Message from the Chair

Sarah Anderson, Pharm.D., BCPS

“When you’re engaged in what you love to do, it’s like driving in the fast lane. Time flies by and more roads open up to you, alternate routes you may not have even known existed.” – T. Harv Eker

As I reflect on the past year as chair of the Adult Medicine PRN, I feel like we’ve been driving in the fast lane, taken a few “scenic routes,” and have now arrived at another annual meeting. The protocol for the Adult Medicine PRN-sponsored survey to characterize pharmacist-hospitalist collaborations was finalized this summer and as of this newsletter has been reviewed by the ACCP Practice-Based Research Network (PBRN). Co-primary investigators Jacky Olin and Antoine Jenkins and the research team are engaged in completing next steps in the process to bring the research project to fruition. We are hopeful that we will have the project ready to launch at the annual meeting.

In a related effort, the Adult Medicine PBRN Research Committee has met several times since this spring and has a year-end goal of creating a dynamic Google Doc to link to the Adult Medicine PRN website that will serve as a forum for research idea discussion and identification of collaborators. This committee will maintain the document and review it for study ideas that the Adult Medicine PRN wants to support moving forward. As we continue to make strides in advancing the research mission of our PRN and of ACCP as a whole, I invite you to get involved and make this a PRN-wide collaboration.

I continue to be amazed by the efforts and dedication of all of our members involved in committee work. I would like to sincerely thank the Archives, Newsletter, Nominations, PBRN Research, Programming, Training & Travel, and Walk-Rounds committees and committee chairs/co-chairs for all of their service and work over the past year. We have been fortunate to have both veteran and new committee members working side-by-side on each of these committees. If you are interested in joining a committee, we will have opportunities for you to learn more about each committee and to sign up at our Adult Medicine PRN business meeting in Hollywood, Florida on Monday, October 24th from 6-9pm in Great Hall 6.

Our Adult Medicine PRN Focus Session entitled, “An Update to the Management of Acute Bacterial Skin and Skin Structure Infections: What is the Utility of the New Agents?” will take place on Monday, October 24th from 1:30-3:00pm EDT in Great Halls 1 & 2. Please attend to learn all about this topic and support the efforts of our programming committee and outstanding speakers!

As we approach another annual meeting, I would like to again personally thank all of the Adult Medicine PRN officers for their leadership, encouragement, and positivity. I would also like to thank all of our members for their involvement and dedication. It is a rewarding experience to see so many outstanding practitioners devote their time to advancing the causes of our PRN and doing so in a such an effective manner. As a PRN we are fortunate to have a large membership and high engagement from our constituents. I know that together we can accomplish great things in moving our PRN, ACCP, and our profession forward!
ACCP Annual Meeting Awards

Resident and Student Travel Awards

Ryan Owens, PharmD
2016 Resident Research Travel Award
“Heart Rate Control as a Marker of Beta-Blocker Efficacy in Hospitalized Heart Failure Patients”

Asha Tata, PharmD, BCPS
2016 Adult Medicine PRN Mentor Award

Kurt Wargo, PharmD, BCPS, FCCP
2016 Adult Medicine PRN Outstanding Paper Award
Wargo KA, McCreary EK, English TM. Vancomycin combined with clindamycin for the treatment of acute bacterial skin and skin-structure infections. Clin

Jacqueline Olin, PharmD, BCPS, FASHP, FCCP
2016 Adult Medicine PRN Service Appreciation Award

Emily Shor
2016 Student Research Travel Award
“Validation of Vancomycin Dosing Strategy in Patients with Morbid Obesity”

ACCP Annual Meeting Awards

PRN Volunteer and Research Opportunities
Looking to get involved in the Adult Medicine PRN? Click HERE to fill out this google survey with your information.

We are looking to increase our ability to have research collaboration within our PRN,

Important Dates for Adult Medicine PRN

- November 30th 2016: Nominations for Fall 2017 awards (Clinical Practice, Education, Russell R. Miller and Elenbaas Service Awards, the 2018 Therapeutic Frontiers Lecture and the 2018 elected offices

- February 15th 2017: Nominations for the 2017 new awards (New Clinical Practitioner, New Educator, New Investigator), 2017 Parker Medal and the 2017 ACCP Fellows (FCCPs)


Cardiovascular disease results in over 2,150 deaths each day in the United States, averaging out to approximately 1 death every 40 seconds according to 2011 data from the American Heart Association. It has been estimated that roughly 635,000 Americans have a coronary attack each year and 300,000 of these patients will have recurrent attacks. These acute coronary syndromes (ACS) and coronary artery disease (CAD) events often result in a cardiovascular procedure or operation. The number of cardiovascular procedures increased by 28% from 2000 to 2010, highlighting the need for optimal treatment for these common disease states. 

Dual antiplatelet therapy (DAPT) is used to reduce thrombotic complications associated with ACS and cardiac stent implantation as well as to reduce atherothrombotic events. Dual antiplatelet therapy generally consists of an aspirin in addition to an oral P2Y12 receptor inhibitor such as clopidogrel, ticagrelor, or prasugrel. While the combination of these medications has been shown to reduce cardiovascular events in patients following an acute coronary syndrome or stent placement2-4, the duration of this therapy has been widely debated.

This year the American College of Cardiology and American Heart Association published an updated guideline regarding the duration of dual antiplatelet therapy in patients with CAD. The recommendations published in these guidelines are presented in Table 1.5 The guideline addresses the duration of DAPT in several clinical situations in addition to recommending to utilize aspirin long-term at a dose of 75-100 mg daily rather than a higher dose of aspirin due to comparable ischemic protection and lower bleeding risks.6

Eleven randomized controlled trials were assessed to determine the optimal duration of DAPT following stent implantation, most of which focused on drug-eluting stents (DES). The DAPT trial was the largest of these, evaluating 9,961 patients. This trial was designed to assess superiority of 30 months of DAPT over 12 months after the placement of newer generation DES. The longer duration of DAPT was shown to reduce the rate of stent thrombosis, major adverse cardiac cerebrovascular events (MACCE), and myocardial infarction (MI) significantly, but was associated with significantly increased rates of moderate or severe bleeding and borderline increased mortality.7,6 Upon further study, the number of cancer-related deaths was found to be significantly different between groups and subsequently it was discovered that the more cancer patients had been enrolled into the longer DAPT duration arm.7 The guideline states a number of writing group members did not believe the data suggests increased mortality is associated with DAPT. Because the data on this subject is conflicting, clinicians are urged to evaluate patients based on factors such as the patient’s bleeding risk, tolerance of DAPT after the minimum suggested time period, and concomitant medications such as anticoagulants.5

A new risk score from the Dual Antiplatelet Therapy Study, the “DAPT score,” may be useful in determining the risk/benefit ratio of prolonged DAPT therapy in patients following coronary stent implantation. Data from this study suggests that a DAPT score of ≥ 2 after 1 year of treatment with aspirin and a P2Y12 inhibitor indicates a favorable benefit/risk ratio whereas a score of < 2 may indicate the potential benefits of prolonged DAPT therapy do not outweigh the risks.5,6 This score illustrates that younger patients are at a lower risk of bleeding and patients with prior history of ACS, or other cardiac risk factors results in a high score, are more likely to experience prevention of an ischemic event than bleeding. A study evaluating this score showed the number needed to treat in order to prevent an ischemic event for patients with a DAPT score ≥ 2 is 34 while the number needed to harm with a bleeding event was 272. Conversely for patients with a score less than 2, the number needed to prevent an ischemic event was 153 and the number needed to harm was 64. The DAPT score is shown in Table 2.5,6

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Table 1: Details of randomized controlled trials evaluating duration of dual antiplatelet therapy following stent implantation.

Table 2: The DAPT score and its interpretation.
### Table 1. American College of Cardiology and American Heart Association Guidelines on DAPT

<table>
<thead>
<tr>
<th>Clinical Presentation</th>
<th>Recommendation</th>
<th>Level of Evidence</th>
</tr>
</thead>
<tbody>
<tr>
<td>SIHD following DES implantation</td>
<td>DAPT for at least 6 months</td>
<td>Class I B-R: Strong recommendation, moderate-quality evidence RCTs/meta-analyses</td>
</tr>
<tr>
<td>SIHD following BMS implantation</td>
<td>DAPT for at least 1 month</td>
<td>Class I A: Strong recommendation, high-quality evidence from RCTs/meta-analyses</td>
</tr>
<tr>
<td>SIHD with DES/BMS implantation at low risk for bleeding</td>
<td>DAPT for &gt; 6 months (DES) or &gt; 1 month (BMS) may be reasonable</td>
<td>Class IIb A: Weak recommendation, high-quality evidence from RCTs/meta-analyses</td>
</tr>
<tr>
<td>SIHD with DES/BMS implantation at high risk of bleeding or development of bleeding</td>
<td>May be reasonable to discontinue P2Y&lt;sub&gt;12&lt;/sub&gt; inhibitor after 3 months</td>
<td>Class IIb C-LD: Weak recommendation, limited data</td>
</tr>
<tr>
<td>ACS following DES/BMS implantation</td>
<td>DAPT for at least 12 months</td>
<td>Class I B-R: Strong recommendation, moderate-quality evidence RCTs/meta-analyses</td>
</tr>
<tr>
<td>ACS treated with medical therapy alone</td>
<td>DAPT for at least 12 months</td>
<td>Class I B-R: Strong recommendation, moderate-quality evidence RCTs/meta-analyses</td>
</tr>
<tr>
<td>ACS following DES/BMS implantation at low risk for bleeding</td>
<td>DAPT for &gt; 12 months may be reasonable</td>
<td>Class IIb A&lt;sup&gt;ss&lt;/sup&gt;: Weak recommendation, high-quality systematic review</td>
</tr>
<tr>
<td>ACS treated with medical therapy at low risk for bleeding</td>
<td>DAPT for &gt; 12 months may be reasonable</td>
<td>Class IIb A&lt;sup&gt;ss&lt;/sup&gt;: Weak recommendation, high-quality systematic review</td>
</tr>
<tr>
<td>ACS following DES/BMS implantation at high risk or bleeding or development of bleeding</td>
<td>May be reasonable to discontinue P2Y&lt;sub&gt;12&lt;/sub&gt; inhibitor after 6 months</td>
<td>Class IIb C-LD: Weak recommendation, limited data</td>
</tr>
<tr>
<td>ACS requiring CABG</td>
<td>DAPT should be resumed after CABG to complete 12 months</td>
<td>Class I C-LD: Strong recommendation, limited data</td>
</tr>
<tr>
<td>STEMI treated with fibrinolytic therapy</td>
<td>DAPT should be continued for a minimum of 14 days, ideally 12 months</td>
<td>Class I A/C-EO: Strong recommendation, high-quality RCTs/meta-analyses and expert opinion</td>
</tr>
<tr>
<td>STEMI treated with fibrinolytic therapy at low risk for bleeding</td>
<td>DAPT for &gt; 12 months may be reasonable</td>
<td>Class IIb A&lt;sup&gt;ss&lt;/sup&gt;: Weak recommendation, high-quality systematic review</td>
</tr>
</tbody>
</table>

SIHD = stable ischemic heart disease  
DES = drug-eluting stent  
RCT= randomized controlled trial  
BMS= bare-metal stent  
CABG= coronary artery syndrome  
STEMI= ST elevation myocardial infarction
The ACC/AHA guidelines have incorporated data from recent trials into their recommendations for duration of DAPT, but they also encourage clinicians to use their judgment to determine which patients might benefit from prolonged therapy and which should have DAPT discontinued after the minimum suggested timeframe. Until more trials evaluate this issue the optimal duration of DAPT is still uncertain. The patient’s individual risk for ischemic events and bleeding events remains the most important factor when making the decision to continue DAPT past the minimum suggested duration.

### References:

Direct oral anticoagulant agents, also known as DOACs, have revolutionized the world of anticoagulation. The DOACs have been shown to be favorable over warfarin due to the need for less monitoring, fewer food and drug interactions, fixed dosing and less inter-patient variability. Agents currently on the market include rivaroxaban (Xarelto®), apixaban (Eliquis®), dabigatran (Pradaxa®) and edoxaban (Savaysa®). Rivaroxaban, apixaban and dabigatran are indicated for treatment of venous thromboembolisms (VTE), VTE prophylaxis following orthopedic surgery, and non-valvular atrial fibrillation. Edoxaban is currently only approved for treatment of VTE and non-valvular atrial fibrillation.

The utilization of these agents in patients with renal dysfunction is also controversial. Table 1 displays either limited pharmacokinetic (PK) and pharmacodynamic (PD) data is available to aid in guidance of the use of DOACs in obesity. Newly approved edoxaban does not currently have weight-specific pharmacokinetic studies, however pooled data suggests that non-renal clearance was higher with increasing body weight. Rivaroxaban has been shown to have similar peak concentrations, area under the curve (AUC) and half-lives in patients > 120 kg versus those 70 to 80 kg, with results bearing uncertain clinical significance. Apixaban has shown significantly lower peak concentrations in those > 120 kg versus 65 to 85 kg in conjunction with a 23% lower AUC. Again, the effect size of these variances was low enough that the authors did not comment on dose adjustments for patients > 120 kg. Finally, dabigatran has been shown to display an inverse relationship between trough concentration and weight, with trough values 21% lower for those > 100 kg versus 50 to 100 kg. In summary, these PK and PD data still beg the question of whether or not patients of extreme body weight are being underdosed, and presently no therapeutic drug ranges have been established for these agents and it is unknown if these differences lead to a change in clinical outcomes.

The Scientific and Standardization Committee of the International Society of Thrombosis and Haemostasis (ISTH) has recommended that DOACs not be used in patients with a BMI ≥ 30 kg/m² or a weight ≥ 120 kg. Furthermore, they recommend monitoring drug-specific peak and trough levels if used in patients meeting this weight criteria, although this practice is likely not feasible or routine at most institutions. Unfortunately, product labeling for the DOACs do not include specific weight cut-offs or recommendations for when to consider an alternative agent.

The utilization of these agents in patients with renal dysfunction is also controversial. Table 1 displays either the mean creatinine clearance (CrCl) or the number of patients with a reduced CrCl enrolled in major efficacy trials. The majority of trials excluded patients with a CrCl < 30 ml/min, with a range of 0.2-1.5% of the total populations falling into this category. Per the package insert, rivaroxaban should be avoided in patients with a creatinine clearance (CrCl) < 30 ml/min. No dosage recommendations are provided for dabigatran at this level of renal dysfunction, although patients were excluded from clinical trials at a CrCl < 30 ml/min.
NOACs, continued.

Apixaban has dosage adjustments for patients with non-valvular atrial fibrillation with two of the following: serum creatinine ≥ 1.5 mg/dL, age ≥ 80 years or body weight ≤ 60 kg. Clinical studies did not enroll patients on hemodialysis, however one PK/PD study displayed similar apixaban concentrations to those observed in the ARISTOTLE trial at usual doses. Long-term safety and efficacy data for apixaban is not available in the hemodialysis population. Edoxaban dosing should be reduced from 60 mg daily to 30 mg daily in CrCl 15 to 50 ml/min, and use in CrCl < 15 ml/min is not recommended. Interestingly, the use of edoxaban at CrCl > 95 ml/min is not recommended in patients with non-valvular atrial fibrillation, as this subgroup had an increased rate of thromboembolism in clinical trials. These variances create challenges for prescribers when trying to select an appropriate agent.

Data regarding the safety of these agents in renal dysfunction is limited, however meta-analyses have been conducted to investigate thrombotic and bleeding outcomes in this subgroup. One such study compared the use of DOACs versus warfarin for atrial fibrillation in renal dysfunction. In mild and moderate renal dysfunction (CrCl 50-80 ml/min and 25-49 ml/min, respectively), the DOACs were comparable to warfarin for safety in terms of risk of major bleeding. Indirect comparisons of the DOACs showed that apixaban had less major bleeding than dabigatran, rivaroxaban, and edoxaban 60 mg daily in moderate renal impairment, however edoxaban 30 mg daily was favorable in comparison to all other agents. The risk in interpretation and extrapolation of these results continues to be the absence of data in CrCl ≤ 30 ml/min. This meta-analysis also assumes homogeneity in the populations as well as safety and efficacy parameters, which is an overall limitation.

Similar to the PK/PD data for the use of DOACs in obesity, variations in renal dysfunction have uncertain correlations to clinical outcomes. In moderate renal impairment (CrCL 30-50 ml/min), dabigatran has been shown to have an increased AUC and half life (from 13 hours to 27 hours) compared to patients with normal renal function. An increase in aPTT has also been observed, albeit with no clinically significant bleeding. Rivaroxaban has shown an increased AUC and mildly prolonged half life in severe renal impairment (average CrCl 15 ml/min) with no associated bleeding events. Subgroup analyses of apixaban have demonstrated increased ischemic stroke coupled with increased major bleeding in CrCI < 50 ml/min. Finally, edoxaban displayed a 2.1% increase in bleeding at a CrCI < 30 ml/min. Overall, data is conflicting in regards to safety and efficacy of the use of DOACs in this special population. No direct investigation of DOACs in renal dysfunction has been conducted, therefore caution should be utilized when considering initiation of DOACs in clinical practice.

It is the responsibility of pharmacists to provide logical, evidence-based recommendations for whom to initiate therapy with one of the direct oral anticoagulant agents. Major societies such as the ISTH recommend avoiding the use of DOACs in patients at the upper extreme of weight. This is due to the lack of clinical data as well as PK/PD data with mixed results. More studies are needed to determine the safety and efficacy associated with the use of DOACs in obese patients and those with renal dysfunction.

<table>
<thead>
<tr>
<th>Trial</th>
<th>NOAC studied-indication</th>
<th>Mean weight, kg (range)*</th>
<th>Weight categories: n (%)</th>
<th>CrCl, mean ±SD (ml/min) OR GFR category: n (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>RECOVER I</td>
<td>Dabigatran-VTE</td>
<td>85.5 (38-175)</td>
<td>≥ 100 kg: 502/2539 (20) BMI ≥ 35: 306/2539 (12)</td>
<td>105.8±40.7</td>
</tr>
<tr>
<td>RECOVER II</td>
<td>Dabigatran-VTE</td>
<td>83.2 (36-184)</td>
<td>&gt; 100 kg: 438/1280 (34.2) BMI &gt; 35: 302/1280 (23.6)</td>
<td>108.2±43.7</td>
</tr>
<tr>
<td>RELY</td>
<td>Dabigatran-AF</td>
<td>82.9 (110 mg group) and 82.5 (150 mg group)</td>
<td>≥ 100 kg: 3099/18113 (17.1)</td>
<td>NR</td>
</tr>
<tr>
<td>REMEDY</td>
<td>Dabigatran-VTE</td>
<td>86.1 (40-188)</td>
<td>≥ 100 kg: 299/1430 (20.9)</td>
<td>104.2±38.6</td>
</tr>
<tr>
<td>RESONATE</td>
<td>Dabigatran-VTE</td>
<td>83.7 (40-151)</td>
<td>≥ 100 kg: 122/681 (17.9)</td>
<td>99.6±35.8</td>
</tr>
<tr>
<td>EINSTEIN OVT</td>
<td>Rivaroxaban-VTE</td>
<td>NR</td>
<td>&gt; 100 kg: 245/1731 (14.2)</td>
<td>&lt; 30: 6 (0.3)</td>
</tr>
<tr>
<td>EINSTEIN PE</td>
<td>Rivaroxaban-PE</td>
<td>NR</td>
<td>&gt; 100 kg: 345/2419 (14.3)</td>
<td>&lt; 30: 4 (0.2)</td>
</tr>
<tr>
<td>ROCKET-AF</td>
<td>Rivaroxaban-AF</td>
<td>NR</td>
<td>&gt; 100 kg: 2035/7131 (28.5) BMI &gt; 35: 792/7131 (13.6)</td>
<td>67 [range 52-88]</td>
</tr>
<tr>
<td>AMPLIFY</td>
<td>Apixaban-VTE</td>
<td>84.6</td>
<td>≥ 100 kg: 522/2691 (19.4) BMI &gt; 35: 349/2691 (13.0)</td>
<td>&lt; 30: 14 (0.5)</td>
</tr>
<tr>
<td>ARISTOTLE</td>
<td>Apixaban-AF</td>
<td>82 (median)</td>
<td>None: NR</td>
<td>&lt; 30: 137 (1.5)</td>
</tr>
<tr>
<td>ENGAGE AF</td>
<td>Edoxaban-AF</td>
<td>NR</td>
<td>≤ 60 kg: NR</td>
<td>&lt; 50: 1361 (19.3)</td>
</tr>
<tr>
<td>HOKUSAI VTE</td>
<td>Edoxaban-VTE</td>
<td>NR</td>
<td>&gt; 100 kg: 611/4118 (14.8)</td>
<td>≥30 to ≤50: 268 (6.5)</td>
</tr>
</tbody>
</table>

Information in this table is limited by data available from clinical trial publications

*Mean weight/BMI in the group receiving study medication
AF = atrial fibrillation, NR = not reported, PE = pulmonary embolism, VTE = venous thromboembolism
NOACs Continued:

References:


PROMOTIONS

- Jaime Foushee, PharmD, BCPS: Promoted to Associate Professor of Pharmacy Practice at Presbyterian College School of Pharmacy
- Lauren Hynicka, Pharm.D., BCPS: Promoted from Assistant Professor to Associate Professor, University of Maryland School of Pharmacy
- Leah Bentley Patel, PharmD, BCPS: Senior Medical Science Liaison, Mallinckrodt Pharmaceuticals
- Rima A. Mohammad, PharmD, BCPS: Promoted to Clinical Associate Professor at the University of Michigan College of Pharmacy, Department of Clinical Pharmacy
- Sarah L. Anderson, PharmD, BCPS: Promoted to Associate Professor, University of Colorado Skaggs School of Pharmacy & Pharmaceutical Sciences
- Jane Bowen, Pharm.D., BCPS: Promoted to Associate Professor of Clinical Pharmacy Department of Pharmacy Practice and Pharmacy Administration, Philadelphia College of Pharmacy, University of the Sciences

NEW ACCP FELLOWS

- Kurt A. Wargo, PharmD, FCCP, BCPS (AQ-ID)- Associate Professor and Regional Dean, Wingate University Hendersonville Health Sciences Center
- Sarah A Nisly, PharmD, BCPS- Wingate University School of Pharmacy
- Rima A. Mohammad, PharmD, FCCP, BCPS- University of Michigan College of Pharmacy and Health System

GRANTS

- Sarah L. Anderson, PharmD, BCPS (Co-Investigator), PI: Joel C. Marrs, PharmD, FCCP, FASHP, FNLA, BCPS-AQ Cardiology, BCACP, CLS; Project Title: Study of the usability and navigability of a clinical pharmacist led Heart360 web-enabled home blood pressure monitoring program within a large safety net health system; University of Colorado Skaggs School of Pharmacy & Pharmaceutical Sciences. Direct Costs: $10,250
- Beth H. Resman-Targoff, Pharm.D., FCCP, Clinical Professor, University of Oklahoma College of Pharmacy- Invited Presentation, “Complex Cases in Joint and Bone Disease” at

Publications