SPRING 2022

ADULT MEDICINE PRN NEWSLETTER

The biannual newsletter of the ACCP Adult Medicine PRN

Message from the Chair

By: Jon Wietholter, PharmD, BCPS, FCCP

But, can you answer the "why?"

I have uttered this grammatically incorrect question countless times over the course of my career. While generally directed at students during an active learning opportunity or during APPE topic discussions, I also think it is important for each of us to contemplate this question when it comes to our careers and our involvement within the ACCP AMED PRN. Can you answer the "why?" Why do you do what you do within the world of clinical pharmacy? Why did you enroll as part of the AMED PRN? Sitting down to write this column two years into the COVID pandemic, I think now more than ever is a great time for us to reflect and to re-answer the "why." So, I'll start…

Why do I do what I do? This question seems easy enough when having noticeable impact through direct patient care. For example, I will never forget how I felt after a 94-year-old Puerto Rican told me "God will bless you" when serving on a humanitarian aid mission with Project Hope after Hurricane Maria in 2017. When in the middle of experiences as impactful as this one, the "why" is easy to see. Unfortunately, this gets significantly more difficult to understand when wandering through mundane day-to-day tasks, especially in times as dark as these last two COVID-filled years. However, we cannot lose sight of our purpose within this profession. As an AMED PRN practitioner, you are bringing medication-based knowledge, skills, and talents to the table that are unrivaled by other healthcare practitioners. As clinical pharmacists, we directly improve patient care, plain and simple.

Next, why did I get involved with the AMED PRN?I believe this is a network of some of the brightest pharmacotherapeutic minds across the globe. As AMED practitioners, we are expected to know the intricate ins-and-outs of ideal pharmacotherapy management for every possible disease state, no matter where we practice.

WHAT'S INSIDE THIS ISSUE?

Message from the Chair Continued…

Without a doubt, this is a difficult task. Yet we do this day after day to improve patient care and work towards furthering the profession of clinical pharmacy. To continue to progress, we must look to expand the boundaries of what a clinical pharmacist can do and the AMED PRN is a phenomenal place to lead this progression. I am thrilled to be serving as your Chair this year because I truly believe we can push the profession forward through PRN-based work. Touching directly on this point, eight PRN Committees will be tackling multiple charges this year that I believe will continue to push clinical pharmacy forward. These include:

- Developing a formal orientation process to be offered to new AMED PRN members
- Beginning discussions regarding development of a repository of essential guidelines and landmark trials stored on the PRN page for diseases commonly encountered by AMED practitioners
- Developing procedures confirming diversity, equity, and inclusion play a vital role in identification of potential speakers for AMED PRN focus sessions at ACCP Annual Meetings
- Developing a survey-based evaluation attempting to determine the clinical impacts of AMED clinical pharmacists across the United States
- Updating the AMED PRN poster scoring rubric to more effectively mirror ACCP's rubric to improve PRN members chances of being recognized as "Top Posters" at ACCP meetings

Now that I've answered my "why" to these two questions, I challenge everyone to take a couple of minutes and answer them as well. Hopefully by re-examining your answers, you can remember or reinforce the reasons why you chose the profession of clinical pharmacy and why you chose to be a part of this PRN. I look forward to catching up with many of you and learn more about your "why" at the 2022 ACCP Annual Meeting in San Francisco, CA this October. I am truly honored to be your AMED PRN Chair for the 2021-2022 year and look forward to the great things to come from the PRN both this year and for the foreseeable future.

ACCP VIRTUAL POSTER SYMPOSIUM

MAY 24TH & 25TH

Pictured Kiya Bennett and Ryan Owens from ACCP Annual Meeting 2017. Photo credit: Beth Resman-Targoff.

AMED PRN Announcements

Nominations Committee

Are you interested in becoming more involved with the Adult Medicine PRN and ACCP? Please consider nominating yourself or another PRN Member for the 2022-2023 AMED PRN officer positions!

The Nominations Committee will set up election slates for the following positions:

Chair-elect

- 3 years of service commitment: 1 year chair-elect term (includes Chairing the AMED Programming Committee), followed by 1 year as PRN Chair, and then 1 year as past Chair (includes Chairing the AMED Nominations Committee)

Secretary-Treasurer

- 1 year service term (includes Chairing the AMED Internal Affairs Committee)

If you are interested in running for office or if you would like to nominate someone, please contact Carmen Smith (csmith2278@gmail.com) or Erin Hennessey (Erin.Hennessey@uhsp.edu) with the name of the nominee by **the end of the day on Friday, May 13th.**

Practioner Award Winner Spotlight

By: Sarah Kessler, PharmD, BCPS, BCGP

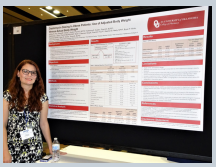
I was honored to have received the New Practitioner Travel Award for the 2021 annual meeting. I am currently the Internal Medicine Clinical Specialist at Denver Health Medical Center, and have had the opportunity to train and work in many different areas of the country. After joining ACCP and the AMED PRN during my PGY-2 in Internal Medicine, I found a group of individuals who practice at the top of their license in a variety of different settings. Given the diversity within the AMED PRN, I believe we are able to work together to improve patient care and the profession of pharmacy.

As a new practitioner, I have been grateful for my mentors who encouraged me to join the AMED PRN as a resident, as well as motivated me to participate in committee work within the PRN. While I have had the opportunity to serve on the External Affairs Committee, and have had the pleasure of getting to know many of our members, the travel award allowed me to continue expanding my involvement with the AMED PRN. During the annual meeting I was able to participate in the Walk Rounds Committee poster review. The outstanding research that our PRN members continue to do daily is inspiring and the variety is unmatched. It was great to speak with other PRN members who are in similar places in their careers and with their research, as well as those who have years of experience. I believe that the variety of research done by AMED PRN members reflects the strength of our group and the commitment the AMED PRN places on improving patient care.

AMED PRN Announcements

Walk Rounds Committee

VOLUNTEER AS A POSTER REVIEWER



Pictured Ashley Fox from ACCP Annual Meeting 2016. Photo credit: Beth Resman-Targoff.

ACCP AMED PRN Walk Rounds Committee will coordinate reviews for any poster with AMED members listed as authors at the 2022 Virtual Poster Symposium. The sessions will take place on **May 24th & 25th from 7:00-9:00PM EST**. In 2021, over 80 posters were presented and reviewed by the AMED PRN!

If you are willing and able to serve as a reviewer, please note your availability on the following survey:

SCAN or Click Here

Assigned posters, instructions and evaluation rubrics will be provided by the Walk Rounds Committee prior to the Symposium. If you have any questions, please contact Melanie Manis (mmanis@samford.edu), Walk Rounds Chair. We thank you for your service!

Link to sign-up:
https://forms.gle/tsv9TmwcEMvU2A9aA

In addition to the Walk Rounds Committee, I had the opportunity to learn about numerous topics, ranging from the AMED PRN focus session on antibiotic resistance to anticoagulation quandaries. In addition to clinical sessions, the diversity, equity, and inclusion opening sessions were impactful, as my institution newly started a DEI subset of our residency advisory committee. While there is still room for improvement, the steps that the national ACCP office has taken have been impressive, and I believe that incorporating a culture of competence into our residency training programs will only further our profession as a whole. I am thankful for all of the learning opportunities this award provided me for 2021, and am looking forward to my continued involvement in the AMED PRN!

Medication Access Services Provided by Pharmacists Decrease 30-day Hospital Readmissions

An AMED PRN Resident Travel Award Winner

By: Heidi King Berman, PharmD

Pharmacists can improve transitions of care at discharge through ensuring patients can afford their discharge prescriptions, but there is limited published data on whether these interventions improve clinical outcomes.

We conducted a single center, retrospective, cohort study of adult patients admitted to Emory University Hospital from January 1, 2014 to August 31, 2020 to evaluate the impact of medication access interventions prior to discharge by pharmacy personnel. One hundred and fifty-four case patients with documented medication access interventions were matched 1:1 with controls by medication, age, Charlson Comorbidity Index, insurance status, and discharging unit. The primary outcome was length of stay (LOS). Secondary outcomes include all-cause readmissions at 7-days, 30-days, and 90-days and a summary of the type of interventions, success in approval, turnaround time, cost savings, acuity based on CCI score, and adherence. Readmissions were tested as either concordant pairs, defined as those with the same discreet outcome (readmitted or not), or discordant pairs. We used applicable normal or non-parametric tests for paired data.

The median age of cases was 57.0 years and age of controls was 57.5 years. Cases and controls were 50.7% and 47.4% male, respectively. Insurance coverage was in effect for 87.5% of cases and 92.8% of controls. Length of stay was not statistically different between the groups (cases 9.1 ± 9.8 days vs. controls 10.7 ± 12.5 days, Wilcoxon p=0.459). Only the 30-day readmission data showed a significant difference with 17 pairs in which the case was readmitted and the control was not vs. 33 pairs where the control was readmitted and the case was not. McNemar Chi-square significance for the 7-day, 30-day, and 90-day readmission differences were 0.327, 0.034. and 0.057, respectively. In terms of the type of interventions pharmacy personnel completed, 40.8% were insurance verification, 30.3% were application of a prescription coupon, 21.1% required a prior authorization to be completed, and 12.5% involved patient assistance program enrollment. For case patients, 52% of interventions included anticoagulants, 29.6% anti-infectives, and 15% diabetes medications.

In conclusion, pharmacist-provided medication access services were associated with improved patient outcomes, statistically significant for 30-day readmissions.

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Spring PGY2 eJournal Clubs

May 18th & June 15th

at 3PM EST/ 2PM CST/ 1PM MT/ 12PM PST

Be on the lookout for calendar invitations for the upcoming PGY2 Internal Medicine eJournal Club Presentations! Please join us as PGY2 Internal Medicine and Pharmacotherapy residents present up-to-date primary literature articles related to Internal Medicine. Questions? Contact Ashley Otto at otto.ashley@mayo.edu

Pharmacist-Led Tobacco Treatment Services to Increase Nicotine Replacement Therapy Access at a Large Rural Academic Medical Center

An AMED PRN Resident Travel Award Winner

By: Erin McMahan, PharmD, BCPS

West Virginia leads the nation in all forms of tobacco use. Patient access to tobacco treatment services, such as nicotine replacement therapy (NRT), tobacco cessation counseling, and referral to local resources, is lacking. At West Virginia University Hospitals (WVUH), pharmacists recognized that many medically-ill patients who actively use tobacco products are discharged from the hospital without plan to address tobacco use. Pharmacists are well-trained to provide education to patients regarding tobacco cessation, and increase access to NRT for patients prior to hospital discharge. Additionally, pharmacists are optimally positioned to refer patients to local resources that can help support them after leaving the hospital. Internal medicine pharmacists at WVUH developed an institutional policy which allows pharmacists to order NRT during inpatient admission, prescribe NRT at discharge for patients interested in tobacco cessation, and counsel patients on how to use NRT prior to discharge.

Pharmacists commonly rise to meet the need of patients by continuously expanding practice to serve their communities. The purpose of our current study is to prove the utility of our institutional policy through prospective patient outreach to increase access to tobacco cessation products in rural areas and enhance the scope of pharmacy practice. We propose an inpatient tobacco treatment service that couples pharmacist-initiated NRT with pharmacist-provided tobacco cessation counseling to combat this major public health problem. The primary aim of this study is to evaluate the impact of pharmacist-led tobacco treatment services on patient access to NRT at hospital discharge compared to the current practices. A secondary aim includes comparing the number of patients who receive NRT during hospitalization in the pharmacist-led tobacco treatment group compared to current practices. We hypothesize that implementation of an inpatient pharmacist-led tobacco treatment process will increase patient access to NRT, improve discharge prescribing of NRT, and positively impact outpatient treatment referrals. The institutional policy is currently approved. Patients are actively being enrolled and grant funding awarded by the American Society of Health-System Pharmacists (ASHP) Foundation will be used for production of education materials and acquisition of NRT for patient use.

WATCH FOR UPDATES TO

STUDENT MEDICINE GRAND ROUNDS CASE PRESENTATIONS

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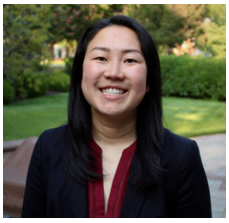

Assessment of Midodrine Prescribing in the Acute Care Setting

An AMED PRN Student Research Award Winner

By: Amy Chan, PharmD Candidate 2022 & Jason Ferrell

Midodrine is used off-label for its peripheral alpha-1 agonist effects to maintain normotension when weaning intravenous vasopressors to potentially shorten ICU and hospital length-of-stay.[1,2] Published studies evaluating midodrine have described a rapid decline in vasopressor rates upon midodrine initiation, but the benefits and risks of the medication remain unclear.[1,2] Midodrine use appears to be safe, with negative effects including risk of bradycardia and continuation of midodrine at discharge in an estimated 34% of patients, especially in those with heart failure.[2,3] A single-center, retrospective chart review of ICU patients administered at least 1 dose of midodrine from April 1, 2020 through March 31, 2021 was conducted to assess the prescribing incidence, factors potentially affecting whether midodrine was prescribed at discharge, and outpatient effects of continuing this medication. Statistical analysis included Wilcoxon rank-sum and Fisher exact tests using SPSS Version 28.0.

There was a high incidence of midodrine continuation at discharge (40.6%, 26/64) and 92.3% (24/26) of prescriptions were written for a 30-day supply with no refills. This trend was attributed to discharge prescribing habits of physicians as patients transitioned to the outpatient primary care setting. Patients that were continued on midodrine at discharge had a higher median inpatient length of midodrine use (7 vs. 4 days, p=0.002) and more days of overlap between oral midodrine and IV vasopressors (5 vs. 1 day, p=0.024), which suggests that those who were discharged on midodrine required a longer duration of vasopressor support while they were still under ICU care. Age, gender, history of hypertension, and vasopressor requirements at midodrine initiation were all insignificantly different between those who were continued on midodrine at discharge (n=26) and those who had midodrine discontinued (n=38), suggesting that initial vasopressor requirements did not predict whether midodrine was continued at hospital discharge. Patients who were continued on midodrine did not have a shorter ICU length of stay after initiation of midodrine (3.5 vs. 3 days, p=0.342).

Results from this project were limited by a small sample size, retrospective chart review relying on prescriber documentation, and an inability to determine midodrine adherence and blood pressure after discharge. Overall, we concluded that patients in the ICU are closely monitored for changes in heart rate and risk of harm from bradycardia from inpatient midodrine use is minimal (incidence of 23.4%, 15/64), especially with nurse education on expected incidence of adverse effects. No patients followed in this study were found to have major negative effects from midodrine, including no additional requirements for medications due to hypertension and no readmissions due to midodrine-related adverse effects, according to hospital chart review. Nonetheless, mindful prescribing during medication reconciliation should be emphasized to prevent unknown negative consequences and potentially unnecessary continuation of midodrine.

References

1. Buckley MS, Barletta JF, Smithburger PL, Radosevich JJ, Kane-Gill SL. Catecholamine Vasopressor Support Sparing Strategies in Vasodilatory Shock. Pharmacother J Hum Pharmacol Drug Ther. 2019;39(3):382-398. doi:10.1002/phar.2199
2. Al-Abdouh A, Haddadin S, Matta A, et al. Impact of Adjuvant Use of Midodrine to Intravenous Vasopressors: A Systematic Review and Meta-Analysis. Crit Care Res Pract. 2021;2021:5588483. doi:10.1155/2021/5588483
3. Rizvi MS, Nei AM, Gajic O, Mara KC, Barreto EF. Continuation of Newly Initiated Midodrine Therapy After Intensive Care and Hospital Discharge: A Single-Center Retrospective Study. Crit Care Med. 2019;47(8):e648-e653. doi:10.1097/CCM.0000000000003814

Characterization of Sleep Aid Medication Prescribing During Transitions of Care for Hospitalized Medical Patients

An AMED PRN Student Research Award Winner

By: Sona Ghorashi, PharmD Candidate 2023

It is well known that factors related to hospitalization can disrupt sleep, resulting in the frequent prescription of neuropsychiatric medications to induce sleep. However, medications prescribed in the inpatient setting are frequently continued unnecessarily across transitions of care.

Our research identified the current practices for prescribing sleep aid medications across transitions of care for hospitalized medical patients at a single large academic medical center. We conducted a retrospective review of 891 electronic medical records of adult patients admitted to an internal medicine service between September 2019 to November 2019. Data for 757 patients were included for analysis.

The results of our study showed that nearly a third of medical patients were prescribed sleep aids during hospitalization, and only half of those patients were prescribed sleep aids prior to admission. However, a small percentage (5.2%) of patients were prescribed a sleep aid at discharge. Overall, the agents prescribed prior to admission and during hospitalization were different. Although melatonin was the most prescribed sleep aid during both care periods, prescribing was increased 2-fold during hospitalization.

We concluded that prescribing of sleep aids in hospitalized medical patients is prevalent, but routine sleep assessment in this setting is less common. The results of this study identified an opportunity for pharmacist-led quality improvement in prescribing sleep aids across transitions of care.

References:

1.Young JS, Bourgeois JA, Hilty DM, Hardin KA. Sleep in hospitalized medical patients, part 1: factors affecting sleep. J Hosp Med. 2008;3(6):473–482.

2. Gillis CM, Poyant JO, Degrado JR, Ye L, Anger KE, Owens RL, Inpatient Sleep Aid Utilization. J. Hosp. Med 2014;10;652-657.

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Review: Updates in the Management of *Clostridioides difficile* Infections

By: Thalia McCann, PharmD, MS and Kathie Le, PharmD, BCPS
Peer Reviewed By: Haley Johnson, PharmD, BCPS

Background

Clostridioides difficile is a pathogenic gram-positive obligate anaerobic bacillus that causes severe colitis and is associated with significant healthcare cost and comorbidity. C. difficile releases Clostridium difficile toxins A (TcdA) and B (TcdB) that bind with receptors in the gut. These endotoxins inhibit Rho guanosine triphosphatases (GTPases) which results in disruption of the tight junctions between colonocytes, causing severe diarrhea and inflammation associated with C. difficile colitis. C. difficile's spores are extremely difficult to eradicate with high tolerance to heat, acid, and many antimicrobial agents, contributing to the prevalence of C. difficile as a nosocomial infection and frequent recurrence despite effective antimicrobial management.[1]

There were an estimated 462,100 cases of C. difficile infection (CDI) in 2017.[2,3] Beyond the significant morbidity associated with these infections is substantial cost and burden on the health system.[2] CDI more than quadruples the cost of hospitalization.[1] One meta-analysis found that hospital-onset CDI was associated with a mean difference in hospital length of stay of 21.6 days compared to 3 days in a propensity-matched group.[3] Clinicians play a critical role in mitigating the risk of CDI in patients through antimicrobial stewardship and infection prevention strategies. Patient characteristics and antimicrobial therapies associated with increased risk of CDI are summarized in Table 1.[4]

Patient Characteristics	Antimicrobial therapy

• Older age
• Recent hospitalization
• Longer hospitalization
• Proton pump inhibitor use
• Chemotherapy
• Chronic kidney disease
• Feeding tube use
	• Prolonged antibiotic use
	• Use of multiple antibiotic agents
	• Use of specific agents:
	  ○ Fluoroquinolones
	  ○ Clindamycin
	  ○ Broad spectrum β-lactams*

Table 1: Risk factors Associated with CDI *broad-spectrum penicillin and β-lactamase inhibitor combinations, carbapenems, 2nd, 3rd, 4th generation cephalosporins.

Diagnosis and Clinical Characteristics

"A case of CDI is defined by the presence of symptoms (usually diarrhea) and either a stool test positive for C. difficile toxins or toxigenic C. difficile, or colonoscopic or histopathologic findings revealing pseudomembranous colitis."[5] Patients presenting with three or more loose stools over 24 hours, without a clear etiology should be tested for C. difficile to rule out CDI. Clinical suspicion for CDI should be increased for patients at higher risk of infection, especially those with recent antibiotic use as the disruption of gut microbiota allows for the overgrowth of pathogenic Clostridioides.

There are multiple diagnostic assays with merits based on their respective sensitivity and specificity, as listed in Table 2.[4] Combination of screening parameters is important in accurately diagnosing active infection and distinguishing from benign colonization. For example, establishing first if a patient is colonized with C. difficile via nucleic acid amplification testing (NAAT) or glutamate dehydrogenase (GDH) antigen testing should be followed by a toxin-specific test probing for the presence of TcdB (and TcdA, though not clinically implicated in pathogen virulence). Clinical diagnostic criteria and the stratification criteria of CDI are listed in Table 3.

Diagnostic Method	Specificity/Sensitivity	Interpretation
NAAT Stool toxin identification:	Sensitivity: 0.87-0.92 Specificity: 0.94-0.96	PCR*assay detecting toxin genes. Positivity indicates colonization but does not distinguish between bacteria which express the toxin and those that do not.
Toxin A/B EIA*	Sensitivity: 0.73-0.87 Specificity: 0.97-0.98	Lower sensitivity than NAAT, positive test result indicates presence of expressed toxin. Testing for toxins A and B increases sensitivity.
GDH EIA	Sensitivity: 0.88- 0.92 Specificity: 0.89- 0.93	Testing for a protein present in both toxigenic and nontoxigenic strains of C. difficile; must be paired with toxin testing via NAAT or EIA for definitive diagnosis.

Table 2: Laboratory Diagnostic Measures *NAAT: nucleic acid amplification testing, PCR: polymerase chain reaction, EIA: Enzyme Immunoassay

Clinical Diagnosis	Clinical severity
• ≥3 unformed stools in 24hour OR radiographic evidence of ileus or toxic megacolon • Positive stool test result for toxigenic C. difficile or its toxins OR colonoscopic/histological findings demonstrating pseudomembranous colitis. • Repeat testing to assess curative response not recommended	• Mild CDI: WBC <15x10^9/L and Scr < 1.5x baseline • Severe CDI: WBC >15x10^9/L OR Scr ≥1.5x baseline • Fulminant or severe, complicated CDI: hypotension or shock, ileus, megacolon

Table 3: Clinical Diagnostic Criteria

Guideline Update Summary

Guidelines on management of CDI in adults was first published in 1995, then updated in 2010, 2017, and again with current Infectious Disease Society of America (IDSA) and Society for Healthcare Epidemiology of America (SHEA) guidelines in 2021. Current guidelines changed drastically in the recommendation of the first-line option. Previously, metronidazole was considered the drug of choice for initial mild and moderate CDI, while oral vancomycin was reserved for severe, complicated CDI. In 2017, the IDSA/SHEA instead recommended either vancomycin or fidaxomicin for initial CDI regardless of severity level. However, based on the outcomes from the recently published randomized controlled trials, the 2021 guidelines now suggest fidaxomicin as the drug of choice for initial CDI, stemming from evidence of its sustained response after therapy, and fewer CDI recurrence. For fulminant CDI, vancomycin is still the recommended choice. For recurrent CDI episodes, previous guidelines recommended using oral vancomycin tapered or pulse regimen. Currently in 2021, fidaxomicin, either as standard or extended-pulsed dosing, is preferred over the intracolonic vancomycin, again due to sustained response after therapy. The 2021 guideline also discussed the use of bezlotoxumab, a monoclonal antibody that targets toxin B, as an adjunct therapy to standard antibiotics for recurrent CDI episodes within six months. Note that while the current guidelines place preference recommendations for fidaxomicin and bezlotoxumab, the cost for these medications are potentially prohibitive in some cases. Oral vancomycin therefore remains an acceptable option for the cases where insurance coverage is limited. Lastly, there are no changes in the guidelines with regards to use of fecal microbiota transplantation.

New Evidence Summary

Fidaxomicin

The newest clinical data used to support the preferential use of fidaxomicin over alternative therapies comes from two phase III studies, a non-inferiority trial and the EXTEND trial. In addition, meta-analysis was included in the 2021 guidelines as part of the panel's justification for their recommendation. In their phase III, vancomycin-controlled, double-blind, parallel-group trial, Mikamo et al. demonstrated higher Global Cure Rate (GCR) with fidaxomicin, defined as the proportion of patients cured at the end of treatment with no recurrence during 28 days of follow up.[6] In particular, in post-hoc analysis of patients who received three or more days of therapy demonstrated a higher GCR with fidaxomicin compared to standard oral vancomycin therapy (fidaxomicin 72.2% versus vancomycin: 67.7%, difference 4.6%, 95% CI -7.9-17,1).[6] Patients treated with fidaxomicin had decreased recurrence within 31 days of treatment compared to those treated with standard therapy of oral vancomycin (fidaxomicin group: 19.5% versus vancomycin: 25.3%).[6] Overall, fidaxomicin was shown to have higher GCR and lower recurrence rate. Notably, this trial excluded patients with life-threatening or fulminant CDI, paralytic ileus, toxic megacolon, prior fidaxomicin use, or 2 or more episodes of CDI in three months prior to the trial, thus fidaxomicin use in these populations was not supported by the trial findings.

The EXTEND trial found that extended-pulsed fidaxomicin therapy (200 mg orally twice daily for 5 days, then once daily on alternate days on days 7-25) is superior to vancomycin in producing a sustained clinical response at 30 days post-therapy (fidaxomicin 70%, vancomycin 59%, OR 1.62, 95% CI 1.04-2.54).[7] However, it is important to note that this trial excluded patients who had 2 or more recurrences in 3 months prior to treatment.

Analyses comparing standard oral vancomycin to fidaxomicin in an initial episode of CDI also included findings from two randomized control noninferiority trials that were published prior to the 2017 IDSA/SHEA guidelines.[8] The first trial by Cornely, et al., demonstrated noninferiority of fidaxomicin therapy compared to vancomycin in clinical cure (defined as resolution of symptoms and no need for further therapy) (per-protocol analysis, fidaxomicin: 91.7%, vancomycin: 90.6%, one-sided 97.5% CI -4.3%).[9] Louie et al. evaluated clinical cure rate (defined as resolution of symptoms and no need for further therapy for CDI at the second day post-therapy completion), and recurrence (defined as diarrhea and a positive stool toxin test within 28 days of treatment), as well as global cure (cure with no recurrence).[10] Notably, the validity of this data is contingent on the trial; concerns regarding blinding, attrition bias, and/or differences in endpoints measured such as global cure rate versus clinical cure for 2 days post-therapy may limit the external validity of these findings.

Pooled analysis of the data from the above 4 trials demonstrated that fidaxomicin is superior to vancomycin in both increased sustained response rate and lower recurrence rate. There was a significantly higher sustained response (defined as resolution of symptoms for 4-weeks post-therapy) with fidaxomicin over oral vancomycin (RR: 1.16, 95% CI 1.09- 1.24).[8] In addition, there was no difference in drug related adverse events (RR: 1, 95% CI 0.96-1.04) or death (RR 0.9, 95% CI 0.66-1.23) between the two treatment groups.[8] Though clinical cure was similar between treatment groups, fidaxomicin was associated with lower recurrence compared to vancomycin (intention-to-treat analysis, fidaxomicin: 15.4%, vancomycin: 25.4%, p= 0.005).[8,10] Further data from the pooled analysis of the 3 randomized controlled trials (RCT) by Louie, Corney and the EXTEND trial, demonstrated that in the treatment of recurrent CDI episodes, fidaxomicin is favored over vancomycin due to higher sustained response of CDI (30 days RR:1.27, 95% CI 1.05-1.54).[8]

However, neither initial clinical cure (RR: 1.03, 95% CI 0.94-1.14) nor sustained response at 90 days (1.56, 95% CI 0.99-2.44) were significantly different between groups.[8] Adverse events and mortality failed to be significantly improved in the fidaxomicin group compared to those treated with vancomycin. This meta-analysis included a trial that utilized patient-reported outcomes, as well as two small studies that were underpowered or had baseline variability of participants in either arm that could skew results. Additionally, treatment approaches between extended fidaxomicin and standard fidaxomicin dosing were not compared, leaving the clinical decision for which strategy to use up to the clinician.

Bezlotoxumab

Bezlotoxumab, a monoclonal antibody active against TcdB, is now recommended in patients with recurrent CDI.[8,11] The MODIFY I/II trials demonstrated bezlotoxumab efficacy in preventing recurrent CDI.[12] In a follow-up analysis, patients were stratified by risk factors, including older age (65 years or older), history of CDI, active severe CDI, or immunocompromised, and the results indicated that patients with one or more risk factor treated with standard of care plus bezlotoxumab had a statistically lower risk of recurrence than those treated with placebo (21.2% versus 37.2%, risk reduction -15.9% (95% CI -21.6, -10.2), and that risk difference increased with each additional risk factor.[13] Notably, there was no higher rate for cure during the episode treated with bezlotoxumab versus placebo, and mortality was similar across both treatment and placebo groups.[12,13]Also, patients with congestive heart failure were at a higher risk of serious adverse events (12.8%) with bezlotoxumab versus placebo (4.8%).[8,12] This effect was not infusion-related but instead occurred over the follow-up period of 12-weeks post-treatment.[11,12] Overall, bezlotoxumab doesn't play a role in clinical resolution of an active CDI, but it is effective in reducing recurrence in patients with risk factors as listed in the trial. The 2021 IDSA/SHEA guidelines recommend treatment with bezlotoxumab in combination with antibiotics (fidaxomicin or vancomycin) for patients with recurrent CDI in the last 6 months.[8] Their pooled analysis of the two bezlotoxumab randomized controlled trials suggested reduced recurrence at 12 weeks post-therapy (RR 0.62, 95% CI 0.51- 0.75), reduced hospital readmissions at 30 days (RR 0.46, 95% CI 0.29-0.71), and no impact on mortality (RR 0.94, 95% CI 0.66-1.34).[8] However, this pooled analysis did not differentiate the effect of bezlotoxumab when used with fidaxomicin versus vancomycin, which leaves interpretation of the true effect size to the clinician.

Fecal Microbiota Transplantation

Fecal microbiota transplant (FMT) has been described as an effective treatment option for patients with multiple recurrences of CDI and was approved for use in this setting by the FDA in 2013. FMT replaces the imbalanced colon microbe of the patient with CDI with a heathy microbiome from a donor, thus preventing regrowth by pathogenic *Clostridium*. One double-blind, randomized controlled trial evaluated FMT in patients who had three or more recurrences of CDI and demonstrated 90.9% cure rate with donor FMT compared to only 62.5% in the control arm. The trial reported no serious adverse events after FMT treatment. However, patients were excluded if immunocompromised or over 75 years of age.[14]There have been multiple trials comparing FMT to drug therapy for CDI, and many support the conclusion that FMT is competitive if not superior to standard antibiotic regimens. However, many of these trials are fraught with limitations, and a lack of quality control regarding the content of the FMT products used across these trials prevents generalization from the results.[15,16] Though the data supporting FMT for patients with multiple recurrences remains convincing, case reports of patients receiving pathogenic enteric bacteria from FMT have promoted an official statement by the FDA warning of potential adverse events associated with FMT.[17]

Costs of Care

The preferential recommendation of fidaxomicin is counteracted by the significant cost associated with its use. Average wholesale cost of each 200 mg tablet of fidaxomicin costs $255.73, therefore a 10-day therapeutic course would come with a $5,114.60 price tag compared to $31 per generic oral vancomycin capsule with a treatment cost of $1,240.[18] Two separate groups disagreed about the cost-effectiveness of fidaxomicin compared to oral vancomycin based on pricing and hospital-related costs associated with recurrence in the United States circa 2013.[19,20] A more recent cost analysis in Germany showed higher cost-effectiveness for standard regimen fidaxomicin versus vancomycin as first-line therapy.[19] Another analysis in Spain demonstrated cost-effectiveness for extended-pulsed fidaxomicin compared to vancomycin as first-line therapy.[21] However, these studies are difficult to extrapolate to the US market, and each study utilized different definitions of cost-effectiveness and the costs associated with hospitalization stays and treatment vary vastly between them.

The average wholesale price of bezlotoxumab costs $4,560 per bottle (1 gram per 40 milliliter).[18] Despite this cost, incremental cost-effectiveness ratio analysis of bezlotoxumab suggests that the cost per quality adjusted life-years (QALY) gained met cost-effective criteria in all patients, but that cost impact was more favorable in patients at higher risk of recurrence including older age, immunocompromised, or those with severe CDI.[22] The cost-effectiveness analyses of both bezlotoxumab and fidaxomicin take into account the financial benefit of reducing recurrence and the associated healthcare costs which may include hospitalization, extensive medical resource utilization as well as the significant morbidity and mortality associated with the disease.

Conclusion and Summary

Infections due to *C. difficile* continue to be prevalent, costly, and difficult to treat. Clinician prudence in antimicrobial stewardship, infection prevention, and mitigating patient risk is paramount to decreasing nosocomial CDI. The IDSA/SHEA 2021 Focused Update highlights increased preference for fidaxomicin for both initial and recurrent CDI episodes and mention a role for bezlotoxumab in high-risk patients. Management of CDI has shifted focus on decreasing recurrence and improving clinical outcomes, albeit with potentially cost prohibitive agents.

References: To access: click references hyperlink or QR code

References

Stock Photo from Canva

AMED PRN Member Accomplishments

September 2021-February 2022

Promotions

- **Sarah Nisly**: Job Transition, Vice President, Outcomes & Clinical Impact at Clinical Education Alliance
- **Ashley Otto**: Assistant Professor of Pharmacy, Mayo Clinic College of Medicine and Science

Awards

- **Paul Boylan**: 2021 Most Collegial Faculty Member, The University of Oklahoma College of Pharmacy Department of Clinical and Administrative Sciences.
- **Alifiya F Hyderi**: ICHP Shining Star Award. Illinois Council of Health-Systems Pharmacists (ICHP)
- **Nicole Metzger**: Mentor Award 2021, ACCP Adult Medicine PRN
- **Mate Soric**: Honorary Inductee, Rho Chi Delta Phi Chapter
- **Jon P. Wietholter**: Top Poster finalist for Personality Type Impact on Second-Year Pharmacy Academic Performance in Integrated Systems-Based Therapy Courses, 2021 ACCP Annual Meeting

Grants

- **Paul Boylan**: Patterns of Care, Outcomes, and Barriers to Treatment Success or Vaccination Associated with Adult Community-Acquired Pneumonia in Medicaid. Pfizer, Inc., $149,974, Co-Investigator [20% Effort].
- **Eliza Dy-Boarman**: Exploring nomophobia in doctor of pharmacy students amid the COVID-19 pandemic, ACCP Education and Training PRN, $1000 awarded, Principal Investigator.
- **Alex Ebied**: Teaching Pharmacy Students How to Interpret Electrocardiograms, ACCP AMED PRN Seed Grant, $5,000, Principal Investigator.
- **Sarah Kessler**: Defining the Future Research Grant, College of Psychiatric and Neurologic Pharmacists, Mentor.
- **Jennifer Austin Szwak:** TELE-TOC: Telehealth Education: Leveraging Electronic Transitions of Care for COPD Patients, $1.9M, Agency for Healthcare Research and Quality R01 Project Grant, Co-Investigator.

Publications

- **Sarah Anderson**- **Anderson SL**, Trujillo JM. Chapter 12: Diabetes Management: Non-Insulin Therapies. Diabetes Secrets, 1st edition. Ed. Michael T. McDermott & Jennifer M. Trujillo. Philadelphia: Elsevier 2022. pp 68-76.
- **Paul Boylan**- **Boylan PM**. Book Review: Transitions of Care in Pharmacy Casebook, First Edition. Laressa Bethishou, Jessica Wooster, and Phung C. On. McGraw-Hill. New York, NY (2021). 160 pp, US $49.95 (paperback), US $37.49 (ebook), ISBN: 978-1-260-47461-9. Curr Pharm Teach Learn. 2022;14(1):120-121.
- **Eliza Dy-Boarman**
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Publications Continued

- **Alex Ebied**
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- **Bethany Ford**
  - Holman SK, Folz HN, **Ford BA**, Moore S, Moody A. Design and Implementation of a Pilot Student Wellness Program at a School of Pharmacy. Curr Pharm Teach Learn. 2021; 13(11): 1471-1477
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- **Joshua Gaborcik** and **Andrew Stone**- **Stone AC**, Dungan K, and **Gaborcik JW**. Insulin NPH for steroid-induced hyperglycemia: Predictors for success. Pharmacotherapy. Oct. 2021; 41: 804-810.
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  - Arnall JR, Maples KT, Harvey RD, **Moore DC.** Daratumumab for the treatment of multiple myeloma: a review of clinical applicability and operational considerations. Ann Pharmacother. 2021. Epub ahead of print.
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Publications Continued

- **Sarah Nisly**
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Publications Continued

- **Jennifer Austin Szwak**
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- **Jon Wietholter- Wietholter JP,** Whetsel TR. Chapter 16: Chronic Obstructive Pulmonary Disease. In: Pharmacotherapy Principles & Practice. 6th ed. New York: McGraw-Hill, January 2022.
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Presentations

- **Sarah L. Anderson**
  - Don't Argue with Me - GLP-1 Receptor Agonists or SGLT2 Inhibitors as First-Line Therapy for Type 2 Diabetes Mellitus, American Society of Health-System Pharmacist Midyear Clinical Meeting, December 2021, virtual.
  - A Tale of Two Conditions: Approaches to Manage Peripheral Artery Disease and Resistant Hypertension, American Society of Health-System Pharmacist Midyear Clinical Meeting, December 2021, virtual.
  - Going Beyond the Major Research Project: Integrating Pharmacy Residents into Scholarly Pursuits, American Society of Health-System Pharmacist Midyear Clinical Meeting, December 2021, virtual.
- **Paul Boylan-** Managing transitions in COPD: a focus on multimorbidity. American Society of Health-System Pharmacists Midyear Clinical Meeting 2021; Orlando, FL. Dec 2021, virtual.
- **Shelby Brooks**- This is a Safe Space…I Think! Creating a Positive Learning Environment for Experiential Students., ULM College of Pharmacy Preceptor Conference, October 2021, Monroe, LA
- **Alifiya F Hyderi**- Road to Residency: The Residency Showcase and Getting Ready for Interviews. ICHP Fall Annual Meeting. Illinois. Virtual Conference September 2021.
- **Nicole Metzger and Carrie Tilton-** Managing Medications in Patients on Dialysis. Southern Hospital Medicine Conference, October 2021, Atlanta, GA.

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Presentations Continued

- **Donald Moore**
  - Updates on Immunotherapy and Best Pharmacy Practice for Multiple Myeloma, American College of Clinical Pharmacy/American Society of Health-System Pharmacy BCOP Clinical Session. Home Study. December 15, 2021.
  - Drug Interactions Relevant in Hematology/Oncology Patients, Area Health Education Center (AHEC) 29th Annual Wilson Medical Center Pharmacy Continuing Education Symposium. Virtual. November 11, 2021.
  - Updates in the Management of Acquired Thrombotic Thrombocytopenic Purpura, Atrium Health Clinical Pharmacy Symposium. Charlotte, NC. November 9, 2021.
  - New Drug Updates: Investigational Therapeutics in the Pipeline, JADPRO Live. Virtual. October 16, 2021.
  - Management of Immune Thrombocytopenia: Examining New Therapies and Advancements in Treatments – Featuring a Patient Perspective, Pharmacy Times Continuing Education™. Live Virtual Symposium. Cranbury, NJ. September 30, 2021.
  - A review of the Bruton Tyrosine Kinase inhibitors in B-cell malignancies, The Journal of the Advanced Practitioner in Oncology (JADPRO) Podcast. Virtual. August 2021.
- **Tiffany Pon**- Flip This Topic Discussion, ASHP National Pharmacy Preceptors Conference, October 2021, virtual
- **Mate Soric-** Study designs: Design and application, American College of Clinical Pharmacy Updates in Therapeutics: Pediatric Pharmacy Preparatory Review and Recertification Course Webinar, November 2021.

Other Notable Achievements

- **Alexandra Tatara** was named Residency Program Director for Internal Medicine PGY-2 Residency Program at Massachusetts General Hospital.
- **Rizah Anwar Assadi** became a Board Certified Pharmacotherapy Specialist in Nov 2021