Adult Medicine PRN Fall Newsletter

Edited by Carmen B. Smith PharmD, BCPS and Sarah E. Petite PharmD, BCPS

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INSIDE THIS ISSUE:

Message from the Chair

Andrew Miesner, PharmD, BCPS

Think of the changes that two decades can bring. In 1999, I didn't have an email address. Now everywhere I go, the internet is buzzing me from my pocket. Chances are you are even reading this from a device that you couldn't have even conceived of twenty years ago. This fall represents not just the 40th anniversary of ACCP, but also the 20th anniversary of the Adult Medicine PRN. Major anniversaries always seem to prompt reflection and I want to ask you take a moment to reflect on the history of your own clinical practice. Did your practice exist two decades ago? What did it look like compared to now? Could it have even existed in 1999? Think of all the things that have changed in pharmacy in 20 years to create a path for today's clinical pharmacists. Although I have only been practicing for a little over half of that time, I recognize that we're not fully where we might have envisioned the profession to be 20 years ago. While the temptation may be to focus on those factors that have stalled our professional momentum in the past two decades or those factors which may threaten further growth, I for one am delighted for the prospect of what clinical pharmacy will look like 20 years from now. I know the Adult Medicine PRN will still be filled with innovators in 2039. Clinicians, researchers, teachers, and learners who will still ready to collaborate and support each other where ever their practice might be… or whatever it may be.

Over the past year, the AMED PRN committees have been hard at work with tasks focused on investing in the future of the PRN.

- The **Internal Affairs Committee** (Chair: *Carmen Smith*, Vice-Chair: *Sarah Petite*) have developed this newsletter using a unique structure: update articles written by students who have been mentored by PRN members. Please be sure to thank and encourage those students who have contributed. The Internal Affairs Committee also deserves special thanks as they have revamped PRN's history document in celebration of the College's 40th anniversary. This document will be available on the PRN website and a summary poster will be on display at the 2019 Annual Meeting in New York City.
- The **Research Committee** (Chair: *Rima Mohammad*, Vice-Chair: *Joel Marrs*) has developed a process for PRN papers and has already archived a number of ideas submitted by the membership. Beginning next year, many of you may be tapped to begin developing these ideas into future publications. They continue to offer funding through the PRN's Seed Grant program and have also identified **Dr. Melanie Manis** as an ACCP MeRIT scholar this year, helping her to secure support for the MeRIT program this past summer.

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UPCOMING JOURNAL CLUBS:

OCTOBER 16TH

NOVEMBER 20TH

DECEMBER 18TH

JANUARY 15TH

FEBRUARY 19TH

MARCH 18TH

JOIN US FOR HAPPY HOUR IN NYC!

5-6PM MONDAY, OCT 28TH

THE IRISH PUB

837 7TH AVE (~1 BLOCK FROM HOTEL)

- The **Training and Travel Awards Committee** (Chair: *Yulia Murray*, Vice-Chair: *Asha Tata*) have also identified award recipients for the Student and Resident Research Awards and the Practitioner Registration Award which will be awarded at the PRN Business and Networking Meeting.
- **Walk Rounds Committee** (Chair: *Jon Wietholter*, Vice-Chair: *Ryan D'Angelo*) expanded their role this spring, conducting a review at both the Updates meeting in April and the Virtual Symposium in May. PRN Top Posters at Updates this year included projects from **Dr. Abigail Yancey** and **Dr. Matea Markovic**. As always, please consider volunteering for Walk Rounds at the Annual Meeting in New York this October.

  If you are interested in participating in Walk-Rounds, please email **jwietholter@hsc.wvu.edu** with the sessions you are available:

  A) Saturday 10/26 from 11:30-1
  B) Sunday 10/27 from 12:45-2:15
  C) Monday 10/28 from 10:30-12
  D) Monday 10/28 from 1-2:30
  E) Tuesday 10/29 from 8:30-10
  F) Tuesday 10/29 from 11:45-1:15

- The **Programming Committee** (Chair: *Ryan Owens*, Vice-Chair: *Andy Crannage*) has developed yet another phenomenal Focus Session for the Annual Meeting: *Post-Op Debate: Anticoagulation vs. Aspirin for VTE Prophylaxis Following Orthopedic Surgery*. This will be held on Monday, October 28, 2019 at 1:45 PM EST. Make every effort to attend!
- The **External Affairs Committee** (Chair: *Jennifer Austin Szwak*, Vice-Chair: *Jamie Sebaaly*) has not only continued coordinating the online Journal Clubs from PRN residents, but also has developed a member spotlight to highlight the innovative practices of the PRN on AMED social media outlets. Be sure to nominate a member, resident, or student chapter to be featured in the AMED Facebook Spotlights!
- Finally, the **Nominations Committee** (Chair: *Leigh Anne Hylton-Gravatt*, Vice-Chair: *Erin Hennessey*) has identified a PRN Mentor and Distinguished Investigator Awards to be awarded at the PRN Business and Networking Meeting. They have also helped facilitate the election process for next set of PRN leaders. Congratulations to **Dr. Carmen Smith** (Chair-elect) and **Dr. Jon Wietholter** (Secretary/Treasurer).

Many thanks to all of the committee members for your service. You have made my time as Chair infinitely more rewarding and have helped set the tone for future of this PRN!

ANNUAL MEETING SAVE THE DATES

- **Saturday, October 26th 11am-1pm:** The History of the Adult Medicine PRN Poster Presentation (Rhinelander Gallery)
- **Monday, October 28th 1:45-3:15pm:** AMED Focus Session (3rd Floor: Trianon Ballroom)
- **Monday, October 28th 5-6pm:** AMED Happy Hour! (The Irish Pub, 837 7th Ave)
- **Monday, October 28th 6:30-8:30pm:** AMED PRN Business Meeting & Networking Forum (3rd Floor: Mercury Ballroom)

2019 ADULT MEDICINE PRN ELECTION RESULTS AND AWARD RECEIPIENTS

PRN NEWLY ELECTED OFFICERS

* **Chair-Elect** - Carmen B. Smith, PharmD, BCPS
* **Treasurer/Secretary** - Jon Wietholter, PharmD, BCPS

PRN AWARDS

* **ACCP Adult Medicine PRN Mentoring Award** - Lindsay Saum, PharmD, BCPS, BCGP
* **ACCP Adult Medicine PRN Distinguished Investigator Award** - Andrew J. Crannage, PharmD, FNKF, FCCP, BCPS
* **Practitioner Award** -Taryn B. Bainum, Pharm.D., BCPS
* **Resident/Fellow Research Award** - Eric Kinney, PharmD; PGY2 Internal Medicine Pharmacy Resident Duquesne University School of Pharmacy & UPMC Mercy Hospital

  "Carvedilol versus metoprolol succinate for heart failure with reduced ejection fraction and concomitant cocaine use"
* **Student Research Award** - Karissa Chow, 2020 PharmD Candidate from Philadelphia College of Pharmacy

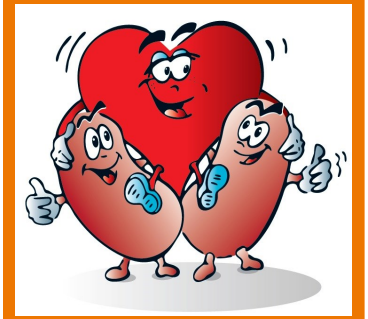
  "Predictors of drug therapy problems and the need for interventions by internal medicine clinical pharmacists"

RESEARCH AWARDS

* **ACCP MeRIT Scholar** - Melanie Manis, PharmD, BCPS

Sweet and Salty: The Cardiovascular and Renal Benefits of SGLT2 Inhibitors

By: Jessica Marie Fraone, PharmD Candidate and
Benjamin Pullinger, PharmD, BCPS



"There is mounting evidence that SGLT2 inhibitors are beneficial in patients with T2DM who have or are at risk for ASCVD or diabetic nephropathy."

In the last decade, treatment of type 2 diabetes mellitus (T2DM) has undergone a substantial shift. Since the FDA mandated phase IV cardiovascular (CV) outcome trials for antidiabetic agents, there has been a focus on new agents that not only provide additional glycemic control but also reduce hard endpoints such as major adverse cardiovascular events (MACE) in patient with or at risk for atherosclerotic cardiovascular disease (ASCVD). Recently, several trials have investigated the role of sodium-glucose cotransporter 2 (SGLT2) inhibitors in reducing the incidence or progression of diabetic nephropathy in addition to the reduction of MACE. SGLT2 is a high capacity and low affinity glucose transporter expressed in the proximal tubule. By blocking this transporter, SGLT2 inhibitors lower the renal glucose threshold, inhibit glucose reabsorption, and induce urinary glucose elimination with concomitant natriuresis and osmotic diuresis.[1]

For several years, we've known about the CV and renal benefits of SGLT2 inhibitors from the EMPA-REG OUTCOME[2,4] and CANVAS[3] trials. In the EMPA-REG OUTCOME trial, empagliflozin was associated with a 14% relative risk reduction (RRR) of MACE in patients with T2DM and established ASCVD (Table 1). One of the most impressive findings in the trial was a reduction in all-cause mortality (5.7% vs 8.3%, hazard ratio [HR] 0.68, 95% confidence interval [CI] 0.57-0.82), which was primarily driven by a reduction in CV mortality. Additionally, empagliflozin significantly reduced heart failure (HF) hospitalizations and a renal composite outcome that represented incident or worsening nephropathy (see Table 1). Two years later, results from the CANVAS program were published. The CANVAS program was comprised of two trials, CANVAS and CANVAS-R, which evaluated the effects of canagliflozin on CV and renal outcomes in patients with T2DM.[3] In contrast to EMPA-REG OUTCOME, the CANVAS program evaluated a mix of primary and secondary prevention patients, since patients could have either established ASCVD or only possess multiple risk factors for ASCVD. Canagliflozin was associated with a 14% RRR in the primary MACE outcome and a 33% RRR in HF hospitalizations (Table 1). Moreover, progression of albuminuria was reduced in the canagliflozin arm. A significant reduction in all-cause mortality was not observed.

In the last year, several landmark trials have strengthened these findings. The CREDENCE[5] trial was a double-blind, multi-site, placebo-controlled randomized trial that assessed the effects of canagliflozin on renal outcomes in 4401 patients with T2DM and chronic kidney disease, defined as an estimated glomerular filtration rate (eGFR) 30 to <90 mL/min/1.73m^2 with albuminuria. All patients were on stable doses of angiotensin converting enzyme inhibitors (ACEi) or angiotensin receptor blockers (ARBs). The trial was stopped early due to observed benefit after a planned interim analysis: In the canagliflozin arm, there was a 30% RRR of the primary renal outcome, defined as end-stage renal disease (ESRD), doubling of serum creatinine (SCr), and renal or CV death (11.1% vs 15.5%, HR 0.70, 95% CI 0.59-0.82). Additionally, secondary endpoints of MACE and HF hospitalizations were significantly reduced with canagliflozin (Table 1). One of the strengths of this study was the inclusion of patients with moderate CKD. The mean eGFR was 56 mL/min/1.73m^2, and 29% and 27% of the study population had an eGFR from ≥45 to <60 mL/min/1.73m^2 or from ≥30 to <45 mL/min/1.73 m^2, respectively. During the first 3 weeks of the trial, a larger initial eGFR decline was observed in the canagliflozin group (–3.72±0.25 vs –0.55±0.25 mL/min/1.73m2), but the eGFR decline was slower in the canagliflozin group than in the placebo group during the remainder of the study. When applying this trial, it should be noted that non-albuminuric patients and patients with

Table 1. Summary of Major Cardiovascular and Renal Endpoints in Published Randomized Controlled SGLT2 Inhibitor Trials

Trial and Study Size	Drug (Daily Dose)	Key Inclusion Criteria	Major CV Endpoint(s)	Major Renal Endpoint(s)	Results	Primary Endpoint NNT
EMPA-REG OUTCOME[2,4] N = 7020	Empagliflozin (10mg, 25mg)	T2DM with established ASCVD eGFR ≥30 mL/min/1.73 m^2	MACE: CV death + MI + stroke‡ HF hospitalization	Renal composite: progression to macroalbuminuria + doubling of SCr + RRT initiation + renal death	MACE: 10.5 vs 12.1%, HR 0.86 (95% CI 0.74-0.99) HF hospitalization: 4.1% vs 2.7%, HR 0.65 (95% CI 0.50-0.85) Renal composite: 12.7% vs 18.8%, HR 0.61 (95% CI 0.53-0.70)	NNT = 63 over 3.1 years
CANVAS and CANVAS-R[3] N = 10,142	Canagliflozin (100mg, 300mg)	T2DM with ASCVD or multiple CV risk factors eGFR ≥30 to <90 mL/min/1.73 m^2	MACE: CV death + MI + stroke‡ HF hospitalization	Progression of albuminuria Renal composite: 40% eGFR reduction + RRT initiation + renal death	MACE: 26.9/1000 patient-yr vs 31.5/1000 patient-yr, HR 0.86 (95% CI 0.75-0.97) HF hospitalization: 5.5/1000 patient-yr vs 8.7/1000 patient-yr, HR 0.67 (95% CI 0.52-0.87) Progression of albuminuria: 89.4/1000 patient-yr vs 128.7/1000 patient-yr, HR 0.73 (95% CI 0.67-0.79) Renal composite: 5.5/1000 patient-yr vs 9.0/1000 patient-yr, HR 0.60 (95% CI 0.47-0.77)	NNT = 62 over 3.6 years
CREDENCE[5] N = 4401	Canagliflozin (100mg)	T2DM with CKD (eGFR 30 to <90 mL/min/1.73m^2 with albuminuria) and on stable ACEi/ARB	MACE: CV death + MI + stroke HF hospitalization	Renal composite: ESRD + doubling of SCr + renal death + CV death‡	MACE: 9.9% vs 12.2%, HR 0.80 (95% CI 0.67-0.95) HF hospitalization: 4.0% vs 6.4%, HR 0.61 (95% CI 0.47-0.80) Renal composite: 11.1% vs 15.5%, HR 0.70 (95% CI 0.59-0.82)	NNT = 23 over 2.5 years
DECLARE-TIMI 58[6] N = 17,160	Dapagliflozin (10mg)	T2DM and established ASCVD or multiple CV risk factors CrCl ≥60 mL/min	MACE: CV death + MI + stroke‡ CV death + HF hospitalization	Renal composite: 40% eGFR reduction + renal death + CV death	MACE: 8.8% vs 9.4%, HR 0.74 (95% CI 0.84-1.03), P<0.001 for non-inferiority CV death + HF hospitalization: 4.9% vs 5.8%, HR 0.83 (95% CI 0.73-0.95) Renal composite: 4.3% vs 5.6%, HR 0.76 (95% CI 0.67-0.87)	N/A
DAPA-HF[7] N = 4744	Dapagliflozin (10mg)	HFrEF (NYHA class II-IV) on GDMT unless not tolerated CrCl ≥60 mL/min	HF composite: CV death + HF hospitalization + urgent HF visit requiring IV therapy‡	Renal composite: 50% eGFR reduction + ESRD + renal death	HF composite: 16.3% vs 21.2%, HR 0.74 (95% CI 0.65-0.85) Renal composite: 1.2% vs 1.6%, HR 0.71 (95% CI 0.44-1.16)	NNT = 21 over 1.5 years

ASCVD = atherosclerotic cardiovascular disease; CAD = coronary artery disease; CKD = chronic kidney disease; CV = cardiovascular; eGFR = estimated glomerular filtration rate; ESRD = end-stage renal disease; GDMT = guideline directed medical therapy; HF = heart failure; HFrEF = heart failure with reduced ejection fraction; HR = hazard ratio; IV = intravenous; MACE = major adverse cardiovascular events; MI = myocardial infarction; NNT = number needed to treat; NYHA = New York Heart Association; PAD = peripheral artery disease; RRT = renal replacement therapy; SCr = serum creatinine

‡ Primary endpoint for trial

severe renal disease (eGFR <30 mL/min/1.73m^2) were excluded. Additionally, early termination of the trial may have limited the power of some secondary outcomes and increased the risk of overestimating effect size. This was the first SLGT2 trial evaluating renal outcomes as a primary outcome and showed that canagliflozin was the first drug since ACEi/ARBs to be disease modifying for diabetic nephropathy.

DECLARE-TIMI 58[6] was a randomized, double-blind, multinational, placebo-controlled trial that evaluated the effects of dapagliflozin on CV and renal outcomes in 17,160 patients who had or were at risk for ASCVD. Dapagliflozin was non-inferior to placebo for the primary MACE outcome but did not show superiority (8.8% vs 9.4%, HR 0.74, 95% CI 0.84-1.03 [p<0.001 for non-inferiority margin <1.3]). Dapagliflozin was associated with a 17% reduction in the secondary endpoint of CV death and HF hospitalization (Table 1), a finding driven by reductions in HF hospitalizations (2.5% vs 3.3%, HR 0.73, 95% CI 0.61-0.88). This finding for MACE differed from EMPA-REG OUTCOME, but it should be noted that EMPA-REG OUTCOME had an exclusively secondary prevention population and had a higher overall mortality rate, which is why it may have been easier to demonstrate a MACE benefit in this trial. A limitation for DECLARE-TIMI 58 was the exclusion of patients with an eGFR <60 mL/min/1.73 m^2, which led to a lower renal risk population. Nevertheless, the primary renal composite endpoint (≥40% decrease in eGFR to <60 ml/min/1.73 m^2, ESRD, or death from renal or CV causes) was still reduced in the dapagliflozin arm (Table 1).

Due to the consistent reduction of HF hospitalizations in the aforementioned studies, trials are being conducted to evaluate the benefit of SGLT2 inhibitors in HF patients with and without concomitant T2DM. Results from the first of these studies, DAPA-HF, were recently released.[7] In this randomized double-blind trial, 4744 patients with heart failure and reduced ejection fraction (HFrEF) were randomized to dapagliflozin or placebo. Only 42% of patients had a history of T2DM at baseline. The primary outcome was a composite of CV death and either HF hospitalization or urgent HF visit requiring intravenous therapy. Over an average follow-up of 18.2 months, dapagliflozin was associated with a 26% reduction in the primary outcome (16.3% vs 21.2%, HR 0.74, 95% CI 0.65-0.85). The primary events were predominantly comprised of HF hospitalizations (9.7% vs 13.4%, HR 0.70, 95% CI 0.59-0.83) and CV death (9.6% vs 11.5%, HR 0.82, 95% CI 0.69-0.98). The CV benefit was consistent across most subgroups (including those with vs without T2DM), although benefit appeared greater in patients belonging to New York Heart Association (NYHA) functional class II. A secondary renal composite endpoint (50% eGFR reduction, ESRD, or renal death) was not statistically significant (Table 1). Limitations to this trial included low representation of black patients (<5%) and those with severe heart failure (majority NYHA class II, median EF 30%). Strengths include good use of background guideline directed medical therapy (GDMT): over 90% of patients were on β-blocker and renin-angiotensin-aldosterone system inhibitors, and 71% were on mineralocorticoid receptor antagonists at baseline. However, doses of background GDMT were not reported, and only 11% of patients were on sacubitril-valsartan.

With all these benefits of SGLT2 inhibitors, professional organizations have weighed in about the evidence-based use of these medications. Canagliflozin and empagliflozin are the only SGLT2 inhibitors approved by the FDA for reducing cardiovascular death in patients with T2DM and established CV disease. The American Diabetes Association (ADA) recommends that patients with T2DM and established ASCVD use an SGLT2 inhibitor or glucagon-like peptide-1 (GLP-1) receptor agonist due to the CV benefits, with SGLT2 inhibitors preferred in patients that have ASCVD and established HF or are at high-risk for HF.[8] The ADA also recommends to consider the use of these medications to reduce the risk of CKD progression, CV events, or both in patients with T2DM and CKD. Metformin is still the preferred first-line oral agent in patients with T2DM. However, if a patient with T2DM and cardiovascular disease cannot tolerate metformin or the patient's hemoglobin A1C is still above their goal, it is strongly suggested that an SGLT2 inhibitor be considered. The American College of Cardiology (ACC) recommends that SGLT2 inhibitors or GLP-1 agonists be utilized in patients with ASCVD, with preference for SGLT2 inhibitors due to strong data supporting reduced MACE and HF hospitalizations.[9] These recommendations will likely continue to evolve as more data emerge.

When prescribing SLGT2 inhibitors, there are some practical considerations to keep in mind. In patients with CKD, SGLT2 inhibitors have been shown to prevent renal progression including albuminuria, doubling of serum creatinine (SCr), renal replacement therapy initiation, and renal death but there are prespecified eGFR cutoffs. Although clinical trials such as CREDENCE studied patients with eGFRs as low as 30 mL/min/1.73 m^2, the FDA deems acceptable eGFR cutoffs for initiation as 60 mL/min/1.73 m^2 (dapagliflozin) and 45 mL/min/1.73 m^2 (canagliflozin, empagliflozin), canagliflozin and empagliflozin were studied at lower eGFRs. There is frequently a modest eGFR decrease when first initiating these agents due to the diuretic effect as observed in the CREDENCE trial.[5] When initiating these agents, clinicians should evaluate concomitant diuretics as a decrease in dose might be warranted in patients at risk for volume depletion. Due to the diuretic effect and direct effects on vascular function, SGLT2 inhibitors can cause a systolic blood pressure reduction of 4 to 6 mmHg.[10] It is important to monitor patients for dehydration and orthostatic hypotension when starting these agents, especially among elderly patients. The increased risk of bone fractures

observed in CANVAS (which was not confirmed in any other SGLT2 inhibitor trial) could in part have been caused by falls due to dehydration or orthostatic hypotension.[10] Additionally, with respect to fracture risk, a recent observational study compared SGLT2 inhibitors to dipeptidyl peptidase-4 (DPP-4) inhibitors and found that the SGLT2 inhibitors (including canagliflozin) had a lower rate of fractures.[11] CANVAS was also the only trial that exhibited an increased risk of amputations primarily at the level of the toe or metatarsal. This has not been established as a class wide effect, but patients taking SGLT2 inhibitors should be educated on conducting regular foot exams and reporting new lesions. It should be noted that patients at the highest risk for amputations in CANVAS were those with prior amputations or peripheral artery disease.[3]

The rate of genital mycotic infections has been repeatedly shown to be higher with SGLT2 inhibitors, but rates of UTIs were no different than placebo in clinical trials. The FDA added a warning label to the SGLT2 inhibitors for Fournier's gangrene (FG) due to post surveillance monitoring, but this finding may be interpreted with some caution due to a potential risk of reporting bias with novel medications. In DECLARE-TIMI 58, the largest trial to date, there were six cases of FG, one in the dapagliflozin group and five in the placebo group.[6] In general, diabetes is a risk factor for FG, and patients taking these medications should be instructed to report any redness or lesions in perineal and genital regions. Euglycemic diabetic ketoacidosis (DKA) has also been reported with these agents; DECLARE-TIMI 58 and CREDENCE confirmed a higher incidence of DKA with SGLT2 inhibitors than placebo, although overall rates were low.[5,6] In these trials, most of the patients that experienced DKA were using insulin at baseline. Patients should be counseled to monitor for signs and symptoms of DKA, and patients should temporarily discontinue SGLT2 inhibitors if they become acutely ill, dehydrated, or have significantly decreased oral intake.

There is mounting evidence that SGLT2 inhibitors are beneficial in patients with T2DM who have or are at risk for ASCVD or diabetic nephropathy. The evidence for CV benefit is most convincing for secondary ASCVD prevention, and SGLT2 inhibitors should be a preferred antidiabetic agent in patients with ASCVD and HF. They should also be a preferred antidiabetic agent in patients with proteinuric diabetic nephropathy. Although a few alarming adverse effects have been reported – albeit inconsistently – we believe that careful initiation, monitoring, and patient education can mitigate these risks, making these drugs valuable agents for glycemic control, cardiovascular risk reduction, and diabetic nephropathy.

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2019 GINA Report Update: Inhaled Pharmacologic Management of Asthma in Patients Over 12 Years of Age

By: Janine Short, PharmD Candidate and Kathleen Adams, PharmD, BCPS

"Instead of as-needed SABAs for the acute relief of symptoms, adults and adolescents should now receive as-needed ICS-formoterol as the preferred reliever therapy "

Background

Following the twice-yearly review of the literature by the Global Initiative for Asthma (GINA) Science Committee, GINA has recently published an updated 2019 global strategy for asthma management and prevention report. The guideline contains multiple updates with the most notable discouraging the use of short acting beta agonists (SABAs) as rescue inhalers.[1]

In the 2018 GINA report, SABAs were recommended as the preferred as-needed inhaler for the rapid relief of acute asthma symptoms across all steps of the treatment algorithm. In step 1 specifically, SABA monotherapy was recommended for the management of asthma symptoms in patients of all ages.[2] At the time of the 2018 report, there was insufficient evidence to support the use of inhaled corticosteroids (ICS) in patients that qualify for step 1 therapy, despite the fact that chronic airway inflammation is found in patients with intermittent symptoms. Additionally, at the time of the 2018 update, data was lacking to confirm the overall safety of SABA monotherapy.[2]

During the course of this past year, substantial data has been published shedding light on the safety risk of SABA monotherapy and the efficacy of ICS in mild asthma (asthma that is well controlled with Step 1 or Step 2 treatment).[1] Taking this current evidence into account, the 2019 report no longer recommends SABA-only therapy for the treatment of asthma in patients over 12 years of age. Furthermore, in steps 1-5, SABAs are no longer recommended as the preferred reliever therapy in patients over 12 years of age.[1]

Instead of as-needed SABAs for the acute relief of symptoms, adults and adolescents should now receive as-needed ICS-formoterol as the preferred reliever therapy in steps 1-5. If SABA reliever therapy is used, patients should either be using a daily ICS or using a low dose ICS whenever the SABA is taken.[1] The risks associated with SABA monotherapy are discussed below.

Summary of the 2018 vs 2019 Treatment Algorithm in Patients ≥12 Years of Age

2018 GINA Asthma Treatment Strategy in Patients ≥12 Years of Age[2]			
Step	**Preferred Controller**	**Alternative Controller**	**Reliever**
1		Consider low dose ICS	As-needed SABA
2	Daily low dose ICS	Once daily leukotriene receptor antagonist (LTRA) [OR] Low dose theophylline	
3	Low dose ICS- long acting beta agonist (LABA)	Medium/high dose ICS [OR] low dose ICS + LTRA [OR] + theophylline	As-needed SABA [OR] low dose ICS-formoterol
4	Medium/high dose ICS-LABA	Add tiotropium [OR] medium/high dose ICS + LTRA [OR] + theophylline	
5	Refer for add on therapy (e.g. tiotropium, omalizumab, benralizumab, etc.)	Add-on low dose oral corticosteroids	

2019 GINA Asthma Treatment Strategy in Patients Over 12 Years of Age[1]				
Step	**Preferred Controller**	**Alternative Controller**	**Preferred Reliever**	**Alternative Reliever**
1	As-needed low dose ICS-formoterol	Low dose ICS taken whenever SABA is taken	As-needed low dose ICS-formoterol	As-needed SABA
2	Daily low dose ICS [OR] as-needed ICS-formoterol	Once daily LTRA [OR] as-needed low dose ICS taken whenever a SABA is taken		
3	Daily low dose ICS-LABA	Medium dose ICS [OR] low dose ICS + LTRA		
4	Daily medium dose ICS-LABA	High dose ICS + tiotropium [OR] high dose ICS + LTRA		
5	High dose ICS-LABA + referral for phenotypic assessment ± add on therapy (e.g. tiotropium, omalizumab, benralizumab, etc.)	Low dose oral corticosteroids		

Supporting Evidence

SABA-only regimens are associated with an increased risk of severe exacerbations and asthma related deaths due to the lack of a maintenance glucocorticoid-containing inhaler.[3,4] As-needed ICS-formoterol reduces the annual number of severe exacerbations and provides better asthma symptom control when compared to as-needed SABA-only reliever therapy.[3,4] The NOVEL-START and SYGMA trials substantially contribute to the pool of evidence that generated the recommendation changes made to the GINA treatment strategy.

SYGMA 1[3]

The SYGMA 1 trial was a double-blind, randomized, parallel group, controlled trial. The trial aimed to evaluate the safety and efficacy of three different regimens for mild asthma. The SYGMA 1 trial included 3,849 adult and adolescent patients over the age of twelve with a clinical diagnosis of asthma for at least six months requiring GINA step 2 therapy for management. Participants were followed over 52 weeks.

Prior to randomization, patients were required to complete a 2-4 week run-in period with inhaled terbutaline to confirm the appropriateness of GINA step 2 treatment. Once the run-in period was complete, patients were randomized to receive one of three regimens: twice-daily placebo controller plus terbutaline 0.5 mg as-needed (N = 1280), twice-daily placebo controller plus budesonide-formoterol 200 µg-6 µg as-needed (N = 1276) or twice daily budesonide 200 µg controller plus terbutaline 0.5 mg as-needed (N = 1290). Inhaler use was recorded via an inhaler monitor and an electronic diary was kept by each patient to record morning and evening peak expiratory flows, asthma symptoms, and nighttime awakenings due to asthma. The electronic diary also provided adherence prompts for the use of the blinded maintenance inhaler.

The primary objective was to investigate superiority of as-needed budesonide-formoterol to as-needed terbutaline defined by number of recorded weeks with well-controlled asthma. Secondary endpoints included the rates of exacerbations and the median daily dose of inhaled glucocorticoids. Results demonstrated that as-needed budesonide-formoterol was superior to as-needed terbutaline, with more weeks of well controlled asthma (34.4% vs 31.1% of weeks; odds ratio, 1.14; CI 1.0-1.3; P=0.046). However, as-needed budesonide-formoterol was shown to be inferior to the budesonide maintenance plus as-needed terbutaline therapy (34.4% vs 44.4% of weeks; odds ratio, 0.64; CI 0.57-0.73). Concerning annual rates of severe exacerbations, as-needed budesonide-formoterol use resulted in a 64% decreased annual rate of severe exacerbations and a 60% decreased annual rate of moderate-severe exacerbations when compared to as-needed terbutaline (0.07 vs 0.20 and 0.14 vs 0.36, respectively; CI 0.27-0.49).

Comparing as-needed budesonide-formoterol to maintenance budesonide plus as-needed terbutaline, the exacerbation rates were similar (0.07 vs 0.09; CI 0.59-1.16 for severe exacerbations). However, patients in the maintenance budesonide plus as-needed terbutaline group were, on average, exposed to six times the metered daily dose of glucocorticoids compared to the as-needed budesonide-formoterol group (57 µg vs 340 µg median daily metered dose).

SYGMA 2[5]

The SYGMA 2 trial was a double-blind, randomized, parallel-group trial that evaluated the safety and efficacy of two different regimens for mild asthma. The trial included 4,176 adult and adolescent patients over the age of twelve with a clinical diagnosis of asthma for at least six months requiring GINA step 2 therapy for management. Prior to randomization, the same run-in period and criteria for randomization as seen in SYGMA 1 were implemented. Participants again were followed for 52 weeks.

After the run-in period, eligible patients were randomly assigned to one of two groups: twice-daily placebo plus budesonide-formoterol 200 µg-6 µg as-needed (N=2089) or twice-daily budesonide 200 µg plus terbutaline 0.5 mg as-needed (N=2087). Inhaler use was recorded utilizing an inhaler monitor. The electronic diary component of SYGMA 1 was not incorporated in attempt to create a more pragmatic design. Due to this, patients did not receive adherence prompts, more closely mimicking medication use outside of a controlled trial setting.

The primary study outcome was to investigate noninferiority of as-needed budesonide-formoterol therapy to maintenance budesonide plus as-needed terbutaline therapy in terms of annual rates of severe exacerbations. Secondary outcomes included time to the first severe exacerbation, use of inhaled glucocorticoids, and adherence.

Results demonstrated that as-needed budesonide-formoterol was noninferior to budesonide maintenance therapy in respect to annual rates of severe exacerbations (0.11; CI 0.10-0.13 vs 0.12; CI 0.10-0.14), with the as-needed budesonide-formoterol group achieving this result while exposing patients to 75% less of inhaled glucocorticoids (66 µg vs 267 µg median daily metered dose). In terms of time to severe exacerbations and measured adherence, there was no statistically significant difference between the groups (hazard ratio, 0.96; CI, 0.78-1.17).

NOVEL-START[4]

The external validity of SYGMA 1 was limited due to the required run-in period. As a result, the NOVEL-START trial looked to expand applicability and more closely mimic real-world practice. The NOVEL-START trial was an open label, parallel-group, controlled trial that evaluated the efficacy of three different regimens for mild asthma. Overall, 668 patients aged 18-75 years were analyzed and followed for 52 weeks. The main inclusion criteria included the use of a SABA-only therapy regimen in the previous three months and patient reported use of the SABA at least twice per week, while averaging two or less doses per day.

Patients were randomized in a 1:1:1 ratio to either as-needed albuterol 100 µg, as-needed budesonide-formoterol 200 µg-6 µg, or twice-daily budesonide 200 µg plus as-needed albuterol 100 µg. Inhaler usage was recorder via an inhaler monitor.

The primary outcome of the trial was annual rates of asthma exacerbations per patient. Secondary measures included the number of exacerbations and the time to the first exacerbation. Concerning annual asthma exacerbation rates, the rate in the as-needed budesonide-formoterol group was approximately half that of the as-needed albuterol group (0.195 vs 0.40; CI, 0.33-0.72; P<0.001), with no significant difference between the as-needed budesonide-formoterol group and the maintenance budesonide plus as-needed albuterol group (0.195 vs 0.175; CI, 0.70-1.79; P=0.65). The number of exacerbations in the budesonide-formoterol group was lower than the number in both the as-needed albuterol group and the maintenance budesonide plus as-needed albuterol group (9 vs 23; CI, 0.18-0.86 and 9 vs 21; CI, 0.20-0.96, respectively). The risk of exacerbation was assessed via a time-to-first-event analysis; the risk of exacerbation in the as-needed budesonide-formoterol group was lower than the albuterol group and did not differ significantly from the budesonide maintenance plus as-needed albuterol group (HR, 0.46; CI 0.29-0.73 and HR, 0.93; CI 0.55-1.57, respectively).

Discussion

As noted in the 2019 GINA report, the use of as-needed ICS-formoterol in moderate and severe asthma (defined as asthma that is well controlled with step 3 treatment and asthma that requires step 4 or 5 treatment, respectively) has been previously well documented. However, prior to 2019, consensus guidelines supporting their use as relief inhalers in mild asthma was limited.[1] Overall, NOVEL-START and SYGMA trials demonstrated the safety and efficacy of ICS-formoterol as reliever inhalers in mild asthma. ICS-formoterol used for the quick relief of asthma symptoms compared to the previous standard of SABAs decreases annual exacerbation rates and reduces average doses of glucocorticoids.[3-5] Of note, potential sources of conflict do exist with members of the GINA committee listed as authors on these studies, which were all sponsored by the manufacturer of budesonide-formoterol. However, GINA implements an extensive screening and review protocol to neutralize any conflicts of interest that may exist during examination of data.[1]

All current evidence supporting the use of an ICS with LABA combination inhaler is with budesonide-formoterol. Beclomethasone dipropionate-formoterol may also be used.[1] Formoterol has an onset of action that closely aligns with that of SABAs. Bronchodilation with formoterol begins to occur within 1-3 minutes of inhalation.[6] In contrast, salmeterol's onset of action is much longer, approaching 10–15 minutes. As a result, there is currently no evidence to support the utility of other LABAs as rapid acting as-needed inhalers and use should be discouraged for acute treatment.[1,7]

Adherence to maintenance inhaled glucocorticoids is low, exposing patients to the risks of SABA-only therapy.[8] Part of this adherence barrier is due to the change in mentality when moving from step 1 to step 2 within the treatment algorithm. Patients must shift their thinking away from the SABA being their primary inhaler. Prescribing ICS-formoterol for maintenance and reliever therapy can assist to mitigate confusion and remove the risk of SABA-only therapy.[1]

Overall, the 2019 GINA report will change how we think about and manage mild asthma. With the new recommendations, ICS-formoterol containing inhalers will become more of an integral part of asthma management therapy. Clinicians will have to work actively to educate the public on the risks associated with SABA monotherapy to ensure proper management and to optimize care.

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Biomarkers to Guide Antibiotic Use in COPD Exacerbations

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"Both PCT and CRP are useful biomarkers in reducing antibiotic use in acute COPD exacerbation [but] should be used in con-junction with clinical judgment."

The Global Initiative for Chronic Obstructive Lung Disease (GOLD) defines chronic obstructive pulmonary disease (COPD) as a preventable and treatable disease characterized by airflow limitation and persistent respiratory symptoms.[1] A COPD exacerbation is characterized by an acute worsening of respiratory symptoms such as dyspnea, increased sputum, as well as coughing and/or wheezing that require additional therapy.[1] Standard treatment for a COPD exacerbation includes antibiotics, corticosteroids, and bronchodilators.[1] According to GOLD guidelines, antibiotics can reduce risk of short-term mortality, treatment failure, and sputum purulence.[1] Due to the absence of evidence for outcome benefits with antibiotics use in all patients, GOLD guidelines recommend antibiotic therapy only in patients with sputum purulence and at least one other cardinal symptom or requiring mechanical ventilation.[1] Analysis of a large retrospective cohort of patients hospitalized for COPD exacerbation found early administration of antibiotics improved mortality (1.04% vs 1.59%; P<0.001), lowered readmission rates (7.91% vs 8.79%; P< 0.001), delayed the need for subsequent mechanical ventilation (1.07% vs 1.80%; p < 0.001), and decreased treatment failure (9.77% vs 11.75%; P<0.001) among hospitalized patients.[2] Furthermore, there are several possible etiologies of acute exacerbation of COPD in addition to bacterial causes, including viruses and common pollutants. As such, the use of antibiotic therapy in the treatment of COPD exacerbations is still controversial. Notably, bacterial infection does play a role in nearly 50% of patients with acute COPD exacerbation and the use of an antibiotic is beneficial for this patient population.[3]

Because of the controversial use of antibiotic in treatment of COPD exacerbations, there is a potential for antibiotic overuse that could contribute to the antibiotic resistant crisis. According to the United States (US) Center for Disease Control, antibiotic resistance has become one of the world's biggest health threats.[4] In the US, every year 2 million people develop a bacterial infection resistant to at least one antibiotic, causing 23,000 deaths.[4] Procalcitonin (PCT) and C-reactive protein (CRP) have been studied as biomarkers to guide the diagnosis of bacterial infection and antibiotic treatment to improve the use of antibiotics and minimize the risk of resistance development.[5,6]

The US Food and Drug Administration approved PCT for the purpose of guiding antibiotic therapy in the setting of acute respiratory infections.[7] (Table 1) PCT is a biomarker of sepsis and bacterial lower respiratory tract infections.[7] PCT is the precursor of the hormone calcitonin, which is secreted by the thyroid C cells.[8] PCT is an acute-phase protein with faster kinetics than CRP. PCT levels increase rapidly during bacterial infection but remain low in viral infections.[9] As a biomarker, PCT has specificity to differentiate bacterial from non-bacterial inflammation and consequently prevent unnecessary antibiotic use and reduce the duration of antibiotic therapy.[10]

CRP is an acute phase reactant protein produced in the liver in response to inflammation. (Table 1) CRP has both pro-inflammatory and anti-inflammatory properties.[6] It can be measured accurately within minutes at the point of care, and is used to assess the presence of acute inflammatory processes.[10]

PCT-Guided Antibiotic Therapy

Procalcitonin to guide antibiotic administration in COPD exacerbations: a meta-analysis[8]

A 2017 meta-analysis including eight randomized trials with 1062 patients with acute exacerbations of COPD evaluated if PCT-guided antimicrobial therapy is associated with significantly reduced antibiotic exposure. The primary outcomes were treatment failure and length of hospitalization. The secondary outcomes include antibiotic exposure, re-exacerbation rate, re-admission rate, and mortality.

Treatment failure was assessed in five out of the eight trials with 834 included patients. Treatment failure occurred in 163 participants with no significant difference between the two groups (RR 0.81, (95% Cl 0.62 - 1.06)). Length of hospitalization was reported in all included trials. There was no significant difference between the two groups (mean difference (MD) -0.76, 95% Cl -1.95 - 0.43).

The length of antibiotic was assessed by six studies with 776 participants. PCT-guided therapy significantly reduced antibiotic exposure by approximately 4 days ((MD) -3.83 (95% Cl -4.32 - 3.35). The rates of re-exacerbation and re-hospitalization were reported in three studies and did not differ significantly between the treatment arms. Mortality at longest follow-up was presented in all included trials and no significant difference was found.

Findings suggest that a PCT-guided protocol may be superior to standard therapy. A PCT guided protocol significantly limits and targets the antibiotic exposure, without impacting clinical outcomes. The meta-analysis concluded PCT-guided antibiotic initiation in patients with acute COPD exacerbations was clinically safe and effective; however, confirmatory trials with rigorous methodology are required.

Impact of Procalcitonin Guidance on Management of Adults Hospitalized with Chronic Obstructive Pulmonary Disease Exacerbations[11]

A retrospective pre-/post-intervention study assessed the safety and efficacy of PCT-guided antimicrobial therapy in management of COPD exacerbations. The primary outcome was duration of antibiotic therapy for COPD exacerbation with secondary outcomes of inpatient length of stay and 30-day readmission rate. PCT guidance resulted in reduced number of antibiotic days (3 days vs. 5.3 days; P=0.01). It also resulted in reduced length of inpatient stay (4.1 days vs. 2.9 days; P= 0.01) with no difference in 30-day hospital readmission (10.8% vs. 9.4%; P=0.25).

Procalcitonin algorithm to guide initial antibiotic therapy in acute exacerbations of COPD admitted to the ICU: a randomized multicenter study[12]

A randomized, controlled, non-inferiority trial compared the efficacy of PCT-guided antibiotic therapy with standard antibiotic therapy in severe COPD exacerbations. It included 302 patients from 11 different intensive care units (ICU) in France with COPD exacerbations with or without pneumonia. Patients in the PCT-guided arm had their PCT levels measured at enrollment, 6 hours, and days 1-3 and 5 after inclusion. The primary endpoint was 3-month mortality and the secondary endpoints were in-ICU and in-hospital antibiotic exposure durations. The study also conducted post hoc subgroup analyses based on the presence or absence of antibiotic therapy at the time of inclusion. The hypothesis was that PCT-guided antibiotic therapy was non-inferior to standard therapy with respect to 3-month mortality and that PCT-guided therapy will reduce ICU and hospital antibiotic exposure.

The three month mortality was higher in the PCT arm than in the control (20% vs 14%; 90% CI -0.3 to 13.5%), and therefore, non-inferiority was not met (non-inferiority margin set to 12%). However, in patients without antibiotic use at baseline (n=119) the use of PCT-guided therapy significantly increased 3-month mortality (31% vs 12%; [90% CI 7.2 - 31.1%]; P=0.015). For patients on antibiotics at baseline (n=182), PCT-guided therapy was non-inferior in regards to 3-month mortality compared to standard therapy (11% vs 15%; [90% CI-10.6 - 4.6%]. Antibiotic exposure in-ICU and in-hospital were similar between the two study groups.

The authors concluded that this study failed to support the non-inferiority of PCT-guided therapy and also failed to reduce antibiotic exposure in-ICU and in-hospital in severe COPD exacerbations. The lack of non-inferiority is mostly due to the subgroup of patients without antibiotic use at baseline, who had higher 3-month mortality. The study advised that PCT might fail to

distinguish between infectious and non-infectious causes of acute COPD exacerbation, patients may benefit from antibiotic regardless of the cause of the exacerbation, and any delay in antibiotic prescription in such patients leads to poorer outcomes.

CRP Guided Antibiotic Therapy

C-Reactive Protein Testing to Guide Antibiotic Prescribing for COPD Exacerbations[13]

Butler et al. conducted a multicenter, open-label, randomized controlled trial that evaluated point-of care testing with CRP to decrease antibiotic use without harming patients who have acute exacerbations of COPD. A total of 653 patients with COPD exacerbation were randomly assigned 1:1 to receive CRP-guided therapy or usual care based on clinical assessment. Primary outcomes were patient reported use of antibiotics for COPD exacerbation within four weeks of randomization and COPD related health status at two weeks after randomization, as measured by Clinical COPD Questionnaire (CCQ). The CCQ is a 10 item scale evaluating COPD health status, with scores ranging from 0 (very good) to 6 (extremely poor). Secondary outcomes were the prevalence of potentially pathogenic organisms in sputum, healthcare use, COPD-related health status, and general health status at six months.

Fewer patients reported antibiotic use within four weeks after randomization in the CRP guided group (n=325) when compared to the usual care group (n=334) (57% vs 77.4%; adjusted OR 0.31; [95% CI 0.20 - 0.47]. The CRP guided group scored better on the CCQ compared to the usual group 2 weeks after randomization. The adjusted mean difference in CCQ score was -0.19 [two-sided 90% CI -0.33 - -0.05] in favor of the CRP guided group. The CCQ result indicates the reduced antibiotic use in the CRP guided group did not compromise disease specific quality of life.

When antibiotic prescribing decisions were reviewed, fewer patients in the CRP guided group received an antibiotic prescription at the initial consultation (47.7% vs 69.7%; adjusted OR 0.31; [95% Cl 0.21 - 0.45] and four weeks after consultation (59.1% vs 79.7% adjusted OR 0.30, [95% Cl 0.20 - 0.461]). Patients in the CRP guided group received 158 antibiotic prescriptions compared to 234 prescriptions in the usual care group. There were no significant differences between the two groups in the secondary outcomes.

The authors concluded that in primary care, CRP guided prescribing of antibiotic for COPD exacerbations resulted in reduced antibiotic use, with no unfavorable effect on clinical outcomes, thus indicating using less antibiotics based on a CRP-guided protocol is safe.

CRP-guided antibiotic treatment in acute exacerbations of COPD in hospital admissions (CATCH) Study[14]

A multicenter, randomized control trial was performed comparing CRP-guided and guideline based antibiotic therapy to reduce over-utilization of antibiotics in COPD exacerbations. The primary endpoint was antibiotic therapy initiated during the first 24 hours after hospital admission. Secondary endpoints were treatment failure rate at 30-days, hospital length of stay, time to re-exacerbation, and quality of life after 30 days and safety profile. Patients were randomized to receive CRP-guided antibiotic therapy if CRP ≥50 mg/L (n = 101) or guideline based antibiotic therapy (n=119).

Fewer patients in the CRP guided arm were treated with antibiotics when compared to the guideline guided arm (31.7% vs 46.2%; OR 0.178, [95% Cl 0.077 - 0.411, P=0.029]). There was no difference observed in treatment failures at 30 days or in time to first exacerbation. The study authors concluded that CRP-guided antibiotic therapy can lead to significant reduction in antibiotic use.

Clinical Application

Both PCT and CRP are useful biomarkers in reducing antibiotic use in acute COPD exacerbation. For PCT, a level of <0.25 µg/L can guide the decision to withhold antibiotics or stop therapy early. (Table 1) However, in critically ill patients in the ICU, evidence suggests that clinicians should not initially withhold antibiotics. When PCT levels drop to <0.25 µg/L or have declined by ≥80% from peak concentration, clinicians could use PCT to guide discontinuation upon patient stabilization.[7,15] When testing for PCT, timing is important. PCT levels might be low early in infection and repeating levels may be necessary. Also, PCT levels are elevated in patients with end stage renal disease due to decreased clearance and a reasonable "cutoff" suggesting active bacterial infection is ≥0.5 µg/L.[15]

CRP and PCT test should be used in conjunction with clinical judgment and shouldn't be a sole element in treatment decisions. PCT levels may be elevated due to non-bacterial causes such as in severe trauma, surgery, and burns.[16] PCT levels are also elevated in newborns less than 48 hours old.[16] CRP elevation is not specific to infection. If a patient has cancer, lupus, rheumatoid arthritis, tuberculosis and other conditions, CRP will already be elevated and it wouldn't be ideal to use CRP to help manage their coexisting COPD exacerbation.[17] CRP is also elevated during pregnancy and with the use of oral contraceptives.[17]

In summary, both CRP and PCT can be utilized to determine appropriate antibiotic use, which in turn, improves antibiotic stewardship strategies in acute exacerbation of COPD.

Table 1: CRP and PCT Values[6,7,10,12,18,19]

Biomarker	Normal value	Bacterial infection	Caveats
PCT	< 0.10 μg/L	≥0.25 μg/L	Sensitive and specific Low sensitivity for localized infection Expensive
CRP	< 10 mg/L	> 10 mg/L	Sensitive but nonspecific No correlation with severity Slower response

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PRN Member Accomplishments

Promotions:

- **Leigh Anne Gravatt:** Vice Chair of Education and Associate Professor for the Department of Pharmacotherapy and Outcomes Sciences, Virginia Commonwealth University School of Pharmacy
- **Kurt Wargo:** Promoted to Interim Dean of the Wingate University School of Pharmacy
- **Angela Miller:** Team Lead Internal Medicine Pharmacy, The University of Kansas Health System
- **Erin Hennessey**: Associate Professor, St. Louis College of Pharmacy

Awards:

- **Mate M. Soric:** Class of 2019 Most Influential Professor, Northeast Ohio Medical University and Ohio Society of Health -System Pharmacists Pharmacy Practice Research Award
- **Kathleen Adams:** Received the Brown University Department of Internal Medicine Teaching Award from the Brown University internal medicine residency program while at Rhode Island Hospital in Providence, RI.
- **Julie A. Murphy:** 2019 Outstanding Teacher of the Year, University of Toledo College of Pharmacy and Pharmaceutical Sciences
- **Julie A. Murphy:** 2019 Donald S. Parks Advisor of the Year, University of Toledo
- **Katherine L. March:** Methodist Performing Excellence Award -- Given bi-annually to select teams who have shown dedication to service, quality, innovation, teamwork, and integrity. Methodist University Hospital, Memphis, TN.
- **Ifeanyi Onor:** Lawrence Ferring Faculty Award (Best Faculty) Xavier University of Louisiana (XULA) College of Pharmacy
- **Brandon Collins:** Preceptor Merit Award – STLCOP
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Publications:

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- **Anderson SL**, Marrs JC. Can Direct Oral Anticoagulants Be Used for Stroke Prevention Among Patients with Valvular Atrial Fibrillation? Curr Cardiol Rep 2019 [In press]

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- **March KL**, **Twilla JD**, Reaves AB, et al. Lorazepam versus Chlordiazepoxide for the Treatment of Alcohol Withdrawal Syndrome and Prevention of Delirium Tremens in General Medicine Ward Patients. Alcohol. 2019 Jun 6.

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- **Smith SM**, Vickery B, Kouzi S, Patel K. Melatonin use in an inpatient academic medical center: Factors affecting provider documentation of patients' sleep quality. J Am Pharm Assoc 2019;59(4):533-538. doi 10.1016/ j.japh.2019.03.010

Other Notable Achievements:

- **Alex Ebied**: ID Stewardship Interview - Insights Into Non-Traditional Doctor of Pharmacy Programs https://www.idstewardship.com/insights-non-traditional-doctor-pharmacy-programs/

Other Notable Achievements (cont.):

- **Sarah L. Anderson:** Finalist; Next-Generation Pharmacist Health-System Pharmacist award (award winner will be announced in late October 2019)
- **Nicole Asal**: Completed year as President of the Rhode Island Pharmacists Association (2018-2019)

Congratulations to AMED's Newest ACCP Fellows

Jennie B. Jarrett

Mate M. Soric

Jennifer Twilla

Thank you to the 2018-2019 Internal Affairs Committee for their work on the spring and fall newsletters!

- Carmen Smith (chair)
- Sarah Petite (vice-chair)
- Leslie Wooten
- Casey Washington
- Kathleen Adams
- Molly Curran
- Jordan Kelley
- Alex Ebied
- Heather Kehr
- Jane Bowen
- Lauren McCluggage
- Beth Resman-Targoff
- Taylor Steuber
- Paul Wong
- Erika Lambert
- Ben Pullinger
- Stanley Luc
- Mary Shreffler

Don't forget to sign up for a PRN committee for the 2019-2020 Year!

See you in New York!