Outpatient Anticoagulation Stewardship

Focusing on DOAC oversight models in Anticoagulation Management Services

Tuesday | July 25, 2023 | 12pm EST

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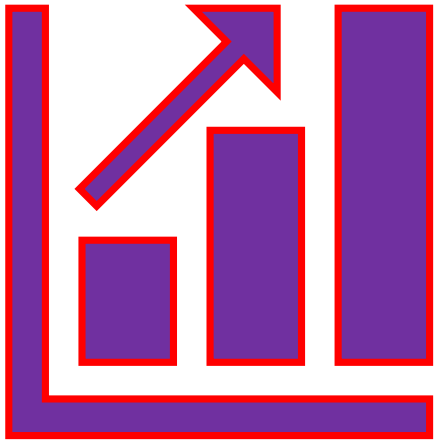
DOAC Use Continues to Increase

- DOAC use continues to increase worldwide:
  - DOACs have replaced warfarin as the primary anticoagulant for atrial fibrillation (AF) and venous thromboembolism (VTE) in practice and guidelines
  - DOACs have also captured some of the patient population that was previously not anticoagulated for AF
- DOACs are "easier" to manage and improve patients' quality of life compared with warfarin
  - No routine anticoagulation monitoring
  - Fixed doses
  - Fewer DDIs and FDIs
  - Less major bleeding

From 2016 → 2020: Number of patients prescribed an OAC increased 17.8%, DOACs increased by 83.6%

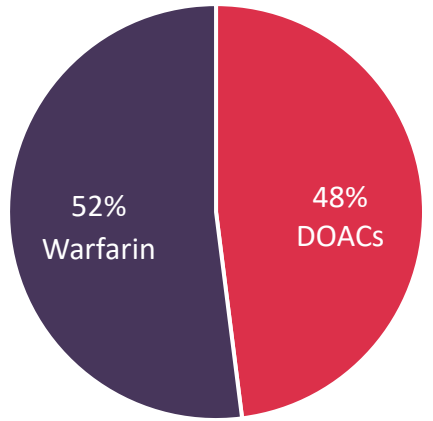


Beier et al. PLoS One. 2022 Oct 6;17(10):e0274237; Tripodi et al. Thromb Res. 2023 May;225:11-15; Geller et al. Thromb Res. 2023 May;225:110-115; Navar et al. J Am Heart Assoc. 2022 Nov 15;11(22):e026723.

Real-World Impact of Bleeding Associated with DOACs

- A decade after the DOACs were introduced, we have a better understanding of the risk of bleeding in the real-world population
- Impact on national healthcare system for bleeding-related adverse drug events:
  - Estimates based on data from a nationally representative public health surveillance system from 2016-2020 (5 years)
  - Over 1.2 million ED visits for oral anticoagulation-related bleeding
    - > 250,000 ED visits annually
    - Bleeding represented 87% of all OAC adverse drug events (resulting in an ED visit)
    - Hospital admission was required for approximately half of the bleeding related visits
  - DOACs accounted for 48% of the visits
    - 5.9 ED visits /100 patients dispensed DOACs, 13 ED visits / 100 patients dispensed warfarin

ED visits for oral anticoagulant-related bleeding (2016-2020)



Geller et al. Thromb Res. 2023 May;225:110-115.

Call to Action

- 1 ED visit for bleeding per 27 patients prescribed a DOAC in 2020!

- We're starting to hear a similar call to action from many different sources nationally and globally
  - Further bleeding prevention efforts are warranted alongside efforts to expand appropriate use
  - Efforts to improve appropriate prescribing and monitoring of OACs remain important in the era of DOACs
  - It is anticipated that both patients and health-systems would benefit from such comprehensive organization (referring to anticoagulation services)

Tripodi et al. Thromb Res. 2023 May;225:11-15; Geller et al. Thromb Res. 2023 May;225:110-115; Burnett et al. J Thromb Thrombolysis. 2016 Jan;41(1):206-32, Witt et al. Chest. 2005 May;127(5):1515-22, van Walraven et al. Chest. 2006 May;129(5):1155-66.

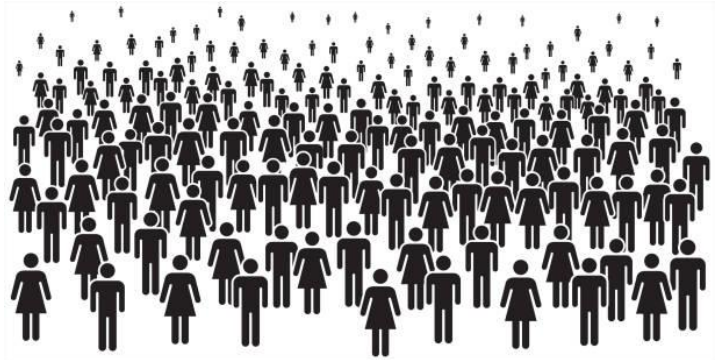
Potential roles of a dedicated anticoagulation service for DOAC oversight

- Evaluate need for concomitant antiplatelet use
- Ensure correct dosing at time of initiation and with changes in clinical status (renal, weight, cancer, absorption, etc.)
- Planning for procedures/surgery
- Assessing for potential DDIs with changes to medication lists
- Ongoing education and support for medication adherence
- Minor/Patient-relevant bleeding events

Sylvester et al. J Thromb Thrombolysis. 2018 Feb;45(2):274-280, https://anticoagulationtoolkit.org/sites/default/files/toolkit_pdfs/toolkitfull.pdf, http://anthostherapeutics.com/wp-content/uploads/2023/06/ISTH-2023-Patient-Relevant-Bleeding-Oral-6-27-FINAL.pdf)

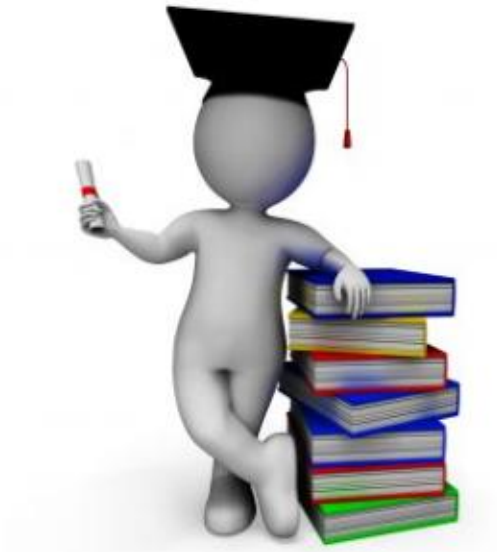
DOAC Management Models

- Models for centralized DOAC oversight
  - Mimic the warfarin management model: Individual patient-focused with scheduled check points in addition to as needed interventions
  - Population health model: Oversight of a large population of patients on DOACs with interventions when certain “rules” are triggered
  - Hybrid approach: small panel of patients that require close management with larger oversight of the lower risk population
  - Anything in between!
- The best fit model will depend on your population, resources, and most importantly will continuously evolve!



BWH AMS Clinic Staffing and Credentials

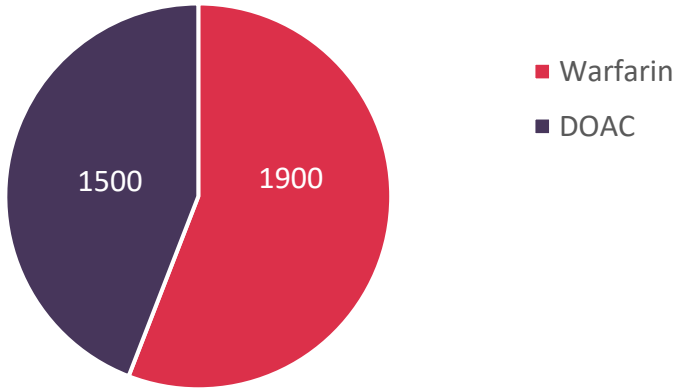
- Leadership
  - Two Co-Medical Directors (Cardiologist and Hematologist)
  - Executive Director of Pharmacy
  - Ambulatory Director of Pharmacy
  - Pharmacy Manager
- Staff
  - 10 Full time pharmacists, 1 part time pharmacist
  - 1 Operations coordinator
  - 3 full time and 1 part time patient navigators
- Recognition and Credentials
  - Recognized as an Anticoagulation Center of Excellence by the AC Forum
  - 15 credentialed Midlevel Practitioners practicing under Collaborative Practice Agreements
  - 6 Pharmacists are certified anticoagulation providers (CACP)
  - 6 Pharmacists are Board Certified (BCPS, BCACP, BCGP)



BWH Anticoagulation Management Services

- Virtual clinic model for warfarin and DOACs
  - Primary method of communication: telephone or patient portal
- Provide anticoagulation services through a collaborative practice agreement which includes:
  - Initiation / selection of anticoagulants
  - Initial dosing and dose adjustments
  - Periprocedural management
  - Transition between anticoagulants
  - Education / counseling on adherence
  - 24/7 emergency support; triage adverse events
- Medication refills
- Prior authorizations and medication procurement

Active Patients by Anticoagulant Type



Pharmacist Panel Distribution (Avg)*	
Total	300
Warfarin	170
DOAC	130

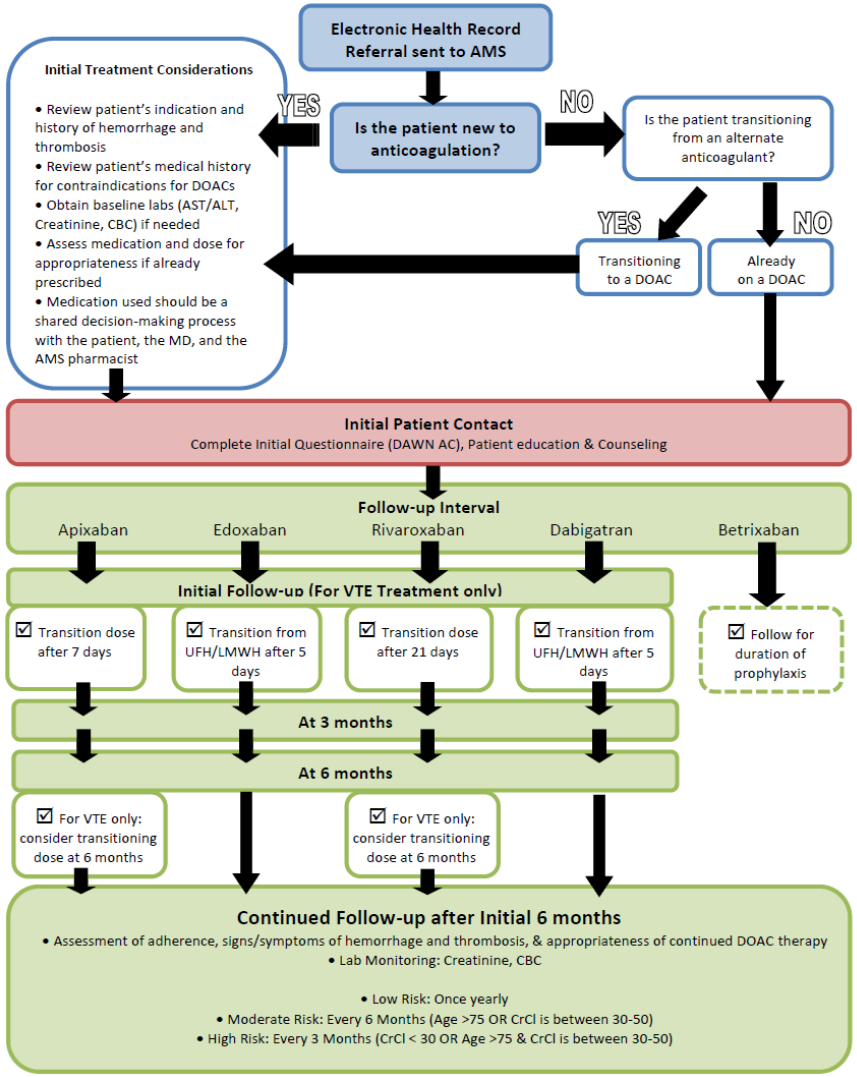
* Pharmacists also have oversight for rate / rhythm control agents for patients with AF

BWH AMS Patient Population

- BWH AMS oversees anticoagulation for:
  - The majority of patients on warfarin associated with the hospital & physicians' organization
  - Approximately 15% of DOACs

- AMS enrollment of DOAC Pts based on referrals
  - Direct referral from providers
  - Warm outreach for pts discharged from ED or inpatient setting with a new DOAC start
  - Warm outreach to targeted PCP groups
  - BWH AMS current warfarin pts transitioned to a DOAC

BWH AMS DOAC Management Plan 2017



	Interval	Comments
Assess compliance	Each visit	• Instruct patient to bring remaining medication: note and calculate average adherence • Re-educate on importance of strict intake schedule • Inform about compliance aids (special boxes; smartphone applications, etc.) Dabigatran must remain in original packaging
Assess for thrombo-embolism	Each visit	• Systemic circulation (TIA, stroke, peripheral) • pulmonary circulation
Assess for bleeding	Each visit	• If minor (nuisance) bleeding, are preventive measures possible? (eg. PPI, saline nose spray, etc.). Motivate patient to diligently continue anticoagulation. • If bleeding with impact on quality-of-life or with significant risk, is prevention possible? (consider changing anticoagulant)
Assess for other side effects	Each visit	• Assess for link to DOAC and decide whether to continue, temporarily stop, or change to different anticoagulant
Assess for new co-medications	Each visit	• Assess for P-gp inhibitors/inducers (if on dabigatran or edoxaban) or dual P-gp/CYP3A4 inhibitors (if on rivaroxaban or apixaban) • Assess for other medications that may increase risk of bleeding such as anti-platelets **NOTE: DOAC dose adjustments may be required if patient starts taking interacting medications (see drug interaction table).**
Assess labs	Yearly Q 6 months Q 3 months As needed	• Hgb, renal and liver function • Renal function if CrCl 30-60 ml/min* or if on dabigatran and >75 years or fragile • Renal function if CrCl 15-30 ml/min* • If clinically indicated for conditions that may impact renal or hepatic function **NOTE: Declining renal function may require a DOAC dose adjustment (see FDA approved anticoagulants for dosing information).** **Edoxaban is contraindicated for atrial fibrillation in patients with CrCl >95.**

BWH Internal Guideline, Sylvester et al. J Thromb Thrombolysis. 2018 Feb;45(2):274-280.

Evolution of the BWH DOAC Services Model

Home › Journal of Thrombosis and Thrombolysis › Article

Published: 22 December 2017

Expanding anticoagulation management services to include direct oral anticoagulants

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ORIGINAL ARTICLE

Optimization of DOAC management services in a centralized anticoagulation clinic

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Patient Follow-Up Categories 2017 vs 2022

2017

Follow-up based on patient's risk factors for bleeding

Risk category	Definition	Follow-interval
High risk	CrCl < 30-ml/min OR age > 75 years and CrCl 30-60 ml/min	Every 3 months
Moderate risk	CrCl 30-60 ml/min or Age > 75 years	Every 6 months
Low risk	None of the above	Yearly

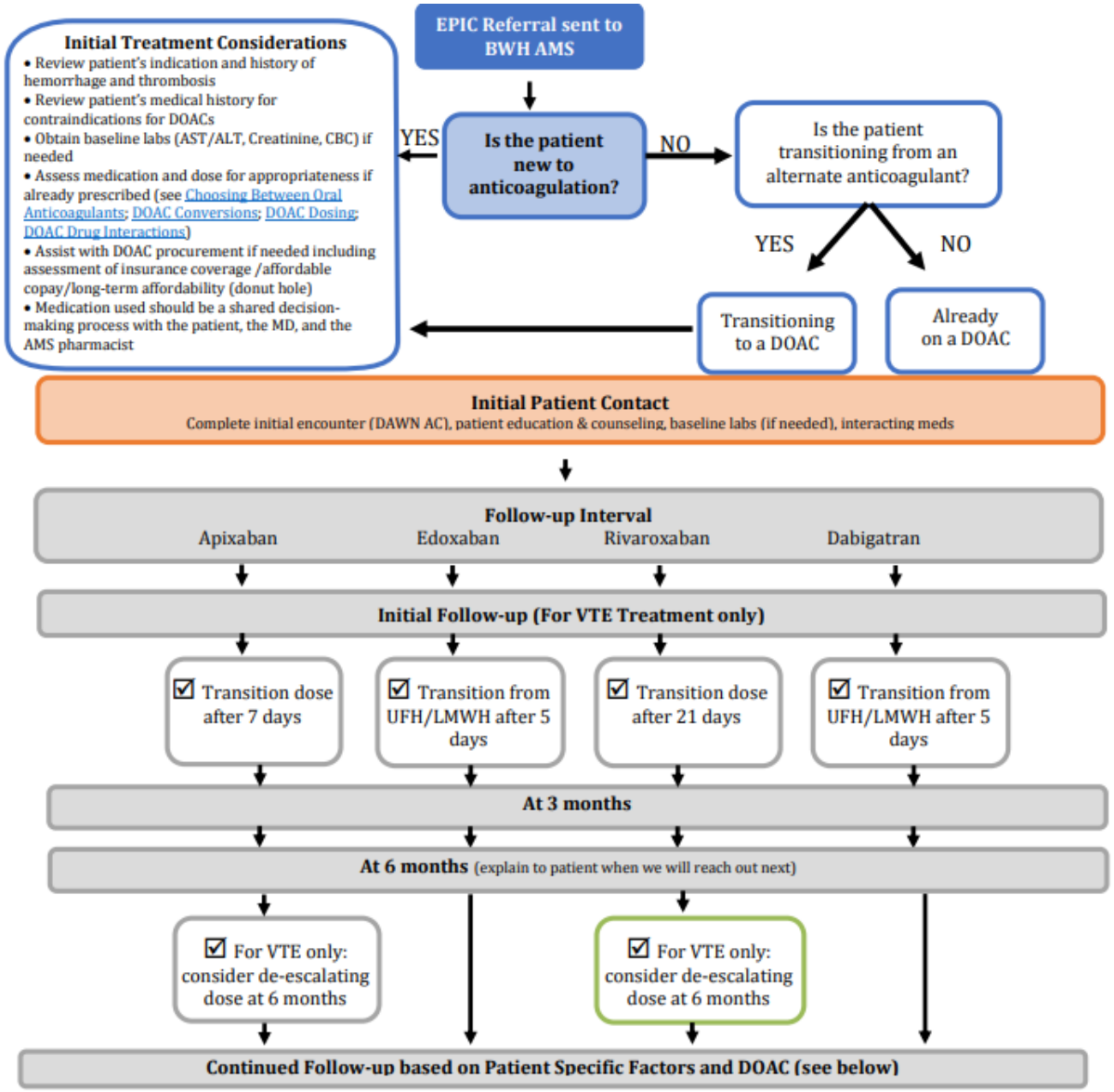
2022

Follow-up based on potential need for DOAC specific dose adjustment

Risk category	Definition	Follow-interval
Active Surveillance	See table on next page; DOAC specific	Chart review every 3 months
Maintenance	See table on next page; DOAC specific	yearly

Sylvester et al. J Thromb Thrombolysis. 2018 Feb;45(2):274-280, Sylvester et al. Res Pract Thromb Haemost. 2022 May 5;6(3):e12696.

BWH DOAC Management Plan 2022



Follow-Up Interval Stratification

DOAC	Indication	Required active surveillance	Reason for active surveillance
Apixaban	Nonvalvular atrial fibrillation	On apixaban 5 mg twice daily and has least 1 of the following characteristics: • Age >80 y • Weight ≤60 kg • Cr ≥ 1.5 mg/dL	Assess for meeting second criterion and needing a dose adjustment to apixaban 2.5 mg twice daily.
	VTE	N/A; no dose adjustments required	N/A
	Extended duration VTE	N/A; no dose adjustments required	N/A
Rivaroxaban	Nonvalvular atrial fibrillation	On rivaroxaban 20 mg once daily and CrCl ≤60 mL/min or fluctuating	Assess for drop in CrCl to ≤50 mL/min requiring dose adjustment to rivaroxaban 15 mg once daily.
	VTE	On rivaroxaban 20 mg once daily and CrCl ≤30 mL/min or fluctuating	Assess for drop in CrCl <15 mL/min requiring a switch to another anticoagulant package insert states to avoid use with CrCl <15 mL/min)
	Extended duration VTE	On rivaroxaban 10 mg once daily and CrCl ≤30 mL/min or fluctuating	Assess for drop in CrCl <15 mL/min requiring a switch to another anticoagulant (package insert states to avoid use with CrCl <15 mL/min).
	CAD/PAD	N/A; no dose adjustments required	N/A

Sylvester et al. Res Pract Thromb Haemost. 2022 May 5;6(3):e12696.

Follow-Up Interval Stratification

DOAC	Indication	Required active surveillance	Reason for active surveillance
Edoxaban	Nonvalvular Atrial fibrillation	On edoxaban 60 mg and CrCl ≤60 mL/min or fluctuating Note: edoxaban is contraindicated for NVAF if CrCl >95 mL/min.	Assess for drop in CrCl ≤50 mL/min requiring dose adjustment to edoxaban 30 mg once daily. If CrCl drops to <15 mL/min, consider changing anticoagulant agent.
	VTE	On edoxaban 60 mg and any of the following: • CrCl ≤60 mL/min • Weight ≤75 kg	Assess for drop in CrCl ≤50 mL/min or weight ≤60 kg requiring dose adjustment to edoxaban 30 mg once daily. If CrCl drops to <15 mL/min, consider changing anticoagulant agent.
Dabigatran	Nonvalvular atrial fibrillation	On dabigatran 150 mg twice daily and CrCl ≤40 mL/min	Assess for drop in CrCl ≤30 mL/min requiring dose adjustment to dabigatran 75 mg twice daily. If CrCl drops to <15 mL/min or on dialysis, consider changing anticoagulant agent.
		On dabigatran 150 mg twice daily and CrCl ≤60 mL/min with concomitant use of a P-gp inhibitor (dronedarone/ketoconazole)	Assess for drop in CrCl ≤50 mL/min requiring dose adjustment to dabigatran 75 mg twice daily. If CrCl drops to <30 ml/min while concomitant use of a P-gp inhibitor, consider changing anticoagulant agent.
	VTE	On dabigatran 150 mg twice daily and CrCl ≤40 mL/min	Assess for drop in CrCl ≤30 mL/min requiring a switch to another anticoagulant (prescribing information recommendation is to avoid use with CrCl <15 mL/min)
		On dabigatran 150 mg twice daily and CrCl ≤60 mL/min with concomitant use of a P-gp inhibitor (dronedarone/ketoconazole)	Assess for drop in CrCl ≤50 mL/min and if requires continued administration of P-gp inhibitor, switch to another anticoagulant.
	Extended duration VTE	Same as above for treatment of VTE	Same as above for treatment of VTE

Sylvester et al. Res Pract Thromb Haemost. 2022 May 5;6(3):e12696.

Phases of Oversight

Active Management

At each visit during active management (first 6 months enrolled at AMS) assess the following:

- Adherence and educational needs
- Signs & symptoms of thromboembolism
- Signs & symptoms of bleeding
- Potential other side effects
- New co-medications (see DOAC Drug Interactions)
  - P-gp inhibitors/inducers (dabigatran / edoxaban)
  - Dual P-gp/CYP3A4 inhibitors (rivaroxaban / apixaban)
  - Other medications that may increase risk of bleeding such as anti-platelets
- Upcoming procedures/surgery (see Procedural DOAC Management)
- Continued need for anticoagulation and appropriate dosing (see Choosing Between Oral Anticoagulants; DOAC Conversions; DOAC Dosing)

After initial 6 months, stratify include maintenance or active surveillance

Active Surveillance

- For patients with moderate or high risk of requiring a dose adjustment due to DOAC specific labeling, move into active surveillance. Active surveillance includes:
  - Chart review every 3 months to assess the need for a dose change and ordering labs as needed
  - Providing perioperative management plans
  - Patient support with education, on-call emergency pager for questions and triage

Maintenance

- For patients with low risk of requiring a dose adjustment due to DOAC specific labeling, move into maintenance mode. Maintenance mode includes:
  - Providing perioperative management plans
  - Patient support with education, on-call emergency pager for questions and triage

All Patients – Annual Review

- All patients regardless of the management plan receive an annual review which includes a chart review and call to the patient to assess:
  - Referring MD still actively managing the patient at BWH
  - Ongoing need for anticoagulation
    - Assess risk of bleeding and thrombosis
  - Need for prescription renewals (and renewal of prior authorizations) and lab order renewal (if standing orders)
  - Asses that yearly labs have been ordered/obtained: AST/ALT, Creatinine, CBC
  - Assessment of any new medications added
  - Assess adherence and ongoing need for education

Patients may move from maintenance to active surveillance based on changes in clinic status at any time

BWH Internal Guidelines

Lab Monitoring & Visit Encounter Checklist

- Baseline: Cr, CBC, LFTs, age, weight
- Ongoing:
  - Creatinine (Q3-12 months or more frequently if fluctuating, or near the limit of a dose change requirement)
    - CrCl Q3 months for patients in Active Surveillance (see Table 1)
  - CBC (at least yearly)
  - Liver function (at least yearly)
  - Age & Weight (at each visit)
- May consider more frequent follow up with patient after adverse bleeding events
  - Asses for signs/ symptoms of bleeding

Encounter Checklist		
	Interval	**Comments**
Assess compliance	Each visit	• Instruct patient to bring remaining medication: note and calculate: note and calculate average adherence • Re-educate on importance of strict intake schedule • Inform about compliance aids (special boxes; smartphone applications, etc.) Dabigatran must remain in original packaging • Assist with medication procurement if needed
Assess for thromboembolism	Each visit	• Systemic circulation (TIA, stroke, peripheral) • Pulmonary circulation
Assess for bleeding	Each visit	• If minor (nuisance) bleeding, are preventable measures possible (e.g. PPI, saline nose spray, etc.). Motivate patient to diligently continue anticoagulation. • If bleeding with impact on quality of life or without significant risk, is prevention possible? (consider changing anticoagulant/ see Choosing Between Oral Anticoagulants; DOAC Conversions; DOAC Dosing)
Assess for other side effects	Each visit	• Assess for link to DOAC and decide whether to continue, temporarily stop, or change to different anticoagulant
Assess for new co-medications	Each visit	• Assess for P-gp inhibitors/inducers (if on dabigatran or edoxaban) or dual P-gp/CYP3A4 inhibitors (if on rivaroxaban or apixaban) • Assess for other medications that may increase risk of bleeding, such as anti-platelets • DOAC dose adjustments may be required if patient starts taking interactive medication (see DOAC Drug Interactions)
Assess for upcoming procedures	Each visit	• Assess need to interrupt DOAC therapy • DOAC periprocedural plans may need to be developed (see Procedural DOAC Management)
Assess labs	Yearly	• Liver function, CBC, Creatinine ○ For Patients in Active Surveillance (see Table 1) CrCl Q3 Months

BWH Internal Guidelines, Sylvester et al. Res Pract Thromb Haemost. 2022 May 5;6(3):e12696.

BWH Data June 2017 to June 2021

Metric	Result
Patient referrals	1622
DOAC (n, %)	
Apixaban	1198 (73.9)
Rivaroxaban	394 (24.3)
Edoxaban	8 (0.5)
Dabigatran	22 (1.4)
Patients requiring medication procurement assistance upon referral (n, %)	149 (9.2)
Follow-up visits	3154
Patients identified as not taking DOAC as prescribed upon follow-up (n, %)	127 (4.0)
Patients requiring medication procurement assistance upon follow-up (n, %)	63 (1.9)
Patients requiring DOAC dose adjustment (n, %)	171 (5.4)
Patients requiring procedural management plans (n, %)	603 (19.1)

Sylvester et al. Res Pract Thromb Haemost. 2022 May 5;6(3):e12696.

Strengths of this Model

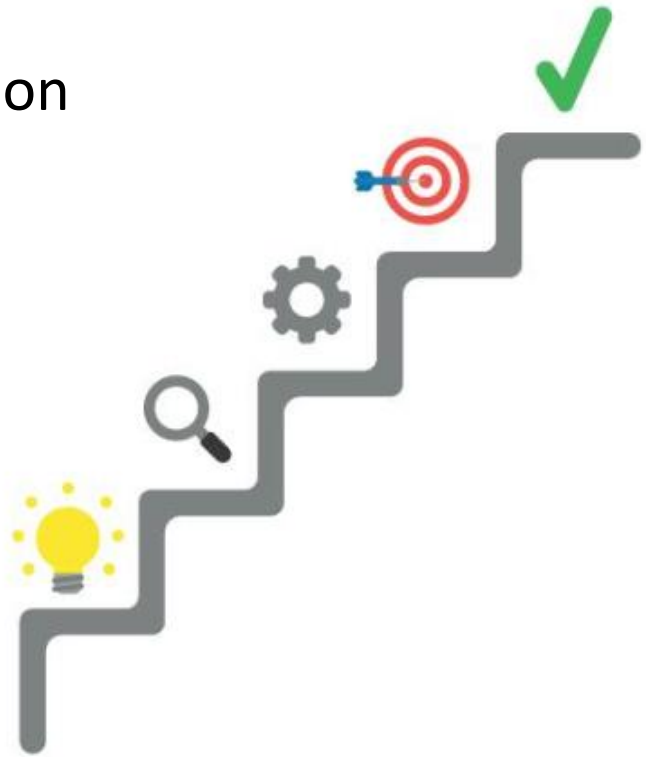
- With minimal IT support can implement in a step-wise approach (we all have to start somewhere)
- Continue to provide care to your patients who are transitioned to DOACs
- Are available for on demand patient needs like 24/7 pager for emergencies, questions / patient education, procedure plans
- Yearly ongoing assessment for need for anticoagulation (every patient gets evaluated at least annually)

Limitations of this Model

- Time intensive chart reviews and patient calls to identify clinical interventions
- Miss potential interventions based on timing between encounters (Cr changes, weight changes, new drug interactions, etc.)
- Patients / providers forget to alert AMS re scheduled procedures

Next Steps – Leverage EMR

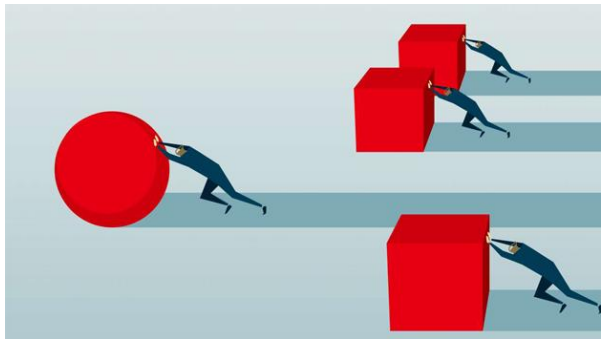
- Population health model / rules-based alerting
- Initial enrollment “hands on”
  - Education, ordering labs & prescriptions, medication selection and dosing, etc.
- Patients transitioned to active surveillance where AMS providers are alerted to review when certain rules are triggered
- Yearly renewal of each patient
  - Ongoing need for anticoagulation, modifiable bleeding risk factors, dosing, prior authorizations, labs, etc.



Population Health

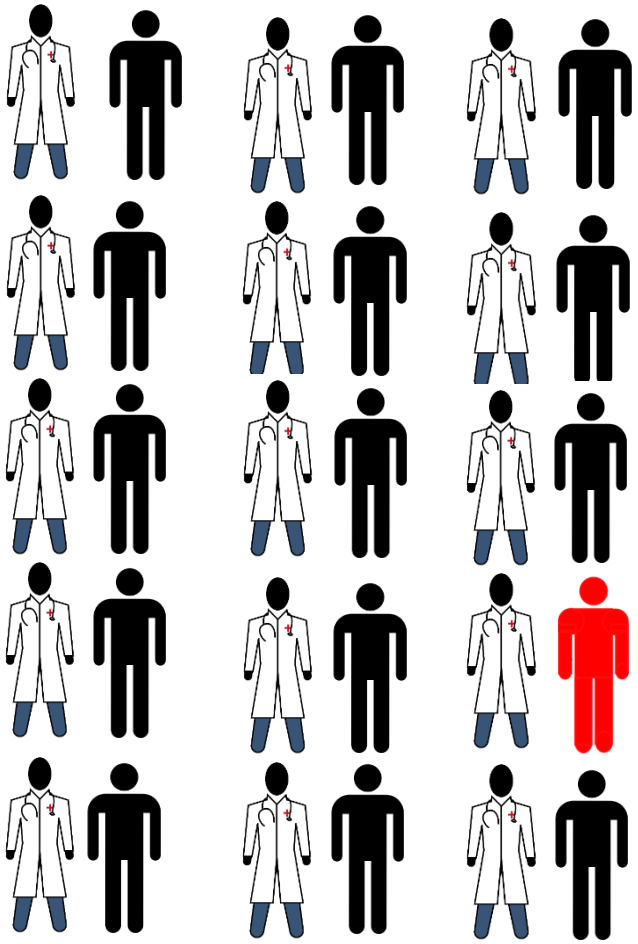
What is it?

work smarter … not harder



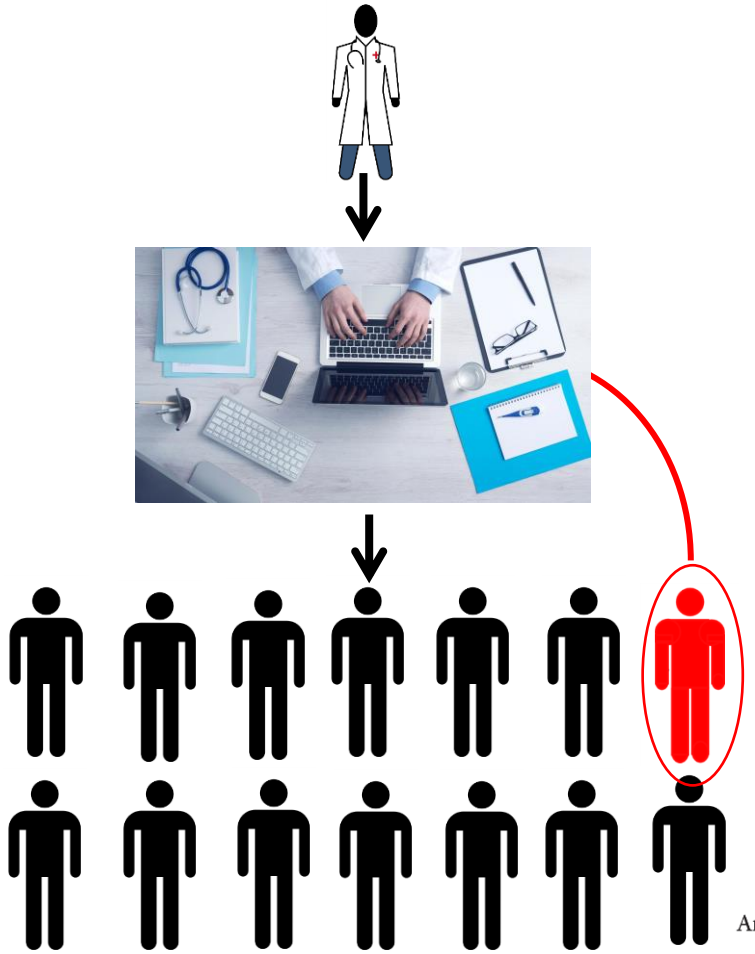
Population Health

Traditional Model

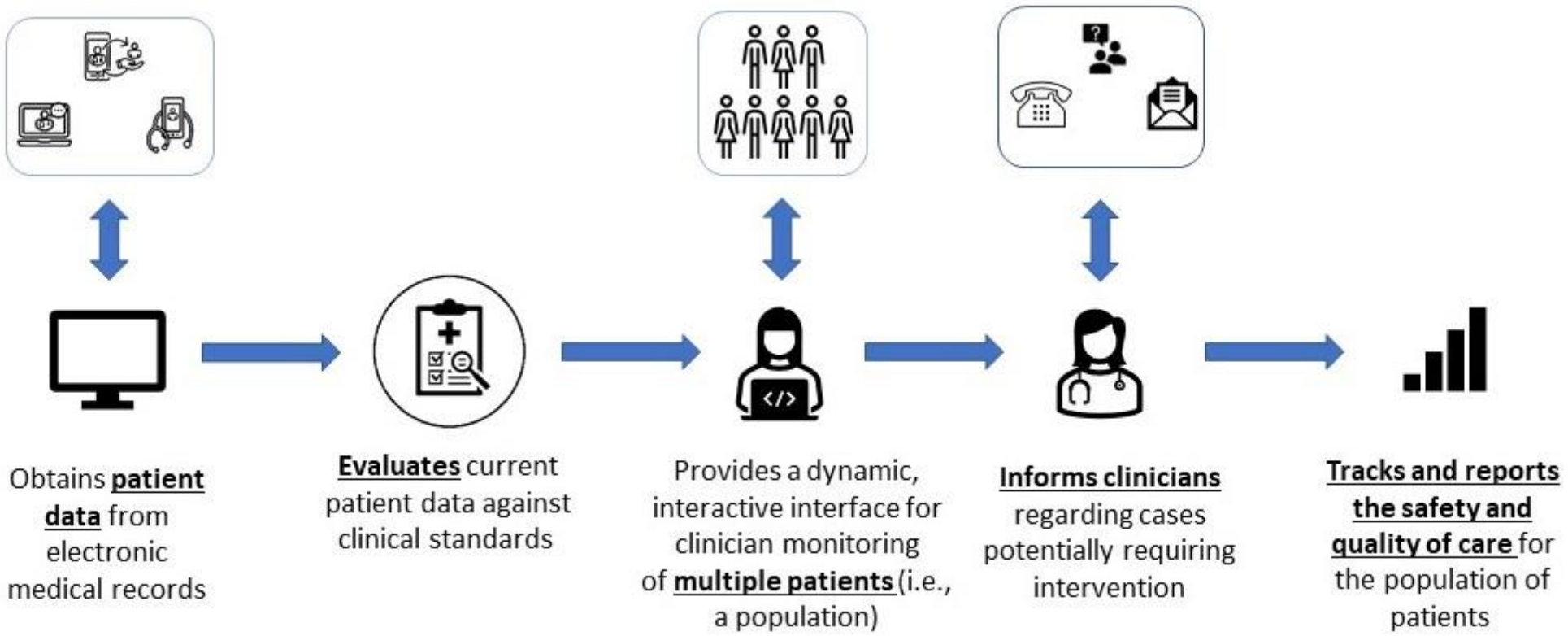


VS

Population Health



What is a “Population Management Tool”



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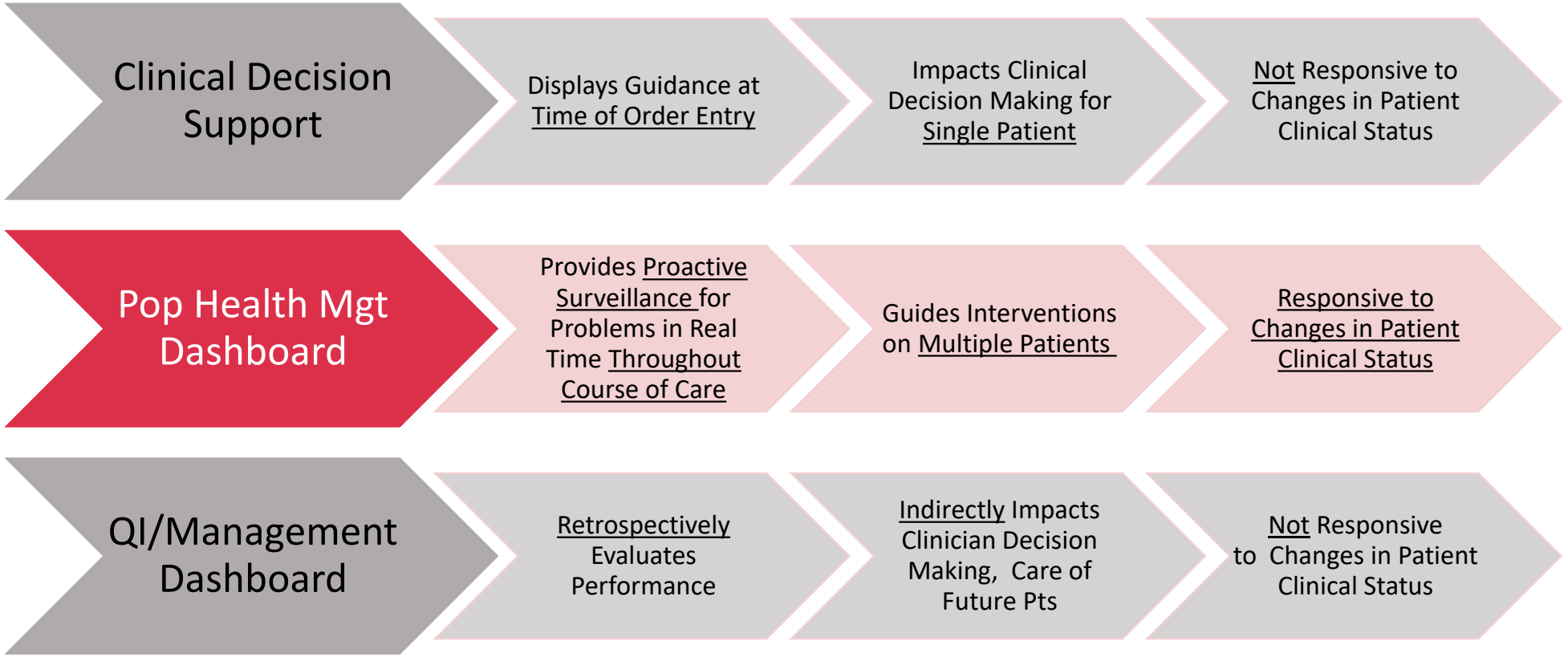
Differentiating Between Digital Tool Models



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What would it look like if we could use technology to DAILY review EVERY PATIENT prescribed a DOAC, spending time only on those that may need something?

- Dosing issues
- Notable labs
- DDIs
- Childbearing potential
- H/o valve replacement, bariatric surgery, or APS
- Due for med renewal
- Medication nonadherence
- Lab monitoring due
- “Lacking indication” for DOAC
- Patients placed “under review” by AC provider

VA's DOAC Population Management Tool: Overview

Patient Counts											
	# Total Patients	Dosing Issue	Notable Hgb/PLT/LFTs	Medication Interactions	Childbearing Potential	Bariatric Surgery or Vlave	Renewal Due Next 30 Days	Potential Nonadherence	Overdue Labs	Lacking Indication	Renewal Due Next 30 Days
Site Name	1286	25	16	3	10	13	1	16	21	13	14
Site Name	786	15	11	7	15	11	0	11	18	7	9

- The home screen provides an overview of the number of flags currently in play for each area of concern.
- This allows the healthcare team to prioritize and filter flags based on the reason for clinical concern.
- Each number serves as a hyperlink to the expanded PMT interface where patients are grouped based on the flag for a focused intervention.
  - When a hyperlink number is clicked, it will expand and provide a more in-depth review of clinically relevant factors and the reason the patient is flagging.

J Am Heart Assoc. 2021;10:e022758.

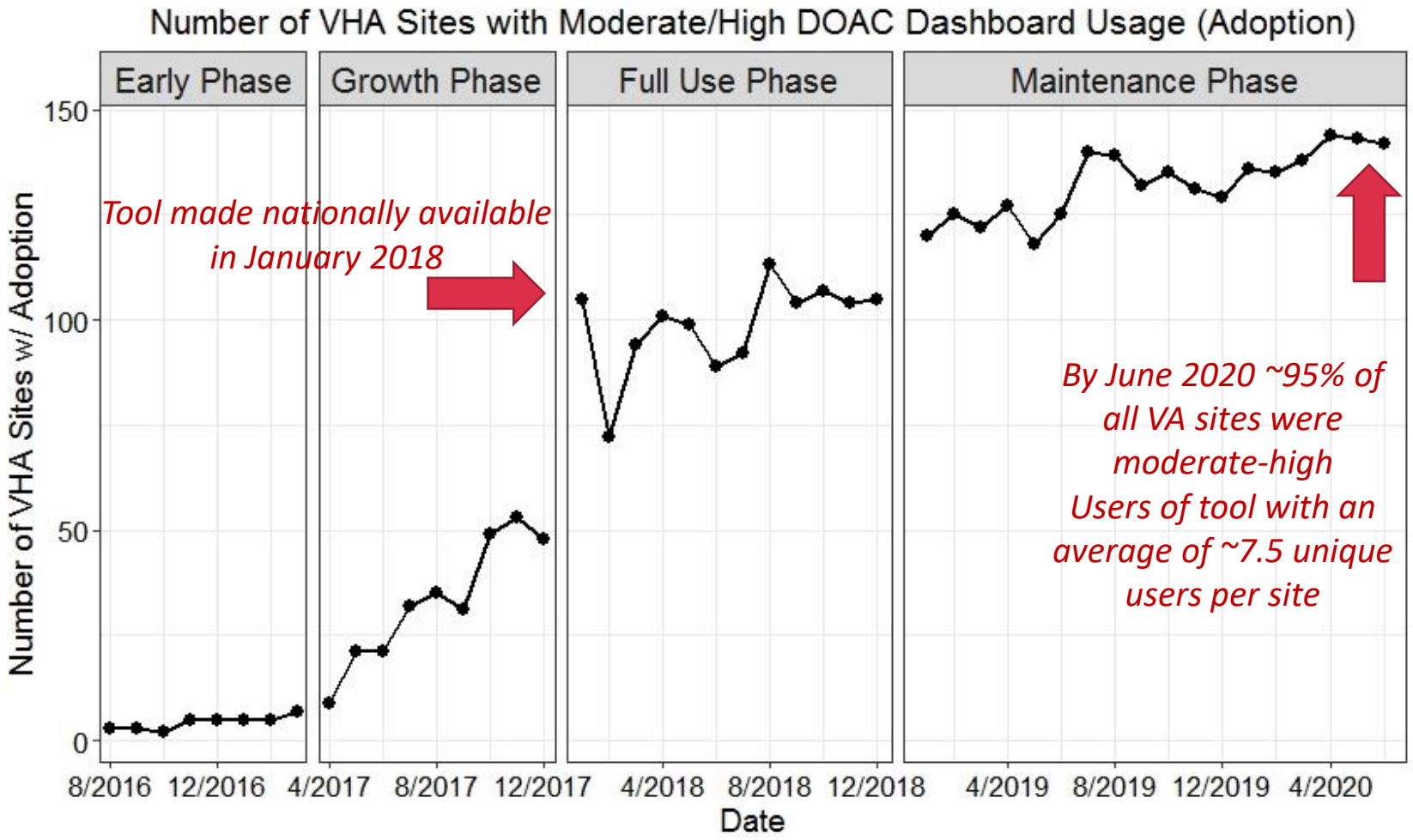
VA's DOAC PMT: Expanded Single-Patient View

Patient Information	DOAC Prescription Information	Labs (value, date, monitoring, frequency)			Appointments	Clinical Concerns - Click on a Clinical Concern to Dismiss
Smith, Joe (1111) 60yoM DOB: 1/1/61 **Wt**: 93kg **Ht:** 67.0 in **BMI**: 32 Diagnosis: Afib/flutter	**Apixaban:** 5.0 mg (5.0 mg total daily) 3 Refills Remaining **Last filled** 90 tabs **for** 90 days supply **on** 8/1/21 **prescribed by** Jones, Arthur **Estimated Duration:** More than 180 days **Drug Interactions:** ASPIRIN TAB, EC	Scr: 1.20 (82.2 ml/min)	7/16/2021	6 Months	**Location:** Crystal Springs HCS Next Primary Care Appt: 8/1/2021 2:30 PM	- Dismiss Dosing Flag: In patients with VTE, on therapy > 6 months, who also have afib/aflutter, apixaban dose should be reduced to 2.5 mg BID for patients meeting two of the following three criteria: serum creatinine >=1.5, either age >=80, or weight <=60.0kg
		Hgb: 11.8	7/16/2021	12 Months		
		Plt: 176	7/16/2021	12 Months	Last Anticoag Visit: 1/26/2021 3:00 PM	
		LFTs: 19 I 20	7/16/2021	Edit		- Click to Place Under Review Oldest Active Flag Date: (Date)

- Each **blue hyperlink** allows the user to review the report in more detail or adjust monitoring frequencies.
  - **Patient Name** provides additional patient-specific detail (e.g., refill history, flag dismissal history).
  - **Diagnosis** provides a comprehensive list of patient diagnoses and gives the reviewer the ability to remove a diagnosis from being included in the report.
  - **Edit** allows the reviewer to adjust monitoring frequency (CBC and Scr)
  - Clinical Concerns box includes the active flags (as hyperlinks) that require review. For the example provided, the patient is flagging for a potential dosing issue. After they have reviewed and addressed the concern, the user can dismiss the flag with one click.
  - The **Click to Place Under Review** function marks a patient for further review at a future date.

J Am Heart Assoc. 2021;10:e022758.

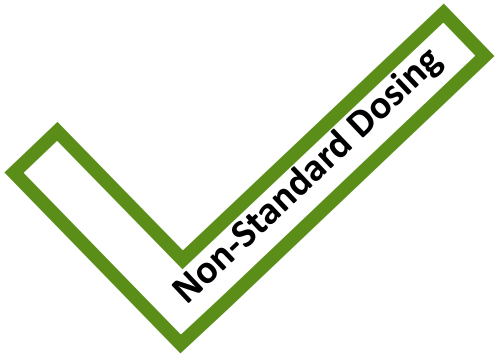
VA DOAC PMT Nationwide Implementation



Circ Cardiovasc Qual Outcomes. 2023;16:e009256.

Benefits of the VA's DOAC PMT

- Valencia *et al*: DOAC PMT model vs. clinic-based model (SOC)
  - Significant interventions made per patient encounter
    - **0.55 (PMT) vs. 0.2 (SOC), P <0.001**
  - **75% reduction in mean time to intervention**
    - 16 min (PMT) vs. 64 min (SOC)

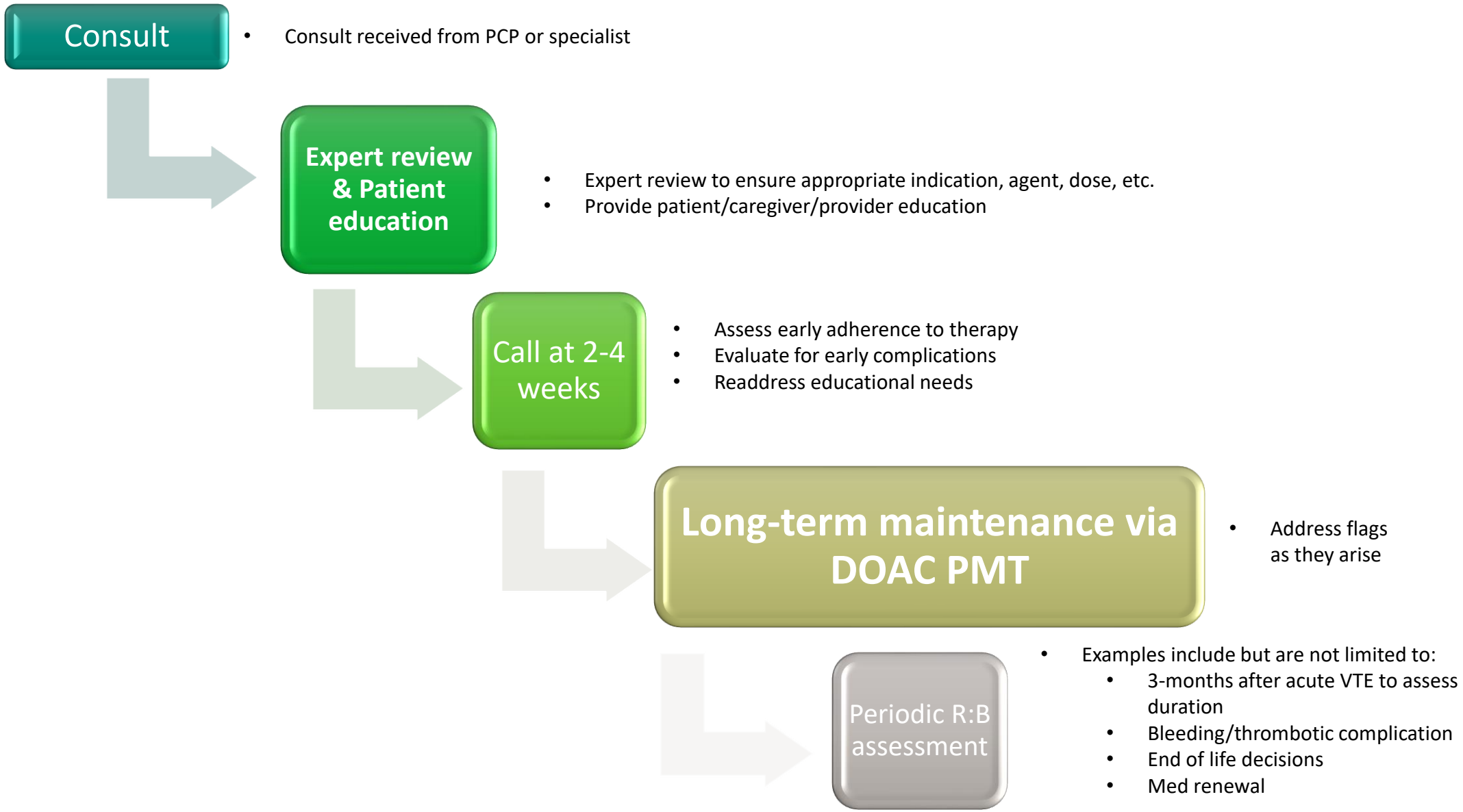


- Rossier *et al*: 20 PMT high-use VA sites vs. 20 non-use sites (SOC)
  - DOAC PMT use was associated w/ **4.3% absolute risk reduction in questionable dosing rates**
    - **13.2% (PMT), vs. 17.5% (SOC) P < 0.001**
    - **In AF subgroup, rates of questionable dosing was nearly twice as high in the SOC group**
      - 5.3% (PMT) vs. 10.4% (SOC) , P < 0.001

Annals of Pharmacotherapy 2019; 53(8), 806–811.

J Thromb Thrombolysis. 2021 Jul;52(1):200-208.

Example Model of Care *(where does PMT fit in?)*



Population Health for Quality Assurance

- Quality Assurance is an important component of AC Stewardship
- Population health tools allow for evaluation of care quality at multiple levels
  - Individual patient
  - Team/provider
  - Practice site
  - Health system
  - Region
  - National

Examples of Population Health QA Tools

Reason For Dose Flag	Local Patients with Dosing Issue	Local Total Patients	Local Dosing Issue Per 1000 DOAC Patients	VISN Dosing Issue Per 1000 DOAC Patients	National Dosing Issue Per 1000 DOAC Patients
After at least six months of therapy for acute VTE, the dose of apixaban and rivaroxaban may be reduced for long-term secondary PE/DVT prophylaxis	285	3165	90.0	127.1	103.0
For patients without PE/DVT, and not meeting the two of three, weight, serum creatinine, and age criteria for reduced dose, apixaban dose should not be reduced to below 5 mg BID	66	3165	20.9	19.6	19.7
For patients with afib/aflutter, without interacting medications, and not meeting the two of three, weight, serum creatinine, and age criteria for reduced dose, apixaban dose should not be reduced to below 5 mg BID	16	3165	5.1	2.6	2.9
Dose of apixaban or rivaroxaban is below recommended dose in first six months of therapy for secondary VTE prophylaxis	16	3165	5.1	7.4	5.9
In absence of VTE, apixaban dose should be reduced to 2.5 mg BID for patients meeting two of the following three criteria: serum creatinine >=1.5, either age >=80, or weight <=60.0 kg	15	3165	4.7	4.2	4.6
Rivaroxaban dose should not be reduced in patients with ABW CrCl >= 50 mL/min	9	3165	2.8	6.0	5.9
A careful risk:benefit assessment is required when serum creatinine > 2.5 or CrCl < 25ml/min, as these patients were excluded from the trials that brought apixaban to market and prospective evidence is limited	7	3165	2.2	5.3	8.4
In patients with VTE, on therapy > 6 months, who also have afib/aflutter, apixaban dose should be reduced to 2.5 mg BID for patients meeting two of the following three criteria: serum creatinine >=1.5, either age >=80, or weight <=60.0 kg	7	3165	2.2	0.8	0.9
Rivaroxaban dose should be reduced for patients without PE/DVT with ABW CrCl < 50 mL/min	6	3165	1.9	2.3	2.4
Given current age and weight, examine apixaban dosing	4	3165	1.3	5.4	5.1
Rivaroxaban is not recommended when ABW CrCl < 30 mL/min	1	3165	0.3	0.7	1

DOAC Dosing

DOAC "Adherence" Rates

	Local Patients with Potential Nonadherence	Local Total Patients	Local Adherence Rate	VISN Adherence Rate	National Adherence Rate
VA facilities	134	2,264	94.08%	93.20%	93.94%
	78	1,232	93.67%	93.20%	93.94%
	241	3,838	93.72%	93.20%	93.94%
	67	1,033	93.51%	93.20%	93.94%
	225	2,898	92.24%	93.20%	93.94%
	330	3,666	91.00%	93.20%	93.94%
	161	3,165	94.91%	93.20%	93.94%
	41	697	94.12%	93.20%	93.94%

Vuong J et al. Defining Success in Anticoagulation Stewardship: The Development of DOAC Population Health Management Quality Reports in Veterans Health Administration. AC Forum 17th National Conference. San Francisco, California. April 2023.

Examples of Population Health QA Tools, cont.

This report identifies bleeding and thrombotic events based on patient prescriptions prior to the event. Data is limited to the prior 6 months. Primary sources of events include:

- Inpatient discharge diagnosis
- Urgent outpatient visit diagnosis
- Events documented via health factors

	Events by Drug Group (Patient may be included in multiple groups)			Total Events (By Patient)
	DOAC Events	Warfarin Events	LMWH/ Fondaparinux Events	
⊟Pending Review	17	2	0	17
Pending - VTE Events	12	1	0	12
Pending - Bleed Events	5	1	0	5

If only pending events are displayed, no events have been validated or dismissed for the selected time period. Once events are validated or dismissed, those categories will be displayed.

Event Information	
Event Date: 1/30/2023 5:27 PM **Event Source:** Inpatient_Discharge_Diagnosis **Event Category:** Bleed **Diagnosis Code:** K29.91 **Diagnosis Description:** Gastroduodenitis, unspecified, with bleeding **Event Medication(s):** APIXABAN 5MG TAB -Rx source: VA Rx	- Click to Confirm Real - Click to Confirm Real - Click to Dismiss as N
Event Date: 1/27/2023 12:00 AM **Event Source:** HealthFactor_Diagnosis **Event Category:** Bleed **Diagnosis Code:** ANTICOAG-MINOR **Diagnosis Description:** BleedEvent **Event Medication(s):** APIXABAN 5MG TAB ASPIRIN 81MG EC TAB CLOPIDOGREL BISULFATE 75MG TAB	- Click to Confirm Real - Click to Confirm Real
Event Date: 2/4/2023 1:35 PM **Event Source:** Inpatient_Discharge_Dia **Event Category:** Bleed **Diagnosis Code:** K92.1 **Diagnosis Description:** Melena **Event Medication(s):** APIXABAN 5MG TAB CLOPIDOGREL BISULFATE 75MG TAB	

Click to Review

- Click to Confirm Real, Appropriately Documented MAJOR Bleed Event
- Click to Confirm Real, Appropriately Documented MINOR Bleed Event
- Click to Dismiss as Not Primary/Initial Documentation of Event
- Click to Confirm Real, Appropriately Documented TE Event
- Click to Dismiss as Not Primary/Initial Documentation of Event

OAC-Related Outcomes

Event Rates

	Warfarin (n=207)	Non-Warfarin (n=3157)	TOTAL (n=3364)
Minor Bleeding	7 (3.4%)	13 (0.4%)	**20 (0.6%)**
Major Bleeding	4 (1.9%)	10 (0.3%)	**14 (0.4%)**
Thrombotic Event	1 (0.5%)	11 (0.3%)	**12 (0.4%)**
TOTAL	**12 (5.8%)**	**34 (1.1%)**	**46 (1.4%)**

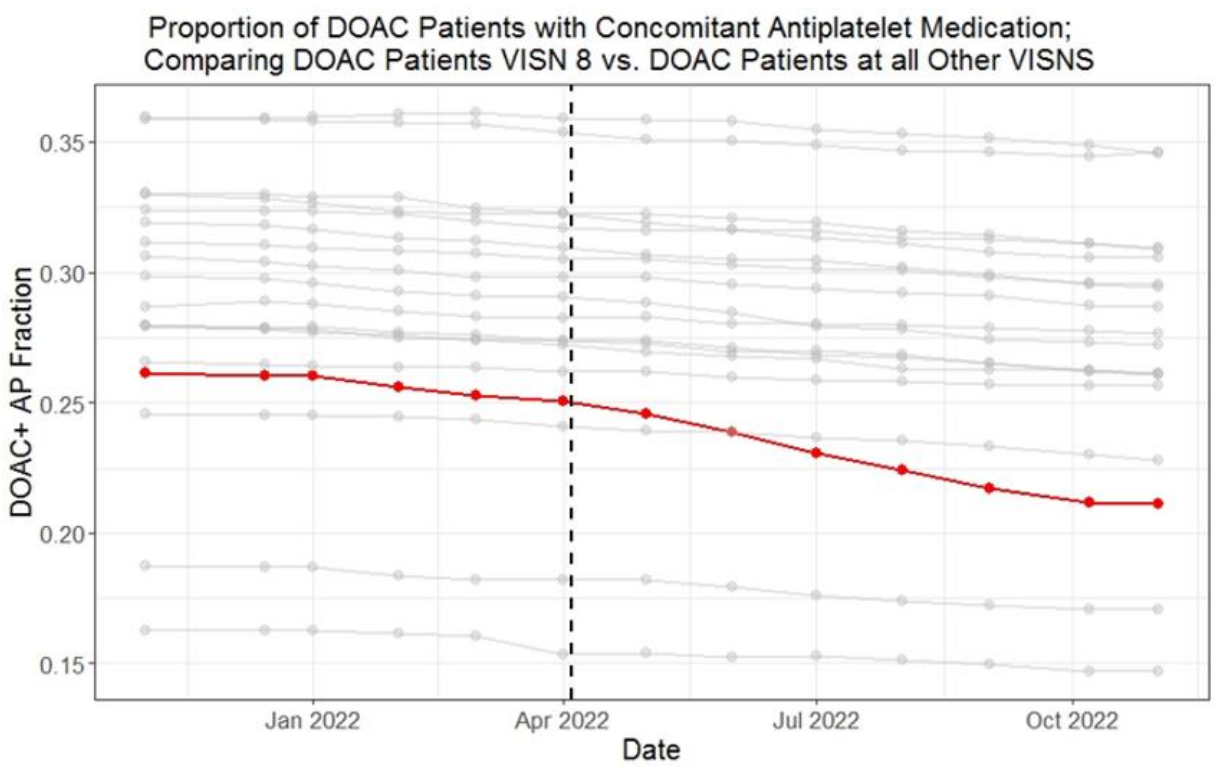
OAC Reversal Agent Utilization

Patient Information	Event Information	Order Start Date & Time	Review
Patient Identifier	Item: COAGULATION FACTOR Xa, INACT-ehoo INJ,LYPHL Ordering Staff Name:	9/29/2022 11:41 AM	Click to Review
	Item: PROTHROMBIN COMPLEX CONC INJ,LYPHL Ordering Staff Name:	9/8/2022 9:39 AM	Click to Review
	Item: COAGULATION FACTOR Xa, INACT-ehoo INJ,LYPHL Ordering Staff Name:	7/7/2022 5:34 PM	Click to Review
	Item: PROTHROMBIN COMPLEX CONC INJ,LYPHL Ordering Staff Name:	6/2/2022 7:02 PM	Click to Review Allen, Arthur (6/30/2022 11:45 AM) Review: Agent Confirmed to Reverse Anticoagulation
	Item: COAGULATION FACTOR Xa, INACT-ehoo INJ,LYPHL Ordering Staff Name:	1/24/2022 10:51 AM	Click to Review
	Item: COAGULATION FACTOR Xa, INACT-ehoo INJ,LYPHL Ordering Staff Name:	1/12/2022 3:30 PM	Click to Review

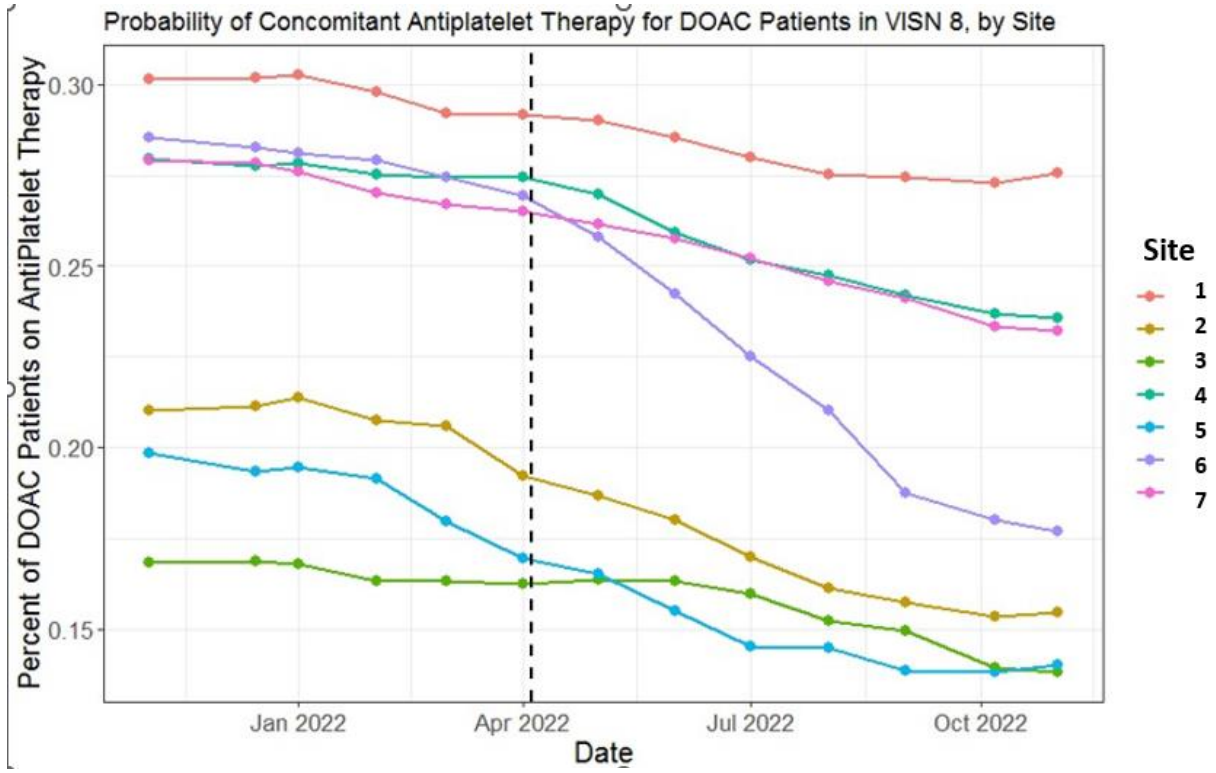
Vuong J et al. Defining Success in Anticoagulation Stewardship:
The Development of DOAC Population Health Management Quality Reports in Veterans Health Administration. AC Forum 17th National Conference. San Francisco, California. April 2023.

Population Health to Address Specific AC Stewardship Efforts

Regional VA Effort: Targeting concomitant DOAC + APT piloting the use of a novel DOAC PMT Flag



DOAC-ATP flags associated with an additional 2.1% decrease in APT co-prescription relative to control group



Some individual sites with dramatic impact on APT co-prescription

Parra D et al. Co-prescribing of Antiplatelets with Direct Oral Anticoagulants: A Medication Safety Initiative. Anticoagulation Forum 17th National Conference. San Francisco, CA. April 1, 2023.

What about patients indicated for but not receiving OAC?

Stroke Prevention in Atrial Fibrillation/ Flutter – Targeting the Untreated While Prioritizing Health Disparities (SPAFF-TNT-D)

- Pilot project using population health to identify patients with AF, non-sex CHA_2DS_2-VASc $\geq$ 2, and no prescribed OAC
- Goals:
  - Validate and refine the data to inform the development of a population health tool for wide dissemination
  - Define reasons and rationale for OAC nonuse
  - Identify potential opportunities for intervention
  - Examine and address health disparities as it relates to OAC non-use in AF
  - Inform a broader VA untreated AF project

Allen A et al. A Population Health Approach to Stroke Prevention in Atrial Fibrillation/Flutter: Targeting the Untreated While Prioritizing Health Disparities (SPAFF-TNT-D). American College of Cardiology National Conference. New Orleans, Louisiana. March 2023.

JAMA Network Open

Original Investigation | Cardiology

Association of Direct Oral Anticoagulation Management Strategies With Clinical Outcomes for Adults With Atrial Fibrillation

Catherine G. Derington, PharmD, MS; Glenn K. Goodrich, MS; Stanley Xu, PhD; Nathan P. Clark, PharmD; Kristi Reynolds, PhD, MPH; Jaejin An, PhD; Daniel M. Witt, PharmD; David H. Smith, RPh, PhD; Maureen O'Keeffe-Rosetti, MS; Daniel T. Lang, MD; P. Michael Ho, MD, PhD; T. Craig Cheetham, PharmD, MS; Angela C. Comer, MPH; Jordan B. King, PharmD, MS

- **Objective:** Compare outcomes associated 3 DOAC care models:
  - Usual Care (UC); UC + PMT; Pharmacists-managed AMS
- **Methods:** Retrospective Cohort study of 44,746 AF patients initiated on DOAC or Warfarin between 8/1/2016 & 12/31/2019 in 3 Kaiser Permanente regions over a median f/u of 2 years
  1. DOAC care models vs. warfarin as a common comparator within each region
  2. DOAC care model compared across regions
- **Outcomes:** First occurrence of a composite outcome (thromboembolic stroke, ICH, major bleeding, death), discontinuation of KP membership, or 12/31/2020

- **Conclusions:** ***"DOACs were associated with favorable outcomes compared with warfarin, but we did not establish superiority of any system-level DOAC therapy management service over UC."***

JAMA Network Open. 2023;6(7):e2321971.

Putting this in perspective

- Single system, retrospective, ICD-based review limited to AF population
- Dabigatran represented **84-93%** of all DOAC use
  - Not representative of most anticoagulated populations
  - Less chance for inappropriate usage/dosing
- KP has a long history of strong AC practices
  - Good practice vs good practice done differently?
  - Details were given about AMS and PMT models, but not about what may have been in place to guide UC (decision support, formulary management practices, etc)

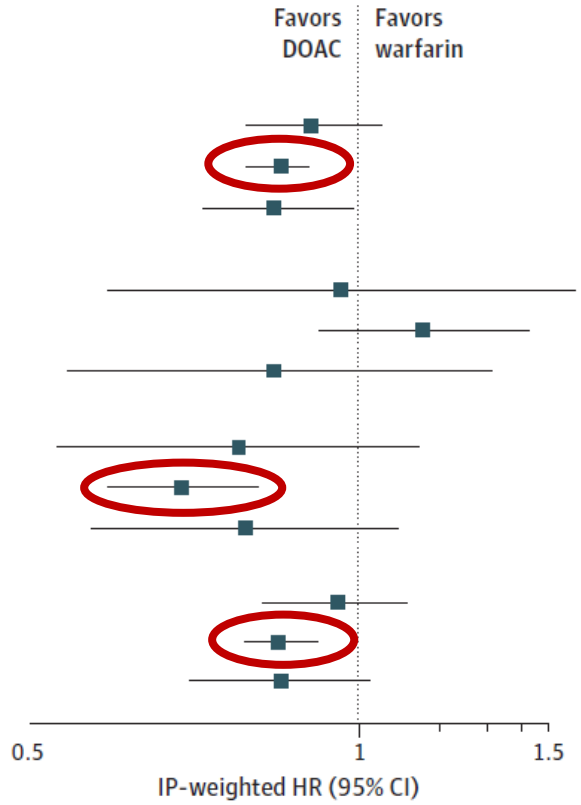
JAMA Network Open. 2023;6(7):e2321971.

Outcomes by DOAC Management Model:
DOAC vs Warfarin

Figure 1. Association of Direct Oral Anticoagulant (DOAC) vs Warfarin Use With Major Clinical Outcomes by DOAC Management Model

Outcome and management model	DOAC, No. of patients with event/ total No. (%)	% Per year	Warfarin, No. of patients with event/ total No. (%)	% Per year	IP-weighted HR (95% CI)
Net clinical benefit[a]					
UC	360/3297 (10.9)	5.4	637/2885 (22.1)	9.1	0.91 (0.79-1.05)
UC plus PMT	2514/21891 (11.5)	6.1	2897/11734 (24.7)	10.5	0.85 (0.79-0.90)
AMS	223/2089 (10.7)	5.1	534/2850 (18.7)	8.0	0.84 (0.72-0.99)
Thromboembolic stroke					
UC	34/3297 (1.0)	0.5	48/2885 (1.7)	0.7	0.97 (0.59-1.59)
UC plus PMT	333/21891 (1.5)	0.8	194/11734 (1.7)	0.7	1.15 (0.92-1.43)
AMS	32/2089 (1.5)	0.7	62/2850 (2.2)	0.9	0.84 (0.54-1.33)
Major bleeding composite					
UC	51/3297 (1.5)	0.8	93/2885 (3.2)	1.3	0.78 (0.53-1.14)
UC plus PMT	442/21891 (2.0)	1.1	487/11734 (4.2)	1.8	0.69 (0.59-0.81)
AMS	59/2089 (2.8)	1.3	132/2850 (4.6)	2.0	0.79 (0.57-1.09)
Death					
UC	301/3297 (9.1)	4.4	549/2885 (19.0)	7.6	0.96 (0.82-1.11)
UC plus PMT	2014/21891 (9.2)	4.8	2542/11734 (21.7)	9.0	0.85 (0.79-0.92)
AMS	158/2089 (7.6)	3.5	414/2850 (14.5)	6.0	0.85 (0.70-1.03)

21,891 patients overseen by THREE pharmacists



Event rates are derived from each site independently and are unweighted; hazard ratios (HRs) are weighted by the inverse of the propensity score. AMS indicates anticoagulation management service; IP, inverse probability; PMT, population management tool; and UC, usual care.

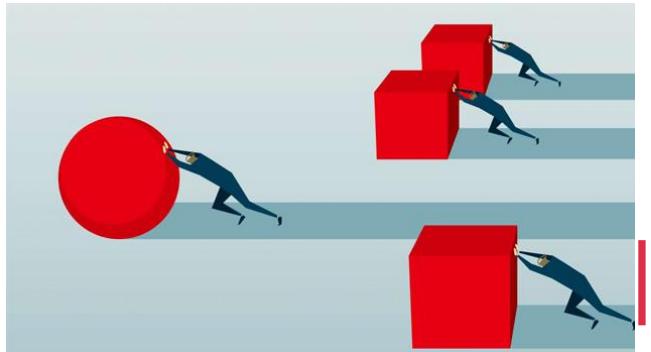
[a] Composite end point of thromboembolic stroke, intracranial hemorrhage, gastrointestinal bleeding, extracranial major bleeding, or death.

JAMA Network Open. 2023;6(7):e2321971.

Summary

- Technology and the move to EHRs have unlocked massive opportunities for the use, study, and operationalization of health data
- For many years, VHA has harnessed the power of population data to improve the quality of care across disease states and has led the way in population health as part of anticoagulation stewardship efforts
  - Spread beyond VHA:
    - Michigan Anticoagulation Quality Improvement Initiative (MAQI^2)
      - Mirrored the VHA approach using EPIC and rolled out across some University of Michigan Hospitals
    - AC Forum
      - Actively promoting population health as a component of anticoagulation stewardship efforts
      - Two ongoing projects surround the use of digital tools
- The recent publication presented only

  highlights the stance that we must strive to …



Panel Discussion

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**Disclaimer: The content herein represents the views of the speaker and do not represent the views of* VA, CDC, or the United States Government

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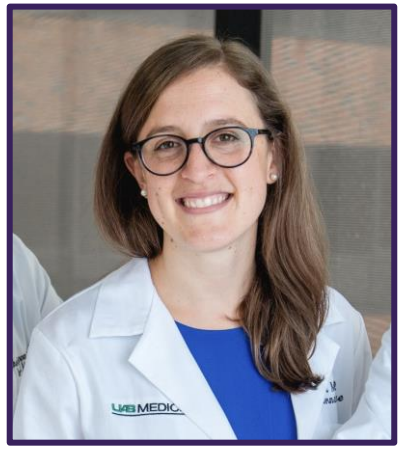

Jori May, MD
University of Alabama at Birmingham (UAB)

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