NOT ANOTHER *Traditional* AFIB TALK!

Transitioning for Community to Hospital and Back

A Sudbury Journal Club Presentation

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Conflict of Interest Declaration

The Sudbury Journal Club is supported by Industry as otherwise this learning opportunity would not exist.

All of our material is original, unbiased, and evidence based in upholding our professional responsibility as pharmacists.

Institute for Safe Medication Practices (ISMP)

ISMP List of *High-Alert* Medications *in Acute Care Settings*

High-alert medications are drugs that bear a heightened risk of causing significant patient harm when they are used in error. Although mistakes may or may not be more common with these drugs, the consequences of an error are clearly more devastating to patients. We hope you will use this list to determine which medications require special safeguards to reduce the risk of errors. This may include strategies such as standardizing the ordering, storage, preparation, and administration of these products; improving access to information about these drugs; limiting access to high-alert medications; using auxiliary labels and automated alerts; and employing redundancies such as automated or independent double-checks when necessary. (Note: manual independent double-checks are not always the optimal error-reduction strategy and may not be practical for all of the medications on the list.)

antithrombotic agents, including:

- anticoagulants (e.g., warfarin, low molecular weight heparin, IV unfractionated heparin)
- Factor Xa inhibitors (e.g., fondaparinux, apixaban, rivaroxaban)
- direct thrombin inhibitors (e.g., argatroban, bivalirudin, dabigatran etexilate)
- thrombolytics (e.g., alteplase, reteplase, tenecteplase)
- glycoprotein IIb/IIIa inhibitors (e.g., eptifibatide)

QuarterWatch

Monitoring FDA MedWatch Reports

Anticoagulants the Leading Reported Drug Risk in 2011

May 31, 2012

New Data from 2011 Quarters 3 - 4

Executive Summary

Annual Report Issue

For the calendar year of 2011 an estimated 2 to 4 million persons suffered serious, disabling, or fatal injury associated with prescription drug therapy, based on our analysis of a full year of reports to the U.S. Food and Drug Administration. The most frequently identified suspect drugs in direct reports to the FDA were the anticoagulants dabigatran (PRADAXA) and warfarin (COUMADIN), showing that inhibiting clotting ranks among the highest risk of all drug treatments. In addition, we identified nine other drugs associated most frequently with five clinically relevant, drug-related injuries, and show the drugs most frequently the target of lawsuits.

Pradaxa Warning

Pradaxa may increase risk for:

Hundreds of
deaths
linked to
Pradaxa
since 2010

Toll Free **1-800-BAD-DRUG**

Overview:

- Provide evidence based drug tables to highlight NOAC indications, dosing, efficacy, and safety
- Dosage reductions as per guidelines
- Managing stroke prevention vs bleed risk
- Case-based discussions for AF patients and CVD
- Guidance on managing drug interactions
- Help to determine which anticoagulant is right for your patient
- Provide practical tools and considerations that can be utilized in your practice (focus on monitoring, compliance, and follow-up)

Drug	AFIB	DVT/PE	TKR/THR	Adjustment (Renal/Hepatic/ Weight)
Dabigatran	150 mg po BID 110 mg po BID	150 mg po BID (after 5-20 days of parenteral)	110 mg po BID x28-35 days (THR) X10 days (TNR	AF: If CrCl is 30-50 ml/min: 110 mg po BID If wt < 60 kg or age >80: 110 mg po BID
Rivaroxaban	20 mg po DAILY	15 mg po BID x3wks then 20 mg po daily	10 mg po Daily x35 days (THR) X14 days (TNR)	AF: If CrCl is 30-49 ml/min: 15mg po DAILY
Apixaban	5 mg po BID	Pending Health Canada approval	2.5 mg po BID x32-38 days (THR) X10-14 days (TNR)	AF: If 2 out of 3: (wt<60 kg/age>80/ srcr>133) then 2.5 mg po BID
Edoxaban	60 mg po DAILY 30 mg po DAILY	Pending Health Canada approval	Pending Health Canada approval	Pending Health Canada approval
Warfarin	5 and 10 mg nomograms (INR 2-3)	LMWH/Heparin bridge to warfarin (INR 2-3)	LMWH/Heparin bridge to warfarin (INR 2-3)	Close monitoring and follow-up

	Rivaroxaban	Apixaban	Dabigatran
Renal 30-50 mL/min	ROCKET-AF: 15mg po Daily AHA/CCS 2014: 15mg po Daily	ARISTOTLE: 5mg po bid until 25 ml/min AHA/CCS 2014: 2.5mg po BID	RELY: 150/110mg po BID AHA/CCS 2014: 110mg po BID
Renal 15-30 mL/min	CCS 2014 recommends against	AHA 2014: 2.5mg po bid	Contraindicated
Drug Interactions	2012 ESC / 2014 AHA: -50% + AUC increase -25-50% AUC increase and age/renal risk factor 15mg po Daily	2012 ESC / 2014 AHA: -50% + AUC increase -25-50% AUC increase and age/renal risk factor 2.5mg po BID	2012 ESC / 2014 AHA: -50% + AUC increase -25-50% AUC increase and age/renal risk factor 110mg po BID
Age/Weight	CCS Recommends: -Age more than 80 15mg po daily	CCS Recommends: -Age more than 80 -2 of age/wt/srcr 2.5mg po BID	CCS Recommends: -Age more than 75 -Weight less than 60 110mg po BID

New OACs Compared to Warfarin

Clinical Trial Data

	Apixaban	Dabigatran 110mg	Dabigatran 150mg	Rivaroxaban
Stroke Prevention	↓	↔	↓	↔
Major Bleeding	↓	↓	↔	↔
Intracranial Hemorrhage	↓	↓	↓	↓
Mortality	↓	↔	↔	↔

Canadian Cardiovascular Society

Leadership. Knowledge. Community.

2014 Recommendation #5:

We recommend that when OAC-therapy is indicated for patients with non-valvular AF, most patients should receive dabigatran, rivaroxaban, apixaban or edoxaban (when approved) in preference to warfarin.

(Strong Recommendation, High Quality Evidence)

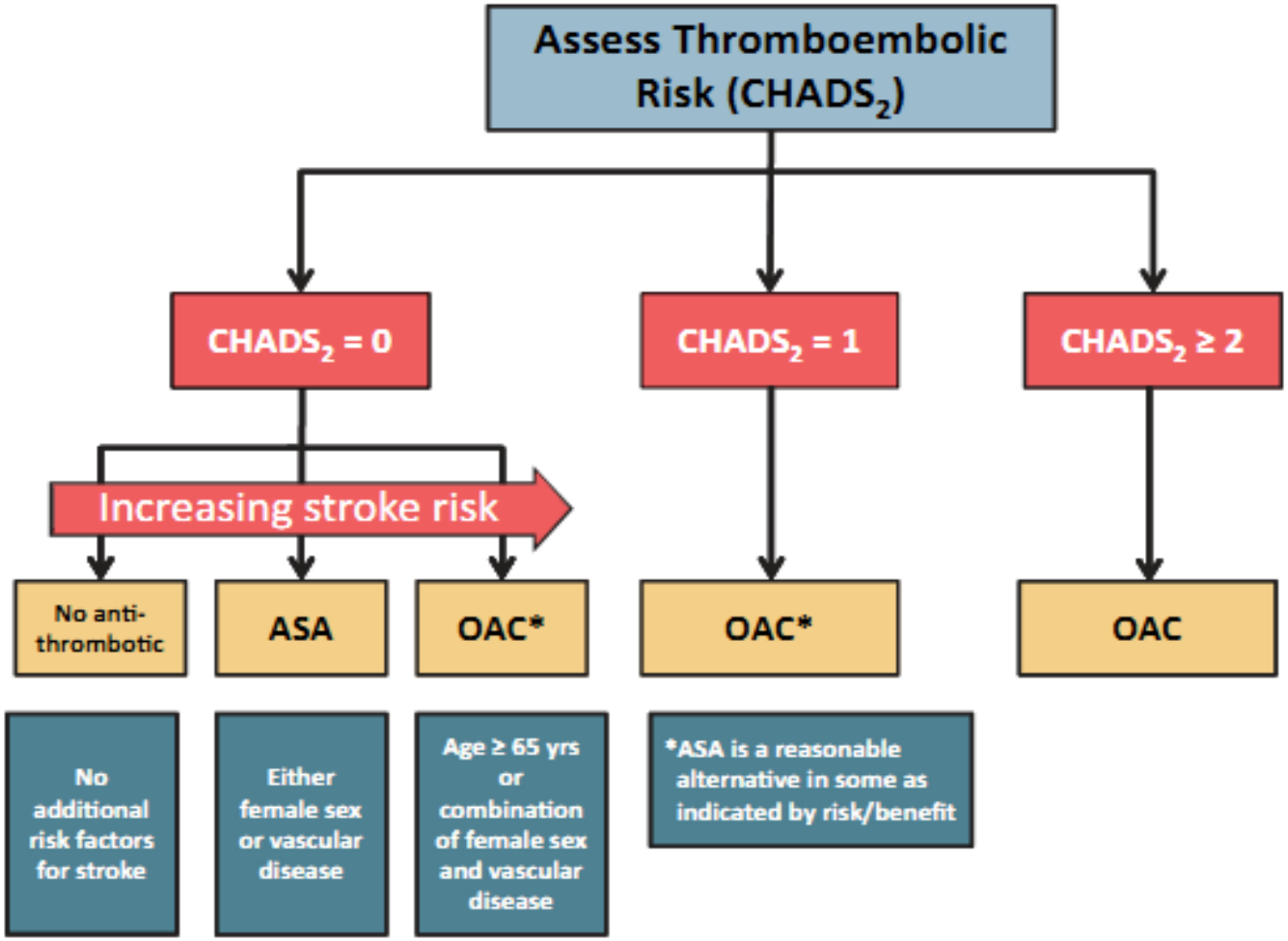
$CHADS_2$: Stroke Risk Score

$CHADS_2$ Score - Sum Of:	Points
Congestive Heart Failure	1
Hypertension	1
Age ≥ 75 Years	1
Diabetes Mellitus	1
Prior History of Stroke / TIA	2

Risk of Stroke in National Registry of Atrial Fibrillation Participants, Stratified by $CHADS_2$ Score

$CHADS_2$ Score	# Patients (n=1733)	Adjusted Stroke Rate %/yr (95% CI)
0	120	1.9 (1.2-3.0)
1	463	2.8 (2.0-3.8)
2	523	4.0 (3.1-5.1)
3	337	5.9 (4.6-7.3)
4	220	8.5 (6.3-11.1)
5	65	12.5 (8.2-17.5)
6	5	18.2 (10.5-27.4)

From the 2012 CCS Guidelines….



New in the 2014 CCS Guidelines....

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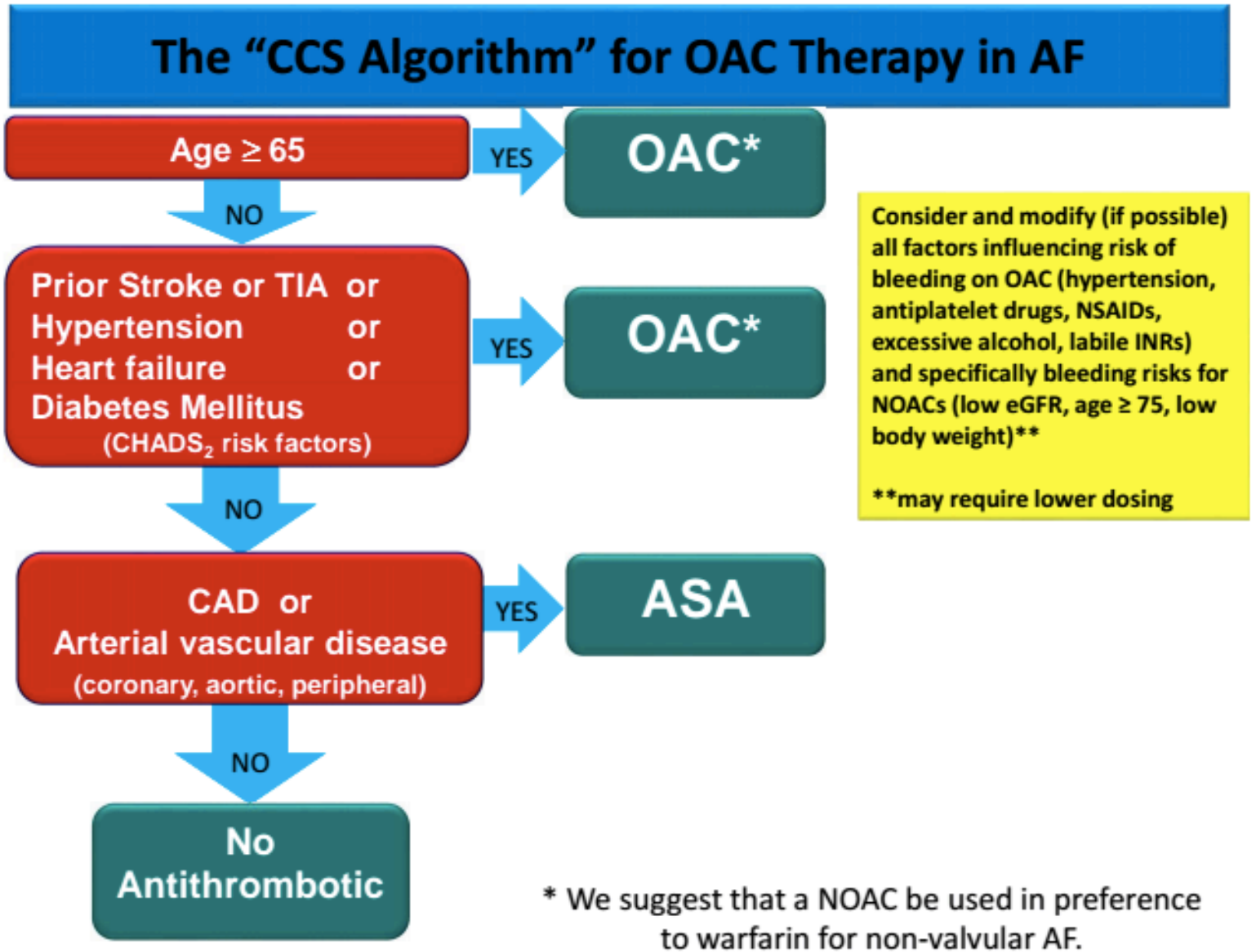
Recommendation #2: We recommend that OAC therapy be prescribed for most patients aged ≥65 years or CHADS2 ≥1.
(Strong Recommendation, Moderate Quality Evidence)

Recommendation #3: We suggest that ASA (81 mg/day) be prescribed for patients with no risks: age <65 years and no CHADS2 risk factors, who have arterial disease (coronary, aortic, or peripheral).
(Conditional Recommendation, Moderate Quality Evidence)

Recommendation #4: We suggest no antithrombotic therapy for patients with none of the risks: age <65 and no CHADS2 risk factors and free of arterial vascular disease (coronary, aortic, peripheral).
(Conditional Recommendation, Low Quality Evidence)

From the 2014 CCS Guidelines....



Estimating Bleed Risk in AF

The bleeding risk depends on BOTH:

i) Specific antithrombotic agent

ii) Variety of patient characteristics

Estimating Bleed Risk in AF

From the CCS guidelines…

i) Specific Antithrombotic Agents

Highest Risk of Major Bleed (Top)

- ❑ Dabigatran 150mg BID
- ❑ Rivaroxaban
- ❑ Warfarin

- ❑ Apixiban
- ❑ Dabigatran 110 mg BID

- ❑ Combination ASA plus clopidogrel

- ❑ ASA (75-325 mg/day)
- ❑ Clopidogrel (75mg/day) alone

Canadian Journal of Cardiology 28 (2012) 125–136

Estimating Bleed Risk in AF

2014 ESC and 2014 CCS AF guidelines recommend:

HAS-BLED	Points
Hypertension (SBP > 160 mmHg)	1
Abnormal renal and liver function (1 point for each)	1 or 2
Stroke	1
Bleeding	1
Labile INRs	1
Elderly (age > 65)	1
Drugs or alcohol	1 or 2
Maximum Score	9

Risk Factor Score	Major Bleeds (%/yr)
0	1.13
1	1.02
2	1.88
3	3.74
4	8.70
5	12.50

HAS-BLED score of ≥ 3 suggests increased bleeding risk and warrants caution and/or regular review.

* Note: bleeding models should not be used as the sole criterion for deciding to initiate therapy

HAS-BLED: How To Use

2014 CCS AF GUIDELINE BOTTOM LINE

"Patients at increased risk of major bleeding warrant extra caution and closer monitoring of antithrombotic therapy"

****PATIENTS WITH HAS-BLED > 3****

HAS-BLED: How To Use

What the tool is not meant to do:

STROKE RISK — BLEED RISK

- 70% of strokes with AF are either fatal or leave severe residual deficits.
- Major bleeding is often less fatal (0.3-0.5% fatal intracranial) and less likely to leave significantly residual effects in survivors.

Canadian Journal of Cardiology 28 (2012) 125–136

BW Presents…

- 71 year old female presents to ER with AF (80–117 bpm)
- ER administers IV diltiazem
- ER - BP 168/98

PMHx:

- Paroxysmal AF
- HTN
- DM
- GERD
- OA

Labs

- CrCl =57 mL/min

Medications on Admission

- Diltiazem CD 240 mg po daily
- ECASA 81 mg po daily
- Metformin 500 mg po daily
- Rabeprazole 20mg po daily
- Takes Advil PRN

Chronic AF Approach

General 3-Step process to selecting therapy:

Step 1: Determine your patient's annual risk of stroke

Step 2: Determine your patient's risk of bleeding

Step 3: Balance the benefits of stroke prevention versus the bleeding risk

What's BW's $CHADS_2$ score?

A) 0

B) 1

C) 2

D) 3

E) 4

F) 5

G) 6

4% annual risk of stroke

What's BW's HAS-BLED score?

A) 0

B) 1

C) 2

D) 3

E) 4

F) 5

G) 6

H) 7

I) 8

J) 9

8% annual risk of major bleed

Any Changes to BW Meds on Discharge?

$CHADS_2$=2 VS HAS-BLED=4

4% stroke **VS** 8% Major bleed

- Are there any modifiable risk factors that can be addressed as a function of the HAS-BLED score?

Any Changes to BW Meds on Discharge?

i) **Advil PRN for OA**
   –Tylenol 650mg QID PRN

ii) **HTN uncontrolled**
   -Add first line agent
   -Aim for ↓SBP<160 over the next 24-48 hrs

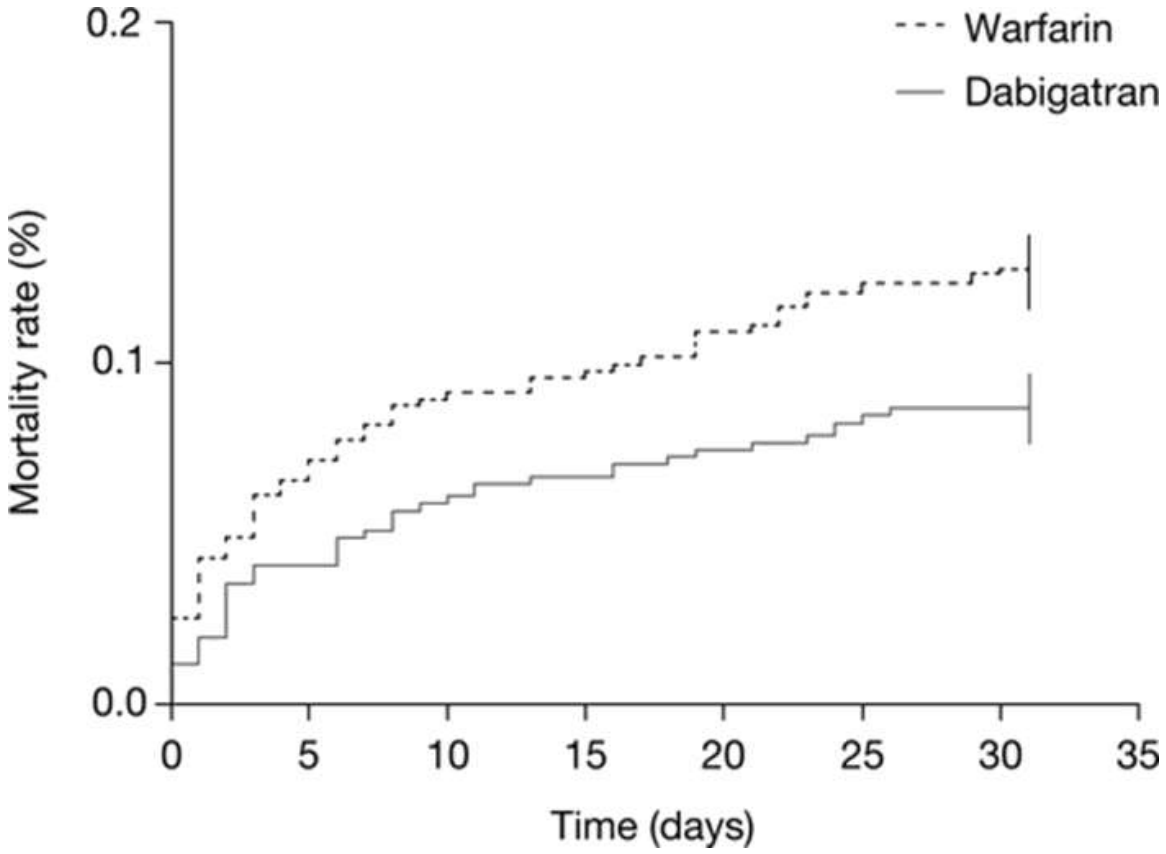
iii) **ASA 81mg?**
   -Something to consider

****GOAL: HAS-BLED < 3****

- Lack of antidote to reverse the anticoagulant effects of NOACs is an overemphasized concern

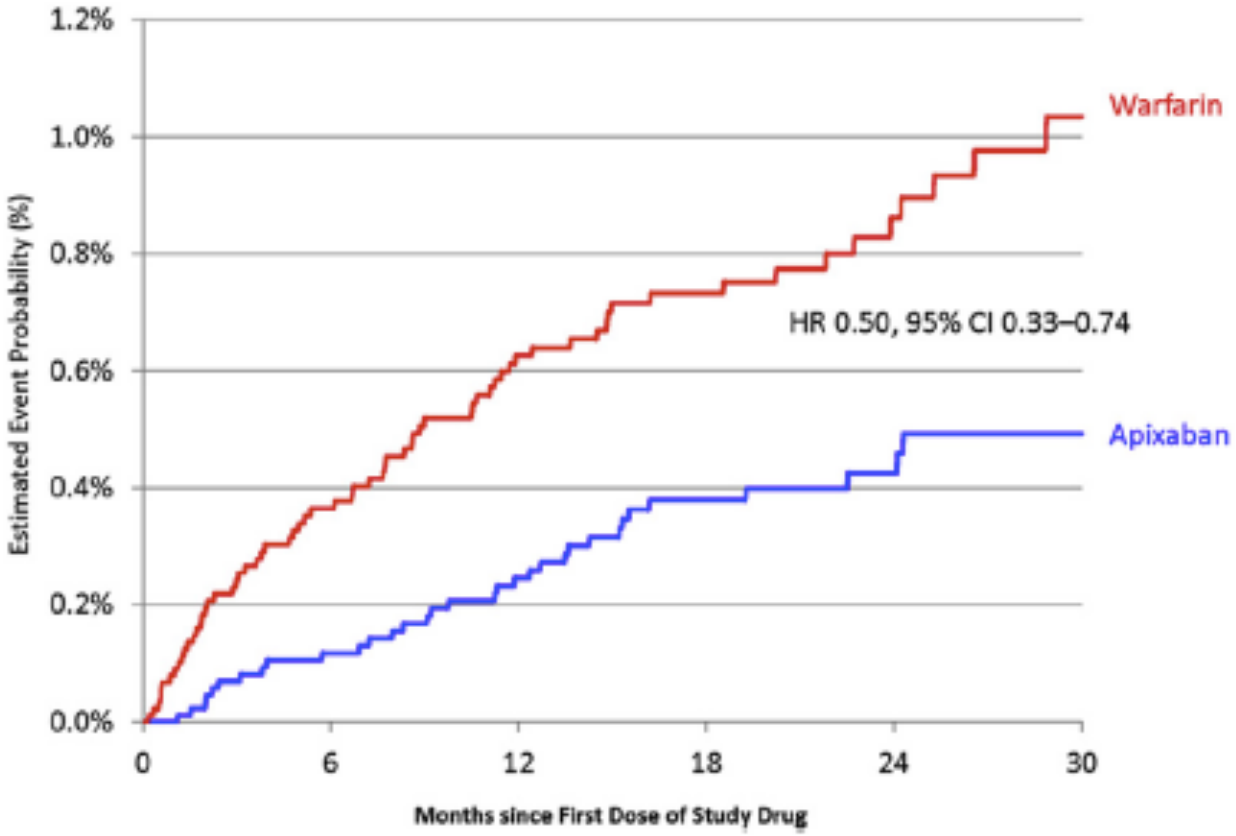
30-day mortality rate after a major bleeding event

("On-treatment" data from five randomized trials)



Majeed A et al. Circulation 2013;128:2325-32

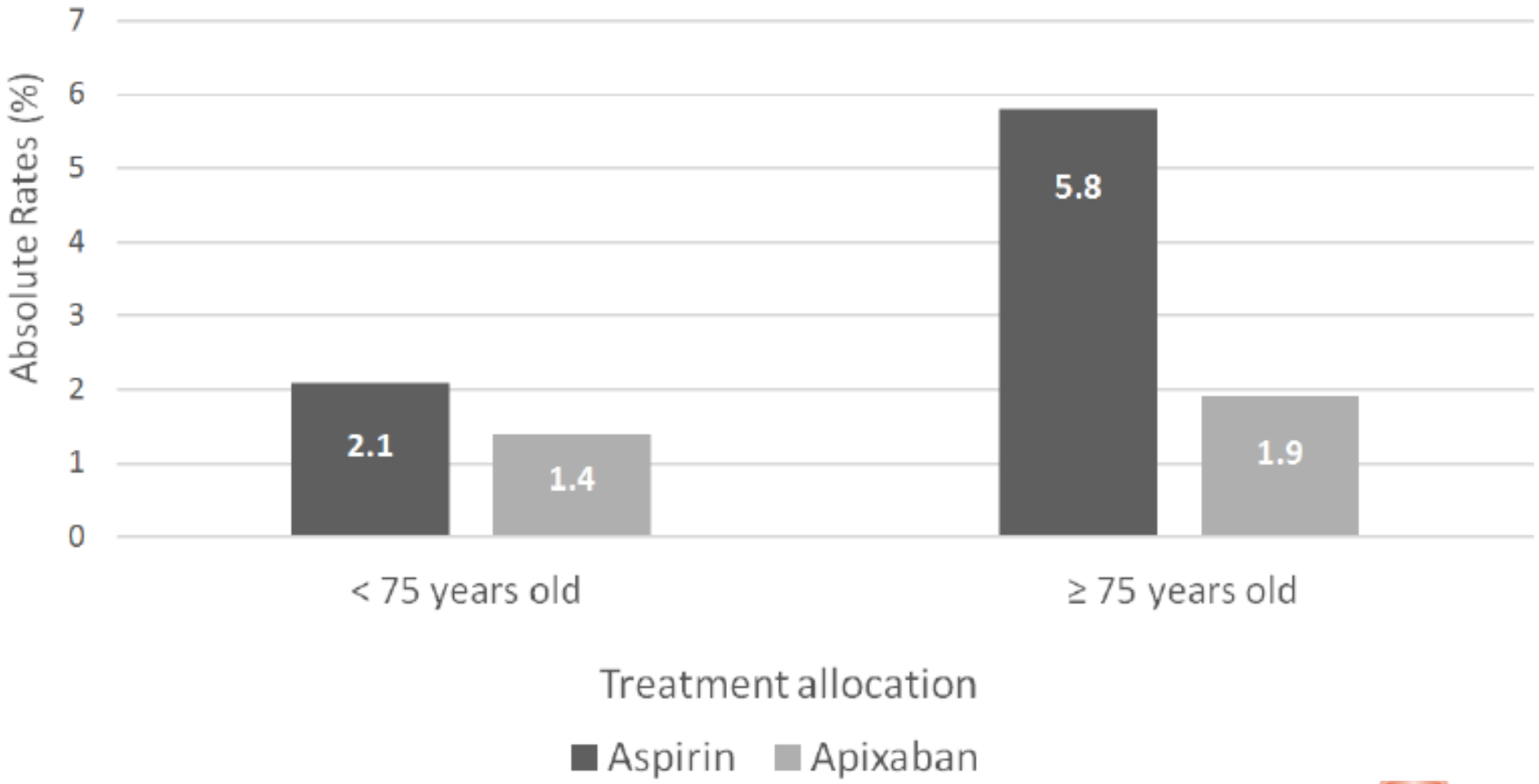
Major Bleeding Followed by Death Within 30 days



Hylek et al. JACC 2014:2141-7

AVERROES Trial: apixaban vs aspirin

Comparison of absolute rates of all strokes between younger and older patients by treatment allocation



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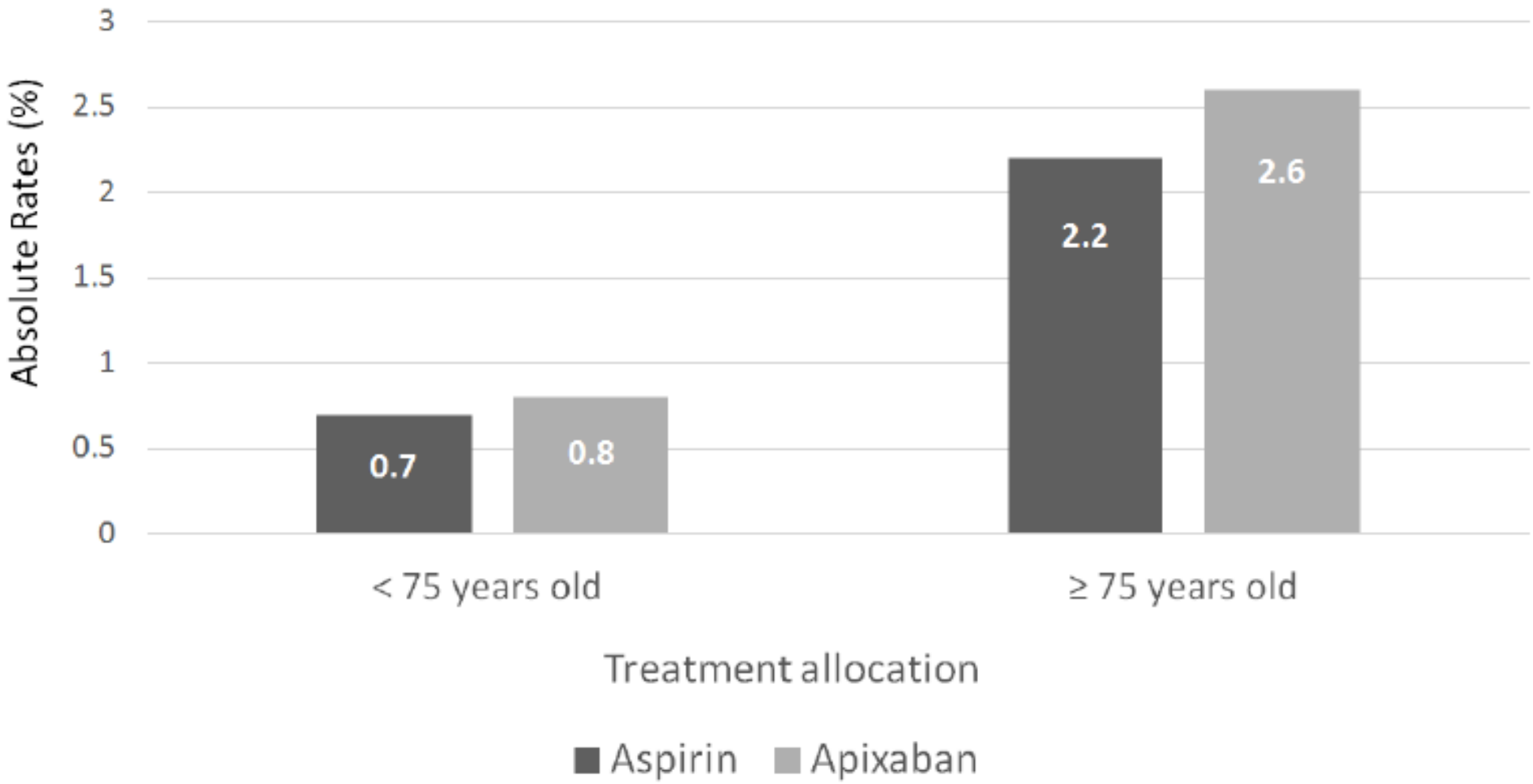


Apixaban and Rivaroxaban Drug Interactions

Potent 3A4 Inhibitors and Potent p-glycoprotein inhibitors


Ketoconazole
Rifampin
Progesterone/Estrogens
Clopidogrel
Ketooconazole
Anticoagulants
clarithromycin
Ticagrelor
Diltiazem
dronaderone
amiodarone
phenobarbital
Fluconazole
Phenytoin
agents
St,John's-wort
voriconazole
Erythromycin
itraconazole
posaconazole
Naproxen
asa
Thrombolytic
Ritonavir
carbamazepine
Word
It Out

Dabigatran Drug Interactions

Potent p-glycoprotein inhibitors


ketoconazole
St,John-wort
Antacids
carmbamazepine
SSRIs
cyclosporine
phenytoin
Verapimil
aspirin
verapamil
dronedarone
itraconazole
tipranavir
prasugrel
SNRIs
systemic
clopidogrel
Ticagrelor
PPIs
nelfinavir
posaconazole
saquinavir
NSAIDs
tacrolimus
amiodarone
ritonavir
Thrombolytic-agents
quinidine
phenobarbital
Progesterone/Estrogens
ketozonazole

Warfarin Drug Interactions

Over 15 different mechanisms of interaction

Clarithromycin Primidone
Amiodarone Devil's Phenylbutazone Levofloxacin
Clofibrate Azithromycin Ciprofloxacin
Citalopram Danaparoid Mesalamine Rifabutin
Danazol Butabarbital Itraconazole Rifampin bark
Nafcillin Argatroban Erythromycin LMWHs Allopurinol
claw Chloral Neomycin avocado Chamomile Clopidogrel
Phenobarbital Fluorouracil Doxycycline Gemfibrozil Anise NSAIDs
Ginseng Red-clover Moxalactam Danshen hydrate Quinidine
heparin Miconazole Amobarbital Ginkgo Grapefruit
Fenugreek Ofloxacin Licorice Garlic Quassia Coenzyme-Q
Feverfew Fish Ritonavir Bactrim Clove
Onion Diltiazem Aspirin Meadowsweet quai Asafoetida
Influenza Propafenone Felbamate Ribavirin oil
Papain Horse Norfloxacin Disulfiram Mango
binge Ginger Disopyramide Alcohol Fenofibrate
Acetaminophen Piroxicam Fluvoxamine Fluconazole
Carbamazepine Dong Metronidazole Green
Isoniazid Phenytoin Mercaptopurine Cimetidine
Omeprazole Chloramphenicol Entacapone
chestnut Dicloxacillin
Cholestyramine Griseofulvin
Propranolol Dipyridamole

Word It Out

	Via	Dabigatran	Apixaban	Edoxaban	Rivaroxaban
Atorvastatin	P-gp/ CYP3A4	+ 18%		No Effect	No Effect
Digoxin	P-gp	No Effect		No Effect	No Effect
Verapamil	P-gp/ CYP3A4	+12-180%		+53%	Minor
Diltiazem	P-gp/ CYP3A4	No Effect	+40%		Minor
Quinidine	P-gp	+50%		+80%	+50%
Amiodarone	P-gp	+12-60%		No Effect	Minor
Dronedarone	P-gp/ CYP3A4	+70-100%		+85%	
Ketoconazole Itraconazole	P-gp/ CYP3A4	+140-150%	+100%		+160%
Fluconazole	Moderate CYP3A4				+42%
Cyclosporin Tacrolimus	P-gp				+50%
Clarithormycin; Erythromycin	P-gp/ CYP3A4	+15-20%			+30-54%
HIV Protease Inhibitors	P-gp/ CYP3A4				+135%
Rifampin; SJW; CBZ; PHT; PHB	P-gp/ CYP3A4	-66%	-54%	-35%	-50%
Antacids	GI Absoprtion	-12-30%		No Effect	No Effect

Other Factors	Via	Dabigatran	Apixaban	Edoxaban	Rivaroxaban
Age>80 years	Increased Plasma Levels				
Age> 75 years	Increased Plasma Levels				
Weight <60kg	Increased Plasma Levels				
Renal Function	Increased Plasma Levels				
Other increased bleeding risk		Pharmacodynamic interactions (antiplatelet drugs; NSAIDS; systemic steroids; anticoagulants) history or active GI bleeding; recent surgery on critical organ; HAS-BLED>3			

For Drug Interaction Tables: H. Heidbuchel et al. Europace 2013:15,625-651

WHICH ANTICOAGULANT IS RIGHT FOR MY PATIENT?

Patient Characteristic	Optimal Oral Anticoagulant (s)	Evidence
Prior Stroke/ CHADS 3 or more	Dabigatran 150mg bid Rivaroxaban 20mg daily Apixaban 5mg bid	-RELY: Conferred the highest reduction of ischemic stroke -ROCKET-AF had the most secondary stroke prevention patients and highest CHADS score of the three trials -ARISTOTLE showed apixaban has the greatest benefit to prevent ischemic stroke, reducing major bleeding, and all-cause mortality in CHADS >3
High Bleed Risk (HASBLED)	Apixaban 5mg bid	-ARISTOTLE demonstrated apixaban's major bleeding benefit over warfarin relative to CHADS2 and HABLED scores of both low and high risk
Moderate Renal Impairment CrCl <30-50 ml/min	Apixaban 5mg bid or dose (reduced when meeting 2/3 age>80, wt<60kg, srcr>133) Rivaroxaban 15mg daily	-ARISTOTLE Subgroup: showed apixaban maintained superior efficacy relative to stroke prevention, superior safety as well as all-cause mortality in moderate renal impairment - ROCKET Subgroup: risk of stroke & systemic embolism and risk of bleeding were both increased in this patient group, however results were still consistent with safety and efficacy non-inferior to warfarin
Mechanical Valve	Warfarin	-Dabigatran trial was stopped early due to 9 Strokes vs 0 with Warfarin -Other 2 NOACs not studied

Patient Characteristic	Optimal Oral Anticoagulant (s)	Evidence
Unsuitable for warfarin	Apixaban 5mg bid	Apixaban 5 mg po bid as safe as aspirin 81 mg daily in patients unable or unsuitable to take warfarin
Older Adults >80	Apixaban 5mg bid (reduced when meeting 2/3 age>80, wt<60kg, srcr>133) Rivaroxaban 20mg daily	-ARISTOTLE Subgroup: Maintained superior stroke efficacy, less major bleeding as well as all-cause mortality -ROCKET Subgroup: Maintained non-inferiority efficacy and major bleeding -RELY Subgroup: In those aged ≥75 years, intracranial bleeding risk is lower but extracranial bleeding risk is similar or higher with both doses of dabigatran compared with warfarin.
Compliance	Rivaroxaban 20mg daily Warfarin	-Once a day dosing regimen was related to greater adherence versus bid regimen in atrial fibrillation patients -Warfarin pharmacotherapy is optimized within therapeutic range more so than community setting
Dialysis	+/- Warfarin	-2012 CCS guidelines advice against warfarin because of 10% annual risk of major bleeding
High risk for GI Bleeding	Apixaban 5mg bid	-Subgroup analysis showed lowest GI bleed rates among the NOACs

Patient Characteristic	Suggested Oral Anticoagulant	Evidence
Hepatic compromise	Warfarin	NOACs require hepatic metabolism and if kinetics are unpredictable, use is not recommended
GERD/ Dyspepsia	Anything but dabigatran	11.6% vs 5 % dyspepsia proven from RELY trial dabigatran versus warfarin
CAD/Recent ACS	Rivaroxaban Apixaban Warfarin	-Dabigatran was found to be associated with a small increase in MI -WARIS II trial demonstrated cardio-protective effect of warfarin

WHICH ANTICOAGULANT IS RIGHT FOR MY PATIENT?

Primary Prevention of a Cardiovascular Event With ASA 81/325 mg Daily

J.D. presents to your pharmacy…

J.D comes in to pick up another bottle of baby aspirin as he has for the past decade

Age: 48 y.o Male

Past Medical History: Afib (diagnosed 3 months ago) HTN, Smoker, Hyperlipidemia, however no diagnosed CAD, ETOH +++

Framingham Risk Score: 10%

Current Meds: Lipitor 40mg po daily, Metoprolol 25mg po bid, Dabigatran 110mg po bid (started 3 months ago) ASA 81mg is an OTC….

BLEED RISK OF ASA + NOAC VS. CVE BENEFIT OF ASA IN PRIMARY PREVENTION

Benefit of ASA in Primary Prevention	Any Benefit NNT = 1667 / year
Bleeding Rate of ASA + Pradax	Major Bleed NNH = 55 / year
Bleeding Rate of ASA + Apixaban	Major Bleed NNH = 100 /year
Bleeding Rate of ASA + Rivaroxaban	Independent bleed risk factor

Antithrombotic Trialists Collaboration. Aspirin in the primary and secondary prevention of vascular disease: collaborative meta-analysis of individual participant data from randomised trials. Lancet. 2009; 373(9678): 1849-60

What could you tell J.D.?

WHICH ANTICOAGULANT IS RIGHT FOR MY PATIENT?

Acute Coronary Syndromes and DAPT

A few years later (59 y.o.)… J.D. gets some chest pain at the golf course and goes to the hospital

- J.D. found to have a NSTEMI, was angioplastied and has 1 DES stent
- You receive his discharge script asking for a Medscheck as well

Discharge Medications Rx:

You notice no ASA?

Lipitor 80mg po od

Apixaban 5mg po bid

Carvedilol 3.125mg po bid

Clopidogrel 75mg po Daily x 1 year

Nictotine Patch 21mg

Ramipril 10mg po Daily

A few years later (59 y.o.)… J.D. gets some chest pain at the golf course and goes to the hospital

- Benefit increases from 1º to 2º prevention — NNT 42 /year
- Bleed risk ASA/Clop/OAC (risk of adding ASA) — NNH 50-100 / **30 Days**
- Total bleed risk of triple therapy — NNH 10-13 / year

Product monographs:

"Concomitant use of ASA or clopidogrel with RIVAROXABAN/ APIXABAN/DABIGATRAN in patients with atrial fibrillation increases the risk of bleeding. Concomitant use of ASA or other antiplatelet agents based on medical need to prevent myocardial infarction should be undertaken with caution"

WOEST Trial Objective

- To test the hypothesis that after percutaneous coronary intervention (PCI) with implantation of a stent in patients on oral anticoagulant therapy, clopidogrel 75mg/d in combination with oral anticoagulation therapy reduces the risk of bleeding and is noninferior to the triple therapy regimen of aspirin 80mg/d, clopidogrel, and oral anticoagulation therapy with respect to preventing thrombotic complications.

Interventions

- All patients pre-treated with a maintenance dose of 75mg clopidogrel/day for at least 5 days, a loading dose of 300mg at least 24 hours before PCI or a loading dose of 600mg at least 4 hours before PCI.

- All patients received 75mg of clopidogrel daily and those in the triple therapy group were also given 80-100mg aspirin daily; a 320mg loading dose was also given to patients who had not been taking aspirin before the study

- During intervention oral anticoagulants were continued if possible with a target INR of 2.

Main Results: Safety

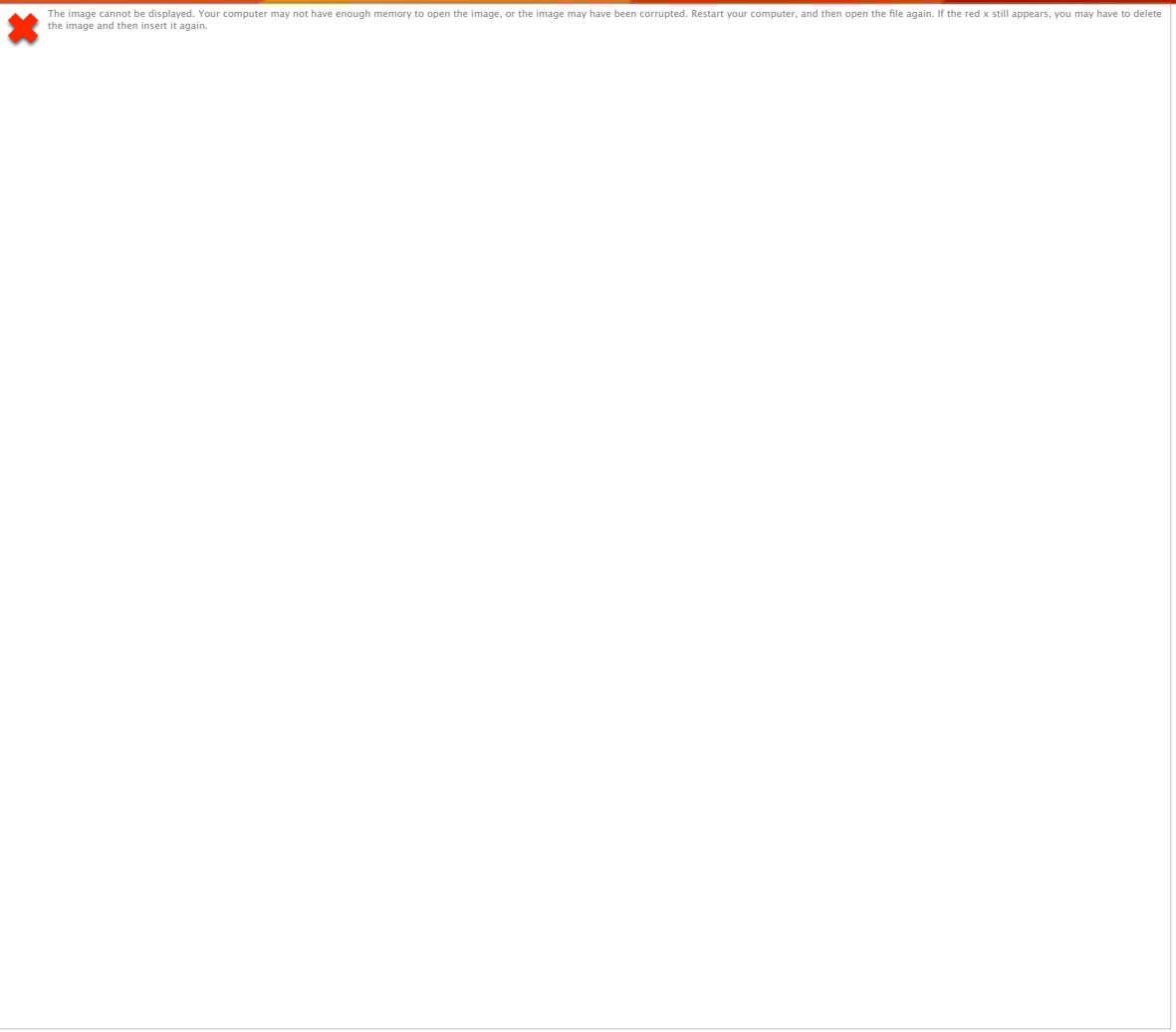
- Significant differences in favour of the double therapy group were seen for TIMI minor, TIMI minimal, GUSTO moderate, GUSTO mild and BARC 3,2,1 major and minor bleeding scales

- There was no difference in the number of intracranial bleeds between both groups.

Main Results: Safety

- For TIMI major, GUSTO severe and BARC 3a and 3b bleeding, double therapy seemed to be associated with fewer cardiac events but differences between groups were not significant.

Main Results cont...



Main Results: Efficacy

- The combined secondary endpoint of death, MI, stroke, target-vessel revascularization and stent thrombosis showed no significant difference amongst groups.

2014 AHA Guidelines

ACCEPTED MANUSCRIPT

January, CT et al.
2014 AHA/ACC/HRS Atrial Fibrillation Guideline

4. **Following coronary revascularization (percutaneous or surgical) in patients with AF and a CHA_2DS_2-VASc score of 2 or greater, it may be reasonable to use clopidogrel (75 mg once daily) concurrently with oral anticoagulants but without aspirin (83).** ***(Level of Evidence: B)***

2014 Canadian Cardiovascular Society ACS/CAD recommendations

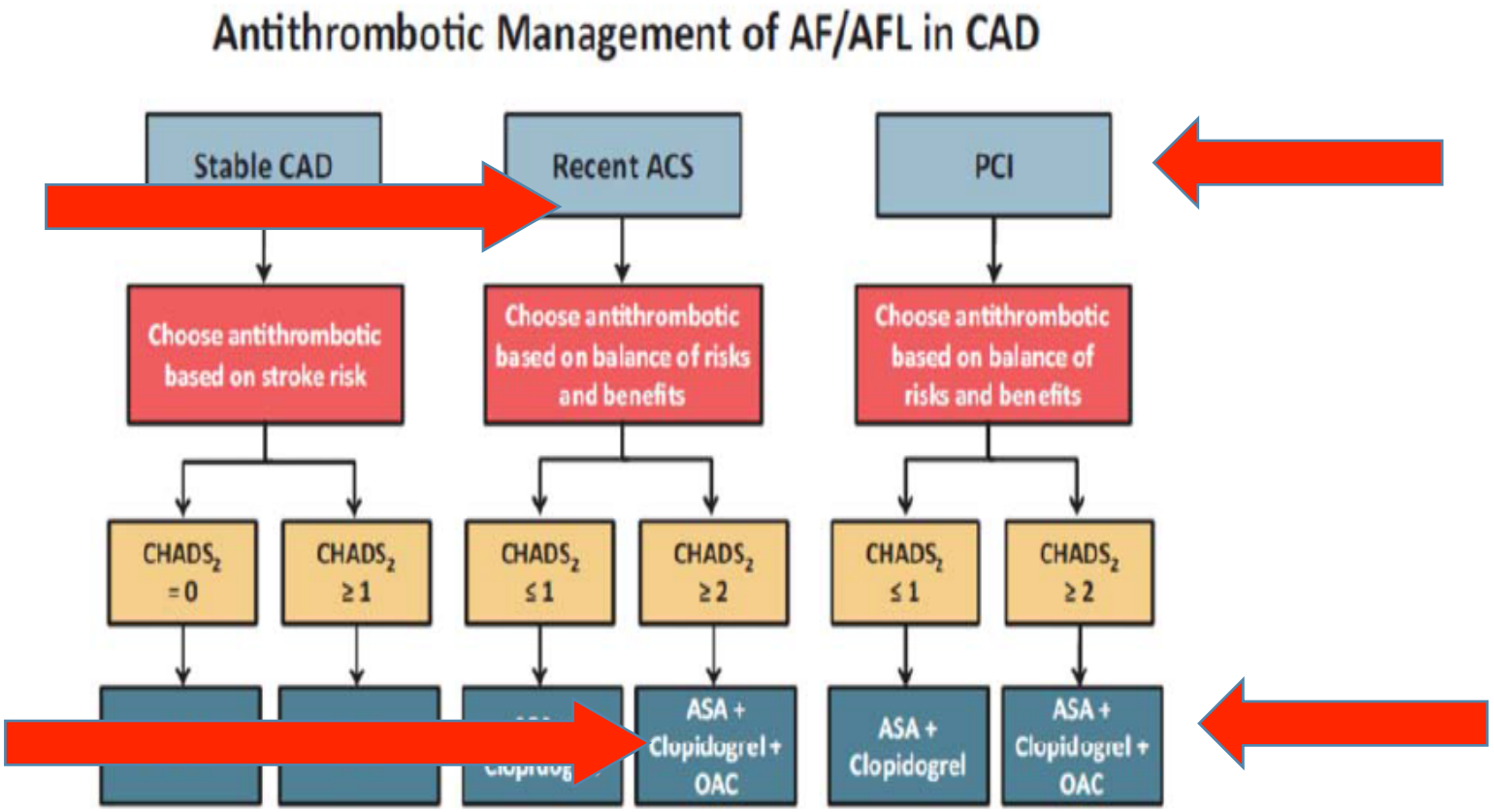


Figure 2. A summary of our recommendations for antithrombotic management in settings of CAD. ACS, acute coronary syndrome; AF, atrial fibrillation; AFL, atrial flutter; ASA, acetylsalicylic acid (aspirin); CAD, coronary artery disease; $CHADS_2$, Congestive Heart Failure, Hypertension, Age > 75, Diabetes Mellitus, and Prior Stroke or Transient Ischemic Attack; OAC, oral anticoagulant; PCI, percutaneous coronary intervention.

Other great things about the discharge Rx…

- They used clopidogrel not ticagrelor
- The dose of apixaban was not reduced, as per the 2013 ESC guideline
- Clopidogrel is prescribed for the suggested amount of time
- Lipitor is optimized
- Medscheck prescribed

WHICH ANTICOAGULANT IS RIGHT FOR MY PATIENT?

Stable CAD/Long Term Secondary Prevention of a Cardiovascular Event With ASA 81/325 mg Daily

A year later… J.D. is in to pick up his refills

-Lipitor 80 po od

-Apixaban 5 mg po bid

-Carvedilol 3.125 mg po bid

-Ramipril 10 mg po daily

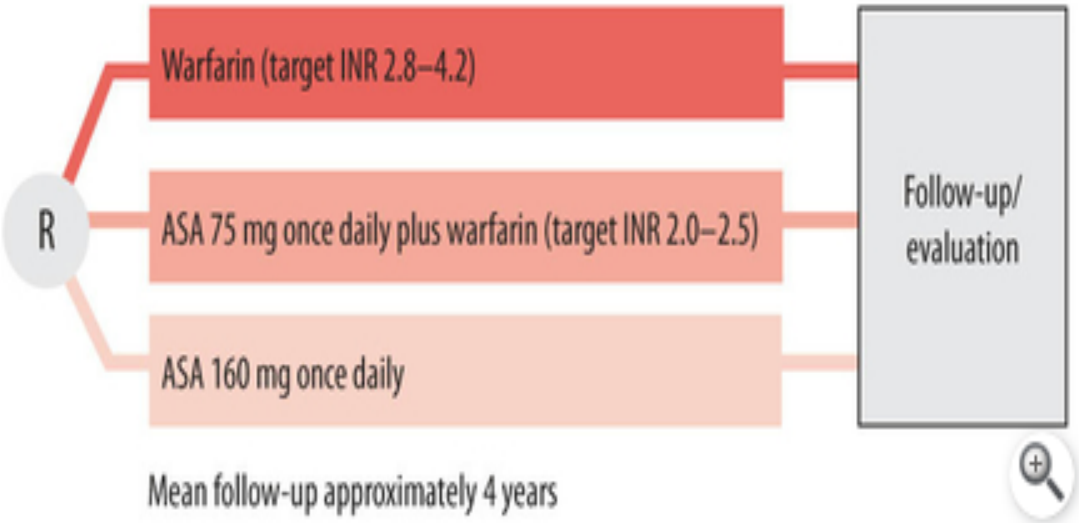
Do you suggest restarting his aspirin 81 mg daily now that the year of Plavix is done?

- ASA is recommended lifelong after stenting/ ACS/CAD according to AHA and CCS guidelines
- Does this apply to our Afib patient?

A year later… J.D. is in to pick up his refills

- Adding ASA causes a major bleed increase of NNH 50-100/year (previous slide)
- Benefit of ASA long term in CAD is NNT of 100 / year
- Do oral anticoagulants have cardio-protective effects? Can the anticoagulant do ASA's job?
  - WARIS II trial

WARIS trial:



Endpoint	Aspirin alone	Warfarin alone	Aspirin + warfarin
Any cardiovascular event/death	241 (20.0%)	203 (16.7%)	181 (15.0%)

- Oral anticoagulation more cardioproctective than aspirin alone over 4 years!
- Mean INR was 2.8

Subgroup Analysis +/- ASA in Aristotle trial

- ARISTOTLE Trial: 20% of patients taking ASA with apixaban for CAD
- Over the 2 year trial, no difference in cardiovascular events or cardiovascular death were found and an increase in bleeding was confirmed by the sub-analysis in those patient receiving ASA
  - Adding ASA to Afib patients already anticoagulated may not lower the risk of cardiovascular events and will likely increase the risk of bleeding

2014 Canadian Cardiovascular Society ACS/CAD recommendations

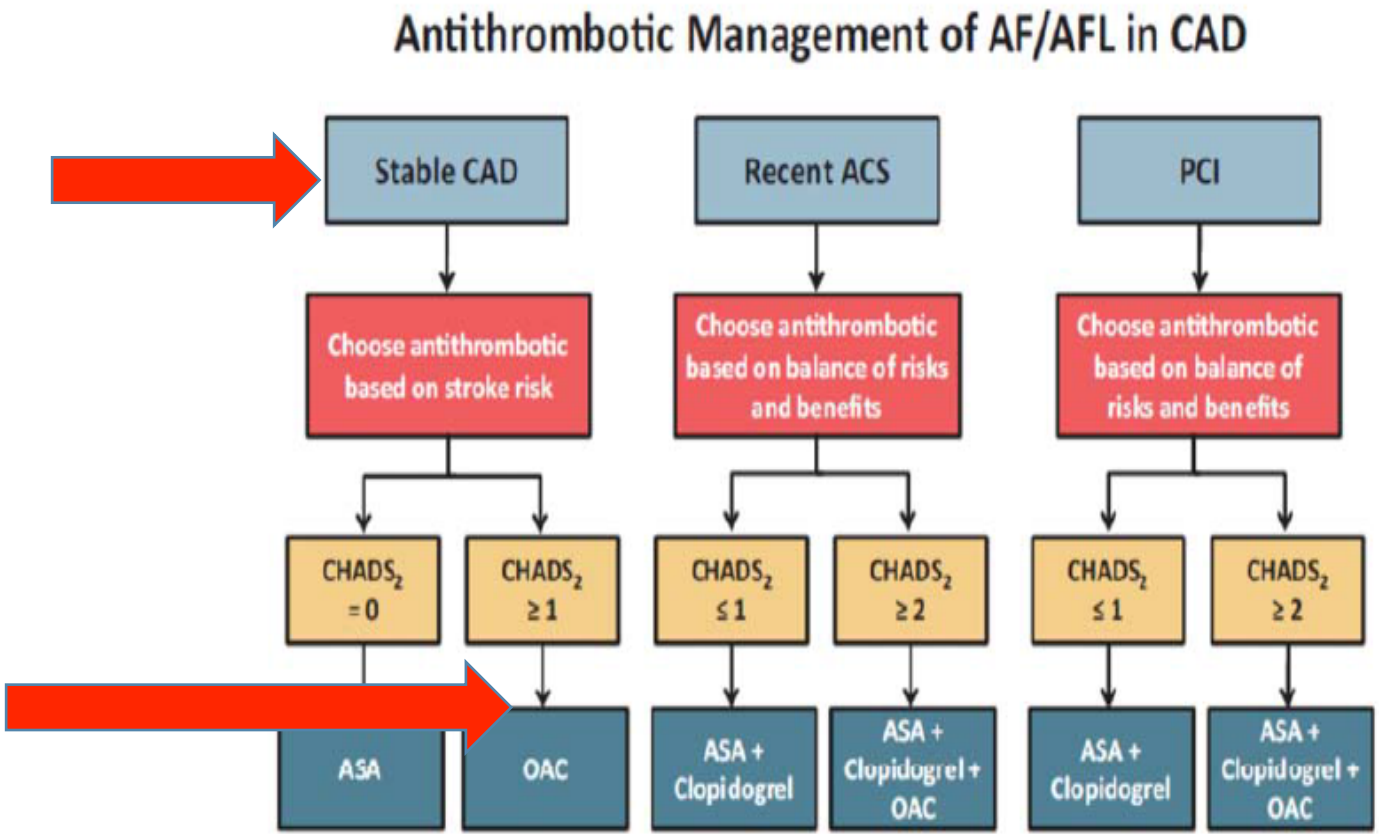


Figure 2. A summary of our recommendations for antithrombotic management in settings of CAD. ACS, acute coronary syndrome; AF, atrial fibrillation; AFL, atrial flutter; ASA, acetylsalicylic acid (aspirin); CAD, coronary artery disease; $CHADS_2$, Congestive Heart Failure, Hypertension, Age > 75, Diabetes Mellitus, and Prior Stroke or Transient Ischemic Attack; OAC, oral anticoagulant; PCI, percutaneous coronary intervention.

Other Important NOAC Considerations

NOAC Medications in a Blister Pack?

- Yes for Apixiban and Rivaroxaban
- Dabigatran must be kept in original packaging

With Meals?

- Dabigatran capsules should be taken with food to reduce the risk of stomach upset or can be taken with water
- Rivaroxaban taken with food enhances absorption (it can be crushed and taken with soft food)
- Apixiban can be taken with a meal but does not need to be

Food Interactions?

- Unlike warfarin there are no known food interactions, also no evidence that grapefruit juice affects efficacy or safety

Alcohol?

- A glass of wine or beer with a meal when taking a NOAC is acceptable but binge drinking or chronic consumption can cause safety concerns

What about PPIs/Antacids?

- Stomach acid issues occur in up to 10% of patients who start dabigatran and is less common with rivaroxaban or apixaban. Taking the medication with meals can reduce the risk of stomach upset. Antacids may help if taken 2 hours after a dabigatran dose.

Checklist for Follow-Up

	Interval	Comments
1. 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; . . .)
2. Thrombo-embolism	Each visit	• Systemic circulation (TIA, stroke, peripheral) • Pulmonary circulation
3. Bleeding	Each visit	• 'Nuisance' bleeding: preventive measures possible? (PPI; haemorrhoidectomy; . . .). Motivate patient to diligently continue anticoagulation • Bleeding with impact on quality-of-life or with risk prevention possible? Need for revision of anticoagulation indication or dose?
4. Other side effects	Each visit	• Carefully assess relation with NOAC: decide for continuation (and motivate), temporary cessation (with bridging), or change of anticoagulant drug.
5. Co-medications	Each visit	• Prescription drugs; over-the-counter drugs (see Section 4) • Careful interval history: also temporary use can be risk!
6. Blood sampling	Yearly 6 monthly 3 monthly On indication	• Haemoglobin, renal and liver function • Renal function if CrCl 30–60 ml/min, or if on dabigatran and >75 years or fragile • If CrCl 15–30 ml/min • If intercurring condition that may impact renal or hepatic function

TIA, transient ischaemic attack; PPI, proton pump inhibitor; CrCl, creatinine clearance (preferably measured by the Cockroft method).

Compliance:

NOACs have a very predictable anticoagulant effect however this effect will fade rapidly 12-24 hours after the last intake.

Compliance is crucial and we can help!

- Leaflets and instructions at the initiation of therapy
- Patient anticoagulation card
- Re-education at prescription renewals
- Involve family members in discussion
- Ensure that there is a pre-specified follow-up scheduled between patient and GP or Cardiologist
- Blister packs, medication boxes, electronic reminders

How to deal with dosing errors?

- **Missed Dosed:**
  - For NOACs with a BID dosing regimen the patient should still take a forgotten dose up till 6hrs after the schedule intake
  - For NOACs with a once daily dosing regimen the patient should still take a forgotten dose up till 12hrs after the scheduled intake

- **Double Dose:**
  - For NOACs with a BID regimen one could opt to forgo the next planned dose and restart BID intake after 24 hours
  - For NOACs with a once daily dosing regimen, the patient should continue the normal dosing regimen

- **Uncertainty about Dose Intake:**
  - Always safest to continue on regular dosing interval and not to risk taking another dose *(great opportunity to discuss compliance aids with the patient or family member)*

Atrial Fibrillation
Oral Anticoagulation Card

for non-vitamin-K anticoagulants

Patient name: **DOB:**

Patient address:

Oral anticoagulant, dosing, timing, with or without food:

Treatment indication:

Treatment started:

Name and address of anticoagulant prescriber:

Telephone number of presciber or clinic:

EUROPEAN Heart Rhythm ASSOCIATION

EUROPEAN SOCIETY OF CARDIOLOGY®

More info:
www.NOACforAF.eu
www.noacforaf.eu

Planned or unplanned visits

Date (or date range):	Site (GP; clinic; cardiologist; ...):	To do / findings:

Recommended follow-up

(see EHRA at **www.NOACforAF.eu** for information & practical advice)

Check each visit:
1. **Compliance (pt. should bring remaining meds)?**
2. **Thrombo-embolic events?**
3. **Bleeding events?**
4. **Other side effects?**
5. **Co-medications and over-the-counter drugs.**

Blood sampling:
- **monitoring of anticoagulation level is not required!**
- **yearly:** Hb, renal and liver function
- **if CrCl 30-60 ml/min, >75y, or fragile:** 6-monthly renal function
- **if CrCl 15-30 ml/min:** 3-monthly renal function
- **if intercurring condition that may have impact:** renal and/or liver function

Date	Serum creatinine	Creatinine clearance	Hemo-globin	Liver tests

Important patient instructions

Take your drug exactly as prescribed (once or twice daily).
No drug is no protection!

Never stop your medicine without consulting your physician.

Never add any other medication without consulting your physician, not even short-term painkillers that you can get without prescription.

Alert your dentist, surgeon or other physician before an intervention.

Concomitant medication

Name:	Dose:

Emergency information

Standard tests do no quantitatively reflect level of anticoagulation!

Name & telephone of patient relative to contact if emergency:

Patient blood group (+ physician signature):


Questions?