the supporting literature about the paradox provides compelling results that seem to validate its existence, it is difficult to locate research with complete death records, which would provide a more definitive conclusion.[20]

The Hispanic Paradox Theories

Possible explanations for this paradox may relate to the overall health of individuals immigrating to the United States, suggesting that healthy individuals are more likely to immigrate to the United States than those who are less healthy. Some data suggest that foreign-born Hispanics have better health than those born in the United States, and those who recently immigrated are healthier compared to those residing in the United States for a longer period of time.[9] Other theories speculate that many Hispanics born outside the United States tend to retire in their native country. In turn, mortality rates are not followed for these individuals and may lead to falsely low statistics.[6,9] This potential bias, also known as the salmon bias hypothesis, suggests that dying Hispanic individuals return to their native country to die and are therefore not reflected in the United States' mortality statistics, but there is little evidence of this.[6,9]

Another hypothesis explains how acculturation affects the health outcomes of the Hispanic population. Acculturation refers to the process by which individuals or groups from different cultures come into contact and exchange ideas, customs, beliefs, and practices leading to changes in one or both cultures.[6,9] This acculturation hypothesis suggests that cultural orientation can represent a protective factor by promoting protective behaviors, and once cultural orientation is affected by the mainstream "American" culture, some of these protective factors can disappear.[6] This theory proposes that immigrants who continue similar lifestyles to their native culture are more likely to have better health outcomes.[9] Additionally, it explains that native Hispanics who are more acculturated in terms of nutrition and behavioral risks tend to lose this advantage.[6,9] Although nutritional changes can both positively and negatively impact Hispanic health outcomes, studies have concluded that changes due to acculturation are more negative than positive.[6] Positive dietary changes often seen in the Hispanic population due to acculturation include a decreased use of cream and sausage, and an increased use of milk and salads.[6] Negative dietary changes include a decrease in consumption of natural, homemade juices and vegetable soups, and increase in consumption of saturated fats such as butter or mayonnaise, or carbohydrates such as cookies.[6] Many traditional Hispanic diets may contain less saturated fat and lower caloric intake, in addition to higher fiber and protein intake compared with non-Hispanics diets. The consumption of legumes such as beans is often widespread in many Hispanics cultures, providing valuable nutrition. Fruit intake is also generally very widespread in the Hispanic population.[9] On the other hand, nutritional intake in the non-Hispanic White population often includes fast foods with saturated fats and sugary drinks.[9] Additional risk factors, such as smoking or alcohol consumption, are also less present in the Hispanic population compared to the NHWs. Research conducted on immigrants from Mexico and Central American countries reported that acculturated women have higher smoking rates compared to less acculturated women.[6] Furthermore, some studies have shown that

acculturation is associated with increased drinking behavior and decreased abstention among Hispanic women.[6] The influence of acculturation in smoking and alcohol consumption is less clear in Hispanic men.[6]

A fourth theory that could help explain the Hispanic Paradox is the dominant resilience hypothesis, which presents the idea that cultural factors positively impact health outcomes.[21] It proposes that cultural values such as social integration, familismo (familism, or supportive family relationship), respeto (respect), simpatía (kindness, or understanding and care for someone else's suffering), and communal coping (the process by which two or more individuals come together to respond to adversity) serve as health-promoting mechanisms.[22–24] Social integration, for example, is thought to help with stress and provide support though the disease course.[21] The dominant resilience hypothesis also supports the idea that the presence of nuclear families is a favorable factor influencing emotional and physical well-being, resulting in lower mortality. In summary, possible explanations to account for the Hispanic Paradox include the healthy migrant hypothesis, the salmon bias, acculturation, and the dominant resilience hypothesis.

Overall, despite some skepticism, several confounding variables, and the lack of a clear explanation for the Hispanic Paradox, it does seem likely, according to the Center for Disease Control and Prevention, that there is an association between the Hispanic population and lower rates of cardiovascular disease.[8] This is primarily evidenced by lower mortality rates due to cardiovascular disease in the Hispanic population, especially among foreign-born, newly arrived, and less acculturated Hispanics, compared to the non-Hispanic White population.[8] Identifying additional protective factors leading to these results in the Hispanic population could help develop additional recommendations for prevention and treatment of CVD disease, which would be relevant not only for Hispanic patients but non-Hispanics as well. Additional studies can further explore factors mediating the protective effects within Hispanics and how to extend these effects to all Americans.

Pharmacist Role

The factors that contribute to Hispanic health and disparities are complex and require additional research, comprehensive strategies, and an interdisciplinary approach. However, pharmacists are in a unique position to guide Hispanic patients in the safe and effective administration of their medications. In order to promote the patient's best therapeutic outcome, the delivery of pharmaceutical care relies significantly on communication between the pharmacist and the patient. As mentioned, a significant portion of the Hispanic population living in the United States has limited English proficiency and often prefers to use their native language of Spanish. The appropriate use of medications by Spanish-speaking patients will therefore depend greatly on the pharmacists' ability to communicate effectively with these patients.[25] According to researchers, Spanish-speaking patients may have difficulty learning how to take their medications. A study found that 47% of Spanish-speaking patients stated that the side effects of their medications were not explained to them, in contrast to only 14% of non-Spanish-speaking patients.[26] Additionally, it has been shown that Hispanics who speak only Spanish are less likely to access a regular source of care than Hispanics who speak English.[25] Even though pharmacists are the most accessible of health care providers, the vast majority of pharmacists in the United States lack adequate proficiency in Spanish to effectively and safely communicate with Spanish-speaking patients.[25,27] A multidisciplinary and interprofessional approach between educators, pharmacies, heath centers, and the community is needed in order to educate and train more pharmacists to provide language-concordant care to Spanish-speaking patients. Pharmacists should make a habit of asking about patients' language preferences and make concerted efforts to accommodate these preferences. Consequently, there is a need to create and use additional resources, such as signage and posters in Spanish, picture diagrams, translated monographs and patient handouts, patient education videos in Spanish, and/or to offer interpretation services to facilitate communication with Spanish-speaking patients. However, focusing on language alone is insufficient, especially if cultural factors are not considered.

It is also important to practice cultural sensitivity in order to provide the best patient care. Pharmacists should not assume that all Hispanics share the same health beliefs, as many do not. However, based on the Hispanic Paradox explanatory theories and possible protective factors, pharmacists should consider assessing a patient's nutrition, psychological and social factors, language and health literacy, socioeconomic status, and use of complementary and alternative medicine (CAM) as part of patient-centered care within the framework of the Pharmacist Patient Care Process. For example, pharmacists can specifically ask about the patient's CAM use, reinforce the importance of a healthy diet, and counsel on the consumption of culturally relevant foods and products that will promote better health. Pharmacists should also be mindful of common Hispanic cultural values such as familismo, respeto, and simpatía, which are not dependent on use of the Spanish language.[28] There is also a need to increase the number of Hispanic pharmacy personnel. Beyond the importance of language concordance, there is additional value in understanding and sharing a patient's culture in order to build strong relationships based on empathy and trust.[29] Pharmacists can also promote/use programs such as church- or school-based screenings or peer-educator programs that avoid the erosion of Hispanics' health status due to diabetes, poor mental health, asthma, or high blood pressure, especially when Hispanics become more acculturated.[30] Additional recommendations for pharmacists are outlined in Table 1.

Conclusion

The Hispanic Paradox is the phenomenon that Hispanics, despite having a higher prevalence of cardiovascular risk factors and greater socioeconomic disadvantage (including lower educational level, employment status, wealth, and environmental factors), have lower or equal mortality rates compared to NHWs. Several theories have aimed to explain this phenomenon and how social and cultural components play a major role in the overall mortality rates of Hispanics living in the United States. Even though there is some conflicting evidence regarding the paradox, it can potentially serve as a base for health care recommendations in Hispanic patients.

Understanding the different aspects of the Hispanic Paradox can help provide pharmacists with an insight on how to provide patient-centered care and potentially improve outcomes by assessing nutritional quality, psychological and social factors, language, health literacy, socioeconomic status, and the use of complementary and alternative medicine.

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TABLE 1. Pharmacist Recommendations Based on Protective and Risk Factors

Protective/ Risk Factors	*Pharmacists Role / Recommendations*
Nutrition Quality	• Personalized assessment of nutritional quality • Assess patient diet and cultural influence in their diet • Reinforce importance of healthy diet/weight and counsel on consumption of culturally relevant foods that will promote better health[31,32]
Psychological and Social Factors, Social Integration	• Include family members in treatment discussions with consent of the patient[33] • Support culturally appropriate community-based interventions (e.g. Community-based screenings with pharmacists, church based interventions, or school-based programs)[34,35,36] • Implement peer-educator or community health worker programs (e.g. Project Dulce)[37,38] • Use LEARN (Listen, Explain, Acknowledge, Recommend, Negotiate) model to facilitate cross-cultural interviewing and bridge cultural gaps[39] • Increase awareness of family and/or traditional cultural values (e.g. simpatía (kindness), respeto (respect), familismo (familism), and communal coping concepts)
Language, Health Literacy	• Encourage and facilitate increased Spanish-communication skills • Hire bilingual personnel to increase language concordance • Provide access to translation and interpreter services • Appropriately use interpretation services • Use the "teach back" method to ensure patient understanding[28] • Allow extra time for patients with limited English proficiency (LEP)[28] • Post bilingual or Spanish-language signage[28] • Provide or enhance culturally sensitive training for staff[28] • Ask patient's language preference and if Spanish, provide Spanish-language medical handouts and patient forms
Socioeconomic Status	• Assess barriers to care (income, transportation, education) • Use available resources to overcome identified barriers (e.g. patient assistance programs, manufacturers' coupons, free clinics, medication delivery options etc.)
Complementary and alternative medicine (CAM)	• Ask about use of CAM including herbals, and know how it may facilitate or impact treatment[40] • Safely accommodate cultural beliefs and practices in patient medication management • If effectiveness of traditional medicine cannot be assessed, assess safety, and involve the patient in decision making toward their treatment • Familiarize oneself with common folk illnesses and healing practices within the Hispanic population (e.g. empacho, mal de ojo, susto etc)[41]

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Review Article

Novel Anticoagulants Affecting Factors IX, XI, and XII

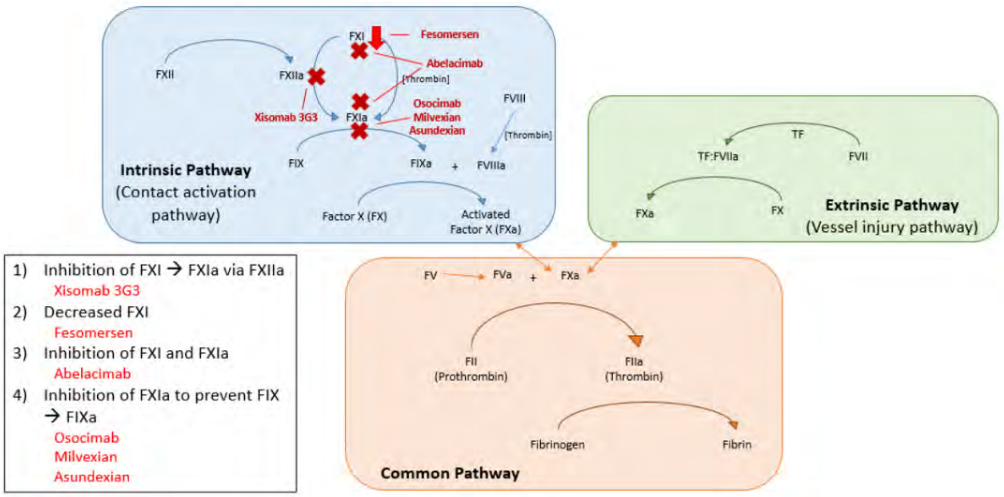
by Kaitlin Bruden, PharmD

When an elderly patient develops atrial fibrillation (Afib) and desires to be placed on anticoagulation, clinicians must think about which agent would be best. It is often difficult to determine a good anticoagulation regimen for patients with a high risk of bleeding; one of the biggest adverse effects of anticoagulation is the risk of bleeding. Some patients decide not to start anticoagulation due to this risk.[1,2]

One thing that unites all anticoagulants currently on the market is that they have an increased risk of bleeding. These agents have differing risks of bleeding (i.e. apixaban has been proven to have lower risk of bleeding than warfarin), but all have certain limitations when it comes to bleeding.[1] Direct acting oral anticoagulants (DOACs) have an estimated rate of major bleeding around 2-4% per year, while warfarin has a rate estimated to be ~0.4-7.2% per year.[3,4] Additionally, DOACs have limitations when it comes to their indications. For example, they have not been shown to be safe and effective for use in patients with antiphospholipid syndrome or mechanical heart valves.[2] These limitations have led to an unmet need for better anticoagulants.

All currently approved anticoagulants work in the same part of the coagulation cascade: the extrinsic pathway. At its simplest, there are three main parts of the coagulation cascade: the intrinsic pathway, the extrinsic pathway, and the common pathway.[5] The intrinsic pathway, also called the contact activation pathway, is more involved with inflammation and innate immunity, as well as being involved with coagulation once activated through the extrinsic pathway via thrombin.[2,5] The extrinsic pathway is considered the "initial spark" for coagulation and is involved with physiological hemostasis.[2] This pathway generates thrombin, which then goes on to involve the intrinsic pathway via factor XI (fXI) as can been seen in Figure 1;

FIGURE 1. Coagulation Cascade Depiction with Novel Agent Mechanisms, Adapted From Nopp et al[2]



thrombin also continues the clotting process in the common pathway.[1] FXI can also be activated by factor XIIa (fXIIa), a step higher in the intrinsic pathway.[6]

Factor XII (fXII) and fXI have gained interest as targets for novel anticoagulants. The major advantage is the hypothesis that these factors will target and decrease the risk of thrombosis while having minimal increased risk of bleeding.[2] What makes these targets different from those of the currently approved agents on the market is that fXI/fXIa and fXII/fXIIa reside within the intrinsic pathway of the coagulation cascade. Recent research seems to support that the intrinsic pathway is involved with pathologic thrombosis, so by inhibiting this pathway, there would be a lower thrombotic risk while leaving physiological hemostasis unchanged.[2,7] There have been discussions about which factor would be a better target.[6] Considerations include that fXI can be activated even without fXII via thrombin and the extrinsic pathway and that fXII-independent processes have been shown to be more significant for thrombosis in some studies. FXI deficiency is a known disorder called hemophilia C; from looking at data on patients with hemophilia C, we know these patients have a mild bleeding disorder–they have a decreased risk of thrombotic events and a low risk of non-trauma related bleeding.[2,5,6,8] Less is known about fXII deficiency than fXI deficiency; current epidemiological data show patients with fXII deficiency are not at lower risk of venous thromboembolism (VTE), stroke, or myocardial infarction (MI) and may actually have a higher risk of thrombotic events.[1]

Discussion

There are many novel agents in Phase II and III studies. These agents have different formulations, so they could have slightly different uses or dosing intervals; for example, monoclonal antibodies are often infused, while small molecule drugs could be an oral option. How the drugs elicit their intended effects can also vary–some agents block the active site of the intended factor while others silence the gene expression of the factor of interest.[2] The differences in mechanisms could also differentiate the agents as we learn more about the intrinsic pathway and the processes involved with thrombosis. The population for which each agent is studied will also affect initial uses. Agents that have been studied in patients undergoing knee replacement include fesomersen (formerly IONIS-FXIRX or

ISIS-416858), osocimab, abelacimab, and milvexian. Many of these novel agents are being researched in patients with end-stage renal disease (ESRD) or patients who are on hemodialysis, which is a population often excluded from clinical trials.

Agents Targeting FXI

Fesomersen is an fXI-directed antisense oligonucleotide (ASO) agent that decreases the amount of fXI and its activity levels with concentration-dependent properties. A phase II study with patients undergoing elective knee replacement compared fesomersen 200 or 300 mg per week, subcutaneously, starting 35 days prior to surgery, with enoxaparin 40 mg daily starting after surgery. Mean fXI levels were reduced to 38% and 28% of baseline values in those receiving the 200 and 300 mg. The 200 mg fesomersen regimen was non-inferior and the 300 mg ASO regimen was superior to enoxaparin for the primary efficacy outcome of VTE. All groups had similar rates of bleeding. This agent has also been looked at in trials of patients with ESRD.[1]

Agents Targeting FXIa

Agents with this mechanism prevent fXIa from activating fIX. Osocimab is a monoclonal antibody that binds to and inhibits FXIa, preventing this from activating FIX. It is a monthly subcutaneous injection or intravenous infusion that has been studied in knee replacement so far with a single intravenous dose given pre- or post-operatively. When compared to enoxaparin 40 mg daily and apixaban 2.5 mg BID, osocimab 0.6 mg/kg post-op, 1.2 mg/kg post-op, and 1.8 mg/kg post-op doses met the criteria for noninferiority compared to enoxaparin while osocimab 1.8 mg/kg pre-op also met the criteria for superiority compared to enoxaparin for VTE rates. Osocimab showed lower bleed rates than enoxaparin in all groups.[9] There is a study with osocimab in patients with ESRD underway that uses a monthly subcutaneous formulation.[1] The two different formulations of osocimab have different doses and frequency recommendations, which makes this agent different from other novel medications mentioned in this article. Milvexian is a small molecule that inhibits fXIa. This is a daily or twice-daily oral medication and has been studied in knee replacement with an upcoming study looking at its effects in ischemic stroke. Seven dosing regimens of milvexian were compared to enoxaparin; four dosing regimens were superior to enoxaparin with all groups having similar bleeding and adverse events.[1,10] Asundexian is a small molecule inhibitor of fXIa; it is a daily, oral option that has been studied in atrial fibrillation. It has no significant drug interactions with CYP3A4, giving it an advantage over the current DOAC agents. Two doses of asundexian were compared to apixaban and showed lower bleed rates than apixaban. There were cases of ischemic stroke in both asundexian arms and none in the apixaban group, showing more efficacy data is needed in Phase III trials.[1,11] There is a completed and ongoing Phase II study in patients with recent myocardial infarction and non-cardioembolic stroke, respectively.[1]

Agents Targeting FXI and FXIa

Abelacimab is another monoclonal antibody; it works by binding to and inhibiting both fXI and fXIa. In a study comparing intravenous doses to enoxaparin in patients undergoing knee replacement, all 3 doses (30-mg, 75-mg, 150-mg) of

TABLE 1. Drug Information for Novel Agents Targeting FXI (fesomersen)

	Fesomersen
Mechanism	FXI-directed antisense oligonucleotide (ASO) agent
Rationale	Decreases amount of FXI and its activity in a concentration-dependent manner
Formulation	Subcutaneous injection
Dosages studied	100 mg per week 200 mg per week* 300 mg per week‡ *Patients received 9 doses over 39 days with first dose 36 days prior to surgery*
Comparator	Enoxaparin 40 mg daily subcutaneous
Population studied	Elective knee replacement (VTE prophylaxis)
Safety	Similar bleeding with comparator
Future studies	Patients with ESRD

*: non-inferior to comparator; ‡: superior to comparator

TABLE 2. Drug Information for Novel Agents targeting FXIa (osocimab, milvexian, and asundexian)

	Osocimab	Milvexian	Asundexian
Mechanism	Monoclonal antibody that binds and inhibits FXIa	Small molecule that inhibits FXIa	small molecule inhibitor of FXIa
Rationale	Prevents activation of FIX	Prevents activation of FIX	Prevents activation of FIX
Formulation	Monthly subcutaneous injection or intravenous infusion	daily or twice-daily oral medication	daily, oral option
Dosages studied	0.3 mg/kg pre-op 0.3 mg/kg post-op 0.6 mg/kg post-op* (enoxaparin) 1.2 mg/kg post-op* (enoxaparin) 1.8 mg/kg post-op* (enoxaparin) 1.8 mg/kg pre-op‡ *All doses given as a single, 60-minute, intravenous infusion*	25 mg BID 50 mg BID‡ 100 mg BID‡ 200 mg BID‡ 25 mg once daily 50 mg once daily 200 mg once daily‡	20 mg once daily 50 mg once daily
Comparator	enoxaparin 40 mg daily and apixaban 2.5 mg BID	Enoxaparin 40 mg daily	Apixaban 5 mg BID
Population studied	Elective knee replacement (VTE prophylaxis)	Elective knee replacement (VTE prophylaxis)	Atrial fibrillation with moderate-high risk of stroke and bleeding
Safety	lower bleed rates than enoxaparin in all groups	All doses similar bleeding and adverse events	Lower bleed rates than apixaban
Future studies	Patients with ESRD on HD (monthly subcutaneous injection)	Ischemic stroke prevention	More efficacy studies needed (in atrial fibrillation)

*: non-inferior to enoxaparin; ‡: superior to enoxaparin

abelacimab showed non-inferiority to enoxaparin 40 mg with superiority met for the 75-mg and 150-mg abelacimab regimens, and rates of bleeding were similar in all groups.[12] There are ongoing studies in atrial fibrillation (for safety outcomes) and cancer-related thrombosis.[1]

Agents acting as FXIIa inhibitors

Xisomab 3G3 is a monoclonal antibody that has been studied in ESRD. It binds to fXI and blocks its activation from fXIIa; fXI activation via thrombin is not inhibited, making this agent unique by acting like an fXIIa inhibitor. In the study of patients with ESRD who need heparin-free dialysis, no bleeding events related to the study drug occurred, and results for efficacy were promising but underpowered. Another study involving artificial surfaces is ongoing; this one is for prevention of catheter-related thrombosis in patients with cancer.[1]

Conclusion

There is a lot of potential from early Phase II and Phase III studies of these novel medications. What is still unknown with these agents is if their efficacy will be similar or better than current agents. It is also unknown if there will be off-target effects from these agents due to their novel mechanism of action.[5,6] While these agents seem to have an increased safety profile from these early studies, larger landmark trials will be needed to determine their safety and efficacy on a larger scale.[13] It is an exciting time to be in the field of anticoagulation, and we'll have to wait and see how the landscape shapes up in the next few years.

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TABLE 3. Drug Information for Novel Agents Targeting FXI and FXIa (abelacimab)

	Abelacimab
Mechanism	monoclonal antibody that binds to and inhibits both FXI and FXIa
Rationale	Prevents activation of FIX
Formulation	Single intravenous infusion
Dosages studied	Intravenous 30-mg abelacimab* Intravenous 75-mg abelacimab‡ Intravenous 150-mg abelacimab‡
Comparator	Enoxaparin 40 mg
Population studied	Elective knee replacement
Safety	Similar bleeding in all groups, none clinically relevant
Future studies	Atrial fibrillation (for safety); Cancer-related thrombosis

*: non-inferior to comparator; ‡: superior to comparator

TABLE 4. Drug information for novel agents targeting FXI conversion to FXIa via FXIIa (xisomab 3G3)

	Xisomab 3G3
Mechanism	monoclonal antibody that binds to FXI (acts like a FXIIa inhibitor)
Rationale	blocks FXI activation from FXIIa without affected FXI activation from thrombin
Formulation	0.25 mg/kg injected into dialysis line 0.5 mg/kg injected into dialysis line
Dosages studied	0.25 mg/kg injection 0.5 mg/kg injection
Comparator	Placebo
Population studied	patients with end-stage renal disease who need heparin-free dialysis
Safety	No bleeding related to study drug occurred
Future studies	Efficacy data needed in patients with end-stage renal disease who need heparin-free dialysis; artificial surfaces for prevention of catheter-related thrombosis in patients with cancer

*: non-inferior to comparator; ‡: superior to comparator

Educational Conference Recap

2023 PSW Educational Conference Recap

by Amanda Egbert, 2024 PharmD Candidate

Over 350 pharmacists, pharmacy residents, student pharmacists, and pharmacy technicians attended the 2023 Pharmacy Society of Wisconsin's (PSW) Educational Conference in April. The statewide event took place over two days at the Monona Terrace Convention Center in Madison, Wis. This year's educational conference focused on fostering change and engaging in storytelling through the theme, "Champions of Change: Blazing a Trail."

The 2023 Wisconsin Pharmacy Residency Conference (WPRC) was held concurrently with the PSW Educational Conference. There were 121 platform presentations given by 81 pharmacy residents during both days of the conference. Presentations were followed by questions from the audience and formal feedback from evaluators. Topics ranged from appropriate prescribing of peri-operative antibiotics and considering pharmacogenomics for the use of opioid analgesics to evaluating medication adherence in patients with cystic fibrosis and pharmacist-led aspirin deprescribing processes in the ambulatory care setting.

In addition to the WPRC, poster sessions took place over the lunch hour during both days of the conference. A total of 88 posters were lined up throughout the Community Terrace where pharmacists and student pharmacists proudly presented their research from the past year. Interested attendees had the opportunity to walk around, ask questions, and learn about the new and important work being done by professionals in pharmacy practice.

Attendees of the conference were encouraged to use the PSW app to create their own personalized schedule, connect with other conference-goers, share photos and reflections on the activity wall, and view available virtual content from the event. Another fun opportunity was the event game, where attendees could earn points by completing challenges, such as "Attend the La Jolla Exhibit Theater," "Meet a PSW Board Member at the Poster Session," and "Share Your Story" at the Grand Terrace video booth.

Day One Details

Steve Bench, founder of Generational Consulting, LLC, jumpstarted the conference by leading the first general session, "Overcoming Generational Differences." Bench, also known as "The Millennial Guy," discussed each of the five generations in the workforce and the traits and stereotypes known to define them. He humorously touched on each generation's motto, talents, and value in the workplace and highlighted that "we are all products of the culture that raised us." Bench explained that putting effort into understanding generational differences can build stronger relationships, improve the culture at work, and increase job satisfaction for all team members.

Following a short networking break, Kari Trapskin, Danielle Womack, and Pamela Appleby led the second general session, "The Pathway Onward: Provider Status Progression and Advancement." Trapskin and Womack introduced the PSW Provider Status Implementation Guide and its anticipated contents as provider status for pharmacists begins to take shape. They continued on to address the question, "What should be done now?" by recommending that pharmacists obtain their National Provider Identifier (NPI), evaluate current services offered, ensure individual liability insurance, and begin discussions with partner physicians about collaborative practice agreements (CPAs). Trapskin and Womack rounded out their portion of the presentation by introducing the Implementation Support Webinar Series. Topics such as medical billing, covered services, and provider enrollment will be addressed as part of the series. Pamela Appleby led the second half of the session, where she explained the general structure and timeline associated with the implementation of Wisconsin Act 98 (2021). She touched on the enrollment pathway for pharmacists as Medicaid providers, the development process for the Medicaid State Plan, and how communication in regard to Wisconsin Act 98 progressions will be handled moving

forward.

Later in the afternoon, exhibit theaters, presentations on the future of the pharmacy workforce and careers in pharmacy, and a spotlight presentation on updates made to the PSW anticoagulation and CKD toolkit took place. A particularly unique and hands-on session, "Saturday Morning Mess: An Interactive Pharmacy Law Escape Room," was led by pharmacists Michael DeBisschop and Kate Rotzenberg. This evening activity gave participants a time limit of one hour to solve eight puzzles in order to successfully (and legally) open the retail store, "Pharmer's Market," in time for the first patient to be served.

Day Two Details

After a successful first day, Karen Kopacek and Megan Grant opened day two of the PSW Educational Conference by leading the discussion, "Champions of Change: Make Your Story, Own Your Story, Tell Your Story." The presentation began with the important concept of professional identity formation (PIF). Kopacek explained that PIF stems from piecing together both your personal and professional identities. By recognizing where your identity comes from, you are more equipped to begin telling your own identity story. She explained that PIF and storytelling go hand-in-hand as revealing your professional identity requires you to engage in self-reflection. Kopacek challenged each audience member to think about how their values and internal standards cause them to feel, think, and act in specific ways both in and out of the workplace. She ended her portion of the session with the following message: "Tell your story to know yourself, tell your story to know what has shaped it, and tell your story to bring about change." From here, Megan Grant took the reins and addressed the components of a good story and how to share that story with peers and colleagues. Grant outlined the four C's of storytelling: character, connection, conflict, and conquest. She instructed the audience to use the four C's to construct a story that was tailored to members of their organizations. The three types of stories that can be told include the involvement story, the impact story, and the thank you story. The involvement story identifies why you got involved with your organization. The impact story focuses on how your organization meets a specific need in the community. The thank you story is a simple acknowledgement to those who helped shape and support your identity formation. Grant encouraged the audience to share their stories during the remainder of the conference through the PSW app and at the "Tell Your Story PSW" booth.

The energy and motivation from the first general session led straight into the second general session of day two, "Upskilling and Reskilling Yourself and Your Team: A Guide to Blazing New Trails on a Professional Journey." Executive Vice President and CEO of PSW, Sarah Sorum, invited Phyllis King, Jon Kaupla, and Sarah Sewell to the stage to discuss current and future workplace dynamics. The goals of this session were to identify factors that are impacting business and health care delivery and pinpoint strategies to best support new learning opportunities and healthy work environments for all team members. The panelists listed a number of realities in the workforce, such as the challenges of meeting the needs of five generations in the workplace, patient care via telehealth, the beginning of Artificial Intelligence (AI), and the importance of supporting the mental and physical wellbeing of employees. Throughout the question and answer session, a number of topics were addressed, including strategies to retain talent, how to attract team members with diverse skillsets, the need for trauma-informed leadership, and the importance of building and maintaining trusting relationships with colleagues in the workplace.

After lunch on day two, conference-goers had the opportunity to attend more exhibit theaters, learn about residency accreditation standard revisions, and engage in a presentation about community health workers. Other learning opportunities during the afternoon included updates in prescribing practices for adeno-associated viral (AAV) gene therapies, opioids for pain management, and antibiotics to treat infectious diseases.

Closing Comments

It's always a joy when the Wisconsin pharmacy community can come together. This year's Educational Conference gave pharmacy professionals the opportunity to develop and share their stories and identities with colleagues from around the state. For one person in particular, the conference made quite an impact. Jéssica Malta, a pharmacist who recently moved to Madison, Wis. from Brazil, wrote to PSW CEO Sarah Sorum to share her experience at the conference. "I am writing to express my gratitude for the opportunity to participate in the PSW Educational Conference. The conference was an excellent experience for me, and I really enjoyed it. I had the chance to practice my English, meet some people, and gain a better understanding of the pharmaceutical area here." Thank you, Jéssica, for attending the conference this year!

Another conference-goer, Marnie Wickizer, said, "The PSW Educational Conference was so well done and just what I needed; it was incredibly uplifting!" Echoing Marnie, members of PSW did an outstanding job developing and hosting a conference that highlighted the importance of self-reflection, discussed challenges and changes occurring in the workplace, and provided updates about current trends in pharmacy practice.

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ROSALIND FRANKLIN UNIVERSITY OF MEDICINE AND SCIENCE STUDENT WRITING CLUB:

Business Member Spotlight: Julie Thiel

by Victoria R. Stang, 2024 PharmD Candidate, Aman Patel, 2025 PharmD Candidate

Julie Thiel, PharmD, is the supervisor for the Children and Youth with Special Health Needs unit within the Division of Public Health at the State of Wisconsin Department of Health Services. She recently transitioned to this role after being a psychiatric pharmacist for the State of Wisconsin, specializing in mental health at Winnebago Mental Health Institute and Wisconsin Resource Center.

Thiel received her Bachelor of Science degree in Pharmacy in 1998 from the University of Wisconsin-Madison and later graduated with her Doctor of Pharmacy degree from the University of Florida in 2015. Thiel believes that she has taken a non-traditional path throughout her career. She first worked as an intern at Shopko and later moved to California to work at a Walgreens training location. With encouragement to move into administration, she became a pharmacy manager, training pharmacists within the San Francisco district. Thiel transferred to a 24-hour HIV specialty location and learned she had an interest in specialty pharmacy. In the summer of 2002, she returned to Wisconsin and assumed the role of pharmacy manager at Walgreens in Appleton. After several years of working as a pharmacy manager there, she transitioned out of retail pharmacy into a clinical pharmacy role at the Winnebago Mental Health Institute and Wisconsin Resource Center Shared Services Pharmacy. In this role, she served as a staff pharmacist for seven years, followed by seven years as the Pharmacy Director and Lab Supervisor. In her role as a director, Thiel served as vaccine coordinator and also oversaw laboratory operations, where she assisted with laboratory workflows related to COVID-19. In September 2022, Thiel moved to the Division of Public Health for the State of Wisconsin, working as a Health Unit Supervisor in the Bureau of Community Health Promotion.

When Thiel is not working or spending time with her family, she can be found volunteering. She is an active member of 5-Stones, an organization working on the prevention of sex trafficking in the state of Wisconsin. Thiel learned about this organization at a Lunch and Learn session, and knew she had to get involved due to her interest in health promotion and education. Some of the other organizations for which Thiel volunteers are Feeding America, which provides food to people facing hunger; Pillars, which helps people experiencing homelessness; and Harbor House, a domestic and sexual violence shelter.

Daily Practice

In her current role, Thiel works within the Family Health Section and oversees three main program areas: the birth defects prevention and surveillance program, facilitation of the newborn screening program, and healthcare access for children and youth with special healthcare needs such as diabetes, asthma, mental health needs, or physical disabilities. Her day-to-day responsibilities include strategic planning and execution, personnel management, and maintaining her program areas as required by state statutes. Thiel is a continuous learner and enjoys taking on new responsibilities in order to effect positive change. One of her focuses is leveraging the strengths of those around her to create a positive work environment.

Overcoming Obstacles

New roles and responsibilities do not come without challenges; Thiel recognizes that different challenges come up in different ways, but acknowledges that it is normal when working with others. One of the biggest challenges she faces in her new role is learning the process for the Title V Maternal and Child Health Block Grant, a federal program that works in partnership with state governments to support mothers, children, and families. Understanding the parameters of the block grant has been a valuable opportunity for Thiel to gain a new skill while applying what she learned from her community-based organization volunteer work. Aside from tackling block grant writing, many of Thiel's other challenges have been administrative in nature, such as managing open positions and hiring, onboarding new team members, and learning the operations and organization within a new division. Thiel believes that "transitions are hard and scary, but having an interest and wanting to learn in that area and having that growth mindset will help to get you through." Though Thiel has made many transitions throughout her career, she believes that every opportunity has given her a new skill set that is transferable to the next new role. It can be easy to forget how much learning happens when there are new people to manage and report to with different organizational structures, but she believes each interaction has presented another opportunity to grow. With that in mind, Thiel says she would not change anything in the path of her career. She credits each job with having given her an opportunity to learn, grow, and work with a diverse group of healthcare professionals, proving that the skills you learn along your journey can help you become a well-qualified professional.

All of the transitions that Thiel has made throughout her career were due to what she needed at the time, and everything she has done has been based on a mindset of personal growth. Getting a PharmD was a personal goal for her, and thus she pursued a non-traditional working professional Doctor of Pharmacy program. This opened up the opportunity to become a pharmacy director in a shared service pharmacy that

provided medication for a hospital setting and correctional setting (~600 beds total). Throughout her career, she's understood the importance of influencing the future of pharmacy practice by educating student pharmacists on rotations. In 2016, she was awarded the Larry Boh Clinical Instructor Excellence Award from the University of Wisconsin-Madison School of Pharmacy, a huge milestone for her. She implemented a mental health advanced pharmacy practice elective and it was exceptionally validating that her students enjoyed the rotation. Thiel was recently awarded the 2022 PSW Pharmacist of the Year Award at the PSW Annual Meeting last August. To Thiel, having a support system is essential. She says, "when you are first starting out, you may not feel like you have the skills or you are not qualified, but just giving it a go is important."

Moving Forward

Over the next few years, Thiel sees many opportunities for pharmacists to get involved in specialty practices and pharmacy practice advancements. One of those unique areas is the correctional system; as different provider shortages grow in the system, there is future potential for pharmacists to step up to help manage chronic conditions such as depression, asthma, and diabetes. She is excited to see administrators become more knowledgeable about the burnout and financial stressors that negatively impact staff. By appropriately encouraging healthy coping skills, completing the stress cycle to prevent holding onto stress, and creating ways for employees to better maintain work-life balance, administrators will be better equipped to support their staff and provide what they need to maintain a healthy work environment. Thiel sees potential for pharmacy practice advancement by focusing on mental health, and specifically how trauma affects long-term health. In ambulatory care and public health settings, pharmacists will be able to connect patients to greater healthcare access and other services related to health promotion rather than treatment. Many areas fall under the umbrella of public health, such as tobacco cessation, immunization, chronic conditions, and substance use disorders—all of which pharmacists are trained in and have the ability to make a significant impact. She believes pharmacists can get into these practices through statewide initiatives and collaborations among different partnerships and organizations. The infrastructure has been set for pharmacists to get involved in these areas; now it is time to take the initiative and get involved to make a difference.

Words of Advice

To aspiring pharmacists and student pharmacists, Thiel advises, "It is important to form connections broader than just pharmacy and to advocate for yourself when you see interest in something, even if you do not have formal training in that specific area. Communicate that interest to your supervisor, especially when you are first starting out or if you do not really know. Ask questions, ask to participate in committees, and look for opportunities to grow. You can expand your knowledge and skills in an informal setting through volunteering and through other opportunities; it does not always have to be done through your career or even be pharmacy specific." Thiel's words of wisdom are, "When you see an interesting opportunity, jump!"

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Below-Left: *Dr. Julie Thiel and Jamie VanDyck, Deputy Director of Winnebago Mental. Health Institute.* ***Below-Center:*** *Julie Thiel with parents David and Nancy Hanson on graduation day at Madison.*
Below-Right: *University of Florida PharmD graduation with husband Todd, daughter Elsa, and son Hunter*

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

Pharmacy Leader Spotlight: Holly Altenberger

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

Holly Altenberger, PharmD, is the director of O'Connell Pharmacy in Sun Prairie, Wisconsin, an independent pharmacy with two locations. In addition to dispensing prescriptions at its retail location, the pharmacy also offers services such as immunizations, healthcare screenings, and compliance programs. At the separate long-term care (LTC) pharmacy location, compliance packaging services are provided to assisted living and skilled nursing facilities. As the Director of Pharmacy, Altenberger oversees the day-to-day operations of both the retail and LTC pharmacies. She is dedicated to providing exceptional patient care, while improving efficiency and lowering error rates at both O'Connell Pharmacy locations.

Altenberger attended Edgewood College and graduated with a bachelor's degree in biology and a minor in chemistry. While completing these degrees, she worked part-time at LensCrafters as an optician. She was a part-time supervisor in her sophomore year of college and, after numerous promotions, held a leadership position at the store management level upon graduation. These positions allowed her to develop valuable leadership skills, in addition to learning about human resources management. Despite appreciating all that she learned at LensCrafters, Altenberger decided she wanted to pursue a career in pharmacy approximately two years after she graduated from Edgewood College. This is when she became a student at the University of Wisconsin-Madison School of Pharmacy. During pharmacy school, Altenberger worked as a pharmacy technician and completed an internship at Walmart Pharmacy. She loved the atmosphere of retail pharmacy, and was able to obtain even more experience during her Advanced Pharmacy Practice Experience (APPE) rotations in her fourth year of pharmacy school. Notably, she had the opportunity to complete one of her eight-week rotations at O'Connell Pharmacy. Following graduation from pharmacy school, Altenberger was hired as a staff pharmacist at O'Connell Pharmacy. Within the first year of her employment, the owner, Mark O'Connell, RPh, began to decrease his hours as he prepared for retirement. Soon after, she became Store Manager at the LTC pharmacy location. She held this role for roughly four years until she was promoted to her current position as the Director of Pharmacy.

Mentor

When asked who has played an influential role in her career, Altenberger was quick to name Mark O'Connell, who owned the pharmacy from 1987 until last May, when he passed. Altenberger says that she had an amazing opportunity to learn directly from him, as there was a good portion of time when it was just her and O'Connell working together. She credits O'Connell with teaching her how to be a calm and respectable leader, seeing patients as people first. Mark O'Connell had the respect of his employees and cared for them like family. Altenberger, having had experience mostly in the corporate world, found O'Connell's leadership style inspiring. Today, she strives to demonstrate her compassion to both her employees and her patients.

Accomplishments

Altenberger says her greatest professional achievement is helping to create an environment where all individuals, employees and patients alike, enjoy their interaction with the pharmacy. She describes an atmosphere that is pleasant yet productive, accurate, and noble. Altenberger makes a great effort to ensure that the pharmacy encourages staff to grow and to do it at their own pace. For instance, she shares that one of her technicians joined the pharmacy while in high school and has, since then, taken on a role as their current project manager. Under her leadership, the pharmacy evolves together, and her team is ready to take on any challenges even if it requires breaking new ground.

Early in her career, Altenberger would often fail to keep what she describes as a "knee-jerk overdrive mode" at bay when plans would go awry. Her immediate response to any issues that arose at the pharmacy was to step in and try to fix everything. However, she has learned over time that there is more harm than benefit done by a knee-jerk reaction, and that her response directly impacts her team morale. Hence, she stresses the importance of being a calm and consistent leader, a lesson carried forward from Mark O'Connell.

Outside of the pharmacy, Altenberger says her greatest personal achievement is having her three kids and trying her best to work through daily hurdles. She values being a part of their growth and having the ability to take on an active role in their lives. Altenberger appreciates the great work-life balance and flexibility that independent pharmacies offer. This enables her and her staff to prioritize family and relations and build a community together with their children.

Concerns Today

As the world of pharmacy practice continues to progress, Altenberger shares her growing concern for the future of independent pharmacies. With changes in reimbursement structure and the cost of goods increasing, independent pharmacies are struggling to continue providing quality care and will continue to be forced into focusing on staying afloat, rather than the incredible services pharmacists are equipped

to provide.

In the next 10 years, Altenberger hopes to see pharmacy practice evolve to provide more clinical services. In recent years, the clinical services at O'Connell Pharmacy have been expanding to accommodate population needs. For example, they now offer COVID-19 testing services in response to the pandemic. Altenberger hopes to continue to see independent pharmacies demonstrating their value and role in society, specifically the ability to provide services that other providers may not be able to. Independent pharmacies are uniquely positioned to provide patients in need with extra resources, as these pharmacists tend to have more time to dedicate to each individual patient.

Altenberger shares that her top priorities today are to continue to expand the clinical services O'Connell Pharmacy offers, while ensuring she retains the necessary staff. She is excited to implement more testing services in the coming year. She is close to this initiative, since she serves on the Pharmacy Society of Wisconsin's (PSW) Seniorcare and LTC Advisory Committee. However, she recognizes that new services would not be possible without the employees to implement them. Altenberger will continue to dedicate her time to showing her appreciation for her staff and allowing them to work towards a fulfilling career in pharmacy.

Advice for Future Leaders

To future leaders, Altenberger emphasizes the importance of keeping an open mind and the value of listening to others. As leaders, it is easy to fall victim to a natural rhythm of seeking out problems, and then immediately finding quick solutions to fix them. However, this underestimates the value of simply sitting down and hearing the perspectives of those directly impacted and the insights they have to offer. Altenberger emphasizes the importance of perpetually adapting to meet the requirements of the industry and employees. She thanks PSW for its support along the way, and for broadening her horizons by enabling her to sit on the LTC board and the Diversity, Equity, and Inclusion committee.

A major lesson adopted from her previous employment at LensCrafters that she carries forward to this day is that a successful leader is one who can step away from their role and still have a seamless operation. To achieve this, leaders must learn the benefit of letting go of control and being able to step back when appropriate. Although Altenberger would no doubt have benefited from learning all these lessons earlier in her life, she is much more appreciative knowing that she gained them through experience over time. A final piece of advice is to always be the best that you can by continuously changing and evolving.

Judy Zheng and Amy Wolff are 2024 Doctor of Pharmacy Candidates at the University of Wisconsin-Madison School of Pharmacy in Madison, WI.

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Telling Their Stories: Transitioning into Ambulatory Care Pharmacy Practice

by Jennifer J Foti, PharmD, BCACP, Sarah C Ray, PharmD, BCPS, FAPhA, Marcus J Pribyl, PharmD, Maija A Anderson, PharmD

The pharmacy profession consists of many different clinical pharmacy practice areas. Ambulatory care pharmacy continues to be a growing area of clinical pharmacy practice, focusing on chronic disease state management. Ambulatory pharmacy roles may differ by state and employer, defining scope of practice, collaborative practice agreements (CPAs), and credentialing or privileging processes.

Aligning with the 2023 Pharmacy Society of Wisconsin (PSW) theme of "Telling Your Story," the authors interviewed pharmacists and pharmacy technicians across the state who have made the transition from a variety of different pharmacy practice areas into ambulatory care pharmacy. They highlight their transition experiences and provide helpful guidance for pharmacists or pharmacy technicians interested in transitioning into ambulatory pharmacy practice.

Below: *Steven Linden, PharmD, Bellin Health, Green Bay, WI.*

Editor's Note:

Contribution from the PSW Ambulatory Care Advisory Committee (ACAC)

Telling Their Story

Steven Linden, PharmD
Bellin Health, Green Bay, WI

Steven Linden is an ambulatory care pharmacist practicing at Bellin Health in Green Bay, Wis. Prior to his ambulatory care role, he practiced in the intensive care unit (ICU) of a 255-bed hospital for over five years. In that role, he was responsible for rounding with the intensivist, attending traumas, and completing pharmacokinetic dosing. Linden was also an active member of the site's antimicrobial stewardship committee, where he created, implemented, and performed inpatient skin tests to rule out penicillin allergies.

What influenced your pharmacy practice change?

Linden's transition into ambulatory care pharmacy practice was driven by his desire for more flexibility to tend to the needs of his family. In his previous ICU pharmacy role, he worked nights, weekends, and holidays, which is common for inpatient pharmacy practice. Unfortunately, Linden's spouse works a similar schedule, which led to long periods without seeing each other and limited family time. In his current ambulatory pharmacy role, he has more flexibility to be able to spend time with his family.

What is your current ambulatory care role?

In Linden's ambulatory care role, he practices under a CPA, provides patient medication reviews and education, and answers provider medication inquiries throughout the health system. Linden is actively involved in the therapeutic management and maintenance of diabetes, opioid titration, anticoagulation, and polypharmacy with an emphasis on behavioral health. Linden feels appreciated in his role as an ambulatory care pharmacist due to the high level of collaboration, and interdisciplinary patient care provided within his ambulatory care setting.

The most enjoyable aspect of Linden's ambulatory care role involves interacting with patients, making therapeutic adjustments under a CPA, and ultimately witnessing improved health outcomes for his patients.

What challenges did you face during this transition and what resources did you use?

Initially, when Linden transitioned into ambulatory care, he struggled with using brand medication names, because they are infrequently used in the inpatient setting. Additionally, he had a strong antimicrobial stewardship background but was challenged by the transition to outpatient antibiotic regimens. He needed to refresh his knowledge on available oral therapy options and empiric treatment recommendations used in this setting.

Some tools that he used to ease this transition included disease-state guidelines and primary literature resources such as PubMed and Cochrane Library. The Natural Medicines Database has been helpful for questions related to herbal and supplement therapy questions. Linden found Lexicomp and UpToDate to be great resources to answer more general drug information questions.

What advice would help in making the transition into ambulatory care?

For anyone interested in transitioning into ambulatory care pharmacy practice, Linden recommends staying up to date on disease state guidelines and literature to maintain a strong foundation in clinical knowledge. For those transitioning from inpatient pharmacy practice, he recommends becoming involved in transitions of care. For students, Linden encourages all students to reach out and shadow or choose multiple ambulatory

Above: *Robert Mueller, PharmD, BCPS, Ascension All Saints, Racine, WI*

care rotations while in school to obtain ambulatory pharmacy exposure.

If you are interested in more information, feel free to contact Linden at: stevenevl@gmail.com.

Robert Mueller, PharmD, BCPS Ascension All Saints, Racine, WI

Robert Mueller is a pharmacist who practices in a variety of pharmacy settings in the Milwaukee area. Currently, he is a faculty member at Concordia University Wisconsin School of Pharmacy, where he serves as an Associate Professor in the Department of Pharmacy Practice. Mueller also practices pharmacy in ambulatory care and acute care settings for Ascension Wisconsin.

In his acute care pharmacy role, he attends rounds, maximizes pharmacokinetic dosing, and monitors patients in the hospital. Mueller also serves as a preceptor for Introductory Pharmacy Practice Experience (IPPE) and Advanced Pharmacy Practice Experience (APPE) students, and Postgraduate Year 1 (PGY1) pharmacy residents. With his transition into ambulatory care, he reduced his acute care pharmacy practice to one day per week.

What influenced your pharmacy practice change?

The major influence that pulled Mueller into ambulatory care involved his background in Spanish. He has a bachelor's degree in Spanish and Portuguese studies and is a certified Spanish interpreter through Ascension Wisconsin. Mueller finds fulfillment in using his expertise in the Spanish language within the medical field, but found these opportunities were limited in his inpatient pharmacy role. Mueller was compelled to use this skill in a meaningful way, which led to his interest in ambulatory care pharmacy serving Spanish-speaking patients.

What is your current ambulatory care role?

Currently, Mueller practices under a CPA to provide medication management services in Spanish to patients with a variety of health conditions, including diabetes, heart failure, hypertension, and hyperlipidemia. With the ability to serve a large Spanish-speaking patient population, he enjoys being able to make an impact on health outcomes and build strong professional relationships with his patients. Mueller is rewarded by the kind, encouraging, and appreciative nature of his patients.

What challenges did you face during this transition and what resources did you use?

Initially, Mueller was challenged by navigating and efficiently documenting ambulatory clinic encounters. He was able to overcome these challenges by shadowing colleagues in similar roles to learn from their experiences about how to manage visits and document efficiently. Mueller also relied on foundational knowledge taught in pharmacy school to improve his essential skills in building patient rapport.

From a clinical perspective, he used specific disease state guidelines and modules from the Pharmacotherapy Self-Assessment Program (PSAP) from the American College of Clinical Pharmacy (ACCP) to help solidify his clinical knowledge. During this transition, Mueller learned to be resourceful to navigate through medication coverage challenges. He uses manufacturer patient assistance programs to ensure patients can acquire the medications they need.

What advice would help in making the transition into ambulatory care?

For anyone interested in ambulatory care, Mueller recommends reaching out to someone who is already practicing in the ambulatory care setting and scheduling a time to shadow. This exposure will offer a better understanding of ambulatory pharmacy encounters and the potential challenges involved in the role. This experience can also help open the door to establish a pharmacy practice mentor relationship.

If you are interested in more information, feel free to contact Mueller at: robert.mueller@cuw.edu.

Ronda Breckler, CPhT Froedtert Health's Anticoagulation Clinic, Milwaukee, WI

Ronda Breckler is a certified pharmacy technician supporting pharmacists and nurses in Froedtert Health's Anticoagulation Clinic. This clinic provides care to patients across much of eastern Wisconsin. Prior to this role, she spent many years as a Senior Technician in an outpatient pharmacy and also served as a sterile compounding technician in a home health care setting.

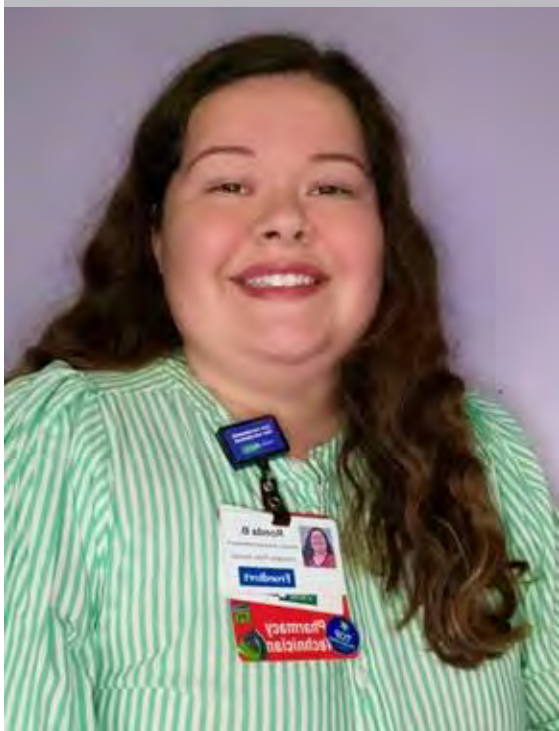
What influenced your pharmacy practice change?

Breckler's main motivation for transitioning into ambulatory care pharmacy is her "deep-seated" passion for providing direct patient care. Being able to foster positive, lifelong relationships with patients has been incredibly rewarding in her ambulatory care role. Breckler is grateful for the opportunity to play an important role in helping patients achieve their health care goals.

What is your current ambulatory care role?

Breckler's role as an ambulatory pharmacy technician in Froedtert Health's Anticoagulation Clinic is to provide support to the pharmacists and nurses managing anticoagulation therapy for patients. In this clinic, ambulatory pharmacy technicians perform administrative tasks and follow

Below: *Ronda Breckler, CPhT, Froedtert Health's Anticoagulation Clinic, Milwaukee, WI*



approved protocols to appropriately assist with patient care and patient education responsibilities.

What challenges did you face during this transition and what resources did you use?

One of the most difficult aspects of starting in ambulatory care was adapting to a new pharmacy practice environment. Ambulatory care is considerably different from other areas of pharmacy. Breckler had to adapt to new workflows, policies, and procedures, and learn to work collaboratively with other health care professionals within the health system. Through this transition, Breckler had to develop a new skill set and knowledge base pertaining to ambulatory care pharmacy. This skill set includes a detailed understanding of anticoagulation medications to triage patient and provider calls and provide patient education within her technician protocol.

Breckler used multiple resources during her transition into ambulatory care, including organizations such as the Pharmacy Technician Certification Board (PTCB) and the National Pharmacy Technician Association (NPTA). These organizations offer a wide variety of resources for continuing education, networking, and professional development, which helped her transition into ambulatory care practice. Additionally, Breckler connected with peers in the ambulatory care field to learn about their experiences and gain insight into the skills that are essential for success in this area of pharmacy practice.

What advice would help in making the transition into ambulatory care?

Breckler encourages anyone interested in pursuing ambulatory care to research the field thoroughly. When the anticoagulation service at Froedtert Health hires new pharmacy technicians, each candidate is offered the opportunity to shadow current technicians to gain a better understanding of ambulatory pharmacy. Networking with peers prior to her transition gave her a small glimpse into what this practice entails. Once she entered ambulatory care pharmacy, she strengthened her knowledge of ambulatory care by reading publications pertaining to the industry. This allowed her to strengthen her communication skills and build confidence in patient interactions.

If you are interested in more information, feel free to contact Breckler at ronda.breckler@froedtert.com.

Jen Slaughter, PharmD, BCACP
SSM Health Dean Medical Group, Madison, WI

Jen Slaughter is an ambulatory care pharmacist with the SSM Health Dean Medical Group in the Madison area. Prior to transitioning into ambulatory care, she practiced in the community and long-term care pharmacy settings. Within her community pharmacy role, she focused on medication dispensing. Through her long-term care pharmacy role, she collaborated with providers at skilled nursing facilities performing chart reviews and recommending medication therapy changes.

What influenced your pharmacy practice change?

Slaughter's main reason to transition into ambulatory care involved the increased level of independence within this practice setting. In her previous role, she was challenged by identifying drug therapy problems that required provider permission for resolution. Slaughter believes that a pharmacist's training encompasses the ability to identify and remedy drug therapy problems. She focused her career goal on working toward a pharmacy position that provided a higher level of autonomy to allow her to utilize these skills.

What is your current ambulatory care role?

Within Slaughter's ambulatory care role, she practices under broad CPAs to autonomously manage multiple chronic disease states. These broad CPAs allow pharmacists to manage diabetes, anticoagulation, and heart failure in patients. Slaughter also collaborates with the hospital pharmacy team to improve transitions of care models within her health system. One of their goals is to reduce polypharmacy within their patient population to improve outcomes. Slaughter practices with a higher level of autonomy, as the ambulatory care pharmacists within Slaughter's health system are not embedded within the same centralized clinic location. This allows the ambulatory care pharmacists to collaborate with a wide range of patients, providers and medical teams. Currently, Slaughter shares an office with an internal medicine physician, providing direct collaboration with providers and clinic staff.

Above: *Jen Slaughter, PharmD, BCACP, SSM Health Dean Medical Group, Madison, WI*

Slaughter says patient interactions and building relationships with her patients on a personal level are the most enjoyable aspects of her ambulatory pharmacy role. "When patients see you are taking the time to get to know them and understand their concerns and health goals, they are very grateful."

What challenges did you face during this transition and what resources did you use?

Initially, Slaughter was challenged by her transition into a new ambulatory pharmacy program collaborating with clinic providers and a medical team who were unfamiliar with the ambulatory care pharmacist role. For example, providers inquired about insulin or medication therapy coverage, but she often had an alternative medication therapy recommendation. Slaughter was challenged to go outside of her comfort zone to be more assertive in recommending more appropriate therapy alternatives and setting up a pharmacist consult to provide patient education.

During Slaughter's transition, she took on multiple roles and responsibilities to gain experience in a variety of pharmacy areas. She collaborated with other pharmacists to build connections. She also broadened her scope through additional trainings, such as the American Pharmacists Association's *Pharmacist and Patient-Centered Diabetes Care Certificate*. These opportunities gave Slaughter the ability to expand her disease state knowledge and take on larger roles within her organization.

What advice would help in making the transition into ambulatory care?

For anyone interested in transitioning into ambulatory care, Slaughter recommends fulfilling additional roles

Above: *Thomas Welke, PharmD, Bellin Health, Marinette, WI*

and responsibilities to build experience in a variety of practice areas. She also recommends taking the necessary steps to enhance clinical knowledge and skills through additional training and certification.

If you are interested in more information, feel free to contact Slaughter at jennifer.slaughter@ssmhealth.com.

Thomas Welke, PharmD
Bellin Health – Marinette, WI

Thomas Welke is an ambulatory care pharmacist with Bellin Health, practicing in Marinette, Wisconsin. Prior to his ambulatory care role, he practiced in community pharmacy. He began his career as a staff pharmacist at Walgreens and transitioned into a pharmacy manager role and third shift pharmacist role. In 2019, he moved into the Bellin Health System to open a new community pharmacy in Seymour, Wis.

What influenced your pharmacy practice change?

The major influence that drew Welke into ambulatory care pharmacy was the desire to try something different in the pharmacy profession. He sought a new challenge to expand his pharmacy experience into an area of practice that would allow him to use all the skills gained throughout his community pharmacy career.

What is your current ambulatory care role?

Ambulatory care pharmacists within Welke's practice location are involved in many patient care responsibilities. His primary role includes answering provider medication questions, providing medication therapy management (MTM) services by referral and collaborating with the anticoagulation team. Ambulatory pharmacists like Welke serve a large geographical region covering multiple sites throughout the health system. This is one of the unique aspects of his ambulatory care role, which allows him to collaborate with a wide range of providers throughout the health system to assist in answering questions surrounding a variety of specialties. Welke's ambulatory practice location in a rural setting has allowed him to cross-train in other areas of pharmacy and serve as a resource to other medical teams within his facility.

The most enjoyable aspect of Welke's ambulatory care role includes the new challenges and unique situations that he is involved in every day, and the ability to dig into a clinical problem to provide the best patient care.

What challenges did you face during this transition and what resources did you use?

Initially, Welke was challenged by the change in work functions between community and ambulatory care pharmacy practices. Within his previous role as a community pharmacist, he was responsible for managing prescriptions in time-sensitive queues and providing clinical decisions based upon instinct and historical clinical knowledge, due to limitations in time and information available. In the ambulatory care setting, he has access to patient clinical information, which allows him to complete an in-depth analysis and apply primary literature and disease state guidelines when making clinical decisions.

Through his ambulatory pharmacy role, Welke is challenged by a wide range of clinical scenarios every day, along with learning to navigate the electronic health record (EHR). To help alleviate these challenges, he uses disease state guidelines to apply his clinical knowledge. He also collaborates with other ambulatory pharmacy colleagues as a resource for continued professional learning. This has paired well with his community pharmacy knowledge of insurance coverage, prior authorizations, and patient assistance programs to help streamline access to medication therapies and enhance patient care.

What advice would help in making the transition into ambulatory care?

For anyone interested in moving into ambulatory care pharmacy, Welke recommends networking with other pharmacists to learn about different areas of pharmacy practice outside of your current role. He encourages you to "go for it" and not be intimidated by a perceived lack of experience, because skills can be transferred from one pharmacy practice setting to another.

If you are interested in more information, feel free to contact Welke at thomas.welke@bellin.org.

Conclusion

Pharmacists and pharmacy technicians can transition into ambulatory care from many different pharmacy practice settings. Pharmacists Linden, Mueller, Breckler, Slaughter, and Welke shared their transition experience, along with the fulfilling patient care they provide within their ambulatory care roles. Pharmacists or pharmacy technicians interested in learning more about ambulatory care pharmacy are encouraged to follow their guidance and reach out for more information.

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