**A Message from the Chair:**

When the leaves return to the trees and the Zyrtec flies off the pharmacy shelves, we know that Spring is coming. With Spring comes the Ambulatory Care PRN newsletter! It is humbling to be leading this outstanding group of 2400+ pharmacists in the Ambulatory Care PRN. With such a large group, we have many great people helping our PRN reach its goals. For the 2015-2016 year, the PRN has 158 committee members on 11 different committees. These appointments serve a dual purpose. First, it allows our PRN the ability to accomplish the 100+ charges set forth and updated annually. Second, it affords our members the opportunity for involvement in national professional service. It is through these types of opportunities that individuals can advance towards their organizational career goals.

At the 2015 Global Conference on Clinical Pharmacy PRN Business Session in San Francisco, we discussed several intended initiatives for our PRN this year in addition to maintaining the excellence for which this PRN is already known. These initiatives include:

- Appoint a PRN liaison to the ACCP Research Institute
- Initiate an update to the Survival Guide
- Separate the Research & Scholarship committee into two committees with distinctly different charges (Research Process; Scholarly Activity)
- Add PRN Networking events at most major pharmacy conferences
- Participate in PRN website revisions per ACCP
- Develop processes for formal mentoring (particularly as it relates to students and residents)
- Re-envision member recognition
- Reach a goal of 2500 members in the PRN
- Increase the PRN members in the ACCP PBRN
- Consider a process for “tracks” in the PRN to more clearly identify organizational career paths

As you can tell, we have some lofty plans for our PRN. Some of these initiatives have already taken place. Others are well on their way to completion. A couple will be multi-year tasks that I am confident 2016-2017 officers will successfully accomplish.

This PRN is the face of Ambulatory Care in ACCP and is consistently making a national impact on Ambulatory Care in our profession.

I want to thank all of the officers, committee chairs & vice chairs, committee members, previous PRN leaders, and (most importantly) current PRN members who make me proud to call the Ambulatory Care PRN my home!

Sincerely,

Daniel M. Riche

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“\[It is unique to be a part of the leading group of Ambulatory Care pharmacists in the world... We are blessed.\]”

- Daniel M. Riche

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**In This Issue**

- 2016 ADA updates
- SGLT-2 Inhibitors and DKA
- Drug Updates: Insulin and Spiriva
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- Nasal treatment for opioid overdose
- Risks with PPI’s
- Advocacy updates
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2016 ADA Standards of Medical Care: Updates and Changes
Jaini Patel, PharmD, BCACP

The American Diabetes Association’s 2016 Standards of Medical Care in Diabetes that were released online on December 22, 2015 and were published in January 2016 issue of Diabetes Care Journal include significant changes in each of its 14 sections. It is vital to note that these changes are tailored to guide clinicians in improving care for special patient populations and utilizing patient-centered strategies. This summary will highlight new recommendations embedded in each of the sections including obesity management, use of new technology, considerations for aspirin therapy, and use of ezetimibe in select individuals.¹

Section 1: Strategies for Improving Care:

Changes in this section guide clinicians in addressing social issues, especially those barriers that are beyond patients’ control and render them vulnerable.

Food insecurity²: The revised section includes definition of food insecurity as “the unreliable availability of nutritious food and the inability to consistently obtain food without resorting to socially unacceptable practices.” Guidelines recommend that providers should refer patients to local resources to overcome barrier of food insecurity to prevent hyperglycemia and/or hypoglycemia associated with lack of access to nutritious food.

Cognitive dysfunction³: New recommendations advise against intensive glycemic control in patients with cognitive dysfunction to prevent severe hypoglycemia that could worsen cognitive function. Despite controversy around statins and dementia, guidelines recommend initiating statin therapy in high-risk patients with diabetes in spite of cognitive function.

Patients with HIV⁴: Given increased risk of diabetes development with use of protease inhibitors and nucleoside reverse transcriptase inhibitors in patients with HIV, updates in this section include screening recommendations for diabetes as well as prediabetes. A fasting plasma glucose level (FPG) should be checked prior to starting antiretroviral therapy and as a follow-up 3 months after initiation of therapy. If FPG is normal, screening should be repeated annually, however, if FPG indicates prediabetes it is recommended to monitor patient’s FPG every 3-6 months to detect progression to diabetes.

Section 2: Classification and Diagnosis of Diabetes:

Recommendations regarding diagnostic methods were worded that no one diagnostic test is preferred over another for diagnosis. Either fasting plasma glucose, 2-h plasma glucose after a 75-g oral glucose tolerance test, or A1C can be utilized for diagnosis of diabetes or prediabetes. New guidelines also recommend screening all patients over age of 45 years regardless of weight, rather than emphasizing importance of screening for overweight or obese patients as stated in 2015 guidelines. Although for patients who are asymptomatic, screening should be performed regardless of patient’s age especially if they are obese or overweight and have additional risk factors. New guidelines also include specific recommendations on management of monogenic diabetes that typically affects patients under 25 years of age.
Section 3: Foundations of Care and Comprehensive Medical Evaluation:

This is a newly combined section of two separate sections on “Initial Evaluation and Diabetes Management Planning” and “Foundations of Care: Education, Nutrition, Physical Activity, Smoking Cessation, Psychosocial Care, and Immunization” from 2015 guidelines. This new section emphasizes importance of incorporating medical evaluation and ongoing care with patient’s lifestyle habits.

Section 4: Prevention or Delay of Type 2 Diabetes:

This section recommends use of technology (i.e. smart phone apps, text messages) to promote adherence to lifestyle modifications for prevention of diabetes progression.

Section 5: Glycemic Targets:

ADA 2016 guidelines recognize the need to grant continued access to continuous glucose monitoring (CGM) for patients over 65 years of age given improved life expectancy.

Section 6: Obesity Management for the Treatment of Type 2 Diabetes:

This is a brand new section in 2016 ADA guidelines that provides clinical pearls on obesity management including weight assessment at each encounter, lifestyle interventions, considerations when choosing pharmacotherapy for diabetes management, and discussion of currently approved medications for weight-loss. Discussion of bariatric surgery was moved to this section from the “Approaches to Glycemic Treatment” section.

Section 7: Approaches to Glycemic Treatment:

There were no major changes to this section except that the discussion on bariatric surgery was removed from this section to be incorporated into Section 6.

Section 8: Cardiovascular Disease and Risk Management:

Several notable changes were made to this section as a result of new clinical evidence, specifically related to lipid management and use of antiplatelet agents.

Terminology change: Of note, the term “Atherosclerotic cardiovascular disease” (ASCVD) has been adapted in the new guidelines to represent cardiovascular disease.

Lipid Management: Recommendations on when low, moderate, or high-intensity statins are indicated based on risk of ASCVD in patients with diabetes has been included. In addition, based on clinically significant evidence from The IMProved Reduction of Outcomes: Vytorin Efficacy International Trial (IMPROVE-IT) by Cannon, et al., recommendations to add ezetimibe therapy to moderate-intensity statin for cardiovascular benefits has emerged in this revised section of the ADA 2016 guidelines. Guidelines recommend considering add-on therapy with ezetimibe in patients >40 years of age with a recent acute coronary syndrome (ACS) with LDL>50 mg/dL or in patients who are intolerant to high-intensity statin therapy. Discussion on the novel PCSK9 inhibitors is included in the revised section, however, there are no specific recommendations regarding use of these agents as phase 4 studies are ongoing and their effects on ASCVD outcomes remains uncertain at this time.

Antiplatelet agents: Recommendations for using aspirin for primary prevention have been revised based on recent clinical trials that shed light on women having equal, if not greater, cardiovascular and cerebrovascular disease risk, as men with diabetes. Previous recommendation to initiate aspirin therapy for primary prevention in women >60 years of age has now been changed to women >50 years of age with diabetes and >1 major risk factor. An additional recommendation was made to evaluate clinical risks (i.e. bleeding) and clinical benefits (i.e. primary or secondary prevention of CVD) associated with use of aspirin therapy in patients <50 years of age with multiple risk factors.
Section 9: Microvascular Complications of Foot Care:

Terminology change: Of note, the term “nephropathy” has been replaced by “diabetic kidney disease” to allow referring to kidney disease that is caused due to diabetes related complications.

Diabetic Kidney Disease: New recommendations regarding referral for evaluation for renal replacement treatment was added for patient with estimated glomerular filtration rate <30 mL/min/1.73 m².

Diabetic Retinopathy: To reflect new evidence regarding superior efficacy of intravitreal antivascular endothelial growth factor (anti-VEGF) agents over monotherapy or even combination therapy with laser in patients with center-involved diabetic macular edema, indication for use of anti-VEGF in these patients was added to the new guidelines. 18-20

Section 10: Older Adults

This section now provides in-depth, patient-centered recommendations to improve care for elderly patients with diabetes. New recommendations have been added to screen patients for neurocognitive functions to tailor self-management strategies, treatment goals, and management approaches. 21 A greater emphasis has been placed on prevention of hypoglycemia and training of long-term facilities or nursing homes staff to optimize management of elderly patients. 22 In order to preserve quality of life for elderly patients enrolled in palliative care, new recommendations are to make treatment goals for hypertension and lipid management less stringent, to the extent of withdrawing therapy if necessary.

Section 11: Children and Adolescents:

Similarly to section 10, this section now provides patient-centered recommendations to improve care for pediatric patients with diabetes by emphasizing importance to address diabetes self-management education and support, psychosocial issues, and therapeutic approaches for these youths. In regards to screening for cardiovascular risk factors, it is now recommended to obtain fasting lipid profile for children ≥10 years of age, which was previously recommended to be starting at 2 years of age.

Section 12: Management of Diabetes in Pregnancy:

Several notable revisions were made to this section of ADA guidelines.

Pregestational Diabetes: New recommendation has been added to discuss family planning and contraception with women of child-bearing age and with preexisting diabetes to ensure they are well equipped prior to becoming pregnant. 23

Gestational Diabetes: Previously targeted A1c goal of <6% has been modified to goal of 6-6.5% with recommendations to set it at <7% if necessary to prevent hypoglycemia. 24 ADA 2016 recommends use of insulin or metformin as preferred first-line treatment option for management of gestational diabetes, while deemphasizing use of glyburide given greater risks associated than benefits with its use. 25

Section 13: Diabetes Care in the Hospital:

The most notable change to this section is shift of emphasis to diabetes in the hospital setting exclusively rather than also including nursing homes and skilled nursing facility as in previous versions of the guidelines.
All of the aforementioned changes to ADA’s Standards of Medical Care in Diabetes for 2016 are intended to allow clinicians to help the most susceptible patient populations. New recommendations are tailored to disparities among individuals with diabetes to ensure disease state management is optimal, safe, and successful. As clinicians in interdisciplinary healthcare teams, pharmacists should especially implement and educate about new recommendations related to obesity management, use of antiplatelet agents, and lipid management.

References:

Sodium-glucose cotransporter 2 (SGLT2) inhibitors are the newest class of oral antidiabetic medications utilized in the treatment of Type 2 Diabetes Mellitus (T2D).1 The three FDA approved agents in this class include canagliflozin (Invokana®), dapagliflozin (Farxiga®), and empagliflozin (Jardiance®). Their mechanism of action is unique as they target the proximal tubule in the kidney to reduce the reabsorption of filtered glucose and lower the renal threshold for glucose. This results in increased urinary glucose excretion and improved plasma glucose concentrations. Clinical trials have studied SGLT2 inhibitors as monotherapy as well as in combination with other antidiabetic medications.2 The average A1C reduction seen with SGLT2 inhibitor therapy ranges from 0.5-1.0%. Common side effects seen in clinical trials include polyuria, urinary tract infections and genital mycotic infections, and symptoms relating to volume depletion such as hypotension and dizziness.

In May 2015, the FDA announced a risk of diabetic ketoacidosis (DKA) in diabetic patients treated with SGLT2 inhibitors.3 Post-marketing surveillance data gathered by the FDA revealed numerous cases of DKA, and uniquely, blood glucose was only slightly elevated compared to more traditional cases of DKA. This warning was issued after a search of the FDA Adverse Event Reporting System (FAERS) identified 20 cases of DKA or related symptoms in patients treated with SGLT2 inhibitors within a 14-month time frame. The safety announcement made no recommendations on altering the use of SGLT2 inhibitors; however, investigations continued.
Diabetic ketoacidosis is a serious and potentially life-threatening condition that is classically characterized by hyperglycemia, ketonemia, and metabolic acidosis. Hyperglycemia is often defined as a plasma glucose greater than 250 mg/dL; however, it can often be markedly higher. Alternatively, significant elevations in plasma glucose are typically not seen in patients receiving SGLT2 inhibitors; and therefore, cases of DKA may not be initially diagnosed causing subsequent deterioration of the patient. It is theorized that euglycemic DKA developed with SGLT2 inhibitors is associated with above average renal glucose clearance, a milder insulin deficiency and insulin resistance, as well as decreased gluconeogenesis. These components prevent extreme hyperglycemia often associated with traditional DKA.

Large clinical trials have reported a low incidence of DKA with concurrent SGLT2 inhibitor treatment. The estimated incidence was 0.8 per 1000 patient-years with canagliflozin (300 mg dose) as reported by Janssen, the manufacturer of canagliflozin. A review article published in late 2015 cites over 30 individual cases of DKA published recently; however, this data includes both Type 1 and Type 2 DM patients. Use of SGLT2 inhibitors in Type 1 DM patients is used as off-label treatment, and may contribute to the higher incidence of DKA seen with these agents.

Ongoing FDA post-marketing surveillance and analysis recently resulted in an update to the SGLT2 inhibitors’ product labeling, with the addition to the “Warnings and Precautions” section of each drug’s labeling stating a risk of ketoacidosis. Additional review of FAERS data found 73 cases of ketoacidosis from March 2013 to May 2015. Detailed review of individual cases identify several factors that may contribute to the risk of developing DKA, including reductions in insulin dosage, decreased caloric or fluid intake, onset of illness, surgery, and use of alcohol. In addition, some T2DM patients who developed DKA on SGLT2 inhibitors were later identified as having latent autoimmune diabetes.

It is recommended that patients stop the SGLT2 inhibitor if symptoms of ketoacidosis develop, which include nausea, vomiting, abdominal pain, and fatigue. Practitioners should be aware of this possible risk of DKA in Type 2 DM patients being treated with SGLT2 inhibitors, to allow for quick diagnosis and treatment to prevent further complications.

References
Insulin Degludec: Two New Drug Treatment Options for Diabetes Mellitus
Sweta M. Patel, PharmD, BCPS

In September 2015, the U.S. Food and Drug Administration approved Tresiba® (insulin degludec) and Ryzodeg 70/30® (insulin degludec/insulin aspart) in adults with type 1 and type 2 diabetes mellitus (DM). Insulin degludec is a long-acting human insulin analog with an onset of 1 hour, time to peak of 9 hours and elimination half-life of 25 hours. Tresiba® and Ryzodeg 70/30® are administered subcutaneously once daily at any time of day and once or twice daily, respectively.

For insulin-naive type 1 and 2 DM patients, insulin degludec is initiated at one-third to one-half of total daily insulin dose and 10 units once daily, respectively. For insulin-experienced type 1 and 2 DM patients, insulin degludec is initiated at the same unit dose as the total daily long or intermediate-acting insulin unit dose. Tresiba® is available as 100 units/mL (U-100) and 200 units/mL (U-200) 3 mL FlexTouch pens. Ryzodeg 70/30® is currently not available in the U.S. markets.

The efficacy and safety of Tresiba® and Ryzodeg 70/30® used in combination with mealtime insulin were evaluated in 1464 type 1 DM patients and with either mealtime insulin or as an add-on to common oral agents (metformin, DPP-4 inhibitors, sulfonylureas, etc.) in 3700 type 2 DM patients. In Tresiba® and Ryzodeg 70/30® trials, they provided similar HbA1c reductions to that of other long-acting or pre-mixed insulins. The most common adverse reactions seen in clinical trials were hypoglycemia, allergic reactions, injection-site reactions, lipodystrophy, pruritus, rash, edema and weight gain. Some studies have demonstrated less hypoglycemic events with the use of insulin degludec compared to other long-acting insulins.

Insulin degludec offers another long-acting insulin option for patients with type 1 or 2 DM. Given its ultra-long duration of action, it allows for a more flexible treatment schedule compared to other long-acting insulins in patients with history of non-compliance secondary to strict treatment schedule. This makes it more convenient for these patients to adhere to their insulin therapy, which may potentially lead to improved clinical outcomes. Additionally, insulin degludec may be beneficial in patients with high risk of hypoglycemia however, long-term studies are needed to evaluate its continued efficacy and safety.

References:
Tiotropium, a long acting muscarinic antagonist (LAMA), is currently available in two different formulations: Spiriva® HandiHaler® - dry powder inhaler and Spiriva® Respimat® - mist inhaler. Both formulations have long been approved for their use in COPD. In September 2015, the FDA approved Spiriva® Respimat®, for the for once-daily, long-term, maintenance treatment of asthma in patients ≥ 12 years of age. The recommended dose is 2 inhalations once daily, but unlike the COPD formulation which delivers 2.5 mcg tiotropium per actuation, the recommended dose/formulation for asthma treatment delivers 1.25 mcg tiotropium per actuation.¹

Tiotropium competitively but reversibly inhibits acetylcholine action at the muscarinic type 3 receptors in the bronchial smooth muscles leading to bronchodilation. The bronchodilator effects are apparent after the 1st dose, but maximum benefit in lung function is not detected until after 4 to 8 weeks of therapy.

The 2016 Global Strategy for Asthma Management and Prevention suggests using tiotropium mist inhaler in persistent asthma as an add-on treatment for patients ≥ 12 years of age with a history of exacerbations despite using ICS ± LABA.² Several studies and a meta-analysis show that adding tiotropium to low to medium dose ICS therapy was better than placebo and non-inferior to addition of LABA.3-5 When added to high dose ICS and LABA combination therapy in patients with at least one severe exacerbation in the past year, tiotropium showed improved lung function and greater mean change in FEV1 than placebo.6 Upper respiratory infections such as sinusitis and bronchitis, sore throat, and headache occurred with an incidence more than 2% in clinical trials.¹

Tiotropium should not to be used as a first line treatment for the treatment of asthma. For uncontrolled asthma, the preferred, first-line choice is the addition of a LABA to low dose ICS.² Then, if further control is desired, the ICS should be increased to high dose. The addition of tiotropium can be considered if a patient’s asthma symptoms remain uncontrolled with a LABA and high dose ICS regimen.³,⁴ Alternatively, tiotropium could be added to an ICS only regimen if the patient is unable to use LABA treatment.³,⁴

References:
The newest class of oral anti-hyperglycemic medications, the SGLT2 inhibitors, have generated a great deal of interest from both patients and providers. Results from the EMPA-REG OUTCOME study, which will be reviewed here, indicate that empagliflozin (Jardiance®) may be associated with a significant mortality benefit. However, clinical trial and post-marketing data have revealed some potentially significant underlying safety concerns related to bone mineral density loss and euglycemic DKA in addition to the well-documented increase in genitourinary infections.

The EMPA-REG OUTCOME study was a multicenter, international randomized, double-blind, placebo-controlled trial. This trial sought to identify the effect of 10 mg and 25 mg empagliflozin (pooled data) vs. placebo in patients with T2DM and existing high-risk cardiovascular (CV) events. Qualifying CV events included myocardial infarction (MI), multi-vessel coronary artery disease (CAD), single-vessel CAD with ≥50% occlusion, unstable angina, stroke, and/or occlusive peripheral artery disease (PAD). Mean baseline characteristics were balanced between the empagliflozin and placebo treated groups. On average, patients were 63 years old, 72% white, and 72% male, with a mean baseline hemoglobin A1C of 8%. More than half of patients had been diagnosed with T2DM for more than 10 years prior to enrollment and were taking various combinations of glucose-lowering therapy. A total of 7020 patients were included, with a median treatment period of 2.6 years and median observation time of 3.1 years.

During the initial 12-week active treatment period, changes to baseline diabetes medications were discouraged unless medically necessary or in the case of a confirmed fasting blood glucose (FBG) >240 mg/dL. After week 12, investigators were encouraged to target glycemic goals per “local guidelines”. Treatment of CV risk factors was encouraged throughout the trial.

Figure 1: Absolute incidence rate reductions by group

<table>
<thead>
<tr>
<th></th>
<th>Placebo (N = 2333) Rate/1000 patient-years</th>
<th>Empagliflozin (N = 4687) Rate/1000 patient-years</th>
<th>Rate difference (95% CI)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cardiovascular death, non-fatal MI, or non-fatal stroke (3-point MACE): primary outcome</td>
<td>43.9</td>
<td>37.4</td>
<td>-6.5 (-12.6, -0.4)</td>
<td>0.04</td>
</tr>
<tr>
<td>All-cause mortality</td>
<td>28.6</td>
<td>19.4</td>
<td>-9.1 (-13.8, -4.5)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Cardiovascular death</td>
<td>20.2</td>
<td>12.4</td>
<td>-7.7 (-11.6, -3.9)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Hospitalization for heart failure</td>
<td>14.5</td>
<td>9.4</td>
<td>-5.1 (-8.4, -1.8)</td>
<td>0.003</td>
</tr>
<tr>
<td>Heart failure hospitalization or cardiovascular death (excluding fatal stroke)</td>
<td>30.1</td>
<td>19.7</td>
<td>-10.5 (-15.3, -5.6)</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>
The primary outcome was the composite of death from any cardiovascular cause, nonfatal MI, and nonfatal stroke. Key secondary outcomes included all-cause mortality and heart failure-related hospitalizations. Outcomes that showed statistical significance in favor of empagliflozin compared to placebo were: the primary composite outcome (both non-inferiority \( p<0.001 \) and superiority \( p=0.04 \)), all-cause mortality (\( p<0.001 \)), CV-related mortality (\( p<0.001 \)), and hospitalizations for heart failure (\( p=0.002 \)). There were no significant differences found in the occurrence of MI, stroke, or hospitalizations for unstable angina. Subgroup analyses demonstrated a significant benefit of empagliflozin on CV-related mortality in all subgroups.

The proportion of patients experiencing adverse events, serious adverse events, and adverse events leading to discontinuation of the study drug was similar between groups. There was a higher incidence of genital infection and urosepsis reported in the pooled empagliflozin group, but the proportion of patients with confirmed hypoglycemic events, acute renal failure, diabetic ketoacidosis, thromboembolic events, bone fracture, and events consistent with volume depletion were similar in the two study groups.

The results from the EMPA-REG OUTCOME study are undeniably impressive; it is the first post-marketing clinical trial to show cardiovascular benefit with a glucose-lowering medication in patients with T2DM and CVD. However, the mechanism of how empagliflozin decreases all cause and cardiovascular mortality is unclear. The EMPA-REG OUTCOME study authors speculate that the mechanism is likely multifactorial. Notably, the favorable outcomes appear to be independent of glycemic control, with only small differences in hemoglobin A1C observed between the empagliflozin groups and the placebo group at study end (-0.24% with empagliflozin 10 mg, -0.36% with empagliflozin 25 mg) One proposed mechanism is related to the diuretic effect of the SGLT2 inhibitors. The diuretic effect may help alleviate volume overload, which can contribute to CV death/hospitalization in the heart failure population. This would potentially explain the 35% reduction in heart failure-related hospitalizations. In the EMPA-REG study fewer patients in the empagliflozin group (16.2%) compared to placebo (22.7%) were started on diuretics post-randomization.

The question of whether or not this is a class effect is also still unclear. Ongoing clinical trials (CANVAS, DECLARE-TIMI58) to assess the impact of canagliflozin and dapagliflozin on CVD will hopefully provide insight on the consistency and mechanism of cardiovascular benefit with SGLT-2 inhibitors.

Finally, despite the good tolerability observed in the EMPA-REG OUTCOME trial there are serious adverse events associated with SGLT-2 inhibitor use, such as genital infections, dehydration, a class-warning on ketoacidosis and an agent-specific warning on bone loss with canagliflozin, which merit a cautious assessment of risks versus benefits for each individual patient.

Reference:

Hypertension predisposes patients to an increased risk of myocardial infarction, stroke, renal failure and death. According to the CDC, approximately one of every three Americans suffers from hypertension, making it one of the most common diseases seen in primary care. Medical professionals continue to debate the ideal blood pressure goal that will provide the most benefit and the least amount of harm. In 2014, the Joint National Committee released new recommendations which relaxed some of the blood pressure targets identified in the committee’s previous guidelines. However, since the publication of this guideline, new research has been published which necessitates further consideration.

The SPRINT trial, published by the New England Journal of Medicine in 2015, was a multi-centered, randomized, open-label study which examined whether a systolic blood pressure (SBP) target of less than 120 mmHg (intensive-treatment) was superior to a SBP target of less than 140 mmHg (standard-treatment). A total of 9,361 patients underwent randomization and were followed for a maximum of 6 years. Patients 50 years of age or older with a SBP of 130-180 mmHg who were at increased risk of cardiovascular events were included in the study. Patients with diabetes, previous stroke, and advanced renal failure were excluded. Blood pressure medications were titrated monthly for the first three months, and every three months thereafter based on the pre-specified treatment algorithms. The primary outcome was a composite of myocardial infarction, acute coronary syndrome not resulting in myocardial infarction, stroke, acute decompensated heart failure, and death from cardiovascular causes. Secondary outcomes included any individual components of the primary outcome, death from any cause, and a composite of both.

The mean SBPs achieved within the intensive- and the standard-treatment groups were 121.4 mmHg and 136.2 mmHg, respectively. Patients in the intensive-treatment group required one more medication on average than the standard-treatment group (mean 2.8 vs. 1.8). Researchers terminated the SPRINT trial early (after 3.26 years) due to superior outcomes in the intensive-treatment arm. Two hundred forty-three patients in the intensive group experienced the primary outcome compared to 319 in the standard group (HR 0.75; 95% CI, 0.64-0.89; p<0.001). Additionally, 155 patients in the intensive group died versus 210 deaths in the standard group (HR 0.73; 95% CI, 0.6-0.9; p=0.003). For the primary outcome and death, the number needed to treat was 61 and 90 patients respectively, for a follow-up of 3.26 years.

When examining the adverse effects associated with each group, there were no statistically significant differences between the number of serious adverse effects reported. Hypotension, syncope, electrolyte abnormalities, and acute kidney injury occurred more frequently in the intensive group. More importantly, there was a statistically significant increase in the number of patients who experienced a reduction in estimated glomerular filtration rate of ≥30 but < 60 mL/min/1.73m² (HR 3.49; 95% CI; 2.44-5.10; p <0.001). Interestingly, orthostatic hypotension occurred significantly less often in the intensive group.

The authors concluded that targeting a SBP of <120 mmHg in non-diabetic patients aged 50 and older resulted in reduced cardiovascular morbidity and mortality. However, targeting a lower SBP may also result in an increased risk for adverse events.

The strengths of the SPRINT trial were the study’s design, large population, and selection of outcomes. One of the limitations of the study is that the mean SBP in the intensive-treatment group failed to meet the goal of <120 mmHg.
Additionally, based on the algorithm, patients in the standard-treatment group experienced step-down of therapy, including discontinuation of medications which may have provided cardiovascular benefit had they been continued. It is also pertinent to remember that patients with diabetes, stroke, and those less than 50 years of age were excluded.

Although the authors point to a 25% relative risk reduction in the primary outcome, it is important to consider that the absolute risk reduction is only about 1.6%. Similarly, the absolute risk reduction of all-cause mortality stands at approximately 1.2%. We also must consider that targeting a lower SBP will require, on average, an additional blood pressure agent resulting in an increased cost to the patient in the form of medication cost as well as an increased number of office visits and more intensive monitoring. Practitioners must weigh the benefits against the increased risk of side effects. The results of the SPRINT trial will undoubtedly be incorporated into the next guideline for the treatment of hypertension; but the exact recommendations that can be taken from this trial remain ambiguous. It is our duty as ambulatory care pharmacists to critically evaluate this trial in order to provide the maximum benefit to our patients.

References:

**Naloxone (Narcan®) Nasal Spray for Opioid Overdose**

Chyrstian Pereira, Pharm.D. BCPS

The FDA recently approved the use of a naloxone nasal spray (Narcan®) for the treatment of opioid overdose. Naloxone is a competitive opioid antagonist which can stop or reverse the effects of an opioid overdose; it has no agonist activity in the CNS. In response to the increased rates of overdose from heroin and other prescription opioids, this product received a fast track and priority review from the FDA. Naloxone, which has long been available in injectable form (IV or IM) is one of the vital tools for first responders. Prior to the recent approval of Narcan® nasal spray (0.4mg/0.1mL; Adapt Pharma), intranasal naloxone was used off-label via an atomizer device. The new Narcan® nasal spray does not require assembly and it can administered by anyone, even those without medical training. The simplified instructions and ease of use give this new formulation an advantage over the atomizer.

In clinical trials, delivering naloxone intranasally achieved the same or slightly higher serum concentrations when compared to the IM route. The nasal formulation has a slightly longer time to effect compared to other formulations. For the reversal of respiratory depression or sedation, the time to effect was 1-2 min, 2-5 min, and 8-13 minute for the IV, IM, and intranasal routes respectively.

The primary adverse effect for this product is the resulting acute withdrawal symptoms in opioid-dependent patients. These symptoms may present as anxiety, piloerection, yawning, sneezing, rhinorrhea, nausea, increased blood pressure, headache, and musculoskeletal pain.

Narcan® nasal spray is available now. The estimated cash price of one package of two 4 mg nasal sprays is ~$130.

References:
The availability of direct oral anticoagulants (DOACs) has added more options for venous thromboembolism (VTE) treatment including deep vein thrombosis (DVT) and pulmonary embolism (PE). However, until recently, DOACs were not recommended for VTE treatment by the American College of Chest Physicians (CHEST) guidelines. In the 9th edition of the Antithrombotic therapy for VTE disease in CHEST guidelines, vitamin K antagonists (VKA) or low-molecular-weight heparin (LMWH) was suggested over DOACs for long-term anticoagulant therapy.¹ This recommendation was made due to lack of evidence comparing DOACs with LMWH.² Since the release of the 9th edition, there have been randomized trials comparing a DOAC with or without initial heparin therapy with VKA therapy for both acute and long-term treatment of VTE, which is defined as 3 months. The results of these trials show an overall moderate to high quality level of evidence for both efficacy and safety. Additionally, the extensive clinical experience using DOACs in patients with VTE has led to an updated recommendation in the 10th edition of the Antithrombotic therapy for VTE disease in the CHEST guidelines. For VTE in patients who do not have cancer, as long-term anticoagulant therapy, dabigatran, rivaroxaban, apixaban, or edoxaban is suggested over VKA therapy, and VKA therapy is suggested over LMWH according to the updated CHEST guidelines. This summary will review the randomized clinical trials which led to this update and discuss important considerations when using DOACs for patients with acute VTE.

Dabigatran was compared to warfarin for symptomatic treatment of acute VTE in two trials, RE-COVER and RE-COVER II.³⁴ All patients received initial parenteral anticoagulation with LMWH or unfractionated heparin (UFH) for 5-11 days then dabigatran 150 mg bid or warfarin targeted to INR 2-3. The trials show that parenteral heparin followed by dabigatran was as effective as heparin overlapped and followed by warfarin. There was no significant difference in the incidence of major bleeding. However, in the RE-COVER trial, approximately one-fourth of all bleeding events with dabigatran were gastrointestinal. Edoxaban was compared to warfarin for treatment of acute VTE in the Hokusai-VTE trial.⁵ All patients received initial parenteral anticoagulation with LMWH or UFH for at least 5 days then edoxaban 60 mg daily or warfarin targeted to INR 2-3. This trial shows that parenteral heparin followed by edoxaban is as effective as heparin overlapped and followed by warfarin and leads to significantly lower incidence of major or non-major clinically relevant bleeding. Rivaroxaban was compared to warfarin for treatment of acute VTE in two trials, EINSTEIN DVT (confirmed proximal DVT without symptomatic PE) and EINSTEIN PE (confirmed acute symptomatic PE with or without DVT).⁶⁷ Patients received rivaroxaban 15 mg bid for 3 weeks followed by 20 mg daily or subcutaneous enoxaparin plus VKA. These trials show rivaroxaban is as effective as enoxaparin/VKA. There was no significant difference in major or non-major clinically relevant bleeding. However, EINSTEIN PE shows rivaroxaban leads to a significant reduction in major bleeding. Apixaban was compared to warfarin for treatment of acute VTE in the AMPLIFY trial.⁸ Patients received apixaban 10 mg bid for 7 days followed by 5 mg bid or subcutaneous enoxaparin plus VKA. The trial shows apixaban is as effective as enoxaparin/VKA. There was a significantly lower incidence of major and non-major clinically relevant bleeding with apixaban. Overall, DOACs demonstrate comparable efficacy and bleeding risk compared to VKA therapy among patients with acute symptomatic VTE.
While the DOACs have been studied extensively in clinical trials and the results demonstrate efficacy and safety in patients with proximal DVT of the lower limb or hemodynamically stable PE, there are many specific subgroups that were excluded or underrepresented. Exclusion criteria varied slightly among the trials, but in general, important exclusion criteria to consider include need for thrombolytic therapy, clinically significant liver disease (acute or chronic hepatitis or cirrhosis), creatinine clearance <30 mL/min (<25 mL/min for apixaban), aspirin use >100 mg/day, and interacting medications. Other considerations include differences in drug characteristics and factors that may influence which oral anticoagulant (OAC) is selected for initial and long-term treatment of VTE (see table 1). The updated CHEST guideline suggests VKA as the preferred agent in renal disease and creatinine clearance <30 mL/min and in patients with poor compliance unless compliance is not expected to be an issue with a DOAC. In summary, DOACs offer patients, physicians, and healthcare systems effective, safe, and convenient treatment for acute VTE. However, there are many considerations that must take place when deciding which patients are good candidates for DOAC therapy and when deciding on which DOAC to select for acute treatment of VTE.

Table 1:

<table>
<thead>
<tr>
<th>Trial</th>
<th>RE-COVER I &amp; II</th>
<th>EINSTEIN DVT &amp; PE</th>
<th>AMPLIFY</th>
<th>Hokusai VTE</th>
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<tbody>
<tr>
<td>Drug</td>
<td>Dabigatran</td>
<td>Rivaroxaban</td>
<td>Apixaban</td>
<td>Edoxaban</td>
</tr>
<tr>
<td>Study duration</td>
<td>6 mo</td>
<td>3, 6, or 12 mo</td>
<td>6 mo</td>
<td>≤ 12 mo</td>
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<tr>
<td>Patients, n</td>
<td>5153</td>
<td>8282</td>
<td>5395</td>
<td>8292</td>
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</table>

<table>
<thead>
<tr>
<th>Recurrent VTE, %</th>
<th>D</th>
<th>W</th>
<th>R</th>
<th>W</th>
<th>A</th>
<th>W</th>
<th>E</th>
<th>W</th>
</tr>
</thead>
<tbody>
<tr>
<td>HR (95% CI)</td>
<td>2.4</td>
<td>2.2</td>
<td>2.1</td>
<td>2.3</td>
<td>2.3</td>
<td>2.7</td>
<td>1.6 †</td>
<td>1.9 †</td>
</tr>
<tr>
<td>Major bleeding, %</td>
<td>1.4</td>
<td>2.0</td>
<td>1.0</td>
<td>1.7</td>
<td>0.6</td>
<td>1.8</td>
<td>1.4</td>
<td>1.6</td>
</tr>
<tr>
<td>HR (95% CI)</td>
<td>0.73 (0.48-1.11)</td>
<td>0.54 (0.37-0.79)</td>
<td>0.31 (0.17-0.55) †</td>
<td>0.84 (0.59-1.21)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Major + CRNMB, %</td>
<td>5.3</td>
<td>8.5</td>
<td>9.4</td>
<td>10.0</td>
<td>4.3</td>
<td>9.7</td>
<td>8.5</td>
<td>10.3</td>
</tr>
<tr>
<td>HR (95% CI)</td>
<td>0.62 (0.50-0.76)</td>
<td>0.93 (0.81-1.06)</td>
<td>0.44 (0.36-0.55) †</td>
<td>0.81 (0.71-0.94)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

A = apixaban; CI = confidence interval; CRNMB = clinically relevant nonmajor bleeding; D = dabigatran; E = edoxaban; HR = hazard ratio; PE = pulmonary embolism; VTE = venous Thromboembolism; and W = warfarin. *Relative risks are reported for the AMPLIFY study. † Recurrent VTE during on-treatment period.


Table 2:

<table>
<thead>
<tr>
<th>DOAC</th>
<th>Parenteral lead-in</th>
<th>Single-drug approach</th>
<th>Switch or Dose de-escalation</th>
<th>Dosing frequency</th>
<th>Renal elimination</th>
<th>Potential for ADE’s</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dabigatran</td>
<td>X</td>
<td></td>
<td>X</td>
<td>BID</td>
<td>++++</td>
<td>MI, GIB, dyspepsia</td>
</tr>
<tr>
<td>Rivaroxaban</td>
<td>X</td>
<td></td>
<td>X</td>
<td>BID x 21 days, then daily</td>
<td>++</td>
<td>GIB</td>
</tr>
<tr>
<td>Apixaban</td>
<td>X</td>
<td></td>
<td>X</td>
<td>BID</td>
<td>+</td>
<td>N/A</td>
</tr>
<tr>
<td>Edoxaban</td>
<td>X</td>
<td></td>
<td>X</td>
<td>daily</td>
<td>++</td>
<td>N/A</td>
</tr>
</tbody>
</table>
Proton pump inhibitors (PPIs) are used to treat a variety of gastrointestinal (GI) disorders such as gastroesophageal reflux disease (GERD), erosive esophagitis, gastric and duodenal ulcers, and eradication of H. pylori infection. They are also commonly used for stress ulcer prophylaxis and prevention of NSAID-induced ulcers. PPIs are one of the most commonly prescribed drug classes with Nexium (esomeprazole) being the 3rd most prescribed drug this past year. However, PPIs are overprescribed and between 53% and 69% of PPI prescriptions were found to be for inappropriate indications. With short-term use, they are generally safe and well tolerated, but studies have brought light to safety concerns, especially with long-term use.

Dementia

One of the most recently published associated risks with PPIs has been dementia. Researchers have found that PPIs can potentially affect amyloid metabolism by enhancing the amyloid beta peptide production which plays a major role in the pathogenesis of Alzheimer’s disease. In addition, vitamin B12 deficiency has also been an associated risk of PPIs, which has been reported to be associated with cognitive decline. Similar to the United States, Germany experienced a fourfold increase in the prescription rate over 10 years and 40–60% of all PPI prescriptions were identified as inappropriate. In 2015, the German Study on Aging, Cognition and Dementia in Primary Care Patients (AgeCoDe) found of 2,911 primary care patients 75 years of age or older, the use of PPI medication had a significantly increased risk of any dementia [Hazard ratio (HR) 1.38, 95 % confidence interval (CI) 1.04–1.83] and Alzheimer’s disease (HR 1.44, 95 % CI 1.01–2.06) compared with nonusers. Then in 2016, Gomn et. al. published a prospective cohort study of 73,679 patients 75 years of age or older and free from dementia at baseline using observational data from the largest German insurer which covers half of its elderly people. Finding similar results compared to the AgeCoDe study, the patients receiving regular PPI use (n = 2950; mean [SD] age, 83.8 [5.4] years; 77.9%female) had a significantly increased risk of incident dementia versus the patients not receiving PPIs (n = 70 729; mean [SD] age, 83.0[5.6] years; 73.6%female) (hazard ratio, 1.44 [95%CI, 1.36-1.52]; P < .001). While the study by Gomen et. al. is significantly larger, they were not able to control for as many variables and cofounders such as amyloid deposition. Consideration should also be given to factors that play a role in PPI use may also be linked to the factors that play a role in risk of dementia; for example, obesity, alcohol consumption, and poorer health and education. These studies show an association between PPI use and risk of dementia but randomized, prospective trials would be needed to establish a causal relationship.

Kidney Disease

PPIs have also been associated with acute interstitial nephritis and acute kidney injury, but most recently have also been reported to be associated with chronic kidney disease (CKD). Lazarus et. al. reports that baseline use of PPIs was independently associated with a 20% to 50% higher risk of incident CKD, after adjusting for several potential confounding variables, including demographics, socioeconomic status, clinical measurements, prevalent comorbidities, and concomitant use of medications. Data was first collected from the Atherosclerosis Risk in Communities (ARIC) cohort, which followed 10,483 patients for a median of 13.9 years. There were 56 incident CKD events among the 322 baseline PPI users (14.2 per 1,000 person years), and 1,382 events among 10,160 baseline non-users (10.7 per 1,000 person-years) with similar results after adjusting for confounding variables (HR, 1.50; 95%CI, 1.14-1.96; P = .003). The results were then validated in the Geisenger Health System cohort of 248,751 patients followed for a median of six years.
In this second cohort, there were 1,921 incident CKD events among 16,900 baseline PPI users (20.1 per 1000 person-years) and 28,226 events among 231,851 baseline nonusers (18.3 per 1,000 person-years). The observational study also found that twice a day PPI use (adj HR, 1.46; 95% CI, 1.28-1.67) was associated with a higher risk compared to once a day use (adj HR, 1.15; 95% CI, 1.09-1.21). While observational studies have their limitations and cannot show a cause and effect relationship, this large observational study shows a significant association of PPI use and the risk of CKD which provides further safety concern with the overuse and inappropriate prescribing of PPIs.\textsuperscript{13,14}

Other Associated Risks

Over the past several years the FDA has made announcements regarding the associated effects of PPIs based on observational studies (Table 2.).\textsuperscript{15}

**Table 2.** FDA Drug and Safety announcements regarding the PPI medication class

<table>
<thead>
<tr>
<th>FDA Drug Safety Communication</th>
<th>Release Date</th>
</tr>
</thead>
<tbody>
<tr>
<td>PPIs may be associated with an increased risk of <em>Clostridium difficile</em>–associated diarrhea (CDAD)</td>
<td>2/8/2012</td>
</tr>
<tr>
<td>PPI drugs may cause low serum magnesium levels (hypomagnesemia) if taken for prolonged periods of time (in most cases, longer than one year)</td>
<td>3/2/2011</td>
</tr>
<tr>
<td>Possible increased risk of fractures of the hip, wrist, and spine with high doses or long-term use of proton pump inhibitors</td>
<td>5/25/2010</td>
</tr>
</tbody>
</table>

FDA also announced in 2009 and in 2010 against the concurrent use of omeprazole and esomeprazole with clopidogrel as they’ve been found to decrease antiplatelet activity by 20% to 40%.\textsuperscript{1,18-17} As PPIs inhibit cytochrome P450 2C19 (CYP2C19), especially omeprazole, it can prevent clopidogrel from being metabolized to its active form.\textsuperscript{17} The GERD guidelines by the American College of Gastroenterology recommend PPI therapy does not need to be altered in concomitant clopidogrel users as there does not appear to be an increased risk for adverse cardiovascular events (Strong recommendation, high level of evidence), highlighting findings from clinical trials and meta-analysis.\textsuperscript{18} However, given the mixed evidence, the American College of Cardiology and the American Heart Association suggest that physicians prescribe drugs other than PPIs, such as histamine H2 antagonists for patients taking aspirin and clopidogrel who require gastroprotection.\textsuperscript{17,19} If a PPI is needed, pantoprazole may be preferred given the lower potential to inhibit CYP2C19.\textsuperscript{19}

The GERD Guidelines also mention that short-term PPI usage may increase the risk of community-acquired pneumonia (CAP), but that the risk does not appear elevated in long-term users (conditional recommendation, moderate level of evidence).\textsuperscript{18} Since the guidelines were published in 2013, there has been a meta-analysis published by Filion et. al. in 2014 that concluded PPIs did not increase the risk of hospitalization for CAP (adjusted OR=1.05; 95% CI 0.89 to 1.25).\textsuperscript{20} However, a meta-analysis published in 2015 concluded PPI use is associated with a 1.5-fold increased risk of CAP, with the highest risk within the first 30 days after initiation of therapy.\textsuperscript{21} Thus, as the association with PPIs and increased risk of CAP remains unclear, caution should be used and risks versus benefits should be weighed with each patient.
Conclusion

While PPIs are used to effectively treat a variety of GI disorders there have been studies showing associated increase risk of certain infections, hypomagnesemia, fractures, and most recently, dementia and kidney disease. Inappropriate PPI use should be discontinued but rebound hypersecretion can be common with symptoms that can last for months. Therefore, it may be helpful to taper patients off PPIs by first reducing the dose and then dosing every other day for a week or longer. Patients can use histamine-2 (H2) blocker for breakthrough symptoms for GERD as needed. To help prevent associated risks, pharmacists can help evaluate the appropriateness and management of patients’ PPI (e.g. indication, duration, dose, tapering, etc.) Pharmacist can also help educate patients on appropriate OTC use as well as non-pharmacological options.

References:


As the second session of the current Congress moves towards the fall elections, ACCP’s Government Affairs and policy staff continues to work diligently on several advocacy efforts to improve chronic care management for Medicare beneficiaries. The Ambulatory Care PRN Advocacy Committee recently spoke with John McGlew, Director of Government Affairs for ACCP, and was encouraged by the demonstrated commitment to legislation that provides opportunities for comprehensive clinical pharmacy services. Although Mr. McGlew expressed realistic expectations in regards to legislation being passed with this Congress due to the upcoming election season, the continued support and discussion is promising and provides momentum to continue these efforts with the next Session of Congress.

ACCP’s Washington office was recently contacted by House Representatives Erik Paulsen (R-MN-3) and Peter Welch (D-VT-At Large) about introducing H.R. 3890, the Better Care, Lower Cost Act, aimed at improving the care for chronically ill Medicare beneficiaries and reform the fee-for-service system to facilitate team-based care. This bill includes pharmacists as eligible members of the proposed “Better Care Practices” that will expand opportunities for Medicare beneficiaries to participate in integrated care delivery models, but does not specify the exact role of pharmacists within these teams. Within its letter of support for the legislation, ACCP urged the Congressmen to include coverage for comprehensive medication management (CMM) as part of the effort. This would more clearly define how pharmacists might contribute as members of inter-professional teams to enhance quality and affordability of services provided to Medicare beneficiaries. You can click here to read the ACCP comments in full.

In the Senate, Johnny Isakson (R-GA) and Mark Warner (D-VA) are leading a bipartisan Congressional working group to begin exploring solutions to support and improve chronic disease state management for Medicare beneficiaries. In response to the Senators call to healthcare stakeholders, ACCP recommended that the working group focus on care delivery models that promote and incentivize a patient-centered, inter-professional approach to medication related clinical care and medication safety. These models would help achieve medication-related outcomes that align with patients’ overall care plans and goals of therapy through the provision of CMM. Within broader payment reform efforts, ACCP urged Congress to enact reforms to the Medicare Part B program for coverage of CMM services provided by qualified clinical pharmacists as members of the health care team.
Last spring, ACCP, in collaboration with the College of Psychiatric and Neurologic Pharmacists (CPNP), extended an offer to the Finance Committee to provide further information, data, and connections with successful practices that provide CMM services. Again, you can [click here](http://www.accpaction.com/signin/index.aspx) to read the ACCP/CPNP comments in full.

The Ambulatory Care PRN Advocacy Committee aims to keep members informed of legislative issues utilizing the PRN’s list-serve, newsletter, and business meetings and to enable members to self-advocate for pertinent legislative issues at the local and state level. Members of the Ambulatory Care PRN can stay updated with ongoing efforts from the Advocacy Committee through:

- Monthly emails regarding updates on legislative issues that affect ambulatory care pharmacists
- Interactive webinars in the spring and fall; planned speakers include a PRN member involved in advocacy efforts at the state level and John McGlew
  - May: State level advocacy
  - September: Federal updates and preparing for a new election season - what you need to know
- YouTube video on how to navigate the Legislative Action Center (You can [click here](http://www.accpaction.com/signin/index.aspx) to view the video in full or access it via the Ambulatory Care PRN’s Facebook page)
- Twitter chat on legislative updates and discussions

The Advocacy Committee is very pleased with ACCP’s ongoing efforts and dedication to legislation that provides opportunities for comprehensive clinical pharmacy services. Last year, Ambulatory Care PRN members donated $585 to the Political Action Committee (PAC) to support ACCP’s goal of CMM legislation, which would recognize pharmacists as providers under CMS. The PRN placed 10th out of 17 PRNs in the annual ACCP-PAC PRN Participation Challenge. This year, the Advocacy Committee strives to improve support and contributions and finish in the top 3! Remember this competition is based on participation and not dollar amount donated. We encourage you to make your donation to support our PRN and our profession today! [http://www.accpaction.com/signin/index.aspx](http://www.accpaction.com/signin/index.aspx).
Upcoming Events:

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<th>Date(s)</th>
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<td>2016 ACCP Virtual Poster Symposium</td>
<td>May 18—19, 2016</td>
</tr>
<tr>
<td>Annual Meeting Abstract Deadlines</td>
<td>June 15, 2016</td>
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<tr>
<td>2016 ACCP Annual Meeting</td>
<td>October 23—26, 2016</td>
</tr>
<tr>
<td>ACCP Updates in Therapeutics 2017</td>
<td>February 17—19, 2017</td>
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2016—2018 ACSAP Book Releases

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<th>May</th>
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<tr>
<td>2016</td>
<td>Endocrinologic/Rheumatologic Care (Jan. 15)</td>
<td>Dermatologic Care (May 16)</td>
<td>Infection Primary Care (Sept. 15)</td>
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<tr>
<td>2017</td>
<td>Oncologic/Hematologic Care (Jan. 17)</td>
<td>Neurologic/Psychiatric Care (May 15)</td>
<td>Fluids and Nutrition/GI Care (Sept. 15)</td>
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<tr>
<td>2018</td>
<td>Cardiologic Care (Jan. 16)</td>
<td>Women’s and Men’s Care (May 15)</td>
<td>Nephrologic/Geriatric Care (Sept. 17)</td>
</tr>
</tbody>
</table>

*Subscribers seeking board certified pharmacotherapy specialist (BCACP) recertification credit from an ACSAP module must submit the required posttest within 4 months after the book’s release.*

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The authors and editors recognize that there may be errors in this newsletter. Drug dosage schedules are, we believe, accurate and in accordance with current standards. Readers are advised, however, to check other published sources to be certain that recommended dosages and contraindications are in agreement with those listed in this newsletter.

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