Direct Oral Anticoagulants: Leading Safety Practices

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December 12, 2017
1:30 PM- 2:45 PM

#IHIFORUM
Session objectives

• Identify transition of care contributing factors of direct oral anticoagulant (DOAC) safety events.

• Implement leading practices to improve the reliability of inpatient and outpatient DOAC management.

• Identify ways to include patients and families in their DOAC safety plan.
Presenter disclosures

- The speakers have no financial disclosures.
- The opinions expressed in this presentation do not reflect the official position of the Agency for Healthcare Research and Quality (AHRQ).
- This information is not being offered as legal or medical advice.
Vizient™ Patient Safety Organization
Vizient Patient Safety Organization

• The Vizient Patient Safety Organization (formerly the University Health System Consortium Safety Intelligence PSO) became federally-listed by AHRQ in 2008
• Certified through 2020
• National participation across 34 states and over 260 providers
• AHRQ Common Formats (v.1.1 and 1.2) integrated with its proprietary taxonomy
• Meaningful comparison data
• National leadership role in PSO activities
• Regular NPSD submissions via PSOPPC

NPSD = Network of Patient Safety Database
PSOPPC = Patient Safety Privacy Protection Center
Patient Safety Organizations

PSOs collect and analyze data in a standardized manner using the AHRQ Common Formats, identify safety improvement opportunities and share learnings widely.
Vizient PSO - Offering Details

Participation in the Vizient PSO provides:

### Educational opportunities
- Safety alerts, checklists and white papers
- Evidence based and expert consensus recommendations
- Patient Safety Evaluation System (PSES) documentation calls
- PSO operations orientation
- Patient safety officer education
- Case law updates

### Collaboration opportunities
- Safe Table participation (minimum of six per year)
- Safety huddles (bimonthly)
  - Leading practice development projects
- 2 in-person PSO conferences
- Quarterly virtual PSO user group
- PSO listserv participation

### Other
- Privilege and confidentiality protection for PSWP
- Multidimensional Analytic Tool access
- Annual evidence-based feedback report with comparative data
- Access to Vizient Performance Management resources
- PSO manager consultation and coaching via telephone and email

### Additional services (incremental fee)
- PSES documentation support
- NPSD reporting
- Quarterly feedback report

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Expert Medication Safety Advisory Team

Jessica Schoenthal, RN, MSN, CPPS
Collaborative Advisor
Vizient PSO
Summary of event types resulting in high harm

• Medication safety
  • Anticoagulants
  • Opioid overdose (pain management)
  • Sedation/Anesthesia management
  • New concentrated insulins (hypoglycemia)
• Falls
• Cardiac alarm monitoring

• Behavioral management
  • Suicide
  • Violence
• Delays in diagnosis
  • Stroke
• Surgical complications associated with patient optimization
• Critical result reporting delays
• Cardiac or respiratory arrest outside of critical care

Vizient PSO Data from 2014-June 2017

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Advisory team roles

**Team members**
- Attend and participate in meetings
- Share knowledge and learnings
- Define project topic
- Define objectives and deliverables
- Share leading practices
- Provide feedback on toolkit
- Participate in safe table meetings and/or webinar

**PSO Collaborative advisors**
- Organize and facilitate meetings
- Analyze data
- Assemble member learnings and leading practices, results of data analysis and evidence-based recommendations
- Communicate materials collected to the advisory team
- Draft and publish toolkit
- Facilitate webinars

**Time commitment:** Approximately 4-6 hours per participant over four months

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Benefits of advisory team collaboration

• Blends complementary perspectives to achieve best outcome.
• Accelerates learning from many organizations.
• Accomplishes more than individuals can do alone.
• Provides everyone an opportunity to teach and learn.
# Medication Safety Advisory Team Members

<table>
<thead>
<tr>
<th>Name</th>
<th>Credentials</th>
<th>Title</th>
<th>Organization</th>
</tr>
</thead>
<tbody>
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Overview of the medication safety project

Feb 2017
Advisory team identified DOACs as the highest priority

Feb 2017
PSO analyzed data, researched literature, and collected leading practices

March 2017
PSO conducted DOAC safe table meeting and reviewed findings with advisory team

April 2017
PSO facilitated team review and revision of safety alerts and leading practices

June - October 2017
PSO distributed Safety Alerts and shared learnings in a topical webinar

Share learnings
Create deliverables
Identify solutions
Define project and deliverables

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Advisory team’s top safety concern

Direct oral anticoagulants (DOAC)

dabigatran
apixaban

Eliquis™
rivaroxaban

XARELTO™
Pradaxa™

Savaysa™
edoxaban
Lixiana™

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Anticoagulants: High risk and problem prone

The Institute for Safe Medication Practices reported that harm from oral anticoagulants ranks as one of the highest priority drug safety problems in 2016 by several measures.

• In clinical trials, oral anticoagulants repeatedly demonstrated high injury rates, causing bleeding in 8% to 19% of patients treated for a year.

• Anticoagulants are used by a large and growing population, notably the elderly.

• Reports of serious injuries and death are also featured prominently in the 2016 U.S. Food and Drug Administration (FDA) Adverse Event Reporting System data
  – Serious injuries (n=18,978) and deaths (n=3,018) in the US

## Warfarin versus DOAC

<table>
<thead>
<tr>
<th>Advantages</th>
<th>Disadvantages</th>
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<tr>
<td><strong>Warfarin</strong></td>
<td><strong>DOAC</strong></td>
</tr>
<tr>
<td>• Broad indications for use</td>
<td>• Slower onset/offset of action</td>
</tr>
<tr>
<td>• Allows adherence to be monitored</td>
<td>• Food-drug interactions</td>
</tr>
<tr>
<td>• Recognized by practitioners as an anticoagulant</td>
<td>• Drug-drug interactions</td>
</tr>
<tr>
<td>• Long half-life</td>
<td>• Routine monitoring required with associated costs</td>
</tr>
<tr>
<td>• Fixed dosing</td>
<td>• Narrow indications for use</td>
</tr>
<tr>
<td>• Less monitoring</td>
<td>• Not readily recognized as anticoagulants</td>
</tr>
<tr>
<td>• Direct mechanism of action with rapid onset</td>
<td>• Reversal protocols and antidotes under development</td>
</tr>
<tr>
<td>• Fewer food and direct drug interactions</td>
<td>• Dose adjustment required for impaired renal function</td>
</tr>
<tr>
<td>• Improved patient satisfaction and quality of life</td>
<td>• Limited availability of assays for measuring drug levels</td>
</tr>
<tr>
<td></td>
<td>• Absence of validated monitoring strategies. to evaluate compliance</td>
</tr>
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<td></td>
<td>• Higher cost to patient</td>
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Analysis of PSO event reports involving DOACs
DOAC event report data

A retrospective review of 273 voluntary PSO reports identified opportunities to improve care for DOAC patients.

Text search for generic and brand names for the following drugs:

- Rivaroxaban (Xarelto™)
- Apixaban (Eliquis™)
- Dabigatran (Pradaxa™, Prazaxa™)
- Edoxaban (Savaysa™, Lixiana™)
Harm scores assigned in DOAC events

72% of all DOAC events reported reached the patient
36% of reported DOAC events resulted in harm  (emotional distress to death).

Period of data: January 2014- July 2017; Number of events= 273
AHRQ Common Format Harm Scale v.11

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Communication breakdowns

- 37%: With other providers WITHIN patient care area
- 16%: With other providers in ancillary departments (e.g., lab, pharmacy, radiology)
- 19%: With other providers in OTHER patient care areas
- 11%: With patient or family
- 17%: No known communication breakdown

Period of data: January 2014 - July 2017
Number of events = 273
Medication-related event subcategories

- Known drug interaction
- Wrong dose
- Prescription/refill delayed
- Wrong drug or substance
- Wrong timing
- Other
- Wrong duration (of administration or course of therapy)
- Unordered drug given
- Wrong frequency
- Monitoring event
- Wrong patient
- Wrong strength/concentration
- Wrong preparation or technique
- Wrong route

Period of data: January 2014 - July 2017; Number of DOAC events = 273
Number of DOAC events categorized as medication-related event type = 175

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Patients received an overdose or extra dose of anticoagulation in nearly 60% of DOAC medication wrong dose events voluntarily reported to the PSO.

Period of data: January 2014 - July 2017
Number of wrong dose events = 39
Opportunities identified in PSO data and safe table discussion

- Decreasing occurrence of unintentional duplicate therapies in anticoagulation
- Individualization of standardized care
- Improving transitions of care - medication reconciliation
- Effective patient and family education
- Selection of the best drug for the patient - indication, age, renal function or drug interactions
- Development of adequate reversal strategies and policies
- Constancy of anticoagulation peri-operative management
- Creation of order sets to eliminate dosing errors
- Reliably dosing morbidly obese patients
High harm event overview

DOAC high harm events were associated with acute bleeding

- GI bleeding
- Epistaxis
- Hematomas
- Intracranial hemorrhage

Common contributing factors in high harm DOAC events

- Therapeutic duplication (35%)
- Inappropriate dose for clinical condition (35%)
- Breakdown in discharge instructions and lack of patient teach back (10%)
DOAC case scenarios
Example 1

- A 64 year old man was admitted with a pulmonary embolism and a history of recent spinal surgery.
- His provider ordered “hold anticoagulation” and completed a pre-authorization request form for rivaroxaban therapy.
- The pharmacy dispensed rivaroxaban, despite the top of the form stating: "This form is not a substitute for a prescription order.”
- This patient was placed at an increased risk for bleeding complications after spinal surgery.

The case described is not an actual case study and does not contain actual patient level data. The case represents an issue or error that can or commonly occurs.
Example 2

- A 70 year old male was admitted to the hospital for evaluation of heart valve disease.

- He takes dabigatran for atrial fibrillation at home, and initial evaluation of laboratory values revealed that patient had a critically elevated INR.

- He had less than optimal renal function, and the dabigatran dose was not adjusted accordingly.

- The dose prescribed was 150 mg twice daily, and it should have been 75 mg twice daily.

The case described is not an actual case study and does not contain actual patient level data. The case represents an issue or error that can or commonly occurs.
Example 3

• A 65 year old female was admitted after a fall and hip fracture. She reported taking dabigatran twice a day at home for atrial fibrillation.

• Her last documented dose of dabigatran was the morning of admission. The provider held dabigatran for 24 hours and then sent the patient to the operating room for a hip repair.

• This organization’s perioperative anticoagulation guideline required dabigatran to be held for at least 72 hours before surgery based on this patient's renal function (CrCl less than 25).

• This patient experienced significant intraoperative bleeding, requiring multiple blood transfusions and admission to a critical care unit postoperatively.

The case described is not an actual case study and does not contain actual patient level data. The case represents an issue or error that can or commonly occurs.
Example 4

• A 44 year old female was admitted as an inpatient and received scheduled apixaban.

• On day three of admission, her physician ordered enoxaparin 1 mg/kg.

• The pharmacist verified and dispensed the enoxaparin.

• This patient received both apixaban and enoxaparin and experienced bleeding from procedural site.
Example 5

- A 55 year old male who was hospitalized was on rivaroxaban, and during the stay, his renal function deteriorated.
- His provider did not adjust or discontinue the rivaroxaban dose in response to the decline in renal function.
- As a result, this patient experienced an upper GI bleed that resulted in a cardiac arrest.

The case described is not an actual case study and does not contain actual patient level data. The case represents an issue or error that can or commonly occurs.
Patient-centered DOAC care coordination
Patient-centered DOAC care coordination

- **Initiation of therapy**
- **Admission to acute care**
- **Discharge from acute care**
- **Ambulatory care**
- **Peri-procedural**

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Safety alert: Discharge from acute care

Vizient PSO

Vizient PSO Safety Message
Consider new DOACs as high alert medications
May 2017

Situation: Earlier this year, Vizient PSO convened an expert multidisciplinary team to discuss their highest priority for medication safety. Experts agreed that the new direct oral anticoagulants (DOACs) were their top safety concern and presented significant safety risks to patients in both the inpatient and outpatient environments.

Background: In the past, Warfarin had been the primary drug on the market to help prevent blood clots and reduce patients’ chances of developing serious conditions such as strokes and heart attacks. Through standardized practices, enhanced education, and closer monitoring of patients in anticoagulant clinics, the safety for patients on Warfarin improved; however the need for frequent blood tests to maintain a safe, therapeutic range for blood clotting places high demand on patients. With no requirements for regular blood testing, no dietary limitations, fewer drug interactions and a rapid onset of action, the new DOACs—rivaroxaban, apixaban, dabigatran and edoxaban—offer an attractive alternative for patients (Institute for Safe Medication Practices, 2015). These benefits led to a rapid increase in their use. Data from 2016 in the Vizient Clinical Data Base (CDB) suggests that while the number of patients on Warfarin is decreasing, the number of patients on the DOACs is on the rise and there may be unintended consequences associated with the introduction of these new medications.

Assessment: An initial review of almost 150 near miss and adverse events involving DOACs in the Vizient PSO database substantiates that these new anticoagulants pose serious risk at discharge. Preventable adverse events resulted from incorrect dosing of DOACs, unintentional duplication of anticoagulants, poor coordination of therapy during transitions in care and before procedures as well as inadequate patient education and engagement. The clinical impact of these events included gastrointestinal or intracranial bleeding, delays in procedures, extended length of stays and readmissions.

The contributing factors identified in these events were:
- Gaps in provider knowledge about DOACs
- The complexity of managing medication orders via electronic health record and paper prescription processes simultaneously
- The failure to create a complete medication reconciliation list
- The failure to perform clinical medication reconciliation of a complete and accurate medication list, including acknowledgment of prescribed medication’s purpose, mechanism of action and drug interactions
- The lack of clear discharge instructions that the patient could teach back
- Insufficient post-discharge follow up to ensure:
  - The patient understands the discharge plan and can carry it out
  - The patient understands appropriate dosing
  - The patient understands signs and symptoms of bleeding
  - The patient is monitored based on their risk for renal impairment complications (e.g. patients on nephrotic medications)
  - The patient is monitored for hepatic dysfunction
  - The patient is monitored for appropriate periprocedural/periprosthetic interruption in therapy

Anticoagulants are often prescribed for older patients. Prescribing medications for older patients requires more care and monitoring (American College of Cardiology, 2017). Over 50% of DOAC events reported to the PSO involved patients 65 years of age and older.

Recommendations: The Vizient PSO, with a team of experts in medication safety, is creating a comprehensive DOAC Tool Kit for PSO members. Below are a few recommendations on how you can begin evaluating your DOAC safety needs at your organization today and mitigating risk. Please watch for further alerts focused on these high risk, high volume and problematic medications.

Raise awareness of the DOACs (rivaroxaban, apixaban, dabigatran and edoxaban) in your organization by placing them on your high alert medication list. In addition, conduct ongoing concurrent surveillance of these medications use and adverse drug events. Report findings of DOAC related adverse drug events to nurses, physicians and pharmacists within your organization. Share findings from the review of safety events with front line providers, pharmacists and nurses. Report near miss and actual DOAC safety events to your PSO to accelerate the pace of learning on this important safety topic.

1. Implement a discharge checklist or “stop list” for patients prescribed DOAC therapy:
   a. The pharmacist must reconcile manual (paper prescriptions) and electronic instructions at discharge to identify therapeutic duplication and/or drug interaction.
   b. Verify if the patient has insurance approval for prescribed DOAC, ensuring there are no roadblocks to drug access.
   c. Prior to discharge, schedule a follow-up appointment with an anticoagulation clinic or with a provider who can monitor post-hospitalization therapy.
   d. Ensure the patient and/or caregiver are able to demonstrate that he/she can teach back their medication plan (including any planned dose changes or therapy discontinuations).
   e. Call all patients discharged on DOACs within 24-48 hours to ensure they received their prescription and that the prescription is accurate. The patient should confirm an understanding how to take the medication, including an ability to describe tapering instructions (if applicable). The provider should also review all home medications to ensure the patient is not taking dual antithrombotic therapy without a provider’s knowledge.

For additional questions or information, please contact Jessica Schwenk or Tammy Williams.

The Vizient PSO Team

This is the first in a series of alerts Vizient PSO will be releasing on this topic.

Resources:
- Management of Patients on Non-Vitamin K Antagonist Oral Anticoagulants in the Acute Care and Periprocedural Setting: A Scientific Statement from the American Heart Association available at http://circ.ahajournals.org/content/early/2015/06/01/CIR.0000000000000472
- 2017 ACC Expert Consensus Decision Pathway for Periprocedural Management of Anticoagulation in Patients with Nonvalvular Atrial Fibrillation available at http://www.onlinejacc.org/content/2017/01/05/jaccc-2016.11.024
- Guidance for the practical management of the direct oral anticoagulants (DOACs) in VTE treatment available at https://www.mdjplus.org/articles/P804770489

This ISMP anticoagulation self-assessment is now live at http://www.ismp.org/selfassessments/anticoagulation/2017/Default.aspx

ISMP Quarterly Watch: Perspectives from new adverse event reports available at http://www.ismp.org/QuarterlyWatch/2015Q2.pdf

- 2017 ACC Expert Consensus Decision Pathway for Periprocedural Management of Anticoagulation in Patients with Nonvalvular Atrial Fibrillation available at http://www.onlinejacc.org/content/2017/01/05/jaccc-2016.11.024

Organizations may use the information in this to evaluate their practices, clinical judgment should always define patient care.

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Improving DOAC management for patients discharged from acute care

Implement a discharge checklist or timeout for patients prescribed DOAC therapy.

- Reconcile manual (paper prescriptions) and electronic instructions at discharge to identify therapeutic duplication and/or drug interaction.
- Verify that the patient has insurance approval for DOAC.
- Schedule a follow-up appointment with an anticoagulation clinic or with a provider who can monitor therapy.
- Include importance of timely follow-up appointments during discharge teaching.
- Ensure patient and/or their caregiver are able to teach back medication plan.
- Call all DOAC patients within 24-48 hours of discharge.

Guidance for the practical management of the DOACs in VTE treatment available at [https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4715848/](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4715848/)
Safety alert: Periprocedural

Vizient Patient Safety Organization safety message
September 2017

Direct oral anticoagulants: The challenge of coordinating periprocedural DOAC therapy

Situation: Patients undergoing invasive procedures may require temporary discontinuation of their anticoagulant therapy. Failure to hold or resume a direct oral anticoagulant (DOAC) correctly puts the patient at risk of bleeding during and after the procedure or a hemorrhagic event from discontinuation therapy. Reliable and safe management of DOACs in periprocedural patients is a high-risk process that is complex and problem-prone.

Background: The number of patients prescribed DOACs is increasing, and there is a lack of validated assessment and monitoring methods, widely available DOA guideline agents, and standardized periprocedural approaches. This increases the risk of adverse periprocedural bleeding for DOAC patients.

Assessment: Vizient™ Patient Safety Organization (PSO) conducted a retrospective review of safety events involving DOAC use from January 2016 to December 2017. A review of the Vizient PSO database revealed 282 DOAC-related events. Of these, 84 (22%) involved bleeding events during periprocedural care.

Table 1 displays the types of periprocedural errors involving DOACs. A common error prior to the procedure involved failure to temporarily hold DOACs, which resulted in protocol delays, cancellations and inappropriate bleeding. Transplant centers may require patients to be switched from a DOAC to warfarin at the time they are placed on the transplant list due to the long half-life of DOACs, lack of reversi agents, and basic monitoring tests. In some cases, patients lost their place on the transplant list because they remained on DOACs and were not properly prepared for surgery.

Periprocedural management of DOACs can be complicated. After the procedure, sometimes orders were written for the incorrect dose or were not written to restart the DOAC, increasing the risk of a thrombotic event. On the other hand, continuous duplication of lab results for anticoagulanthypocoagulation in patients prescribed multiple interacting drugs, which exacerbated the risk of causal bleeding. Some post-procedural orders set arbitrarily order pharmacologic versus thrombotic treatment prophylaxis. This standardized work process does not individualize care for patients on DOACs and placed them at risk for and resulted in therapeutic duplication.

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<th>Table 1: Distribution of DOAC periprocedural event types</th>
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<tbody>
<tr>
<td>Type</td>
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<tr>
<td>Atrial fibrillation</td>
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<tr>
<td>Cardiac surgery planning</td>
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<tr>
<td>Thrombus prophylaxis</td>
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<td>Anticoagulation reversal</td>
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<tr>
<td>Oral anticoagulation therapy</td>
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<tr>
<td>Venous thromboembolism prophylaxis</td>
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<tr>
<td>Warfarin therapy</td>
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</tbody>
</table>

Contributing factors identified in DOAC events include:
- Lack of consensus among the healthcare teams related to procedural bleeding risk and reversal strategy (from initiating DOACs)
- Unproven processes for assessing coagulation and renal status prior to procedures
- Inability to confirm DOAC was not completed before anticoagulant and discontinuation
- Medication administration and assessment that was initiated for DOAC therapy
- Lack of availability reversal agents/ reversal protocols and ways to reverse DOAC effect on patient
- Complex patient instructions and lack of a patient medication instruction, teach back and planned follow-up with the patient before admission and after discharge

Recommendations
- Review the Vizient PSO Safety Message: Discharge Care for Patients on DOACs from May 2017.
- Develop standard processes, guidelines, and protocols for managing DOAC therapy in the periprocedural setting, specifically:
  - Convolve a multidisciplinary team to define standard work for pre-procedural and post-procedural DOAC patients (see UV Medicine Pharmacy Services online reference guide) and Michigan Anticoagulation Quality Improvement Initiative Anticoagulation Toolkit 3.7
  - Outline institutional policies and procedures, standardization of order sets, clinical pathways and clinical decision support tools for management of patients in periprocedural situations to avoid delays that could adversely affect patient outcomes.
  - Ensure wide availability of antidotes for bleeding induced by direct oral anticoagulants.
  - Define consistent pre-procedural processes to review the medical history, medication list, including over-the-counter medications and any supplements and herbal preparations, and laboratory test results to identify factors that may increase a bleed risk.
  - Create a checklist for transplant patients that assess if the patient takes a DOAC. Review the transplant guidelines, consider switching based upon evidence-based recommendations, and measure the frequency of patients unexpectedly removed from the transplant list related to anticoagulation.
  - Document the anticoagulant management plan and patient concurrence in the patient’s medical record before undertaking the procedure.
  - Develop a process for individualization of standard work based on patient risk factors (consider a tissue test with the patient).
  - Develop explicit documentation of presurgical education, prescribing and dispensing procedures within the transplant teams to assure timely procurement, dispensing and administration of DOACs.
  - When presurgical hold for a DOAC is completed, the transplant medical record/prescription administration, review the process to ensure there is no possibility of conflicting procurement with dispensing and administration.
  - Review Joint Commission standard H 06.01.01 work with a multidisciplinary team to identify when and if anticoagulants should be administrated before pharmacy review. Include in the policy that a resident or independent pharmacist on the presurgical team
  - Ensure patients can teach back DOAC and instructions, build this into defined standard work in each phase of the periprocedural care.

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Improving periprocedural care coordination

• Convene a multidisciplinary team to define standard work for pre-, intra- and post-op DOAC patients.\textsuperscript{i,ii}

• Outline institutional policies and procedures, standardized order sets, clinical pathways, and clinical decision support tools for management of patients in urgent situations to avoid delays that could adversely affect patient outcomes.\textsuperscript{iii}

• Document the anticoagulant management plan and patient concurrence in the patient’s medical record before undertaking the procedure.

• Develop a process for individualization of standard work based on patient risk factors (consider a team huddle with the patient).

\textsuperscript{i}Michigan Anticoagulation Quality Improvement Initiative Anticoagulation Toolkit (V 1.7): A consortium-Developed Quick Reference for Anticoagulation. \url{http://anticoagulationtoolkit.org/sites/default/files/toolkit_pdfs/toolkitfull.pdf}

\textsuperscript{ii}UM Medicine Pharmacy Services (2014). \url{http://depts.washington.edu/anticoag/home/content/uw-medicine-alternative-monitoring-antithrombotic-agents#apixaban}

Improving DOAC quality and safety

• Share DOAC events, root cause analyses (RCAs) and failure mode effects analyses (FMEAs) with your PSO to promote national learning.
• Raise awareness of DOAC utilization and safety events within your organization.
  - Safety alerts
  - Case studies, safety stories and huddles
• Review DOAC related events with a multidisciplinary team.
  - Identify contributing factors
  - Review workflows
• Develop standard processes, guidelines and protocols for managing DOAC therapy in all phases of care.
• Review Joint Commission standard MM.05.01.01 - pharmacy review.
One organization’s approach

Steve Meisel, Pharm.D., CPPS
Director of Patient Safety
Fairview Health Services
Fairview Health Services
Provides a full continuum of health and medical services.

- Not-for-profit organization established in 1906
- Partner with the University of Minnesota since 1997
- 22,000+ employees
- 2,300 aligned physicians
- 7 hospitals and medical centers (1,602 staffed beds)
- 45+ primary care clinics
- 55+ specialty clinics
- 47 senior housing locations
- Home care, home medical and hospice
- Urgent care and retail clinics

2015 data
- 67,682 inpatient admissions
- 345,000 assigned/attributed lives
- $3.9 billion total revenue

2017: acquired Healtheast with its 4 hospitals and 12 clinics
Fairview Pharmacy Services

For consumers and patients
• Retail pharmacies (36)
• Hospital pharmacies (7)
• Specialty pharmacy (serves patients in all 50 states)
• Infusion services
• Medication therapy management (33 clinics)
• Mail service pharmacy
• Compounding pharmacy (IntegraDose©)
• Central packaging
• Long-term care/assisted living pharmacy
• Clinical trials services
• Anti-coagulation clinics (30)
• Wholesale pharmacy
• Center for Bleeding and Clotting Disorders

For employers and health systems
• ClearScriptSM prescription benefit management
• Fairview Purchasing Network
• Excelera© Network

1,500+ FPS and inpatient pharmacy employees
2.5 million ambulatory prescriptions filled in 2015
$14 million in 1996 to over $1.1 billion in revenue

2016 data
• > 8,000,000 annual inpatient doses dispensed
• 1.7 million annual retail pharmacy prescriptions
Organizational approach to safety
Organizational approach to safety

- Leadership and culture
- Adaptive change: resilience, teamwork, communication
- Technical and process: deploy all known best practices
- Innovation: invent new best practices

Patient safety

Training

Measurement
Designing reliable systems of care

- Prevent
- Detect
- Mitigate
Prevent

• Order sets
• Computer alerts
• Double-checks
• Smart-pumps
• Hard stops
• Floor stock limits

• Pharmacist oversight
• Prospective risk assessment
• Medication reconciliation
• Bar coding
Detect

- Computer alerts
- Double-checks
- Smart-pumps
- Monitoring devices and schedules
- Critical value management
Mitigate

Protocols for recovery: prior to calling physician

- Narcotic oversedation
- Hypoglycemia
- Extravasation
- Rapid response teams
Basic tenet #1

Shame on us if we don’t learn from the experiences of others.
Basic tenet #2

If it has happened elsewhere, it can happen here. Complacency is an independent risk.
Basic tenet #3

If someone else has dreamed up a solution, we should implement it unless we can prove we can solve the problem better or differently.
Basic tenet #4

We will implement the same best practice universally across the company.
Basic tenet #5

If we have identified and/or solved a problem it is our obligation to share our experiences so others can benefit.
Errors with DOACs
No reported A, F, G, H, or I events due to error. 4 ADEs unrelated to error (one D & 4 F) also occurred during this time.
Error types

“Standard errors” (10)
- Missed dose or wrong time
- Omission (4)
- Failure of medication reconciliation (3)
- Wrong frequency ordered
- Capsule inappropriately opened

DOAC-specific errors (6)
- Overlap with heparin or aspirin (2)
- Renal dosing error (2)
- Transitions with heparin (2)
Case scenario 1

Patient had renal failure with estimated CrCl < 20 ml/min. Pharmacist misunderstood the renal dose adjustment chart in the guideline table and mistakenly adjusted the dose of apixaban down to 2.5mg bid (vs 5mg bid). Two other pharmacists reviewed this chart over the next 4 days and did not change the dose. (Harm D)
Patient was going for cardioversion. Cardiologist wanted apixaban started before cardioversion. Med ordered at 0900, pharmacy verified at 0915 after discussing apixaban use while on heparin drip with him. Heparin Xa came back about same time as all of this, and was sub-therapeutic. Pharmacist ordered a heparin bolus and increased drip rate. The pharmacist was approached after lunch by the nurse; she said she did not see orders for apixaban and heparin bolus and rate change because she had already released and "signed off on cardioversion orders." (Harm D)
Case scenario 3

- Patient on Heparin protocol given 4,000 unit bolus late in the evening subsequent to a low anti Xa level.
- Rivaroxaban 15mg orally daily with supper ordered at 22:46 and given at 00:36.
- 05:00 anti Xa level canceled, due to questionable specimen.
- Redraw of anti Xa level = 1.94 (critical); heparin discontinued

Problems
- Transition from IV heparin to rivaroxaban, which is supposed to start 2 hours after heparin discontinuation. No orders to discontinue heparin.
- Due to recent IV bolus of heparin, rivaroxaban should have been delayed until morning.
- The incorrect dose of rivaroxaban was prescribed. (should have been 15mg PO BID for 21 days then decrease to 20mg PO daily. (Harm D)
Actions to prevent errors with DOACs
Order search

<table>
<thead>
<tr>
<th>Name</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>apixaban ANTICOAGULANT (ELIQUIS) DVT/PE - initial dosing</td>
<td></td>
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<tr>
<td>apixaban ANTICOAGULANT (ELIQUIS) tablet</td>
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</tbody>
</table>
Choosing the tablet
Choosing the tablet

Apixaban is an oral anticoagulant which works by inhibiting factor Xa.

APIXABAN (ELIQUIS) Dose

DVT or PE treatment: 10 mg PO BID x 7 days; then 5 mg PO BID

DVT or PE prophylaxis: 2.5 mg PO BID (following a minimum of 6 months with full treatment dosing)

Atrial fibrillation: 5 mg PO BID. Reduce dose to 2.5 mg PO BID if patient has 2 or more of the following criteria:

1. ECF > 1.5 mg/dL
2. Age > 80 years old
3. Body weight < 60 kg

Apixaban does NOT dose reduction with moderate renal dysfunction (Cl > 5 mL/min). Do not use apixaban if Cl < 15, or in those undergoing dialysis.

CONVERSIONS FROM APIXABAN

From | To | Instructions
--- | --- | ---
Argatroban | Apixaban | Stop apixaban. Start parenteral anticoagulant 12 hrs later. In cases of high bleeding risk, consider omitting initial bolus when transitioning to heparin drip.
Dabigatran (Edoxaban) | Apixaban | Stop apixaban. 12 hours later, start dabigatran/edoxaban/riboxaban.
Warfarin | Apixaban | Stop apixaban. 12 hours after last apixaban dose, start a parenteral anticoagulant (e.g. heparin, enoxaparin, argatroban) AND start warfarin. Once the INR is over 2, can stop the parenteral anticoagulant.

*Note: Apixaban increases INR. Until apixaban has cleared from the body, the INR may not be an accurate measure of warfarin anticoagulation.

CONVERTING TO APIXABAN

From | To | Instructions
--- | --- | ---
Argatroban | Apixaban | Start apixaban within 2 hrs after stopping argatroban/lowmolecular-weight heparin.
Dabigatran (Edoxaban) | Apixaban | If Cl > 30, start dabigatran 12 hrs after last dose of dabigatran given. If Cl < 30, start dabigatran 24 hours after last dose of dabigatran given.
Edoxaban | Apixaban | Wait 24 hours after last dose of edoxaban to initiate apixaban.
Enoxaparin | Apixaban | If taking 1 mg/kg (full dose) enoxaparin start apixaban when NEXT dose of enoxaparin would have been due.
If taking prophylaxis (30-40 mg) enoxaparin start apixaban when clinically indicated, irrespective of when last enoxaparin dose given.
Fondaparinux | Apixaban | If taking 5-10 mg (full dose) fondaparinux start apixaban when NEXT fondaparinux dose due.
If taking 2.5 mg (prophylaxis dose) fondaparinux start apixaban whenever
# Transition of Anticoagulants 2016

**Van Hellerslia, PharmD, BCPS, CACP**, Clinical Assistant Professor of Pharmacy Practice, Temple University School of Pharmacy, Philadelphia, PA

**Pallav Mehta, MD**, Assistant Professor of Medicine, Division of Hematology/Oncology, MD Anderson Cancer Center at Cooper

**Reviewer**: Kelly Rudd, PharmD, BCPS, CACP, Clinical Specialist, Anticoagulation, Bassett Medical Center, Cooperstown, New York

<table>
<thead>
<tr>
<th>Brand</th>
<th>Generic</th>
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<tbody>
<tr>
<td>Angiomax</td>
<td>bivalirudin</td>
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<tr>
<td>Arixtra</td>
<td>fondaparinux</td>
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<tr>
<td>Coumadin</td>
<td>warfarin</td>
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<tr>
<td>Eliquis</td>
<td>apixaban</td>
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<td>Fragmin</td>
<td>dalteparin</td>
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<td>Lovenox</td>
<td>enoxaparin</td>
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<td>Pradaxa</td>
<td>dabigatran</td>
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<td>Savaysa</td>
<td>edoxaban</td>
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<tr>
<td>Xarelto</td>
<td>rivaroxaban</td>
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<table>
<thead>
<tr>
<th>From</th>
<th>To</th>
<th>Action</th>
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<tbody>
<tr>
<td>Apixaban</td>
<td>Argatroban/Bivalirudin/Enoxaparin/Dalteparin/Fondaparinux/Heparin</td>
<td>Wait 12 hours after last dose of apixaban to initiate parenteral anticoagulant. In cases of high bleeding risk, consider omitting initial bolus when transitioning to heparin infusion.</td>
</tr>
<tr>
<td>Apixaban</td>
<td>Warfarin</td>
<td>When going from apixaban to warfarin, consider the use of parenteral anticoagulation as a bridge (eg, start heparin infusion/enoxaparin and warfarin 12 hours after last dose of apixaban and discontinue parenteral anticoagulant when INR is therapeutic ≥2).</td>
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</table>
## Anticoagulation Resources

<table>
<thead>
<tr>
<th>Policies</th>
<th>Labs</th>
<th>Reversal</th>
<th>Guidelines</th>
<th>Patient Education</th>
<th>Other Resources</th>
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<tr>
<td><strong>Policies</strong></td>
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<td>Rivaroxaban (Xarelto®), Apixaban (Eliquis®) and Edoxaban (Savaysa®) Bleeding Treatment Algorithm (2016)</td>
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<td><strong>Guidelines</strong></td>
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<td>Argatroban/Lepirudin/Fondaparinux Guidelines*</td>
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<td>Suggestions for Management around Dental Procedures</td>
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<td>*Lepirudin is No longer manufactured as of May 2012: This was a business decision and not due to safety concerns. There are no other manufacturers of lepirudin injection</td>
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Panel for initial dosing

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<tr>
<td>apixaban ANTICOAGULANT (ELIQUIS) tablet</td>
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</tbody>
</table>
Panel for initial dosing

Apixaban is an oral anticoagulant which works by inhibiting factor 10a.

DVT or PE treatment: 10 mg PO BID x 7 days, then 5 mg PO BID

DVT or PE prophylaxis: 2.5 mg PO BID (following a minimum of 6 months with full treatment dosing)

Atrial Fibrillation: 5 mg PO BID. Reduce dose to 2.5 mg PO BID if patient has 2 or more of the following criteria:
1. Scr > 1.5 mg/dl
2. Age > 80 years old
3. Body weight < 60 kg

Apixaban does NOT dose reduction with moderate renal dysfunction (CL > 15 mL/min). Do not use apixaban if CL < 15, or in those undergoing dialysis.

<table>
<thead>
<tr>
<th>CONVERSIONS FROM APIXABAN</th>
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</thead>
<tbody>
<tr>
<td>From</td>
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<tr>
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</tr>
<tr>
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<td>Warfarin</td>
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<td>Apixaban</td>
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</table>
Dabigatran “SIDE-PANEL” Wording

Dabigatran (Pradaxa) is an oral anticoagulant which works by directly inhibiting thrombin.

DVT or PE Treatment/Prophylaxis Dose:
If CrCL is GREATER than 30 mL/min, give 150 mg PO BID.
Use dabigatran with caution in those ≥ 75 years of age. (Consider reducing dose to 110 mg if ≥ 75 year old)
If CrCL is LESS than/equal to 30 mL/min, DO NOT USE.

Nonvalvular AFib Dose:
If CrCL is GREATER than 30 mL/min, give 150 mg PO BID.
If CrCl is 15-30 mL/min, give 75 mg PO BID.
If CrCL is LESS than 15 mL/min or if on dialysis, DO NOT USE.

Postoperative prophylaxis following hip replacement
If CrCl > 30 mL/min: Give 110 mg PO once, followed by 220 mg PO daily for 28-35 days.
If CrCL is LESS than/equal to 30 mL/min, DO NOT USE.
Guidance when transitioning FROM another anticoagulant over to Dabigatran

<table>
<thead>
<tr>
<th>Converting FROM</th>
<th>Instructions for transitioning TO Dabigatran</th>
</tr>
</thead>
<tbody>
<tr>
<td>Apixaban</td>
<td>Give first dose of dabigatran when next apixaban dose would have been due.</td>
</tr>
<tr>
<td>Argatroban</td>
<td>Start dabigatran at the <strong>same time</strong> that argatroban/bivalirudin is stopped.</td>
</tr>
<tr>
<td>Edoxaban</td>
<td>Wait 24 hours after last dose of edoxaban before starting dabigatran.</td>
</tr>
</tbody>
</table>
| Enoxaparin     | If taking high dose (1 mg/kg) enoxaparin: start dabigatran when NEXT dose of enoxaparin would have been due.  
|               | If taking low dose (30-40mg daily) enoxaparin: start dabigatran whenever clinically indicated, irrespective of when last enoxaparin dose given. |
| Heparin drip   | Start dabigatran at the **same time** that heparin drip is stopped. |
| Warfarin       | Stop warfarin. Start dabigatran when the INR/chromogenic factor 10 is below the therapeutic goal range. |
| Fondaparinux   | If taking fondaparinux 5-10 mg daily, start dabigatran when NEXT fondaparinux dose due.  
|               | If taking fondaparinux 2.5 mg daily, start dabigatran whenever clinically indicated (irrespective of when last fondaparinux dose given). |
Other actions

- Renal dosing protocols
- Medication reconciliation
- Anticoagulation clinics
  - Discharged from clinic once INR <2 and on DOAC
  - Considering quarterly visits
- Reversal protocols
- Required education for pharmacists
- Patient discharge teaching
  - New starts (some hospitals)
- Interventional radiology hold protocol
**IR protocol**

<table>
<thead>
<tr>
<th>Anticoagulants</th>
<th>Hold</th>
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<tbody>
<tr>
<td>apixaban (ELIQUIS)</td>
<td>24 HOURS</td>
</tr>
<tr>
<td>argatroban (ACOVA)</td>
<td>NO HOLD</td>
</tr>
<tr>
<td>bivalirudin (ANGIOMAX)</td>
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</tr>
<tr>
<td>dabigatran (PRADAXA)</td>
<td>NO HOLD</td>
</tr>
<tr>
<td>edoxaban (SAVAYSA)</td>
<td>24 HOURS</td>
</tr>
</tbody>
</table>
| enoxaparin (LOVENOX)            | OUTPATIENT: Minimal bleeding risk Q12H and Q24H dosing: Hold enoxaparin dose the AM of procedure  
INPATIENT: Minimal bleeding risk Q12H and Q24H Dosing: Hold enoxaparin dose the AM of procedure |
| fondaparinux (ARIXTRA)          | 24 HOURS                  |
| heparin                         | 2 hour IV Heparin hold for the University and 4 hour IV heparin hold for the community sites due to workflow issues.  
"SQ heparin Q8hrs -- hold for 8 hrs....  
SQ heparin Q12 hrs-- hold for 12 hrs...." |
| rivaroxaban (XARELTO)           | 24 HOURS                  |
| warfarin (COUMADIN)             | Check with the interventional radiology department on the hold time for the warfarin (COUMADIN).  
The hold time length will be based on the INR of the patient and the discretion of the provider based on the level of the procedure risk. |
IR protocol

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Duplicate drug or drug interactions

Drug-Drug: heparin (porcine) and apixaban ANTICOAGULANT
Use of Direct Factor Xa Inhibitors with Heparin & Factor Xa Inhibitors may increase the risk of bleeding. The coadministration of Heparin & Factor Xa Inhibitors and Direct Factor Xa Inhibitors should be avoided according official package labeling.

Details

Override Reason...

Duplicate Therapy: heparin (porcine), apixaban ANTICOAGULANT
HEPARINS AND RELATED. No Abuse/Dependency Potential.
Details

Override Reason...
Pending actions

• Surgical hold protocol
• Best practice alert for procedure order
• Consider failure rates as a potential adverse drug event (ADE)
Questions?

Comments?
# Medication Safety Advisory Team Members

<table>
<thead>
<tr>
<th>Name</th>
<th>Credentials</th>
<th>Title</th>
<th>Organization</th>
</tr>
</thead>
<tbody>
<tr>
<td>Vanessa B. Bibbs</td>
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<td>Accreditation Nurse Specialist</td>
<td>Vidant Health</td>
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<td>University of Iowa Hospitals &amp; Clinics; University of Iowa Carver College of Medicine;</td>
</tr>
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<td>Vizient</td>
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<td>MD</td>
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<td>Center for scholarship in patient care quality and safety; UWMC</td>
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<td>AVP Safety Program</td>
<td>Vizient</td>
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<td>SSM Health</td>
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<td>Director of Clinical Pharmacy Services Director</td>
<td>Albany Medical Center</td>
</tr>
<tr>
<td>Jim Lichauer</td>
<td>Pharm.D., BCPS, FASHP</td>
<td>Project Manager, PI Collaborative and Advisory-Pharmacy</td>
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<tr>
<td>Elena Meeker</td>
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<td>Medication Safety Pharmacist</td>
<td>University of Washington Medical Center</td>
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<tr>
<td>Steven B. Meisel</td>
<td>Pharm.D., CPPS</td>
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<td>Fairview Health Services</td>
</tr>
<tr>
<td>Joe Melucci</td>
<td>RPH, MBA,</td>
<td>Medication Safety Officer</td>
<td>The Ohio State University Wexner Medical Center</td>
</tr>
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<td>Pharm.D.</td>
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<td>Upstate University Hospital</td>
</tr>
<tr>
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<td>DHS-Pharmacy Affairs</td>
<td>LA County</td>
</tr>
<tr>
<td>Christi Quarles Smith</td>
<td>Pharm.D., MBA</td>
<td>Assistant director Pharmacy for medication safety</td>
<td>University of Arkansas</td>
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<tr>
<td>Jessica Schoenthal</td>
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<tr>
<td>Robert Sikorski</td>
<td>MD</td>
<td>Assistant Professor, Medical Director of Trauma Anesthesiology, Department of Anesthesiology and Critical Care Medicine</td>
<td>The Johns Hopkins Hospital</td>
</tr>
<tr>
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<td>Denver Health</td>
</tr>
<tr>
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<td>Pharm.D., and MPH Student</td>
<td>PSO Intern</td>
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<tr>
<td>Tammy Williams</td>
<td>RN, MSN, CPPS</td>
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</table>
PSO Advisory Teams

Vizient is currently looking for experts to collaborate with Vizient PSO in the following topics:

• Telemetry alarm fatigue
• Reliable electronic communication among the healthcare team
• Behavioral health management

If you or someone in your organization is an expert and interested in partnering on these teams, please contact Bobbi Kosloski at bobbi.kosloski@vizientinc.com.
References

ISMP Quarterly Watch: Perspectives from new adverse event reports available at http://www.ismp.org/QuarterWatch/pdfs/2016Q2.pdf

Management of Patients on Non–Vitamin K Antagonist Oral Anticoagulants in the Acute Care and Periprocedural Setting: A Scientific Statement From the American Heart Association available at http://circ.ahajournals.org/content/early/2017/02/06/CIR.0000000000000477

2017 ACC Expert Consensus Decision Pathway for Periprocedural Management of Anticoagulation in Patients With Nonvalvular Atrial Fibrillation available at http://www.onlinejacc.org/content/early/2017/01/05/j.jacc.2016.11.024


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