Straight to the Point of Care: DOACs from Hospital to Home

May 11th, 2018
11:45 AM – 12:45 AM
American College of Cardiology – Rhode Island Chapter
For the CV Team by the CV Team

Ralph J. Riello III, PharmD, BCPS
Cardiovascular Critical Care Pharmacist
Coronary Intensive Care Unit (CICU)
Yale-New Haven Hospital

Disclosures

- Dr. Riello has the following conflicts of interest:
  - Advisory boards and/or consulting fees: Bristol-Myers Squibb, Johnson & Johnson, Pfizer, Portola
  - Speaker's bureau: Janssen, Portola
  - Stock Ownership: Portola
- Off-label or investigational uses of medications will be discussed

Objectives

1. Review evidence-based strategies for the safe use of direct oral anticoagulants to prevent stroke, systemic thromboembolism, and minimize bleeding
2. Discuss best practices for ensuring optimal transitions of care across the healthcare continuum for patients prescribed anticoagulation

Direct Oral Anticoagulants

Nomenclature

- DOAC vs. NOAC vs. TSOAC
- **D**irect **T**hrombin Inhibitor
  - o**D**abiga**T**ran (Pradaxa®)
- Factor **Xa** Inhibitors
  - oApi**Xa**ban (Eliquis®)
  - oBetri**Xa**ban (Bevyxxa®)
  - oEdo**Xa**ban (Savaysa®)
  - oRivaro**Xa**ban (Xarelto®)

J Thromb Haemo. 2015;13:1154-6

DOAC Comparison

	Dabigatran	Rivaroxaban	Apixaban	Edoxaban
Target	IIa (Thrombin)	Xa	Xa	Xa
Administration	Do not crush	G, NG, but not J tube	Any feeding tube	G, NG, but not J tube
Drug-Drug Interactions	PPI's, potent CYP3A4 inducers & P-gp Inhibitors	Potent CYP3A4 inducers & P-gp inhibitors	Potent CYP3A4 inducers & P-gp Inhibitors	P-gp inhibitors
Indication Based Dosing	• AF: 150 mg BID; if CrCl 15-30 mL/min: 75 mg BID • VTE: 150 mg BID s/p 5-10 days parenteral lead-in	• AF: 20 mg QD; if CrCl 15-50 mL/min: 15 mg QD • VTE: 15 mg BID x 21 days then 20 mg QD	• AF: 5 mg BID; if ≥2 of 3: 1) Age ≥80 y/o; 2) Weight ≤60 kg, 3) SCr ≥1.5 mg/dL: 2.5 mg BID • VTE: 10 mg BID x 7 days then 5 mg BID	• AF: 60 mg QD; if CrCl 15-50 mL/min: 30 mg QD • VTE: 60 mg QD s/p 5-10 days parenteral lead-in; if CrCl 15-50 mL/min or ≤60 kg: 30 mg QD
Clinical Pearls	• Cannot remove from original packaging • Dyspepsia & gastritis very common side effects (35%) • Greater GI bleed risk than warfarin & other DOACs • 75 mg BID dose not studied in RE-LY trial	• Once daily dosing convenience • Take with meals • Safe in patients s/p gastric bypass surgery • Preferred DOAC in obese & underweight patients • Recent label update for hemodialysis patients	• 5 mg BID superior to warfarin for NVAF • All-cause mortality benefit compared to warfarin in NVAF • Lowest bleeding risk of all DOACs, warfarin, & even aspirin • May be preferred DOAC in hemodialysis, but dosing controversial • Avoid intentional under-dosing	• Once daily dosing convenience • 60 mg dose superior to warfarin for NVAF • Contraindicated in CrCl <15 mL/min or >95 mL/min • Not covered by many insurance plans • May be preferred DOAC in cancer associated thrombosis

P-gp inhibitors: amiodarone, azithromycin, captopril, clarithromycin, verapamil
CYP 3A4 inhibitors: atazanavir, darunavir, clarithromycin, ketoconazole, ritonavir
CYP 3A4 Inducers: carbamazepine, dexamethasone, fos/phenytoin, oxcarbazepine, phenobarbital, rifampin, St. John's wort

Guideline Excerpts

Panel	Condition	Recommendation
	Atrial Fibrillation	Warfarin (IA), Dabigatran (IB), Rivaroxaban (IB), Apixaban (IB)
ACCP	Venous Thromboembolism	DOACs over VKA (2B)
	Valvular Heart Disease	DOACs over VKA (2C)

Circulation. 2014;130(23):2071-104
Chest. 2016;149(2):315-352
Circulation. 2017;135(25):e1159-e1195

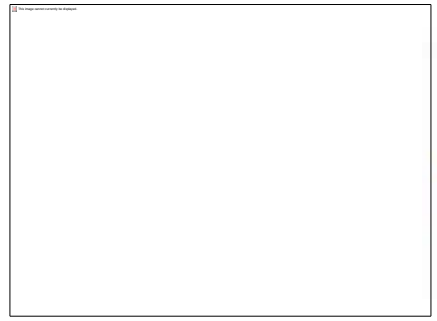
Special Populations

Condition	Eligibility
Mechanical prosthetic valve	Contraindicated
Mitral stenosis (moderate or severe)	Contraindicated
Aortic stenosis (mild, moderate, or severe)	Included in all RCTs except RE-LY
Following PCI w/ stent placement w/ DAPT	Preferred to triple therapy w/ VKA
Bioprosthetic valve	Acceptable if >3 months post-operatively
Transaortic Valve Replacement (TAVR)	RCTs underway, may also require DAPT

Eur Heart J. 2018;00:1-64

Upcoming Indications

- Extended duration VTE prophylaxis
- Heparin induced thrombocytopenia
- Cancer associated thrombosis
- Transaortic valve replacement
- Coronary / peripheral artery disease
- Heart failure
- Reversal



Atlantis

Hokusai VTE CANCER

ANNEXa 4

Transitions of Care

Transitions of Care

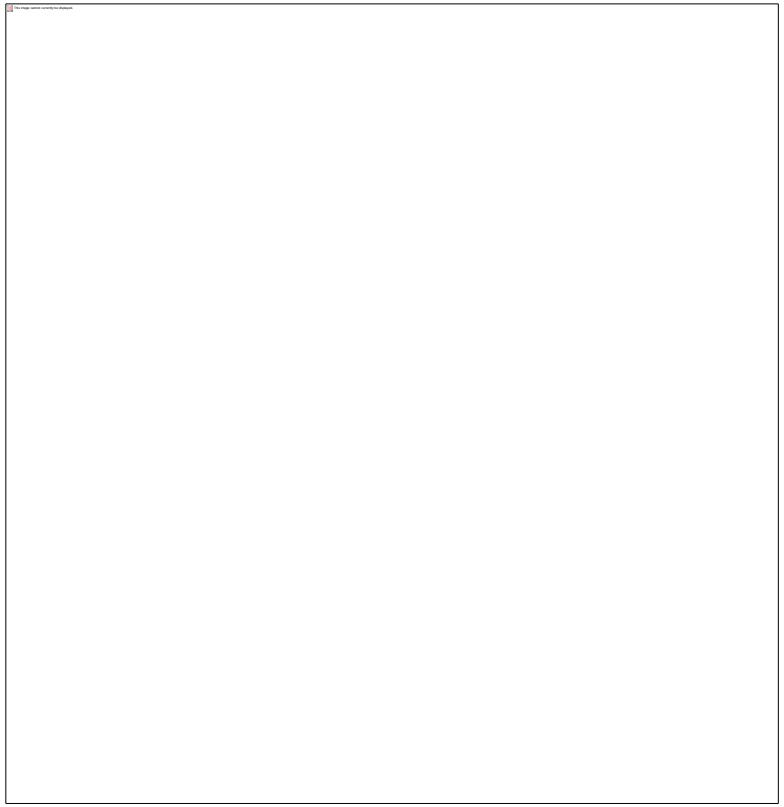
Transitions of Care

- "Random events connected to highly variable actions without only a remote possibility of meeting implied expectations"
  - Roger Resar, MD

  Agent of tremendous change and global innovation seeker

  Senior Fellow, Institute for Healthcare Improvement

  Assistant Professor of Medicine – Mayo Clinic



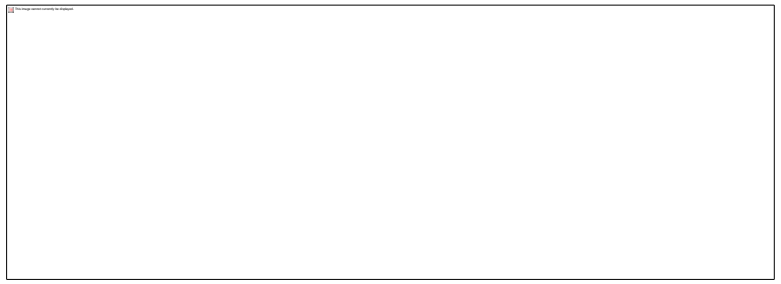
Hospitals. 1979;53(10):79-83

Transitions of Care

- "Continuity of patient care between different healthcare settings has been advocated **for nearly 20 years**, but little has been done to affect it. The study described here emphasizes the current lack of effort by healthcare providers in hospitals and nursing homes to find a workable solution"
  - Rosenthal & Miller

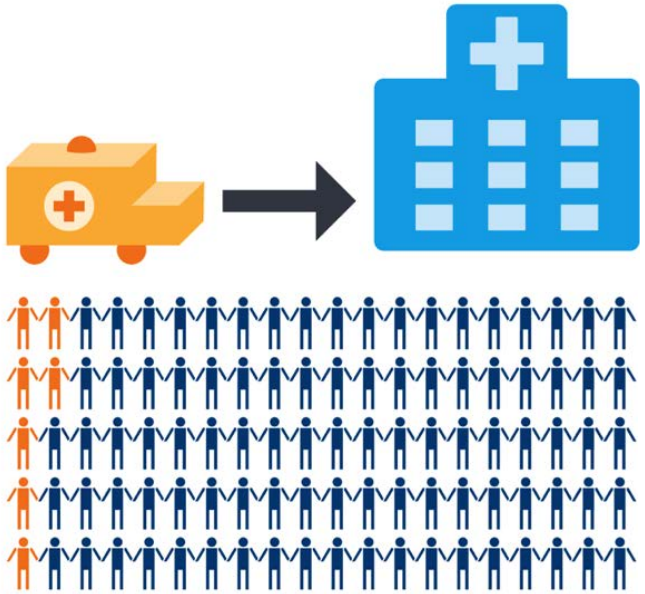
Hospitals. 1979;53(10):79-83

Gaps in Care



Adverse drug events during transitions of care are attributable to **medication changes**

Patients discharged from the hospital have at least 1 unintentional **medication discrepancy**

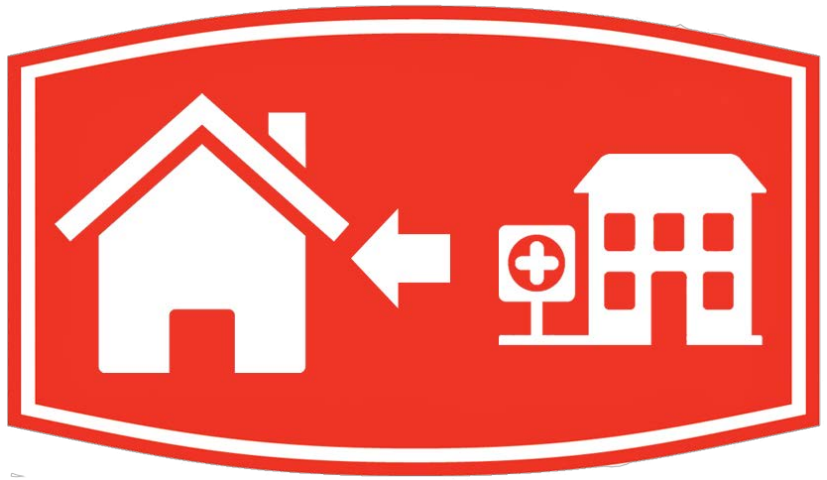


7% of all discharged patients end up in the emergency department **within 30 days**

Ann Pharmacother. 2008;42:1373–1379
JAMA. 2007;297(8):831-841
Arch Intern Med. 2004;164:545–550

Vitamin K Antagonists

- "Warfarin implicated in 33.3% of all emergency hospitalizations due to an adverse effect"
  1. Delayed onset of action
  2. Variable dosing regimen
  3. Education & compliance
  4. Monitoring & follow-up required
  5. Drug / diet / disease interactions



N Engl J Med. 2011;365(21):2002-2012

Direct Oral Anticoagulants

- "Safer bridge from hospital to home?"
  1. Immediate acting
  2. One size fits *most* dosing
  3. Education & compliance
  4. Minimal monitoring & follow-up
  5. Limited drug interactions

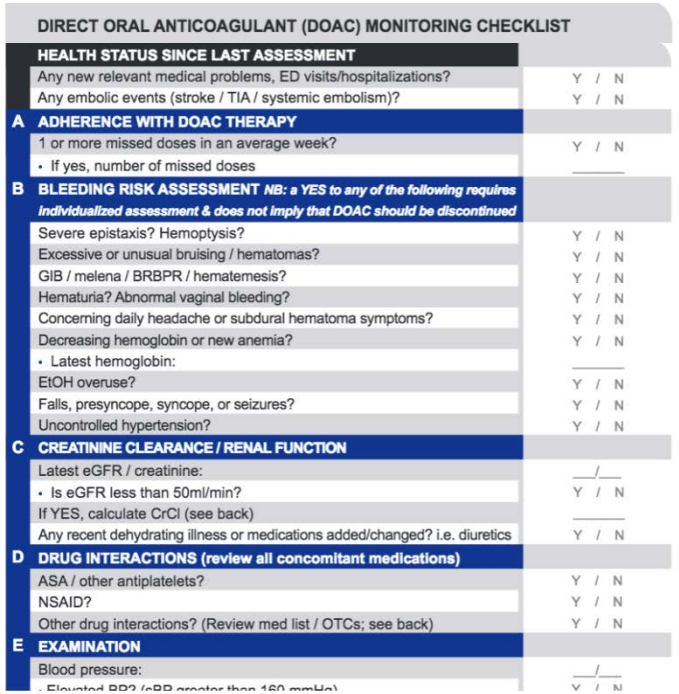
DOAC Checklist

1. Affordability
   - oPrior authorization
   - oOut-of-pocket costs
   - oCo-pay assistance
2. Prescribing
   - oAppropriate indication
   - oOptimal DOAC selection
   - oCorrect regimen
     - – Dose, frequency, duration, adjustments

Can Pharm J (Ott). 2018;151(2):102-106

DOAC Checklist

3. Monitoring
   - oCreatinine checks
   - oDocumentation
   - oPeriodic follow-up
4. Patient counseling
   - oAdherence, risk of non-compliance
   - oAvoiding NSAIDs, etc.
   - oBleeding triage techniques
     - – Lifeline to call with questions



DIRECT ORAL ANTICOAGULANT (DOAC) MONITORING CHECKLIST

	HEALTH STATUS SINCE LAST ASSESSMENT	
	Any new relevant medical problems, ED visits/hospitalizations?	Y / N
	Any embolic events (stroke / TIA / systemic embolism)?	Y / N
A	**ADHERENCE WITH DOAC THERAPY**	
	1 or more missed doses in an average week?	Y / N
	• If yes, number of missed doses	_____
B	**BLEEDING RISK ASSESSMENT** *NB: a YES to any of the following requires individualized assessment & does not imply that DOAC should be discontinued*	
	Severe epistaxis? Hemoptysis?	Y / N
	Excessive or unusual bruising / hematomas?	Y / N
	GIB / melena / BRBPR / hematemesis?	Y / N
	Hematuria? Abnormal vaginal bleeding?	Y / N
	Concerning daily headache or subdural hematoma symptoms?	Y / N
	Decreasing hemoglobin or new anemia?	Y / N
	• Latest hemoglobin:	_____
	EtOH overuse?	Y / N
	Falls, presyncope, syncope, or seizures?	Y / N
	Uncontrolled hypertension?	Y / N
C	**CREATININE CLEARANCE / RENAL FUNCTION**	
	Latest eGFR / creatinine:	__/__
	• Is eGFR less than 50ml/min?	Y / N
	If YES, calculate CrCl (see back)	_____
	Any recent dehydrating illness or medications added/changed? i.e. diuretics	Y / N
D	**DRUG INTERACTIONS (review all concomitant medications)**	
	ASA / other antiplatelets?	Y / N
	NSAID?	Y / N
	Other drug interactions? (Review med list / OTCs; see back)	Y / N
E	**EXAMINATION**	
	Blood pressure:	__/__
	• Elevated BP? (eBP greater than 160 mmHg)	Y / N

Can Pharm J (Ott). 2018;151(2):102-106

Take Home Points

- DOACs offer at least as efficacious, if not safer and more convenient anticoagulation than warfarin
- More data is still needed to establish the safety and efficacy for DOACs beyond traditional indications
- Any phase of care change represents a vulnerable gap in care where preventable errors are prone
- Anticoagulation increases risk of harm across care settings, though DOACs may help streamline care continuum

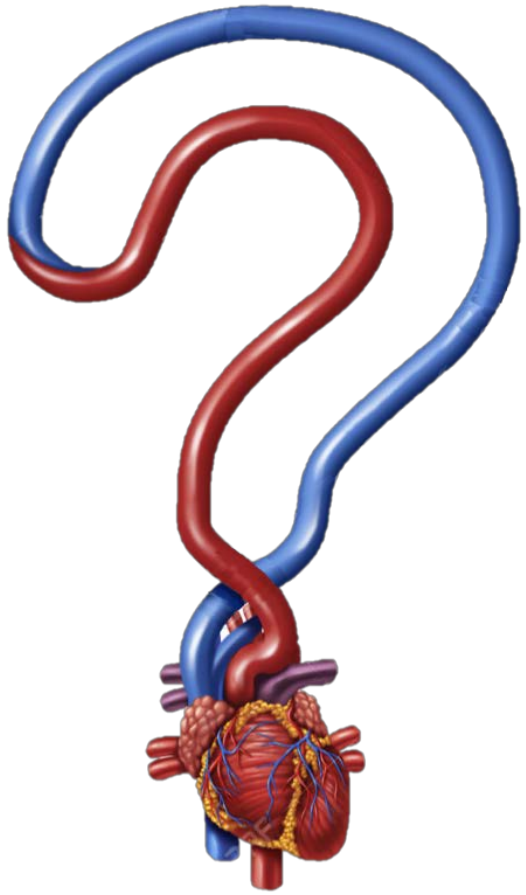
Thank You!


BRACE YOURSELVES
Factor Xa
Andexanet
APPROVED
Lacks Membrane-Binding Domain
DOACS ARE COMING

References

1. Barnes GD, Ageno W, Ansell J, Kaatz S, for the Subcommittee on the Control of Anticoagulation. Recommendation on the nomenclature for oral anticoagulants: communication from SSC of the ISTH. *J Thromb Haemo*. 2015;13:1154-6.
2. Steffel J, Verhamme P, Potpara TS, et al. The 2018 European Heart Rhythm Association Pracitical Guide on the use of non-vitamin K antagonist oral anticoagulants in patients with atrial fibrillation. *Eur Heart J*. 2018;00:1-64.
3. January CT, Wann LS, Alpert JS, Calkins H, et al. 2014 AHA/ACC/HRS guideline for the management of patients with atrial fibrillation: executive summary: a report of the American College of Cardiology/American Heart Association Task Force on practice guidelines and the Heart Rhythm Society. *Circulation*. 2014;130(23):2071-104
4. Kearon C, Aki EA, Omelas J, et al. Antithrombotic Therapy for VTE Disease: CHEST Guideline and Expert Panel Report. *Chest*. 2016;149(2):315-352
5. Nishimura RA, Otto CM, Bonow RO, et al. 2017 AHA/ACC Focused Update of the 2014 AHA/ACC Guideline for the Management of Patients With Valvular Heart Disease: A Report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines. *Circulation*. 2017;135(25):e1159-e1195
6. Rosenthal JM, Miller DB. Providers of failed to work for continuity. *Hospitals*. 1979;53(10):79-83
7. Kripalani S, LeFevre F, Phillips CO, Williams MV, Basaviah P, Baker DW. Deficits in communication and information transfer between hospital-based and primary care physicians: implications for patient safety and continuity of care. *JAMA*. 2007;297(8):831-841
8. Wong JD, Bajcar JM, Wong GG, et al. Medication reconciliation at hospital discharge: evaluating discrepancies. *Ann Pharmacother.* 2008;42:1373–1379
9. Boockvar K, Fishman E, Kyriacou CK, et al. Adverse events due to discontinuations in drug use and dose changes in patients transferred between acute and long-term care facilities. *Arch Intern Med*. 2004;164:545–550
10. Budnitz DS, Lovegrove MC, Shehab N, Richards CL. Emergency hospitalizations for adverse drug events in older Americans. *N Engl J Med*. 2011;365(21):2002-2012
11. Leblanc K, Semchuk WM, Papastergiou J, et al. A pharmacist checklist for direct oral anticoagulant management: Raising the bar. *Can Pharm J (Ott)*. 2018;151(2):102-106

Questions?



Contact Information

Ralph J. Riello III, PharmD, BCPS
Cardiovascular Critical Care Pharmacist
Adjunct Assistant Professor of Pharmacy Practice
University of Connecticut School of Pharmacy
Coronary Intensive Care Unit (CICU)
Yale-New Haven Hospital
20 York Street, PS LL-01
New Haven, CT 06510
Email: ralph.riello@ynhh.org
Office Number: 475-246-4679
Office Location: SP 5-329
Pager: 203-128-2049