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Comprehensive Atrial Fibrillation Guidelines: A fresh look for 2020

October 2020

Andrade J, et al., *Canadian Journal of Cardiology*, DOI: https://doi.org/10.1016/j.cjca.2020.09.001 October 24, 2020

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Disclosures

Hippocrates refusing the gift of Artaxerxes by Anne-Louis Girodet 1792

Disclosure

- Speaker has no conflict of interest

Learning objectives

- As a result of attending this session, participants will be able to:
  - Identify which patients with a.fib require anti-coagulation
  - Know how to interrupt anti-coagulation for elective procedures
  - Choose between rate vs. rhythm control
  - Determine which patients should be on both anti-platelets and anti-coagulants
  - Find true happiness in their lives

Canadian Cardiovascular Society Atrial Fibrillation Guidelines 2010: Implementing GRADE and Achieving Consensus

Gillis et al. Canadian Journal of Cardiology 2011;27:27-30

Focused 2012 Update of the Canadian Cardiovascular Society Atrial Fibrillation Guidelines: Recommendations for Stroke Prevention and Rate/Rhythm Control

Skanes et al. Canadian Journal of Cardiology 2012;28:125-36

2014 Focused Update of the Canadian Cardiovascular Society Guidelines for the Management of Atrial Fibrillation

Verma et al. Canadian Journal of Cardiology 2014;30:1114-30

The 2014 Atrial Fibrillation Guidelines Companion: A Practical Approach to the Use of the Canadian Cardiovascular Society Guidelines

Macle et al. Canadian Journal of Cardiology 2015;31:1207-18

2016 Focused Update of the Canadian Cardiovascular Society Guidelines for the Management of Atrial Fibrillation

Macle et al. Canadian Journal of Cardiology 2016;32:1170-85

2018 Focused Update of the Canadian Cardiovascular Society Guidelines for the Management of Atrial Fibrillation

Andrade et al. Canadian Journal of Cardiology 2018;34:1371-92

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2020 CCS/CHRS Comprehensive Guidelines for the Management of Atrial Fibrillation

Authors

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2020 CCS/CHRS Comprehensive Guidelines for the Management of Atrial Fibrillation

Methodology: Grading of Recommendations Assessment, Development and Evaluation (GRADE)

Quality of Evidence:

- **High:** Further research is very unlikely to change our confidence in the estimate of effect
- **Moderate:** Further research is likely to have an important impact on our confidence in the estimate of effect and may change the estimate
- **Low:** Further research is very likely to have an important impact on our confidence in the estimate of effect and is likely to change the estimate
- **Very Low:** Any estimate of effect is very uncertain

For more information on the GRADE process and development of recommendations visit www.ccs.ca.

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2020 CCS/CHRS Comprehensive Guidelines for the Management of Atrial Fibrillation

Methodology: Grading of Recommendations Assessment, Development and Evaluation (GRADE)

Strength of a Recommendation:

- **Quality of evidence:** The higher the quality of evidence, the greater the probability that a strong recommendation is indicated
- **Difference between desirable and undesirable effects:** The greater the difference between desirable and undesirable effects, the greater the probability that a strong recommendation is indicated
- **Values and preferences:** The greater the variation or uncertainty in values and preferences, the higher the probability that a conditional recommendation is indicated
- **Cost:** The higher the cost, the lower the likelihood that a strong recommendation is indicated

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Overview of Topics

Content

I. Classification and Definitions
II. Epidemiology
III. Pathophysiology
IV. Clinical Evaluation
V. Screening and Opportunistic AF Detection
VI. Detection and Management of Modifiable Risk Factors
VII. Integrated Approach to AF Management
VIII. Stroke Prevention
IX. Arrhythmia Management
X. Sex Differences
XI. Atrial Fibrillation and Special Populations

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Key Considerations for Stroke Prevention in AF

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CCS Stroke Risk Assessment and Antithrombotic Rx

- 2010 – $CHADS_2$
- 2012 – based on CHA_2DS_2-VASc
- 2014 – Present – CHADS-65
- Decision based on:
  - A cut off for OAC at annual risk of stroke ≥ 1.5% / year
    - OAC increases the risk of bleeding 0.5 – 1% / year
    - OAC reduces the risk of stroke by 66+%
    - Risk of major bleeding increases < risk of stroke as risk factors accumulate
    - Impact of stroke > Impact of major bleeding
  - No role for ASA in SPAF

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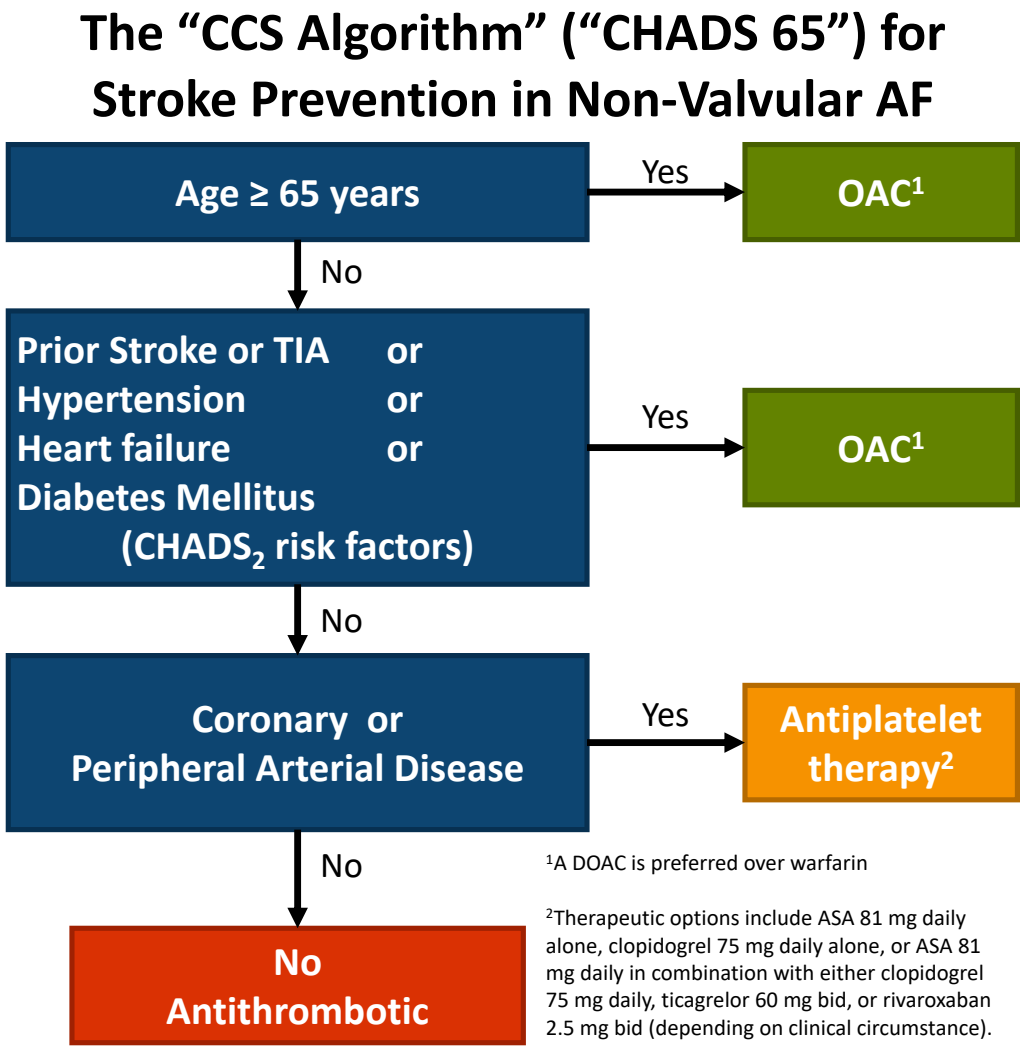
Annual Stroke Rate by Risk Factor

Risk factor	Annual risk (95% CI)	Hazard ratio (95% CI)	*P*
CHA_2DS_2-VASc = 0	0.69 (0.59-0.81)	1.0	
CHA_2DS_2-VASc = 1			
Heart failure	2.35 (1.30-4.24)	3.39 (1.84-6.26)	< 0.0001
Diabetes mellitus	2.28 (1.42-3.66)	3.31 (2.00-5.46)	< 0.0001
Hypertension	1.60 (1.26-2.01)	2.32 (1.75-3.07)	< 0.0001
Age 65-74 years	2.13 (1.85-2.46)	3.07 (2.48-3.80)	< 0.0001
Vascular disease	1.40 (0.91-2.15)	2.04 (1.29-3.22)	0.002
Female sex	0.86 (0.70-1.06)	1.25 (0.96-1.63)	0.10

Olesen JB, Lip GY, Hansen ML, et al. BMJ 2011;342:d124

CHADS-65



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Definition of Risk Factors

Table 1. Definitions of stroke risk factors in the Canadian Cardiovascular Society Atrial Fibrillation Guidelines update

Factor	Definition
Congestive heart failure	Documented moderate to severe systolic dysfunction; signs and symptoms of heart failure with reduced ejection fraction; or recent decompensated heart failure that required hospitalization irrespective of ejection fraction
Hypertension	Resting blood pressure > 140 mm Hg systolic and/or > 90 mm Hg diastolic on at least 2 occasions or current antihypertensive pharmacological treatment
Age 65	Age ≥ 65 years
Diabetes mellitus	Fasting plasma glucose concentration ≥ 7.0 mmol/L (126 mg/dL) or treatment with oral hypoglycemic agents and/or insulin
Stroke/transient ischemic attack/peripheral embolism	Ischemic stroke: focal neurologic deficit of sudden onset diagnosed by a neurologist, lasting > 24 hours, and caused by ischemia; Transient ischemic attack: focal neurological deficit of sudden onset diagnosed by a neurologist, lasting < 24 hours; Peripheral embolism: thromboembolism outside the brain, heart, eyes, and lungs, or pulmonary embolism (defined by the responsible physician)
Vascular disease	Coronary artery disease, peripheral artery disease, or aortic plaque

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Choice of Anticoagulant

- DOAC preferred over Warfarin
  - Efficacy at least as good
  - Bleeding less particularly ICH
  - Convenience
- No head to head comparisons between DOAC
- “Real World” data plentiful but too subject to bias for decision making

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Valvular AF

- *We recommend that warfarin be used for those patients with a mechanical prosthetic valve and those with AF and moderate-to-severe mitral stenosis (Strong Recommendation; Moderate-Quality Evidence).*
- RE-ALIGN -> ↑ TE and bleeding events in patients with mechanical valves
- No current RCT of DOAC in mitral stenosis
  - RIVER (bioprosthetic mitral valve)
  - INVICTUS (rheumatic heart disease)

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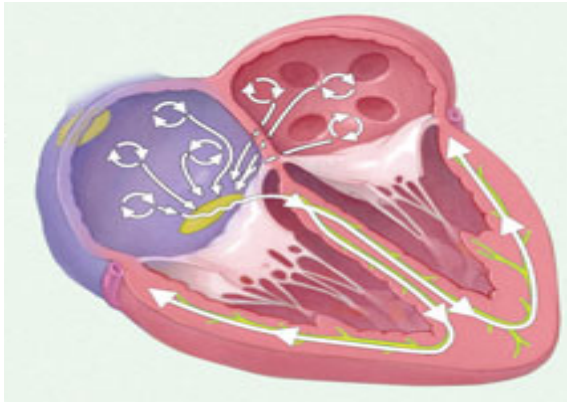
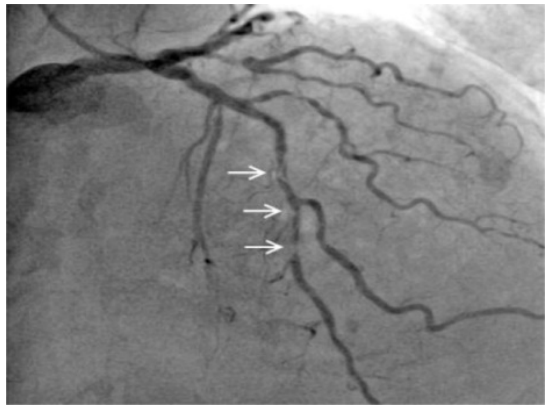
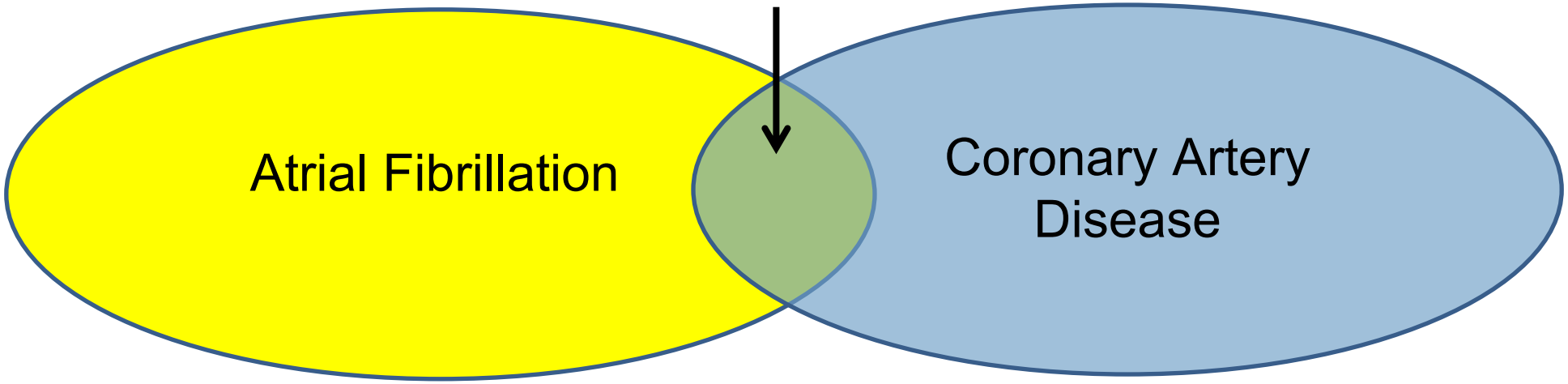
Concomitant AF and CAD





Up to 30% of patients with AF also have CAD



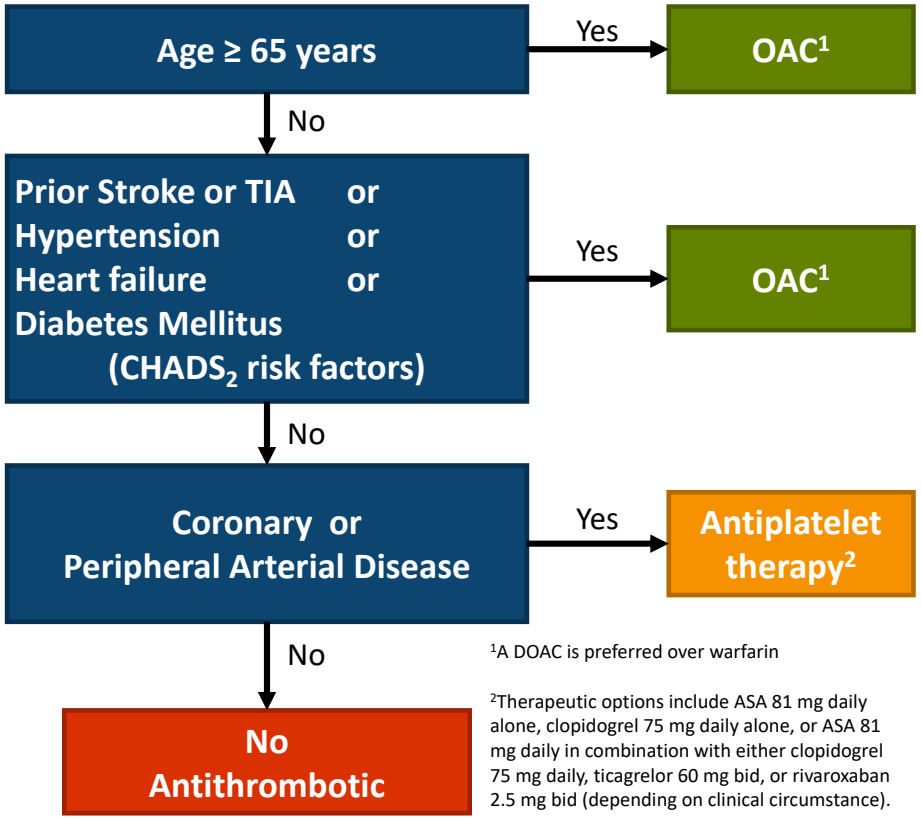
Singer DE, et al. Ann Intern Med 2009;151:297-305

Andrade J, et al., *Canadian Journal of Cardiology*, DOI: https://doi.org/10.1016/j.cjca.2020.09.001 October 24, 2020

Management of CAD + AF

STROKE RISK

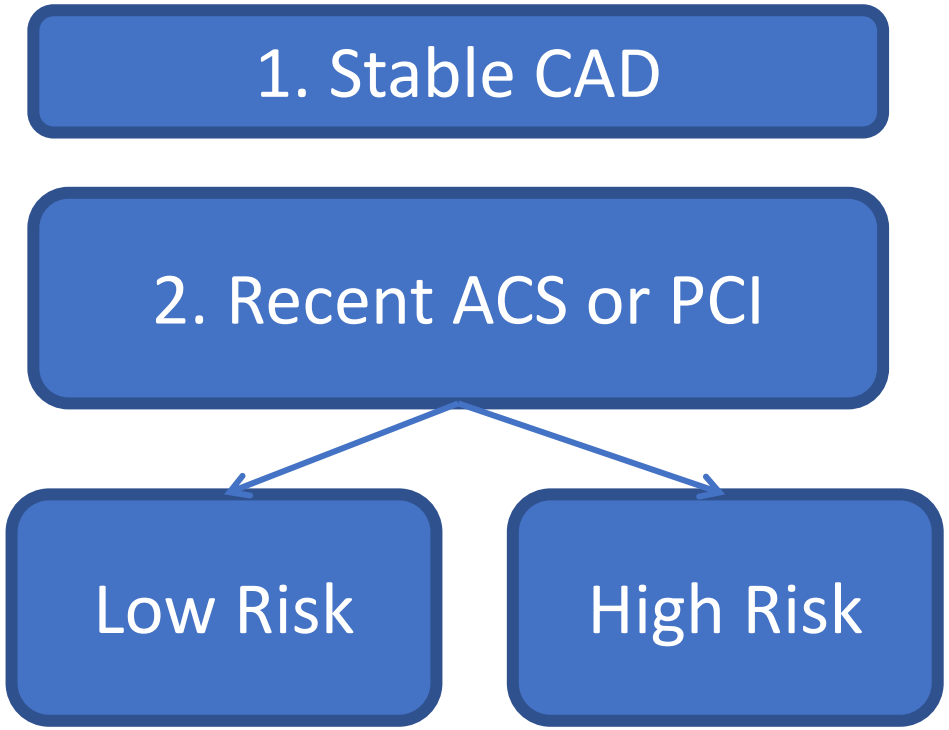
The "CCS Algorithm" ("CHADS 65") for Stroke Prevention in Non-Valvular AF



[1]A DOAC is preferred over warfarin

[2]Therapeutic options include ASA 81 mg daily alone, clopidogrel 75 mg daily alone, or ASA 81 mg daily in combination with either clopidogrel 75 mg daily, ticagrelor 60 mg bid, or rivaroxaban 2.5 mg bid (depending on clinical circumstance).

CORONARY RISK



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Where we were 6 years ago

REVIEW

Additional research studies are required to further optimize treatment strategies in this high-risk population

David Fitchett[a], *Atul Verma*[b], *John Eikelboom*[c], *Mina Madan*[d], *Eric Cohen*[d], *Alan Bell*[e], *and Paul Dorian*[a]

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Where we are now

RANDOMIZED CONTROLLED TRIALS

AF + PCI / ACS

- WOEST – WARFARIN
- PIONEER AF PCI – RIVAROXABAN
- RE-DUAL PCI – DABIGATRAN
- AUGUSTUS – APIXABAN
- ENTRUST AF – EDOXABAN

AF + STABLE CAD

- AFIRE - RIVAROXABAN

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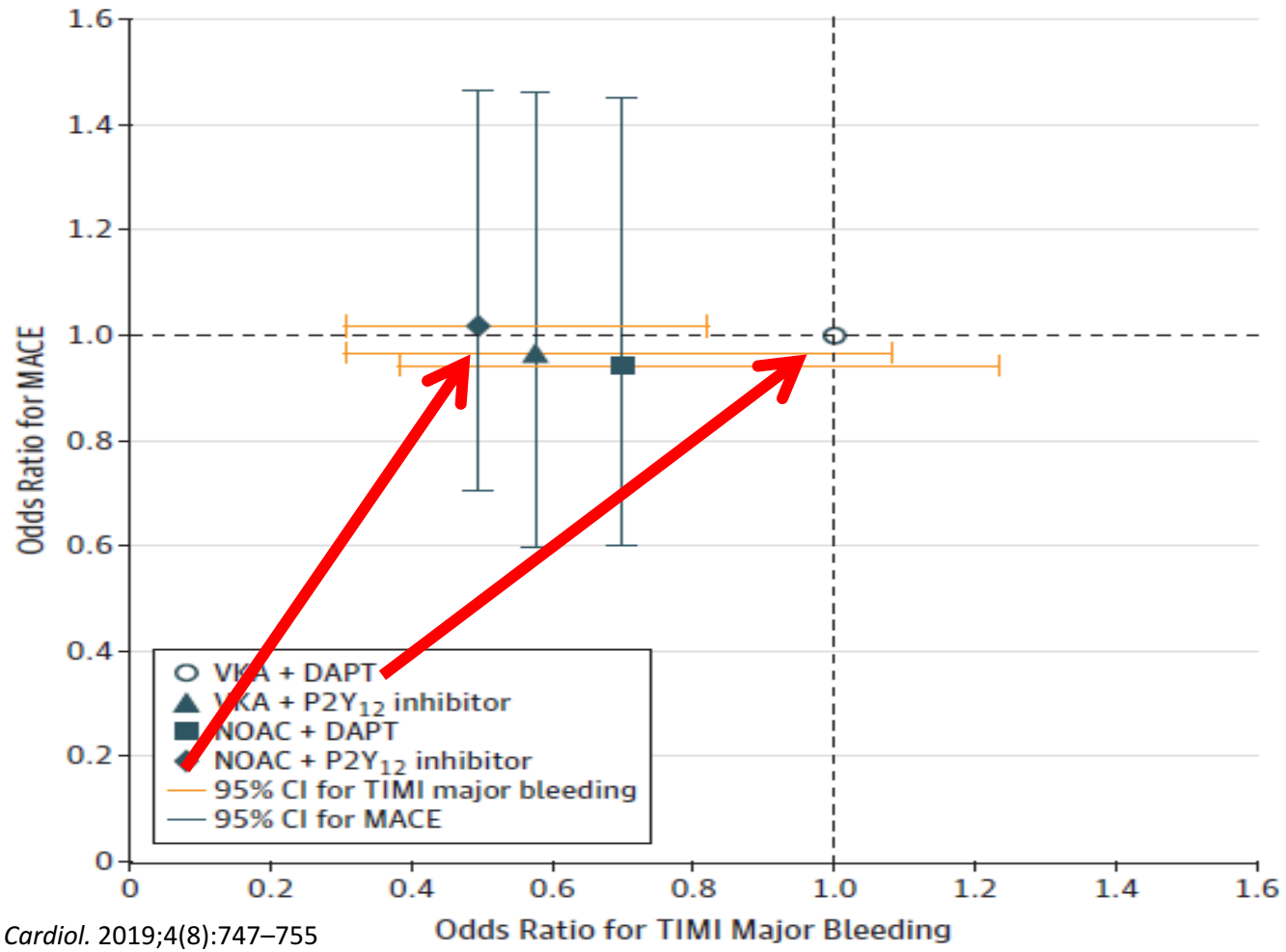
Dual Pathway vs Triple RX Metanalysis

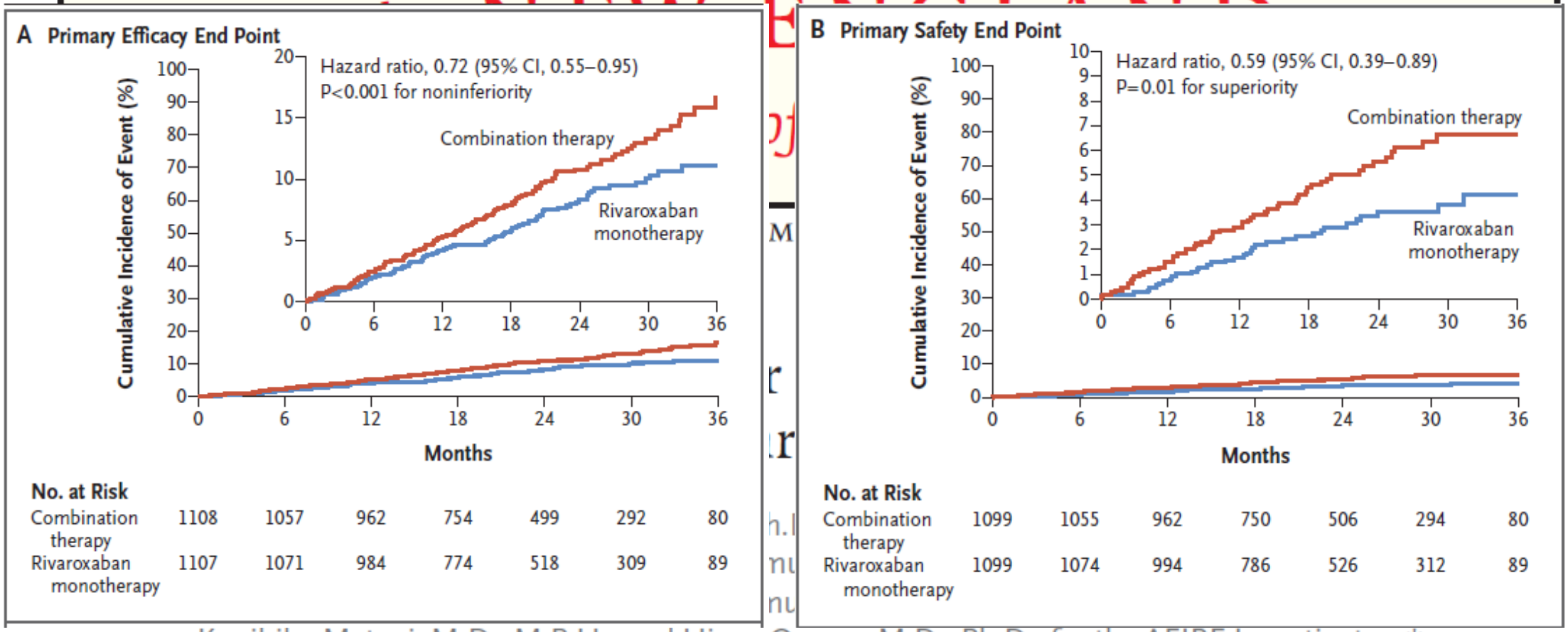
Figure 4. Odds Ratios for TIMI Major Bleeding and MACE



Lopes RD, Hong H, Harskamp RE, et al. *JAMA Cardiol.* 2019;4(8):747–755

Andrade J, et al., *Canadian Journal of Cardiology*, DOI: https://doi.org/10.1016/j.cjca.2020.09.001 October 24, 2020

AF + Stable CAD



Kunihiko Matsui, M.D., M.P.H., and Hisao Ogawa, M.D., Ph.D., for the AFIRE Investigators*

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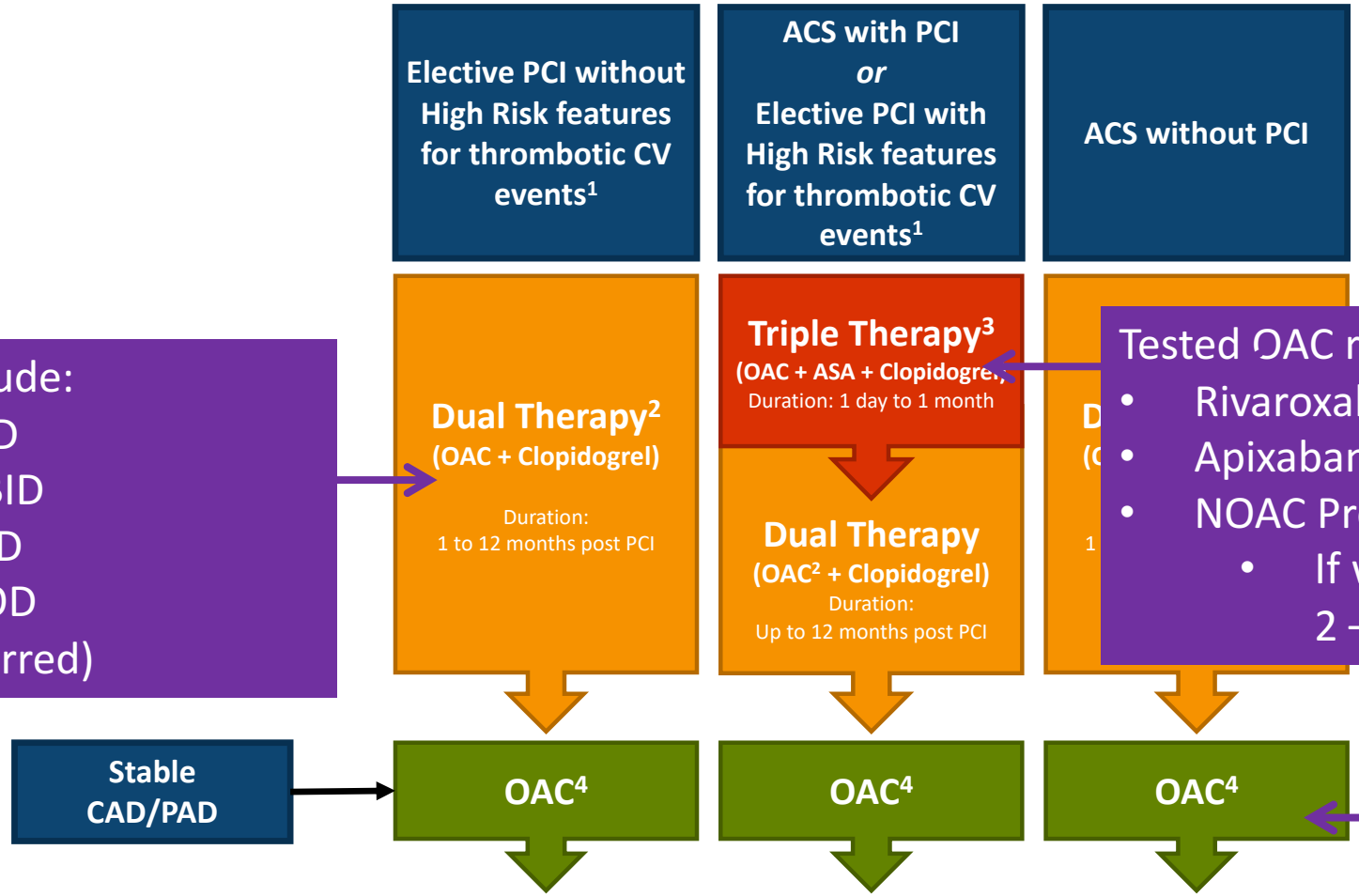
AF Patients with Coronary or Vascular Disease and an Indication for OAC (Age ≥ 65 years or $CHADS_2$ ≥ 1)



Tested OAC regimens include:
- Rivaroxaban 15 mg OD
- Dabigatran 110/150 BID
- Apixaban 5/2.5 mg BID
- Edoxaban 60/30 mg OD
- Warfarin (DOAC preferred)

Tested OAC re
- Rivaroxab
- Apixaban
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  2 – 2

Tested OAC regimens include
- Apixaban 5/2.5 BID

Tested OAC regimens include
- Rivaroxaban 15/10 mg OD
- Single antiplatelet may be added only in highly-selected patients with high-risk for ischemia and low risk of bleeding

1. PCI is considered high-risk based on clinical and angiographic features such as: diabetes mellitus, current smoker, chronic renal dysfunction (eGFR < 60 mL/min), prior ACS, multi-vessel disease, multiple stents implanted, complex bifurcation lesion, total stent length > 60 mm, prior stent thrombosis, chronic total occlusion intervention, or bioabsorbable vascular scaffold.

2. The OAC component of Dual pathway regimens includes: warfarin daily, apixaban 5 mg BID (reduced to 2.5 mg if they met two or more of the following dose-reduction criteria: age > 80 years of age, weight < 60 kg, or Cr > 133 µmol per liter), dabigatran 110 mg or 150 mg PO BID, edoxaban 60 mg PO daily (30 mg in patients with CrCl 15–50 mL/min, bodyweight ≤ 60 kg, or concomitant use of specified potent P-glycoprotein inhibitors), rivaroxaban 15 mg PO daily (10 mg in patients with CrCl 30-50 mL/min). A DOAC is preferred over warfarin, however if warfarin is to be used the lower end of the recommended INR target range is preferred. All patients should receive a loading dose of ASA 160 mg at the time of PCI (if previously ASA naïve).

3. The OAC component of triple therapy regimens includes: warfarin daily, rivaroxaban 2.5 mg PO BID, or apixaban 5 mg BID (reduced to 2.5 mg if they met two or more of the following dose-reduction criteria: age > 80 years of age, weight < 60 kg, or Cr > 133 µmol per liter). A DOAC is preferred over warfarin, however if warfarin is to be used the recommended INR target is 2.0-2.5. All patients should receive a loading dose of ASA 160 mg at the time of PCI (if previously ASA naïve). Thereafter, ASA may be discontinued as early as the day following PCI or it can be continued longer. The timing of when to discontinue ASA will depend on individual patient's ischemic and bleeding risk.

4. The dose of OAC beyond one year after PCI should be standard stroke prevention doses. A combination of an OAC and single antiplatelet therapy may be used only in highly-selected patients with high-risk features for ischemic coronary outcomes, and who are also at low risk of bleeding

Patient Factors

- Age (> 65 years)
- Low body weight (< 60 kg)
- Hypertension
- History of bleeding (esp. within 1y)
- Prior Stroke or intracranial bleed
- Excess alcohol consumption
- Labile INR (TTR <60%)

Patient Factors

- Diabetes mellitus
- Current smoker
- CKD (eGFR < 60 mL/min)
- Prior acute coronary syndrome
- Prior stent thrombosis

Clinical Presentation

- Acute coronary syndrome

Factors that Increase Risk of Bleeding

Factors that Increase Risk of Ischemic Coronary Events

Concomitant use of:

- antiplatelet use
- NSAIDs
- prednisone

Laboratory

- Anemia (hemoglobin <110 g/L)
- Abnormal liver function
- CKD (eGFR < 60 mL/min)

Angiographic factors

- Multi-vessel disease
- Multiple (≥ 3) stents implanted
- Stenting of a bifurcation lesion
- Total stent length > 60 mm
- Left main or proximal LAD stenting
- Chronic occlusion intervention
- Bioabsorbable vascular scaffold

Andrade J, et al., *Canadian Journal of Cardiology*, DOI: https://doi.org/10.1016/j.cjca.2020.09.001 October 24, 2020

Bleeding and Bridging

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Outline

Bleeding

- Bleeding risks of antithrombotic therapy
- Mitigation of bleeding risks
- Management when bleeding occurs including use of antidotes

Periprocedural management: OAC Interruption and Bridging

- Decision regarding OAC interruption
- Management of OAC for emergency, urgent, non-urgent procedures
- Bridging needs for OAC interruption: who, how, and when?

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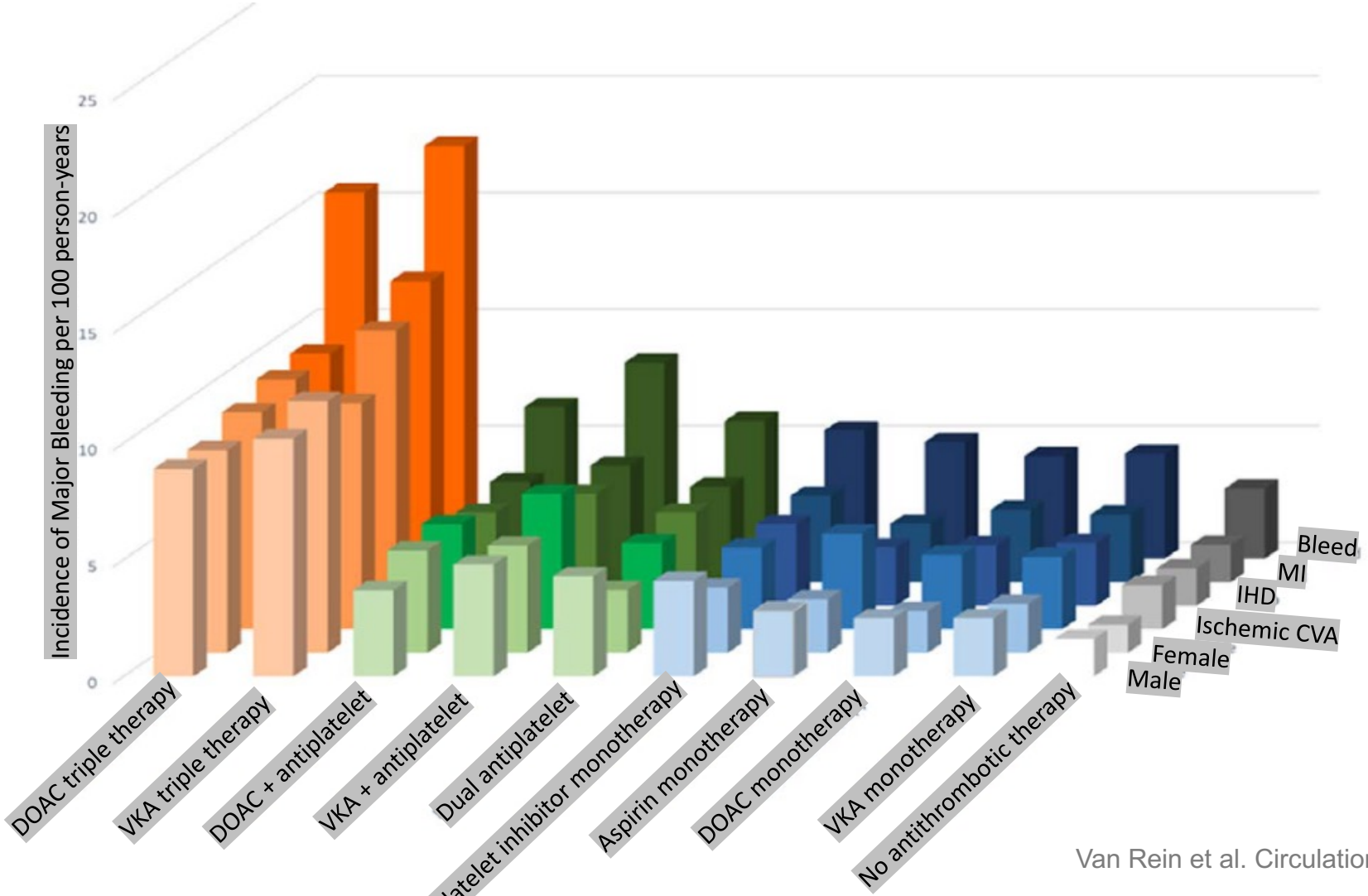
Incidence Rate of Major Bleeding: Single, Dual and Triple Therapy: Nationwide Danish Cohort (N=272,315)



Van Rein et al. Circulation 2019: 139

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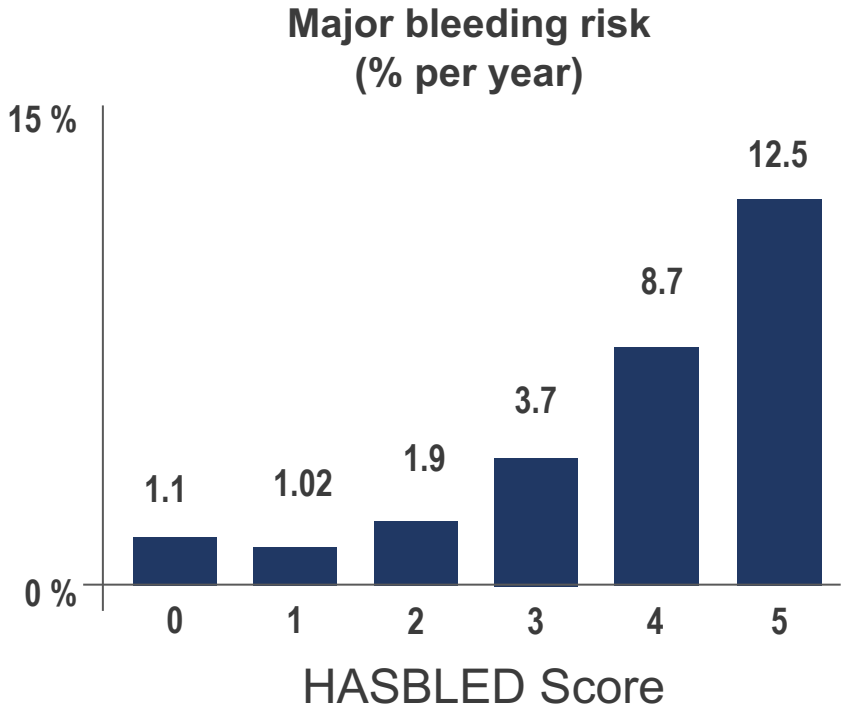
HASBLED Bleeding Risk Score and Risk Mitigation

HAS-BLED	SCORE
Hypertension (SBP>160 mm Hg)	1
Abnormal renal function (Cr>200 umol/L) or liver function (cirrhosis, bilirubin >2x upper normal, or AST/ALT/ALP >3 x upper normal	1 1
Stroke history	1
Bleeding (major) or tendency (prior GI bleed, PUD, prior cerebral hemorrhage)	1
Labile INR (unstable INR, time in therapeutic range <60%)	1
Elderly: Age >65 years	1
Drugs (antiplatelet, NSAIDS, anti-inflammatory medications, steroids); alcohol or drug abuse	1



*__Other conditions__ with increased bleeding risk: Thrombocytopenia, coagulation defects, anemia, Lower body weight, drug interactions

*__Correct dosing of DOACs__ with changing renal function; effective INR monitoring

*PPI to decrease the risk of gastrointestinal adverse effects, for patients who require daily antithrombotic therapy that includes acetylsalicylic acid (ASA) (Weak Recommendation; Moderate-Quality Evidence).

Pisters R, et al. Chest. 2010;138:1093-100

Andrade J, et al., *Canadian Journal of Cardiology*, DOI: https://doi.org/10.1016/j.cjca.2020.09.001 October 24, 2020

General Principles for Treatment of Bleeding and Anticoagulation Management

- Best strategy: proactively reduce risk of bleeding
- Most bleeding not severe and can be treated with supportive measures: compression at bleeding sites, fluid and blood products where necessary.
- Bleeding difficult to stop, hematuria, GI bleed, hemoptysis need urgent assessment and treatment.
- Warfarin: hold off, let INR comes down; reversal with vitamin K, 2-10 mg IV; prothrombin complex concentrates (PCC) 30-50 IU/kg; FFP. If life-threatening, consider also tranexamic acid and aminocaproic acid.
- DOACs: Delay next dose; Idarucizumab specific for Dabigatran; PCC 50 IU/kg (non- specific reversal). If life-threatening, consider also tranexamic acid and aminocaproic acid.
- OAC should be reintroduced as soon as medically appropriate.

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Bleeding while on OAC

Assess hemodynamic status, coagulation parameters (PTT, INR ± dTT), blood counts, renal function
Obtain anticoagulation history (OAC agent and dose, and timing of last administration)

	Mild Bleeding[1]	Significant Bleeding[2]	Life-Threatening Bleeding[3]
Bleeding on VKA	Delay VKA until INR < 2	**Source control** - Local hemostatic measures and/or procedural/surgical intervention **Supportive Measures:** - Fluid replacement - RBC transfusion (symptomatic anemia) - Platelet transfusion if <50 x 10^9/L **Consider Vitamin K PO/IV 2-5 mg**	**Consider PCC or aPCC[4]** **Consider tranexamic acid or aminocaproic acid** **Consider Vitamin K IV 5-10 mg** **Consider FFP**
Bleeding on DOAC	Delay next DOAC dose	**Source control** - Local hemostatic measures and/or procedural/surgical intervention **Supportive Measures:** - Fluid replacement - RBC transfusion (symptomatic anemia) - Platelet transfusion if <50 x 10^9/L **Consider activated charcoal if DOAC ingestion within 4 hours**	**Consider Antidotes:** idarucizumab[5] or andexanet alfa[6] **Consider PCC or aPCC[4]** if no antidote available[7] **Consider tranexamic acid or aminocaproic acid**

Initiate OAC as soon as possible after the cause of bleeding has been identified and corrected[8]
Re-evaluate concomitant medications which may contribute to bleeding (e.g. ASA, NSAIDs)

Andrade et al. 2020 Canadian Cardiovascular Society/Canadian Heart Rhythm Society Comprehensive Guidelines for the Management of Atrial Fibrillation Canadian Journal of Cardiology.

Andrade J, et al., *Canadian Journal of Cardiology*, DOI: https://doi.org/10.1016/j.cjca.2020.09.001

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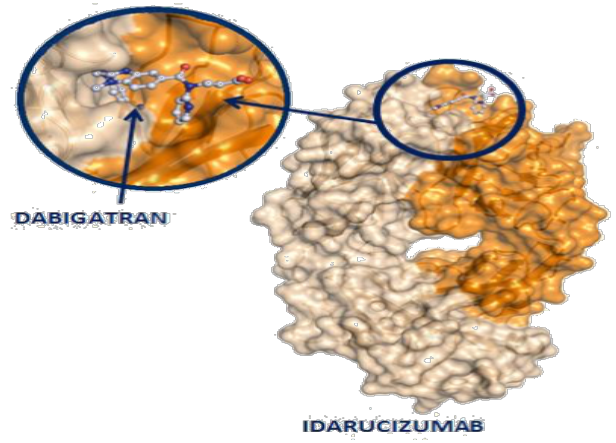
DOAC Antidotes

Idarucizumab (Praxbind®)-Dabigatran-specific reversal

- RE-VERSE AD Trial*: No serious adverse safety signals
- Two IV doses, each 2.5 g, within 15 minutes
- Binds specifically to dabigatran
- Primarily renal excretion
- Short half-life (half-life: initial 45 min; terminal:10.3 hours)
- No interaction with other drugs
- No intrinsic pro-coagulant or anticoagulant activity
- Acts immediately with complete and sustained reversal



*Pollack C et al.NEJM 2017; 377: 431-441

Recommendation: Administer idarucizimab for emergency reversal of dabigatran's anticoagulant effect in patients with uncontrollable or potentially life-threatening bleeding and/or requiring urgent surgery.

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Other DOAC Antidotes (PIPELINE)

Andexanet Alpha: Factor Xa reversal agent.

- Recommendation: Administer andexanet alfa for emergency reversal of Factor Xa inhibitors: apixaban, edoxaban, and rivaroxaban in patients presenting with uncontrollable or potentially life-threatening bleeding who have received any of these agents within the preceding 18 hours. Patients who are anticipated to require unfractionated or low-molecular-weight heparin within 12-24 hours should NOT receive andexanet alfa.
- Dosage of Andexanet based on the specific FXa inhibitor, the dose of DOAC patient is taking, and the timing of the last DOAC dose prior to the bleed.
- OAC should be reintroduced as soon as medically appropriate.

Ciraparantag (PER-977, aripazine): “universal” reversal agent.

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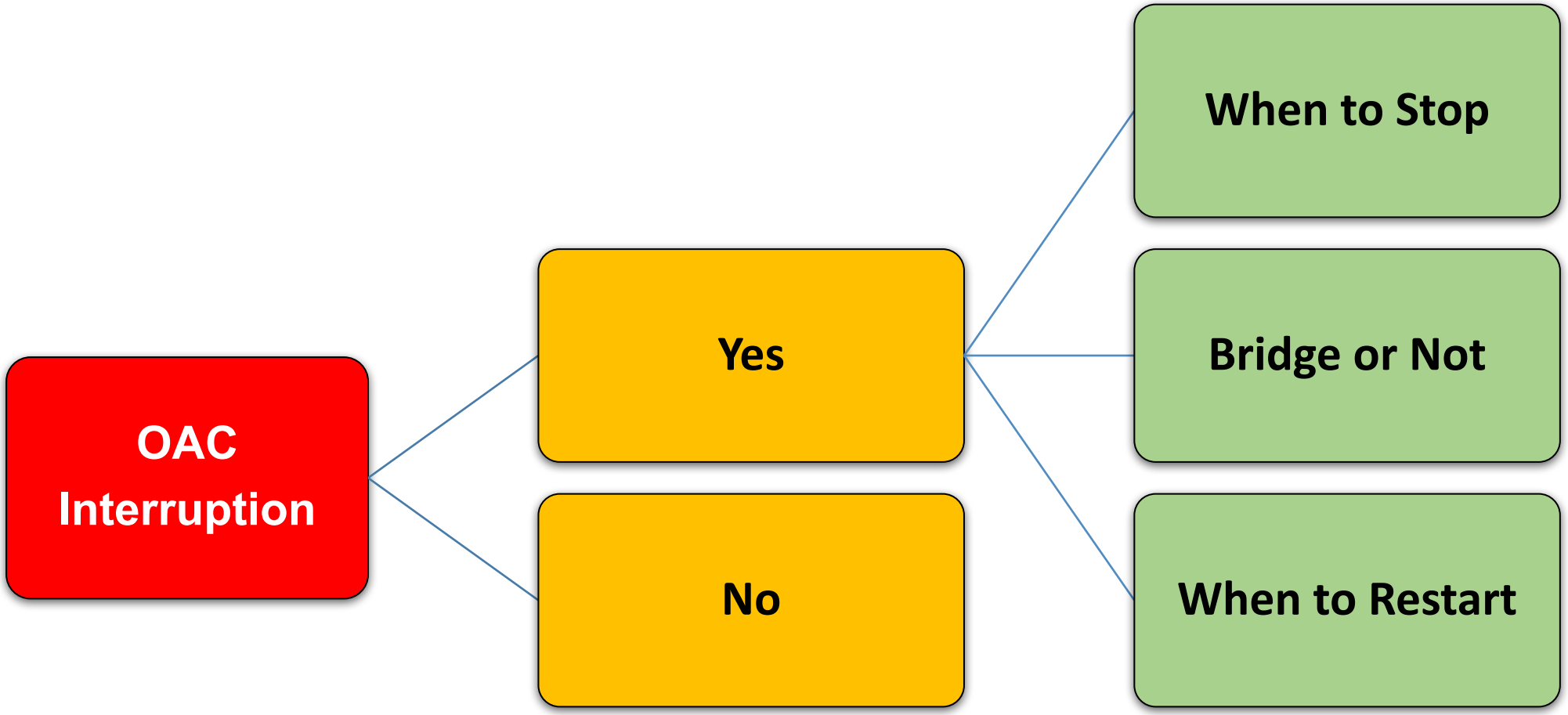
Periprocedural Management of Anticoagulation
OAC Interruption and Bridging Considerations



Andrade J, et al., *Canadian Journal of Cardiology*, DOI: https://doi.org/10.1016/j.cjca.2020.09.001 October 24, 2020

Interrupting Anticoagulation for a Procedure

Bleeding Risks:

1. Procedural risks
(High, low-moderate, minimal)

2. Patient bleeding risks
(HASBLED Score)

Thromboembolic Risks:

1. CHADS2 score 5-6
2. Mechanical valve
3. Thromboembolism <3 m
4. Moderate-severe mitral stenosis

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Anticoagulation Interruption

Decision to interrupt antithrombotic therapy for an invasive procedure must balance the risks of a thromboembolic event with those of a peri-procedural bleeding event.

Recommendations:

Minimal risk procedures: No need to interrupt

Low-moderate, high, uncertain risks: Recommend interruption

Practical Tip: Thrombosis Canada (http://thrombosiscanada.ca) Perioperative Anticoagulant Management Algorithm.

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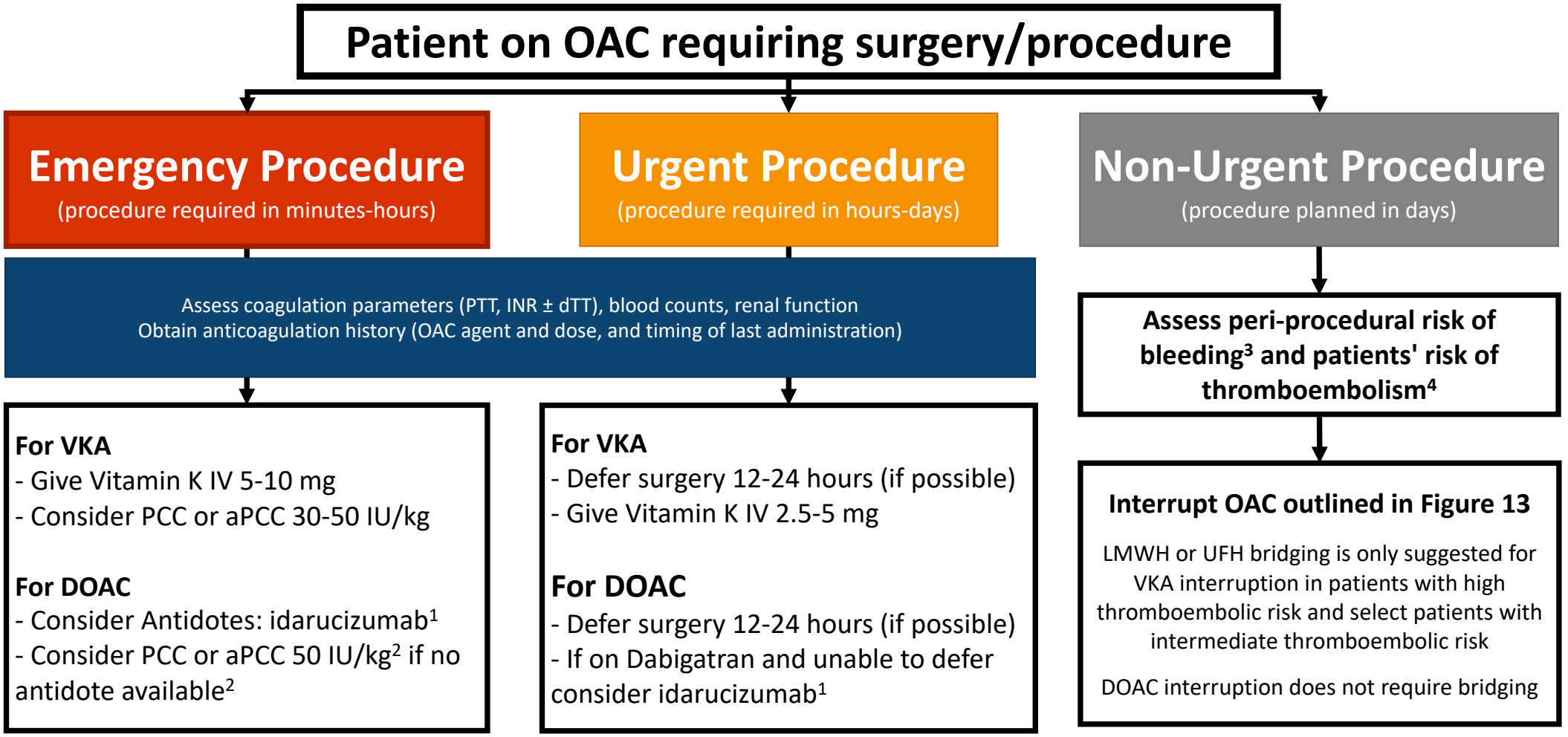
Risk Categories of Procedures

Minimal Bleed Risk	Low/Moderate Bleed Risk	High Bleed Risk
• **Cataract surgery** • **Dermatologic procedures (e.g. biopsy)** • **Gastroscopy or colonoscopy without biopsies** • **Coronary angiography (using radial arterial approach)** • **Permanent pacemaker insertion or internal defibrillator placement (if bridging anticoagulation is not used)** • **Selected procedures with small-bore needles (e.g. thoracentesis, paracentesis, arthrocentesis)** • **Dental extractions (1 or 2 teeth)** • **Endodontic (root canal) procedure** • **Subgingival scaling or other cleaning**	• Abdominal surgery (e.g. cholecystectomy, hernia repair, colon resection) • Other general surgery (e.g. breast) • Other intrathoracic surgery • Other orthopedic surgery • Other vascular surgery • Non-cataract ophthalmologic surgery • Gastroscopy or colonoscopy with biopsies • Coronary angiography* • Selected procedures with large-bore needles (e.g. bone marrow biopsy, lymph node biopsy) • Complex dental procedure (e.g. multiple tooth extractions)	• Any surgery or procedure with neuraxial (spinal or epidural) anesthesia • Neurosurgery (intracranial or spinal) • Cardiac surgery (e.g. CABG, heart valve replacement) • Major vascular surgery (e.g. aortic aneurysm repair, aortofemoral bypass) • Major orthopedic surgery (e.g. hip/knee joint replacement surgery) • Lung resection surgery • Urological surgery (e.g. prostatectomy, bladder tumour resection) • Extensive cancer surgery (e.g. pancreas, liver) • Intestinal anastomosis surgery • Reconstructive plastic surgery • Selected procedures involving vascular organs (e.g. kidney biopsy, prostate biopsy) or high bleed risk interventions (e.g., colonic polypectomy, spinal injection, pericardiocentesis)



[1]idarucizumab is unlikely to improve outcomes in patients taking dabigatran with a dilute thrombin time TT <30 ng/mL, normal thrombin time, or a drug level <50 ng/mL
[2]Inform patients/families regarding small thrombotic risk of PCC (e.g. stroke, myocardial infarction, venous thromboembolism), but consequences of uncontrolled bleeding likely exceed this risk
[3]Procedure bleeding risk is outlined in **Table 6**
[4]Patients considered to be high risk of thromboembolism include those with valvular AF (mechanical heart valves or moderate-severe mitral valve stenosis), non-valvular AF with a $CHADS_2$ score of 5-6, and those with recent TIA/Stroke (within 3 months).

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Interruption of OAC for Non-Urgent Procedures

OAC		Day -5	Day -4	Day -3	Day-2	Day-1	Procedure	Day +1	Day +2	Day +3	Day +4
Warfarin Usually no need to interrupt VKA for procedures with low bleeding risk	*VKA*	No VKA	No VKA	No VKA	No VKA	INR[2]	None	VKA[5,6]	VKA[5,6]	VKA	VKA
	Heparin Bridging[1]	No LMWH	No LMWH	LMWH	LMWH	INR[2,3]	None	LMWH[6,7]	LMWH[6,7]	LMWH	LMWH
DOAC[4]	*Low/Moderate bleeding risk*	DOAC	DOAC	DOAC	DOAC	None	None	DOAC[6,7]	DOAC[6,7]	DOAC	DOAC
	High bleeding risk	DOAC	DOAC	DOAC	None	None	None	None	DOAC[6,7]	DOAC	DOAC
Dabigatran + CrCl <50 mL/min	*Low/Moderate bleeding risk*	DOAC	DOAC	DOAC	None	None	None	DOAC[6,7]	DOAC[6,7]	DOAC	DOAC
	High bleeding risk	DOAC	None	None	None	None	None	None	DOAC[6,7]	DOAC	DOAC

[1]Patients in need of bridging during interrupted VKA therapy include those with valvular AF (mechanical heart valves or moderate-severe mitral valve stenosis), non-valvular AF with a $CHADS_2$ score of 5-6, and those with a recent stroke or transient ischemic attack).

[2]INR should be performed the day prior to the procedure. If >1.5 then consider administering vitamin K PO/IV.

[3]Give morning LMWH for bid dosed regimens (or ½ daily LMWH dose for once daily dosed regimens).

[4]This schedule applies to factor Xa inhibitors (apixaban, edoxaban, rivaroxaban) and dabigatran (but only when dabigatran is used in patients with a CrCl ≥50 mL/min).

[5]VKA therapy resumption following an invasive procedure may occur almost immediately given it will take several days for the INR to become therapeutic.

[6]Consider withholding anticoagulation therapy for the first 72 hours following cardiac surgery

[7]DOAC/LMWH resumption following an invasive procedure should only occur once hemostasis has been achieved.

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Bridging in Patients on Warfarin

No Bridging for Interrupted VKA in Patients with Low Thromboembolic risks

When a decision to interrupt VKA therapy for an invasive procedure has been made, we suggest interruption to begin 5 days prior to the procedure, and that a procedure with a low bleeding risk may proceed when the INR is ≤1.5, and a procedure with an intermediate or high bleeding risk may proceed when the INR is ≤1.2.

Bridging for Interrupted VKA in Patients on VKA with High Thromboembolic Risks

When a decision to interrupt VKA-therapy for an invasive procedure has been made, we suggest that bridging therapy with LMWH or UFH be started when INR is below therapeutic level only in patients at high risk of thromboembolic events (mechanical heart valves, moderate-severe mitral valve stenosis, nonvalvular AF with a CHADS2 score of 5-6, and those with a recent stroke or TIA).

Andrade et al. 2020 Canadian Cardiovascular Society/Canadian Heart Rhythm Society Comprehensive Guidelines for the Management of Atrial Fibrillation Canadian Journal of Cardiology.

Andrade J, et al., *Canadian Journal of Cardiology*, DOI: https://doi.org/10.1016/j.cjca.2020.09.001 October 24, 2020

No Bridging for Patients Needing DOAC Interruption

When a decision to interrupt a DOAC for an invasive procedure has been made for a patient with AF, we suggest that the duration of interruption be based on the risk of bleeding associated with the procedure and the patient's renal function. No bridging is necessary.

Resumption of OAC after Interruption

When OAC has been interrupted for an invasive procedure, we suggest that such therapy be restarted when hemostasis is established (within 24 hours for a procedure with a low risk of bleeding and 48-72 hours for a procedure with an intermediate or high risk of bleeding).

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Screening for AF / Device-detected AF / Embolic Stroke of Unknown Source (ESUS)

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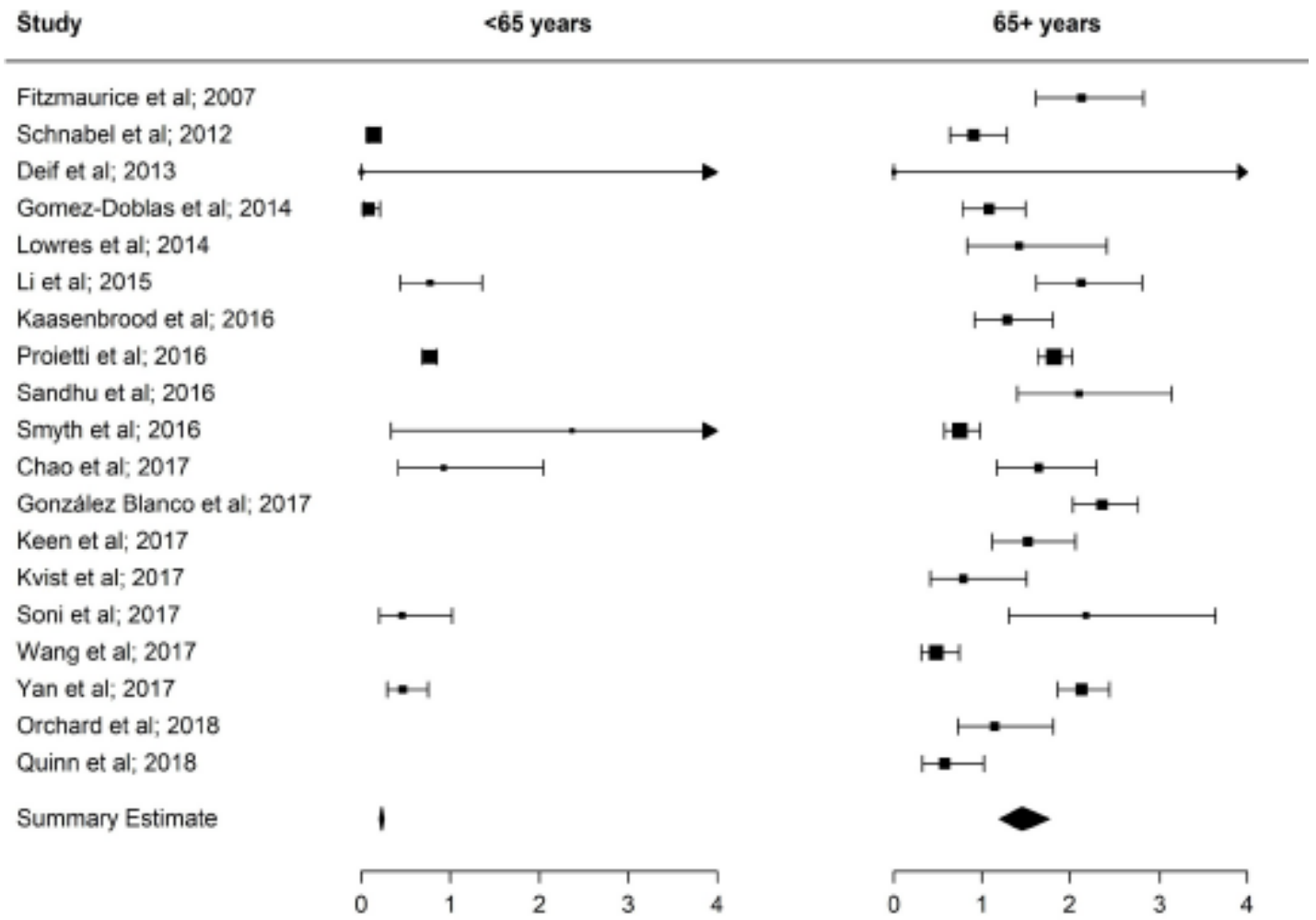
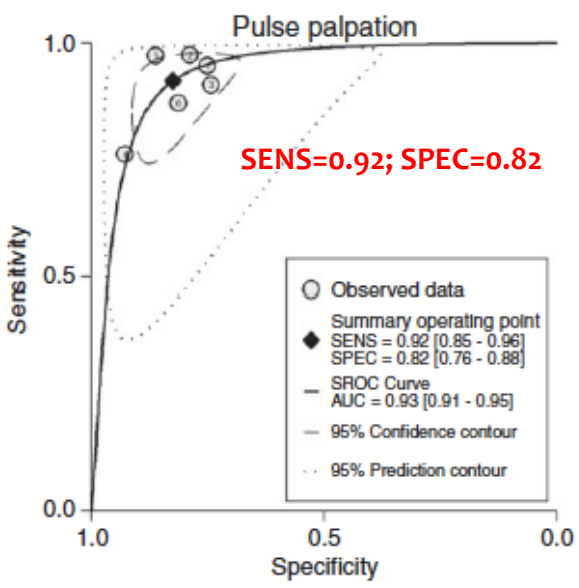
Opportunistic AF Detection in General Population

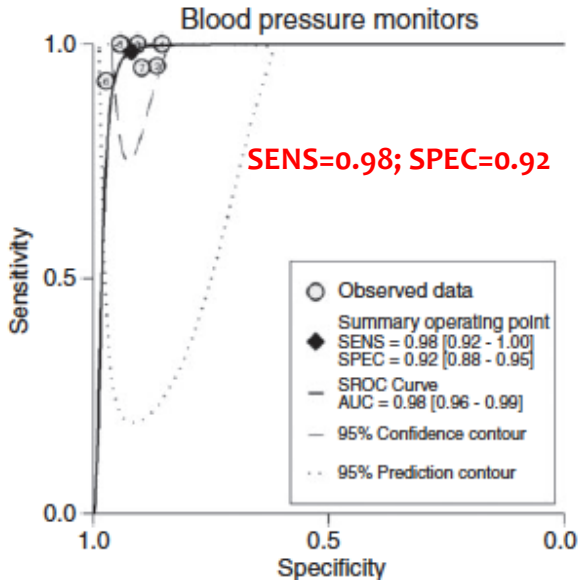


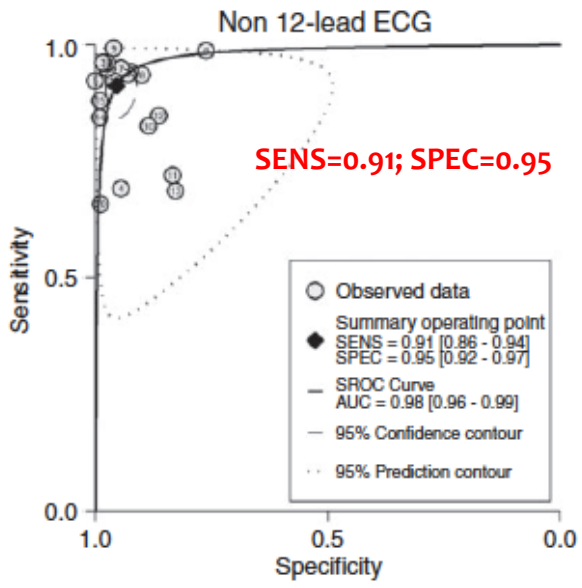
Lowres et al. PLOS Medicine 2019;16:e1002903.

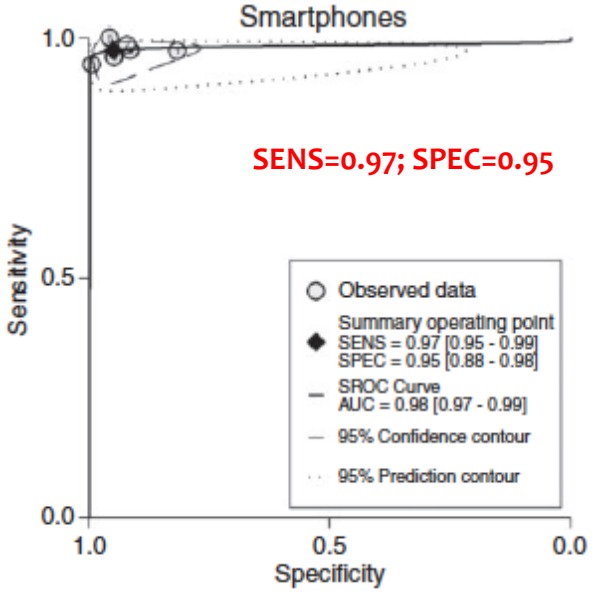
Andrade J, et al., *Canadian Journal of Cardiology*, DOI: https://doi.org/10.1016/j.cjca.2020.09.001 October 24, 2020

ROC plots of AF screening tools



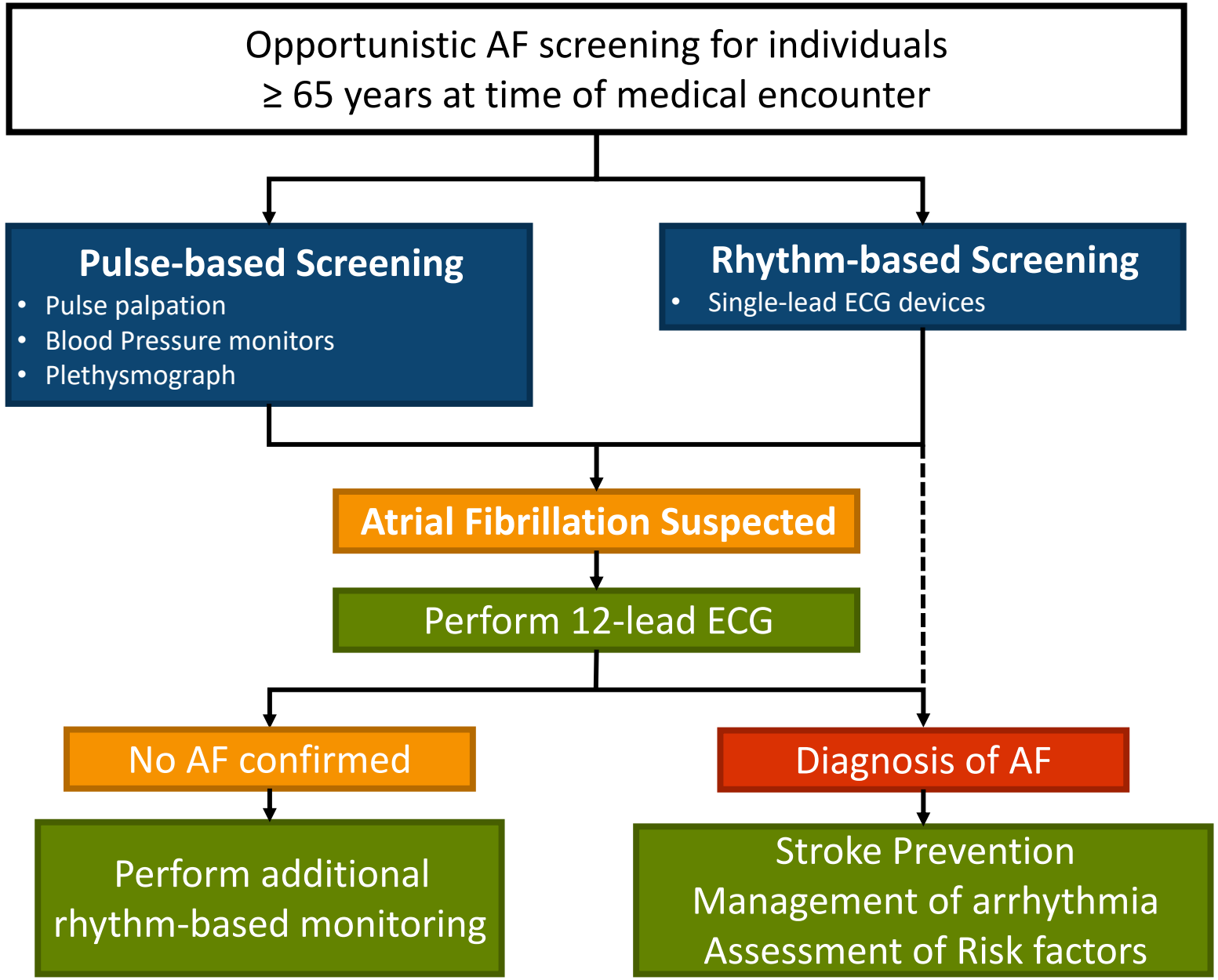






Tagger et al. Eur J Prev Card 2016;23:1330-1338.

Andrade J, et al., *Canadian Journal of Cardiology*, DOI: https://doi.org/10.1016/j.cjca.2020.09.001 October 24, 2020



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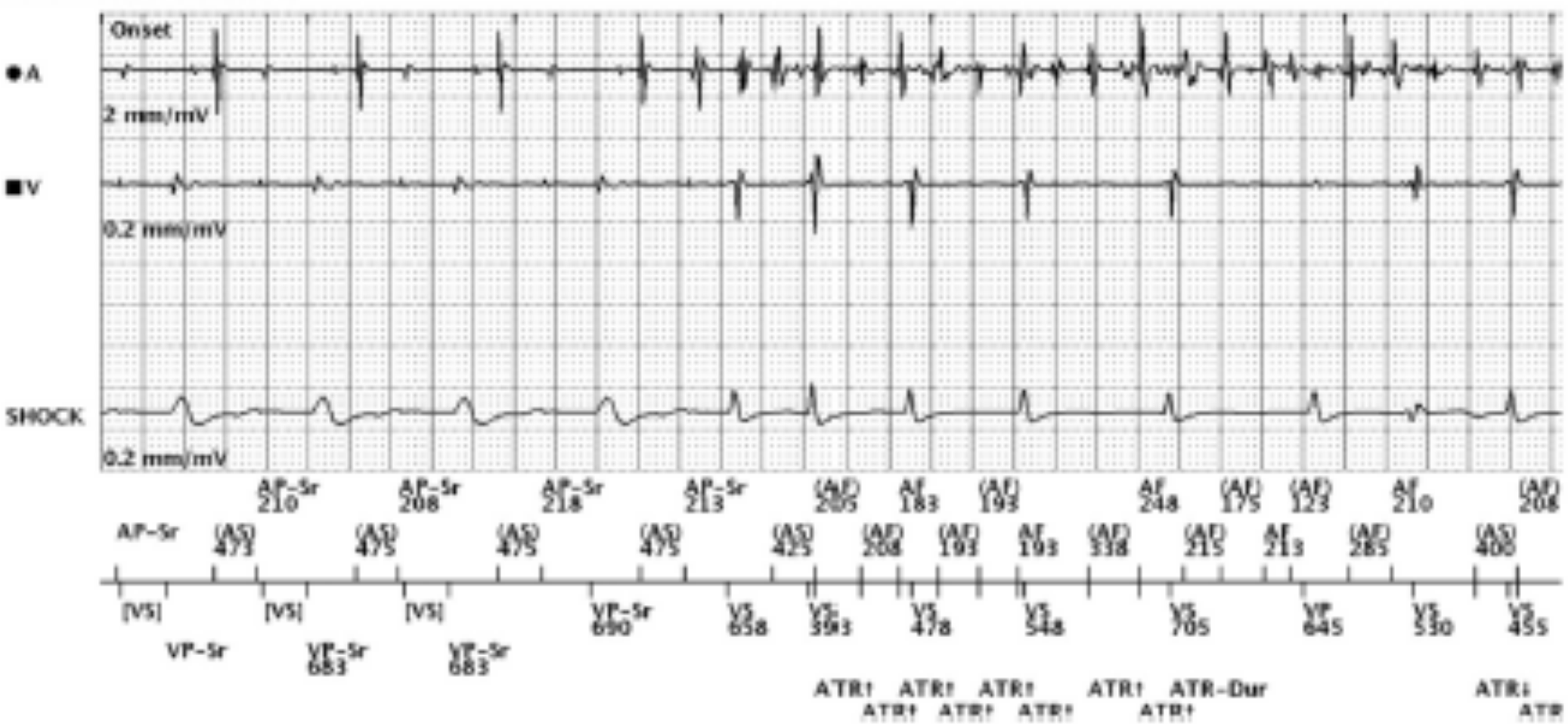
Opportunistic AF Detection in Patients with Cardiac Implantable Devices



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Link Between AHRE and TE

Year	Trial	Number of patients	Duration of follow-up	Atrial rate cut-off	AF burden threshold	Hazard ratio for TE event	TE event rate (below vs. above AF burden threshold)
2003	Ancillary MOST[5]	312	27 months (median)	>220 bpm	5 min	6.7 (*P*=0.020)	3.2% overall (1.3% vs. 5%)
2005	Italian AT500 Registry[18]	725	22 months (median)	>174 bpm	24 h	3.1 (*P*=0.044)	1.2% annual rate
2009	Botto *et al.*[19]	568	1 year (mean)	>174 bpm	$CHADS_2$+AF burden	n/a	2.5% overall (0.8% vs. 5%)
2009	TRENDS[20]	2486	1.4 years (mean)	>175 bpm	5.5 h	2.2 (*P*=0.060)	1.2% overall (1.1% vs. 2.4%)
2012	Home Monitor CRT[22]	560	370 days (median)	>180 bpm	3.8 h	9.4 (*P*=0.006)	2.0% overall
2012	ASSERT[7]	2580	2.5 years (mean)	>190 bpm	6 min	2.5 (*P*=0.007)	(0.69% vs. 1.69%)
2014	SOS AF[23]	10016	2 years (median)	>175 bpm	1 h	2.11 (*P*=0.008)	0.39% per year Overall

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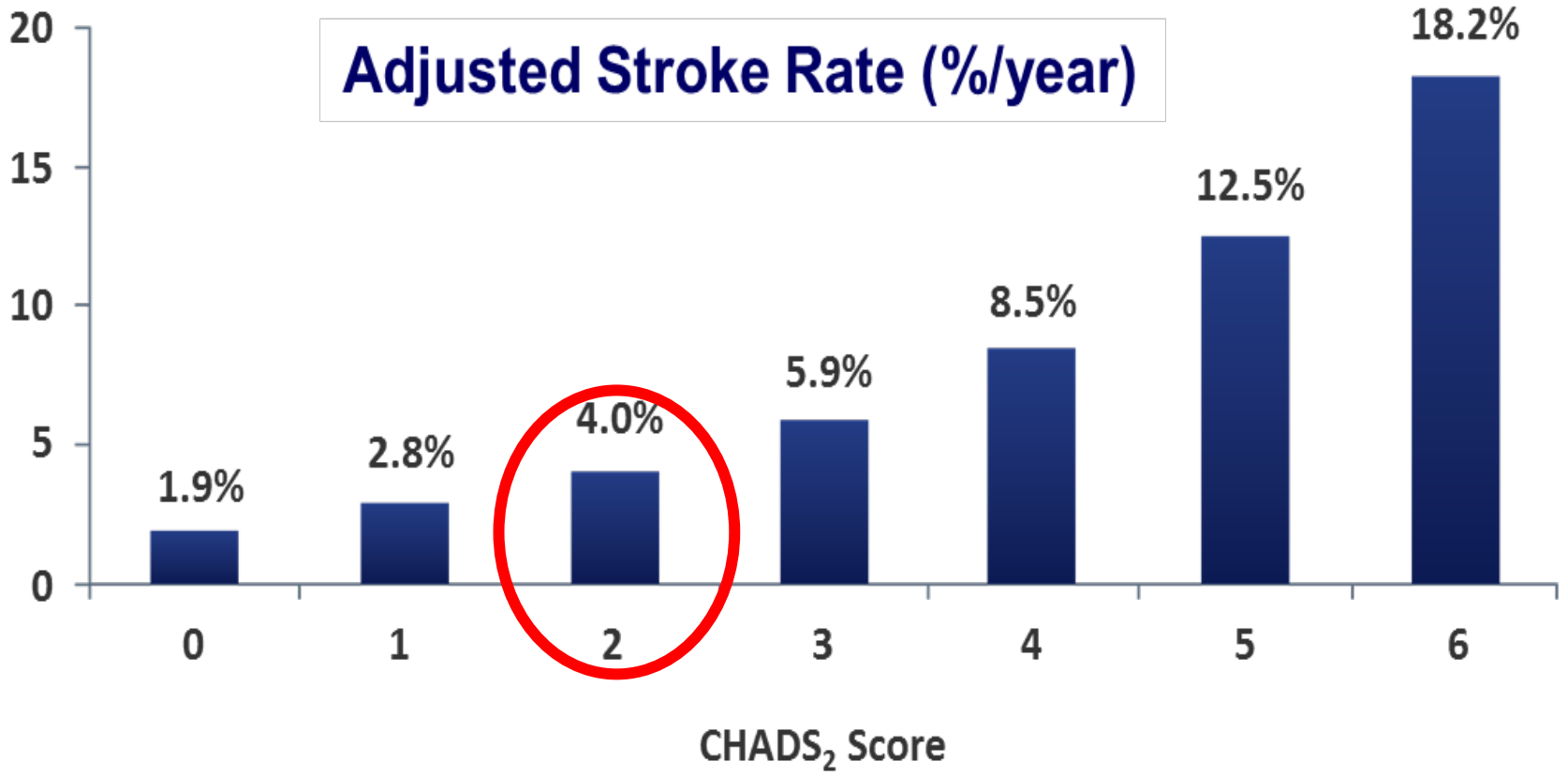
Stroke Risk for AHRE and AF

TRENDS Study:

Overall mean $CHADS_2$=2.2±1.2; Stroke rate AHRE ≥ 5.5 h=2.4%/year



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SOR	QOE	Recommendation
Strong	Low Quality	Atrial high-rate episodes (AHREs) be assessed at the time of cardiac implantable electronic device (loop recorder, pacemaker, or cardioverter-defibrillator) interrogation.

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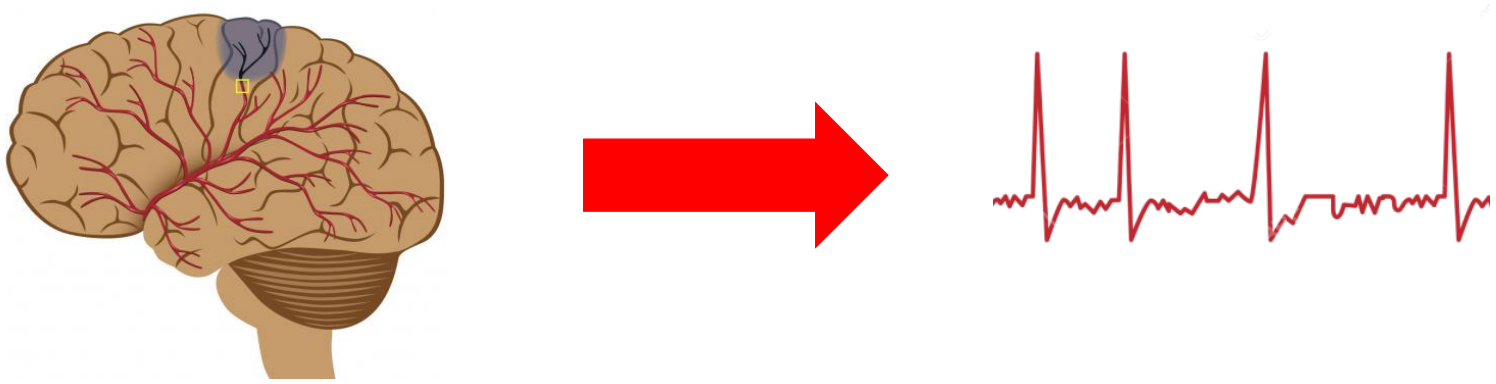
AF Detection After ESUS



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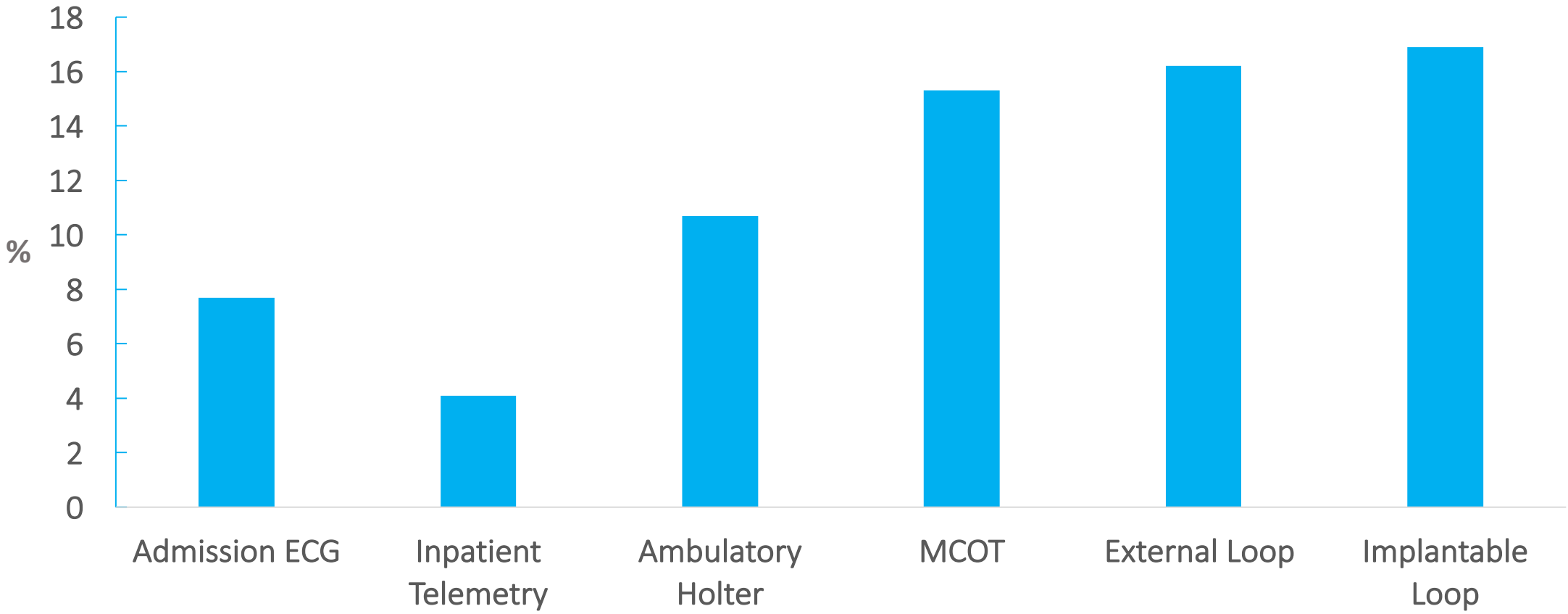
Yield of Monitoring Tools for AF



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The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

EMBRACE (N=572)

- AF detection (30s) at 3 months was 16.1% 30-d event recorder versus 3.2% control group

Gladstone DJ LA et al. NEJM 2014;370:2467-2477.

CRYSTAL AF (N=441)

- AF detection (30s) at 6 months was 8.9% ICM versus 1.4% control group.

Sanna t et al. NEJM 2014;370:2478-2486.

SOR	QOE	Recommendation
Strong	Low Quality	At least 24 hours of ambulatory ECG monitoring to identify AF in patients with non-lacunar ESUS.

SOR	QOE	Recommendation
Weak	Moderate Quality	Additional monitoring for AF detection be performed for selected older patients with non-lacunar ESUS in whom AF is suspected but not proven.

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Secondary Stroke Prevention

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Stroke on OAC – Potential Causes

- Inadequate intensity of anticoagulation
  - INR (warfarin), dose (DOAC)
- Suboptimal adherence or persistence
- Alternate Stroke Etiology
  - Eg. Carotid stenosis, ICAD, dissection, vasculitis, hemodynamic
- Suboptimal Risk Factor management

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Stroke on OAC – Recommendation

- We recommend that patients with AF who experience an ischemic stroke while receiving OAC be managed acutely according to the secondary stroke prevention practice guidelines (e.g. Canadian Stroke Best Practice Recommendations), with emphasis on addressing OAC medication adherence, ensuring correct OAC dosing and avoidance of drug interactions, identifying and treating other potential causes for the stroke other than AF, and promoting general vascular risk factor modification and healthy lifestyle choices (Strong Recommendation; Moderate-Quality Evidence).

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Stroke on OAC – Practical Approach

- Confirm diagnosis
  - CT/MRI, clinical evaluation to exclude mimics
  - TIA over diagnosed
- Etiologic investigation
  - Vascular imaging critical
- Medication adherence
  - Dosing/intensity, medication interaction
- Risk factor optimization
- Determine if change required to OAC
  - Interruption, change on reinitiation

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Timing of OAC initiation after ischemic stroke in patients with AF

- We recommend that the timing of initiation of anticoagulant therapy following an ischaemic stroke should be individualised and take into account the competing risks of recurrent stroke against the risk of haemorrhagic transformation of infarction (Strong Recommendation; Moderate-Quality Evidence).

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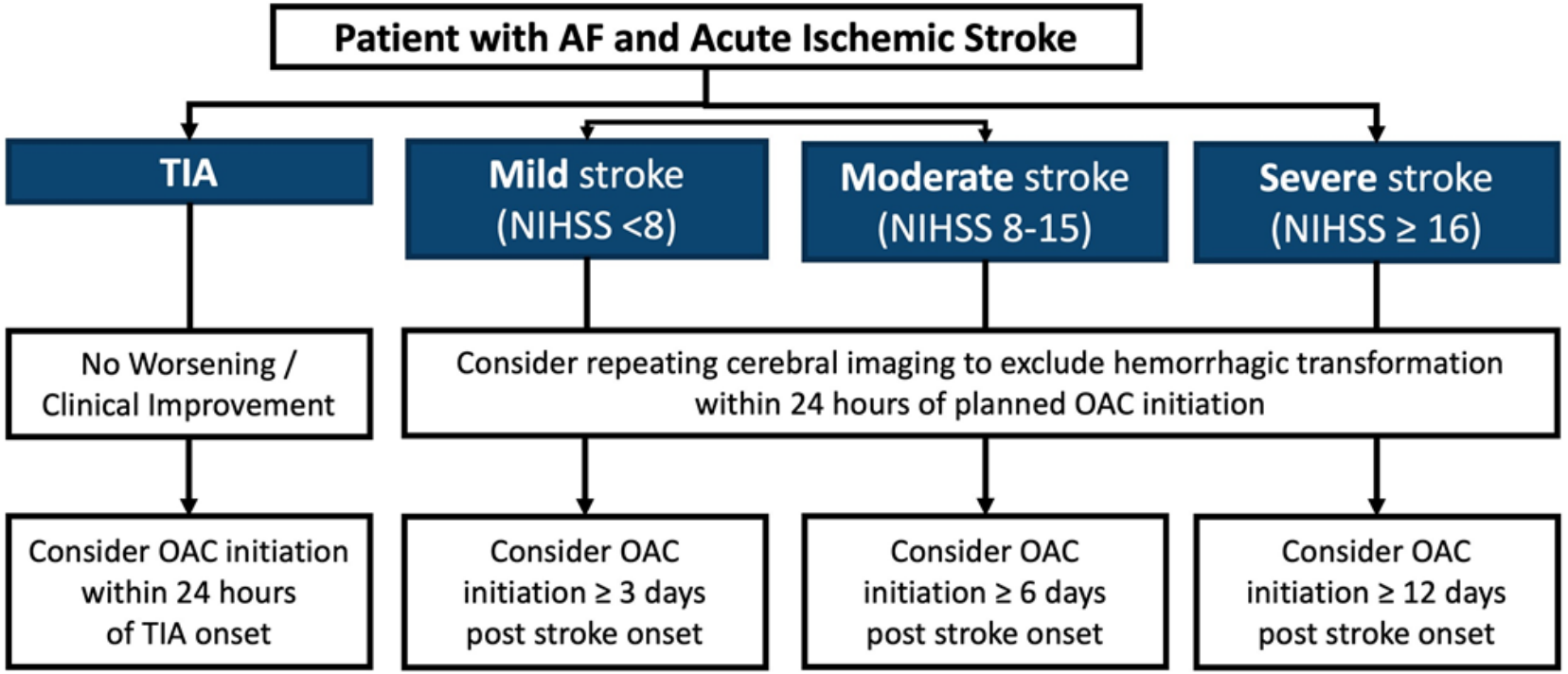
Timing of initiation of OAC – Practical approach



Factors Favouring Delayed Initiation of OAC	Factors Favouring Early Initiation of OAC
Hemorrhagic transformation	Mechanical heart valve
Large/moderate volume infarction	Intracardiac thrombus
High NIHSS	Intraluminal thrombus
Fluctuating neurologic status	Left atrial spontaneous echo contrast
Uncontrolled hypertension	Hypercoagulability
Coagulopathy	

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Rate and Rhythm
Acute and Non-Acute

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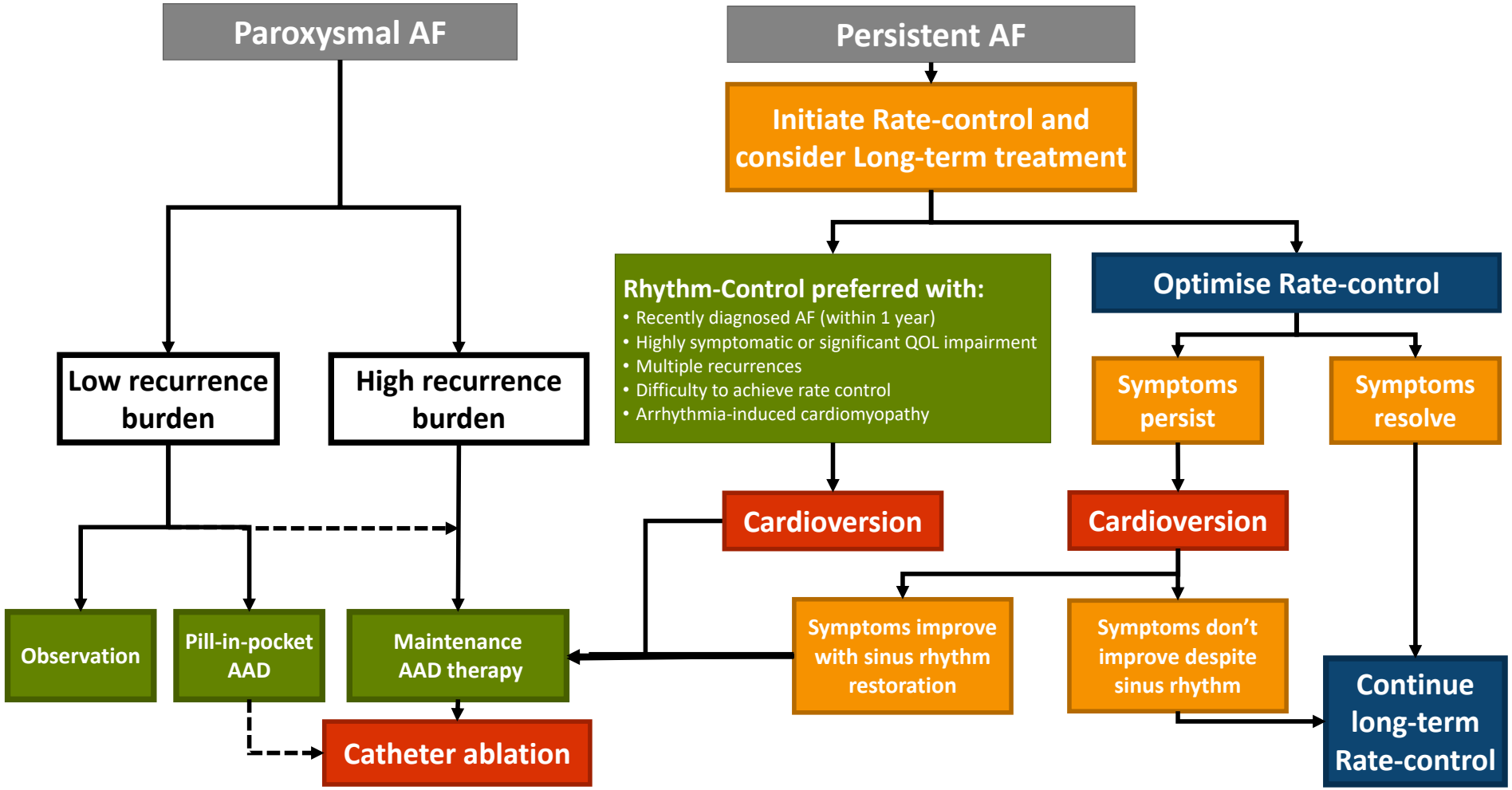
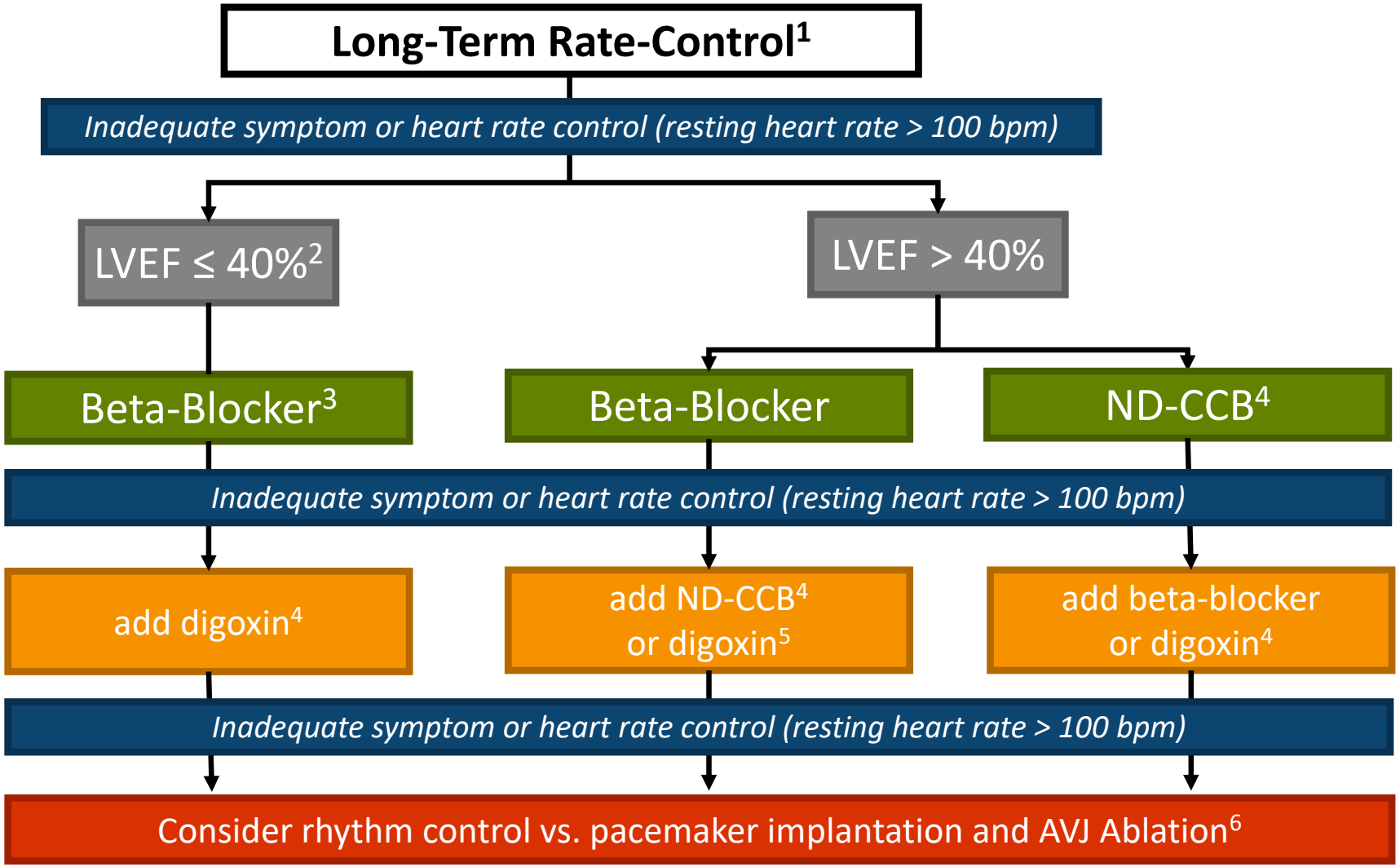
Approach to Rate and Rhythm for AF



Andrade JG et al. Can J Cardiol (in press)

Andrade J, et al., *Canadian Journal of Cardiology*, DOI: https://doi.org/10.1016/j.cjca.2020.09.001 October 24, 2020

Long-Term Rate Control



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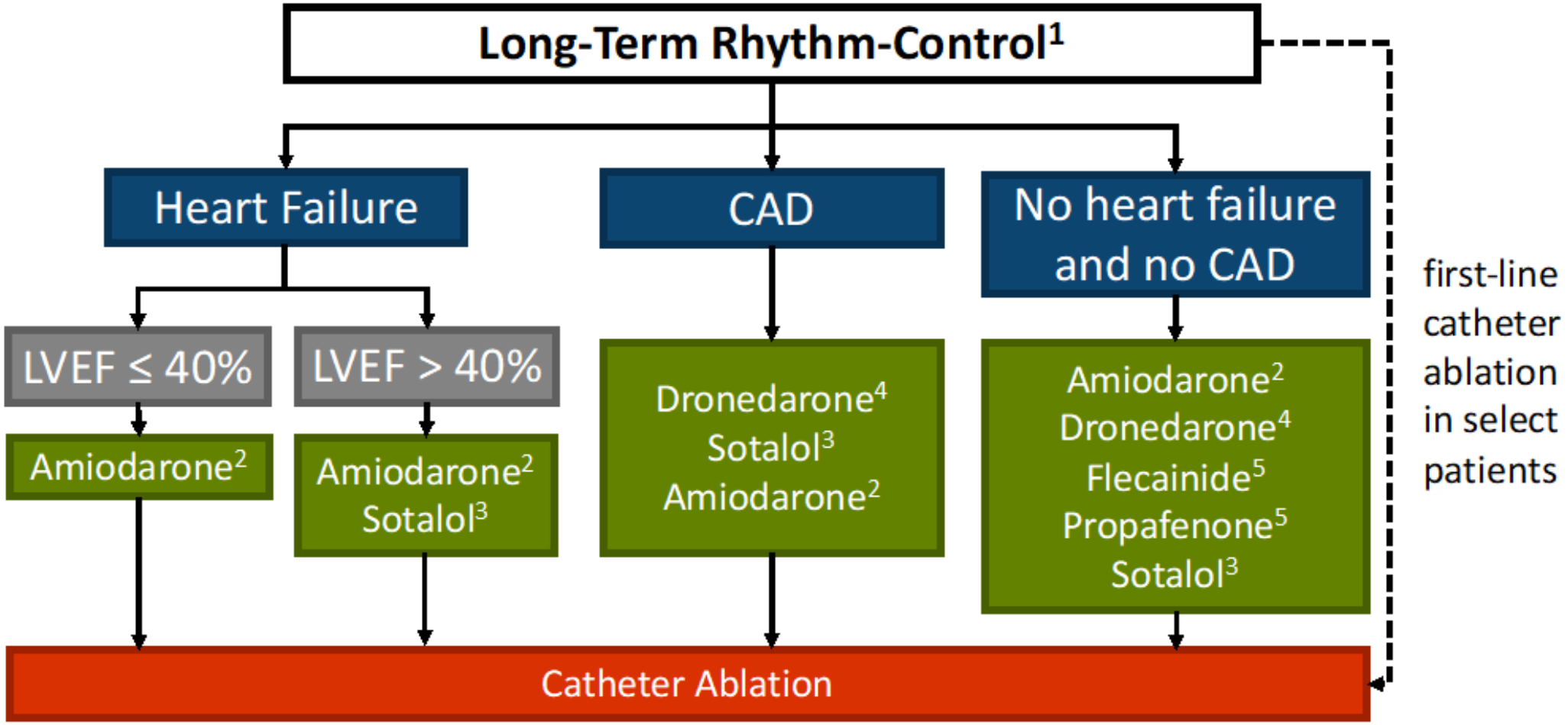
Long-Term Rhythm Control



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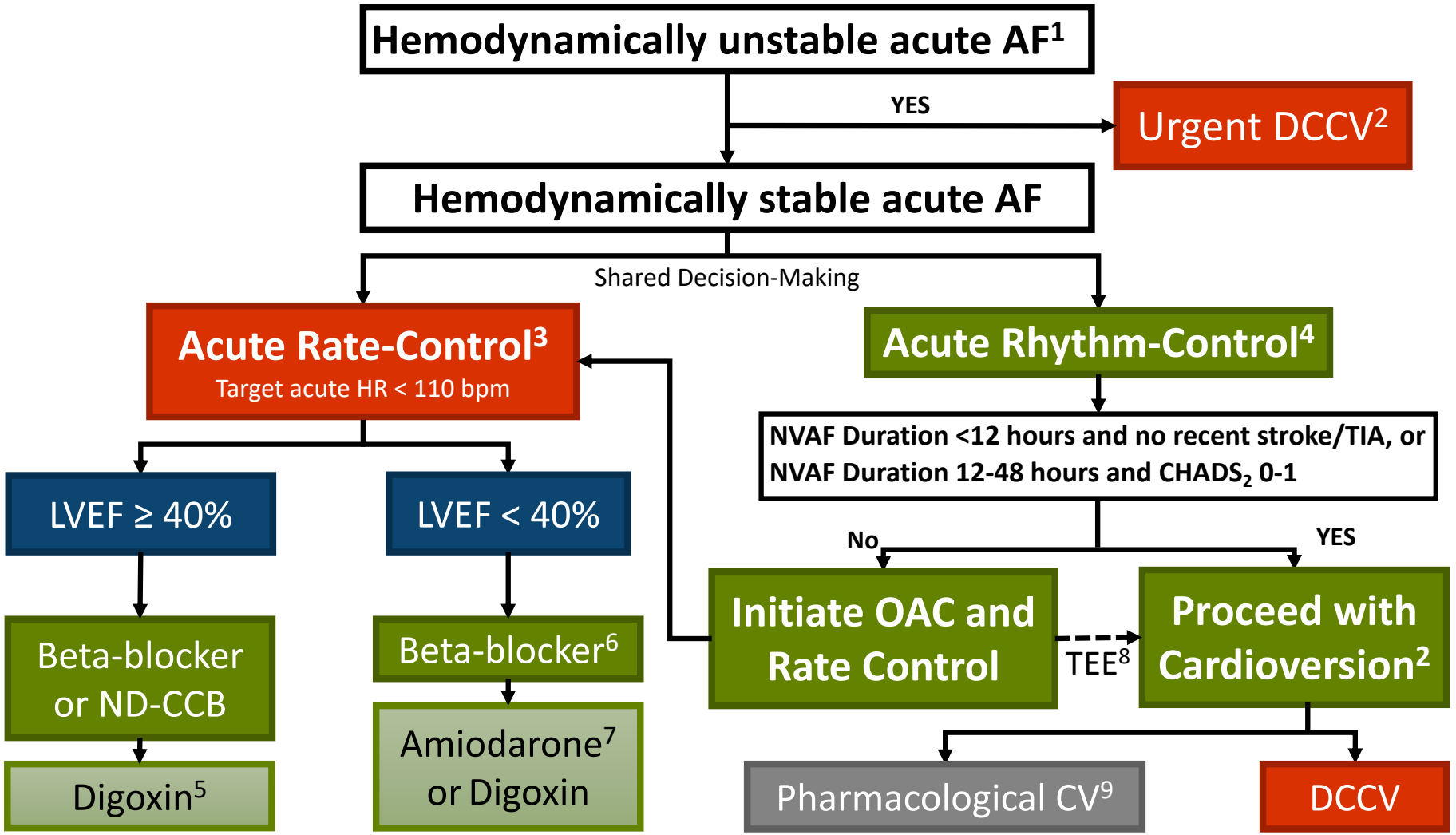
Approach to Acute AF/AFL



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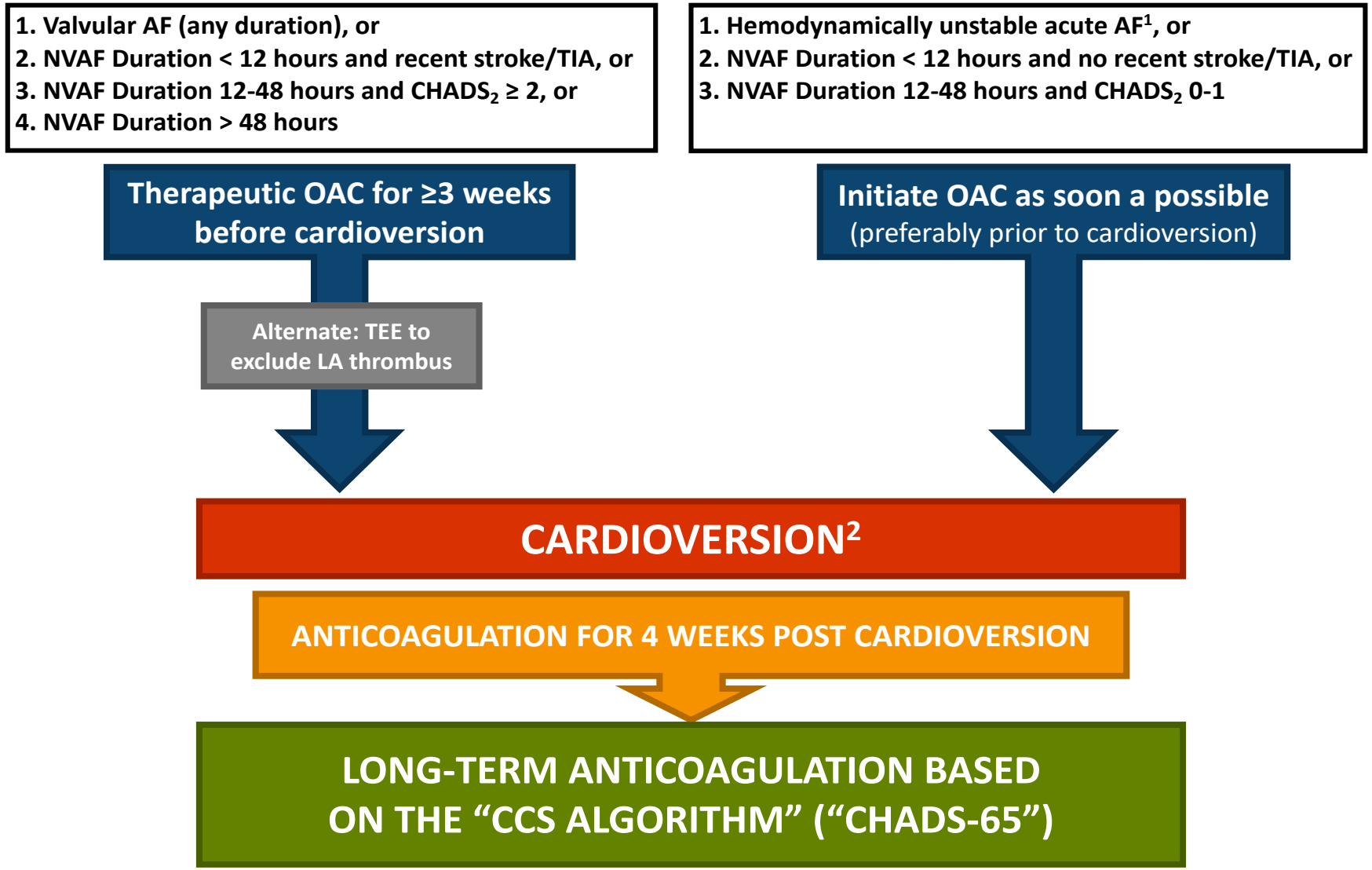
Anticoagulation Considerations for CV



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Risk Factors and Other Considerations

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Risk Factors

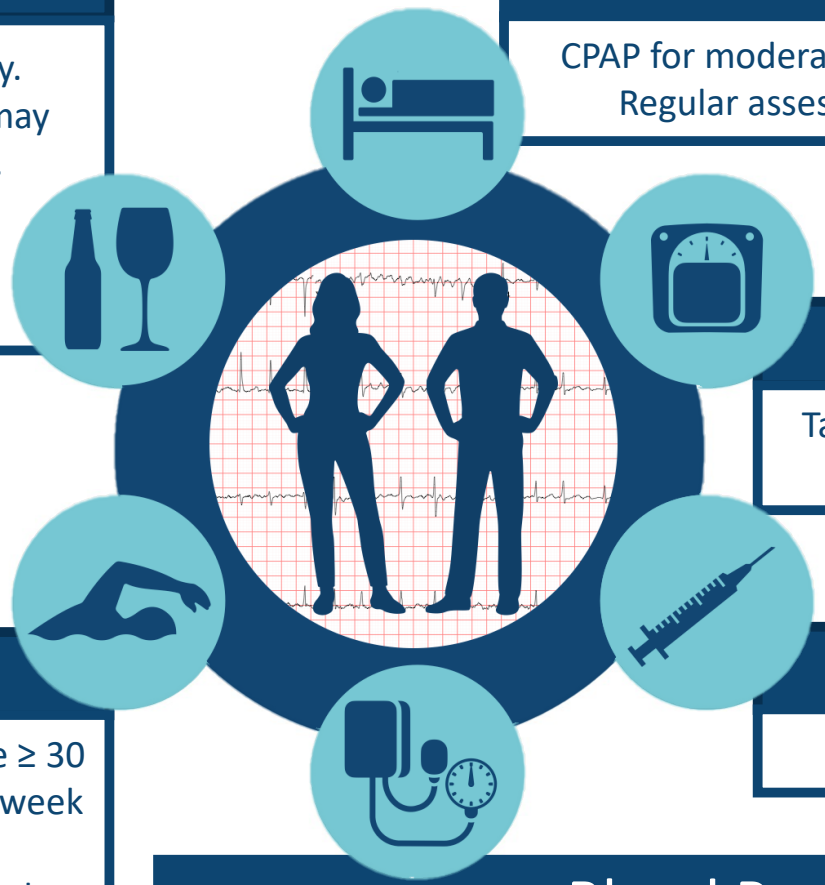
Alcohol and Tobacco

Limit to ≤ 1 standard drink[1] per day. Complete abstinence from alcohol may be preferred in selected patients.

Target complete abstinence from tobacco-related products.

Sleep Apnea

CPAP for moderate-severe OSA (AHI ≥ 15/hour)
Regular assessment of CPAP adherence.



Weight Loss

Target a weight loss of ≥10% to a BMI of less than 27 kg/m^2.

Diabetes

Target a HbA1c of ≤7.0%.

Exercise

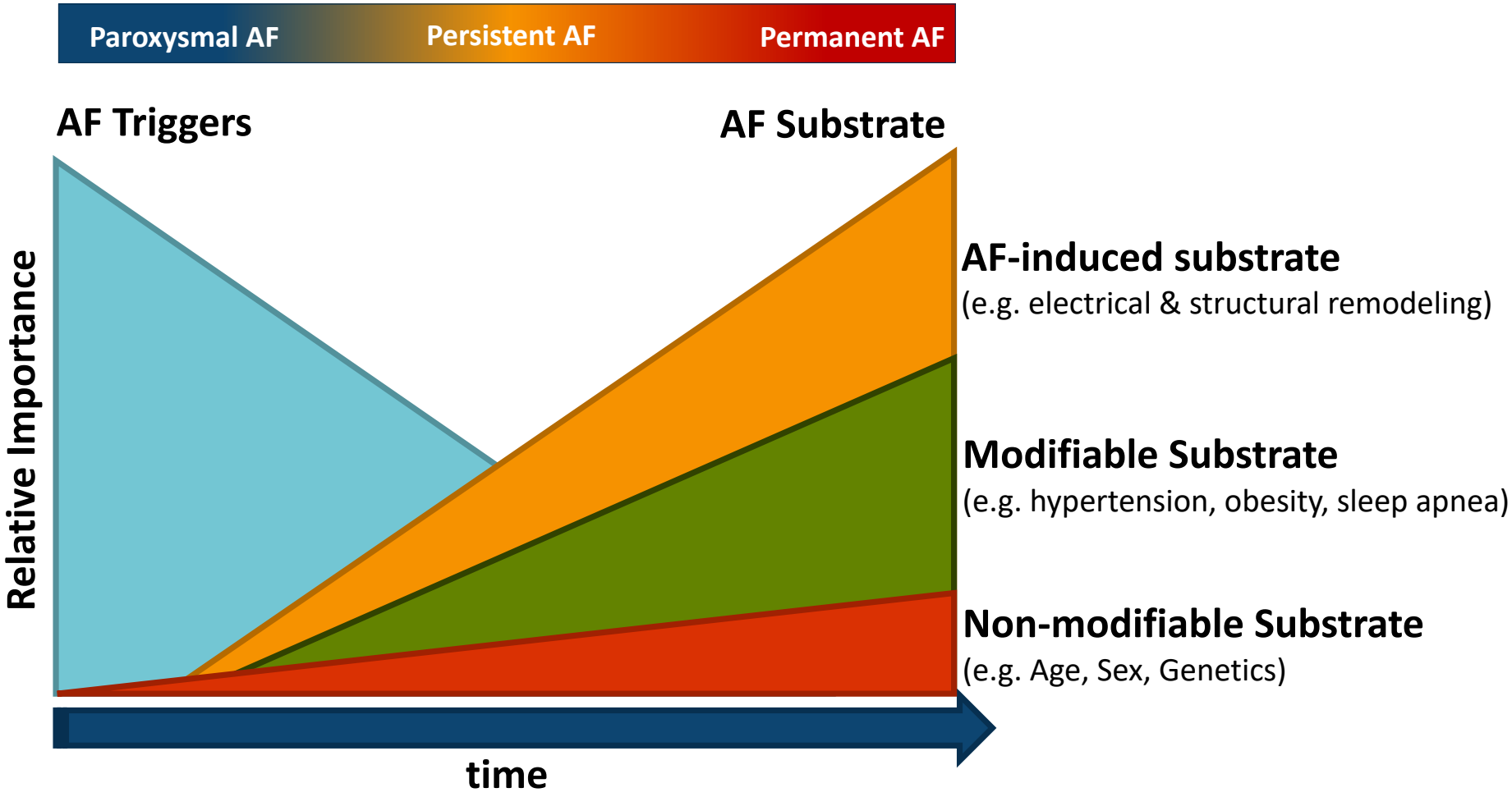
1. Moderate intensity aerobic exercise ≥ 30 minutes a day at least 3-5 days per week (target ≥ 200 minutes weekly).
2. Resistance exercise 2-3 days per week.
3. Flexibility exercises at least 10 minutes per day at least 2 days per week in those >65 years of age.

Blood Pressure

Target ≤ 130/80 mmHg at rest and ≤ 200/100 mmHg at peak exercise.
ACE-I or ARB may be preferred.

[1]defined as containing 14 g of alcohol; 44 mL (1.5 fluid oz.) of 80-proof liquor, 148 mL (5 fluid oz.) of wine or 355 mL (12 fluid oz.) of beer

Risk Factors



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Risk Factors

Conventional risk factors

- Advancing age
- Male sex
- Hypertension
- HF with reduced ejection fraction
- Valvular heart disease
- Overt Thyroid disease
- Obstructive sleep apnea

Emerging risk factors

- Obesity
- Excessive alcohol intake
- Pre-hypertension and Increased pulse pressure
- Chronic obstructive pulmonary disease
- HF with preserved ejection fraction
- Congenital heart disease (e.g. early repair of atrial septal defect)
- Subclinical hyperthyroidism
- Coronary artery disease
- Morphometric (increased height, increased birth weight)

Potential risk factors

- Familial/genetic factors
- Tobacco Use
- Left atrial dilatation
- LV hypertrophy
- Inflammation
- Diabetes
- Pericardial fat
- Subclinical atherosclerosis
- Chronic kidney disease
- Excessive endurance exercise
- Electrocardiographic (atrial conduction delay, PR interval prolongation)

Legend: AF, atrial fibrillation; HF, heart failure; LV, left ventricular.

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Risk Factor	Role in AF	Mechanism
Hypertension	Hypertension is a strong and independent predictor of incident AF.[30] AF incidence is linearly related to blood pressure (BP), with increased risk noted even in the pre-hypertensive range (adjusted HR ~1.3 for systolic BP 130-139 mmHg vs. <120 mmHg).[119, 834] Increased pulse pressure has been associated with an increased AF risk (adjusted HR ~1.25 per 20 mmHg increase).[119]	Hypertension may induce AF through: • Neurohormonal activation (sympathetic nervous system and the renin-angiotensin-aldosterone system) • Structural remodeling (atrial fibrosis) • Electrical remodeling (conduction disturbances)
Diabetes	Diabetes has been associated with ~1.5x increased risk of AF.[835, 836] AF risk is independently associated with a longer duration of treated diabetes (3% increased risk for each additional year of diabetes) and with worse glycemic control (13% increased risk with each 1% increase in HbA1c; and 33% increased risk with each 1 mmol/L increase in fasting glucose).[836-840] Co-existence of AF and diabetes portends a worsened prognosis, increasing all-cause mortality, cardiovascular death, and heart failure.[841]	Diabetes may induce AF through: • Structural remodeling (atrial fibrosis) • Electrical remodeling (conduction slowing) • Autonomic remodeling
Tobacco	Tobacco use has been associated with increased risk. [30, 842-844] • Active smokers having a higher risk than former smokers. • Risk is linked to cumulative exposure (greatest risk in the highest tertile, >675 cigarette-years). Continued tobacco use is associated with worse outcomes following catheter ablation.[845] Pooled analyses have not established a relationship between smokeless tobacco products and AF, and there is limited data regarding electronic cigarettes or second-hand smoke.[846]	Tobacco use may induce AF through: • Electrical remodeling (altered atrial conduction and refractoriness [direct effects of nicotine]) • Structural remodeling (atrial fibrosis) • Inflammation and oxidative stress
Alcohol	Acute paroxysms of AF have been reported after binge consumption (>5 standard drinks on a single occasion; "holiday heart" syndrome).[847-849] Heavy habitual consumption has been associated with risk of incident AF in a dose-dependent relationship (8% increase in incident AF with each additional drink/day).[847, 849, 850]	Alcohol use may induce AF through: • Neurohormonal activation (increased sympathetic activity, impairment of vagal tone) • Electrical remodeling (increase in inter- and intra-atrial conduction time, shortening of atrial effective refractory period) • Structural remodeling (atrial fibrosis)

Christopher Labos: One more reason to reduce your alcohol consumption

A new study tested whether abstinence prevented episodes of a type of arrhythmia known as atrial fibrillation.

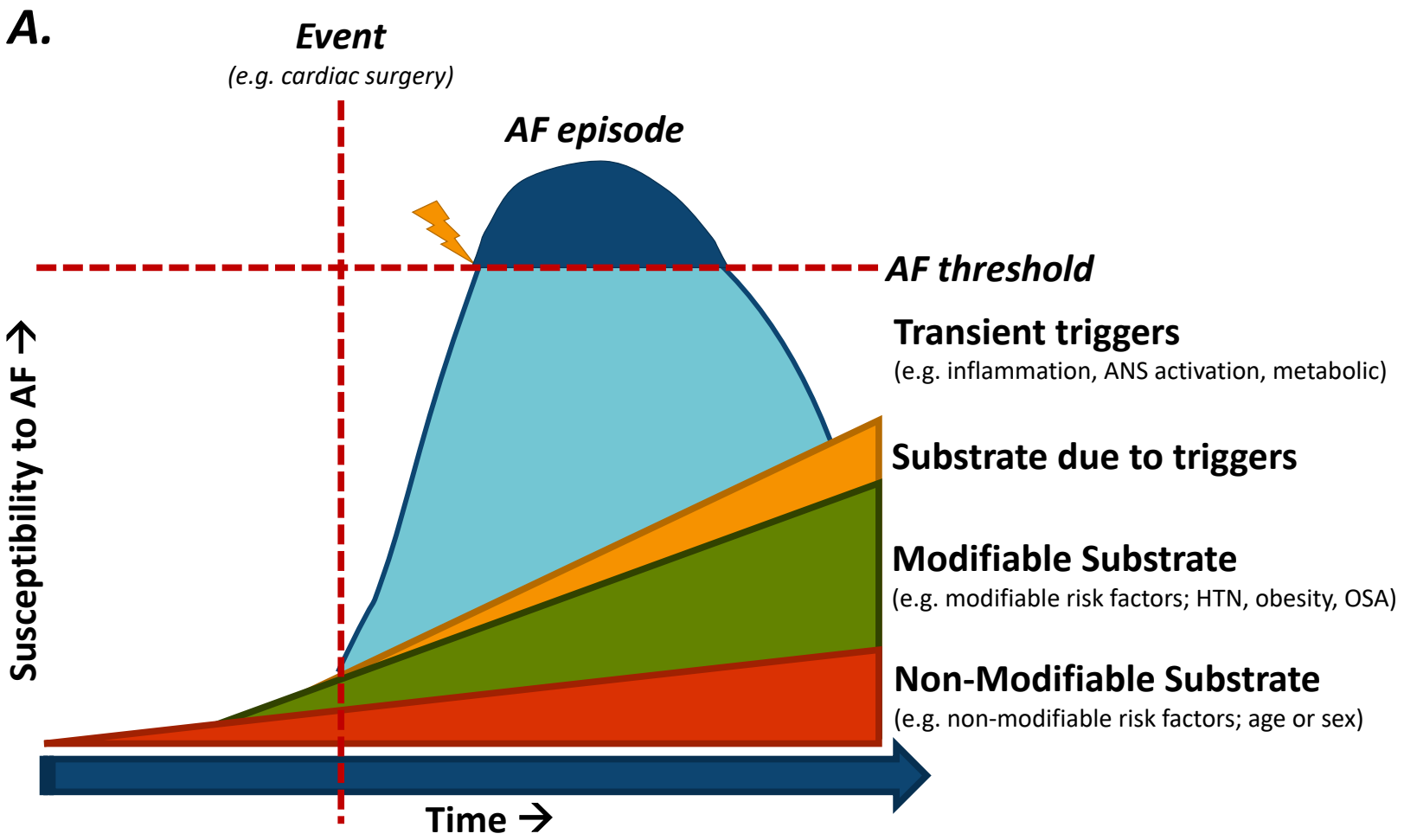
Christopher Labos • Special to Montreal Gazette
Jan 14, 2020 • Last Updated 10 months ago • 3 minute read

2020 AF Guidelines Recommendation

In patients with established AF or at high risk of developing AF, we recommend a systematic approach to the identification of traditional modifiable cardiovascular risk factors and/or conditions associated with AF, with strict guideline-adherent management in order to reduce major cardiovascular events *(Strong Recommendation; High-Quality Evidence)* and to prevent recurrence of the arrhythmia and/or decrease its symptom burden *(Strong Recommendation; Low-Quality Evidence)*.

Andrade J, et al., *Canadian Journal of Cardiology*, DOI: https://doi.org/10.1016/j.cjca.2020.09.001 October 24, 2020

Secondary AF



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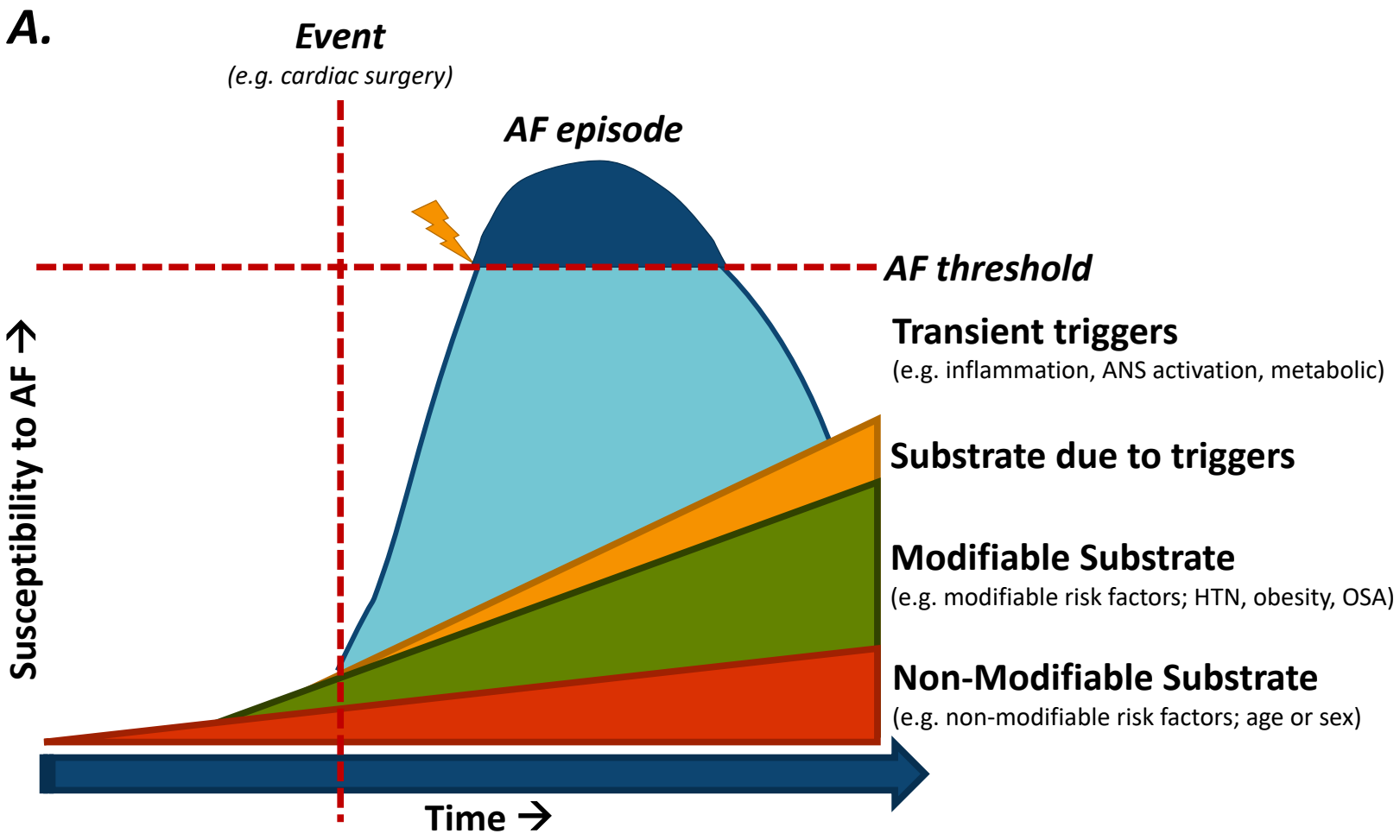
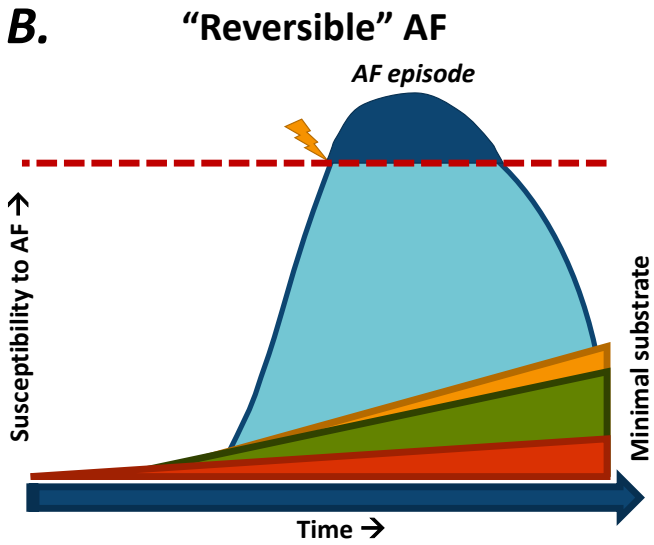
Secondary AF





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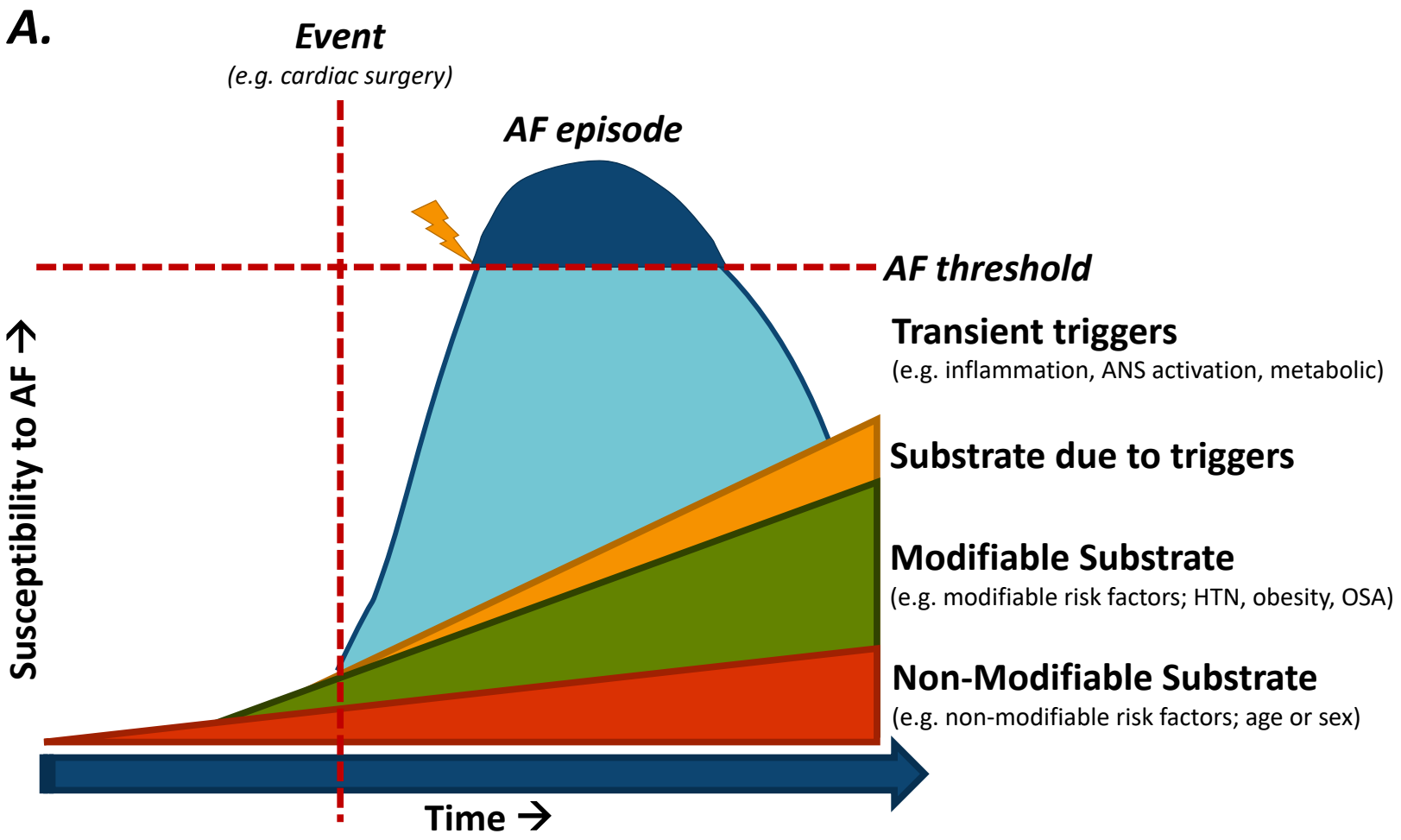
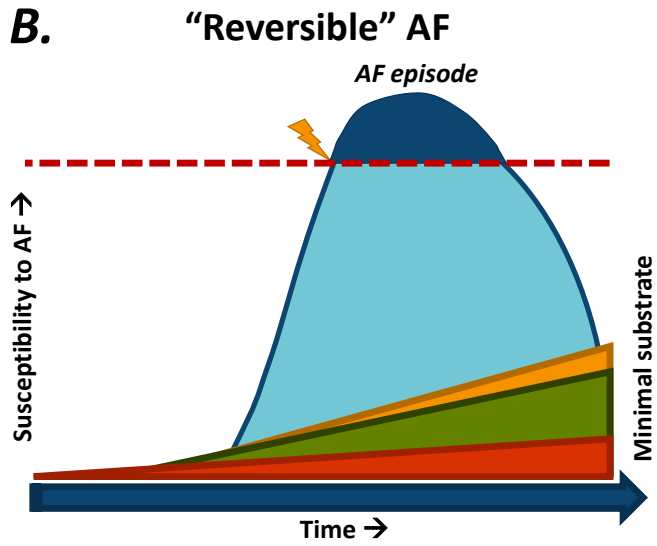
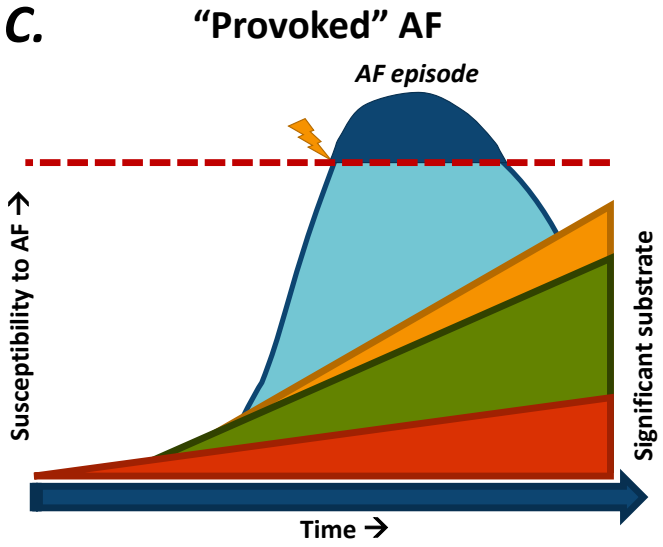
Secondary AF







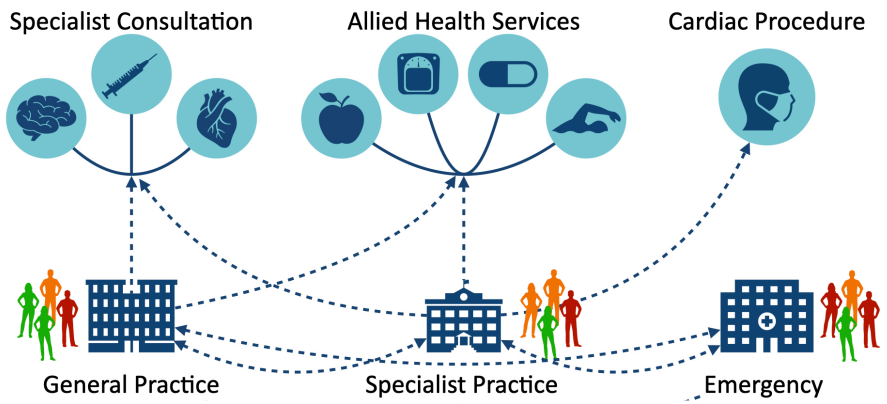
Andrade J, et al., *Canadian Journal of Cardiology*, DOI: https://doi.org/10.1016/j.cjca.2020.09.001 October 24, 2020

2020 AF Guidelines Recommendations

- We recommend that the management of patients presenting with recent-onset AF due to a reversible or secondary cause should be directed at the primary illness *(Strong Recommendation; Low-Quality Evidence).*
- We suggest that most patients with secondary AF due to thyrotoxicosis be anticoagulated until a euthyroid state is restored *(Weak Recommendation; Low-Quality Evidence).*
- We suggest that patients with secondary AF, which has resolved, not be routinely anticoagulated in the absence of recurrence *(Weak Recommendation; Low-Quality Evidence).*
- We recommend that patients who have experienced secondary AF be followed indefinitely for the possible emergence of recurrent clinical AF, with opportunistic screening for AF conducted at the time of medical encounters *(Strong Recommendation; Moderate-Quality Evidence).*

Andrade J, et al., *Canadian Journal of Cardiology*, DOI: https://doi.org/10.1016/j.cjca.2020.09.001 October 24, 2020

AF Clinics and Multidisciplinary AF Care



Low risk patients
Well-managed

Moderate Risk patients
Needs complex intervention

High Risk patients
Requires acute intervention

Cardiology and Electrophysiology

Nursing

Pharmacy / Medication management

Weight management

Smoking cessation

Nutrition / Dietary counselling

Exercise physiology

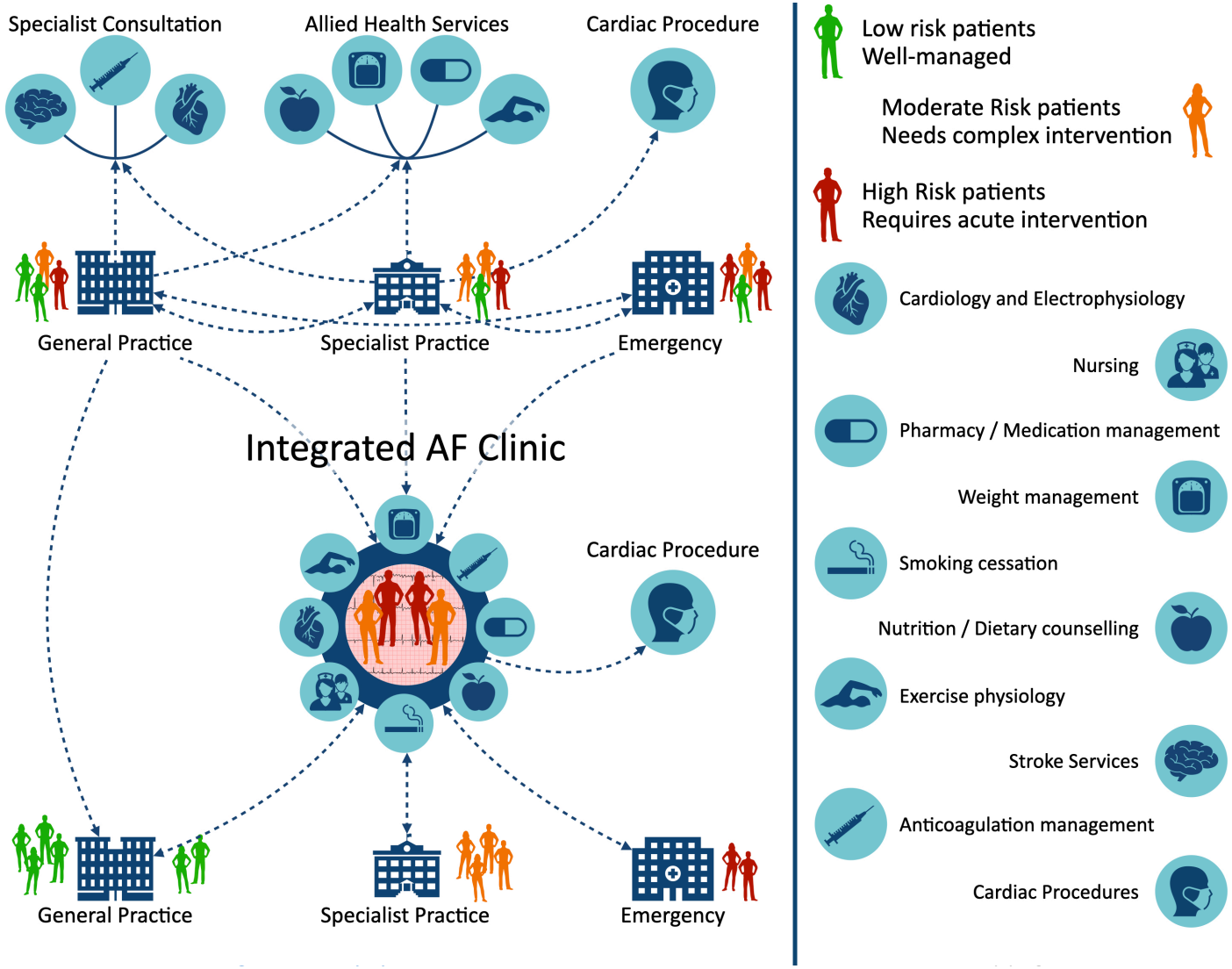
Stroke Services

Anticoagulation management

Cardiac Procedures

Andrade J, et al., *Canadian Journal of Cardiol*

AF Clinics and Multidisciplinary AF Care



Andrade J, et al., *Canadian Journal of Cardiol*

2020 AF Guidelines Recommendation

We suggest a structured, integrated, multidisciplinary, patient-focused approach to care should be implemented for patients with AF (Weak Recommendation; Moderate-Quality Evidence).

- ***Values and Preferences –*** *This recommendation recognises that AF is a multi-factorial disease that requires long-term treatment. An integrated patient-focused team-based approach to care has been shown to improve guideline adherence, reduce adverse clinical outcomes such as hospitalization and mortality, and improve quality-of-life*

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Sex Differences

10. Sex Differences in AF

Recognition of sex differences offers an opportunity to impact outcomes in women with AF.[659]

10.1. Epidemiology and Pathophysiology

Age and sex are the two most powerful predictors of incident AF. While the prevalence of AF doubles with each decade of age (increasing from 1-4% at 60 years to 6-15% at 80 years), male sex is associated with a 1.5-fold risk of AF, even after adjusting for age and predisposing conditions. While the age-adjusted prevalence of AF is consistently observed to be higher in men (e.g., a sex-based prevalence of 9.2% for women vs. 15.0% for men in a community-based, randomised, controlled AF screening study performed in Sweden)[31, 85] the absolute number of female patients with AF exceeds the number of male patients with AF due to the longer life span of female patients.

While the exact mechanism responsible for the reported sex-related differences in AF remains inadequately understood, several theories have been suggested. Firstly, anthropomorphic differences between the sexes result in a larger LA dimension and volume in male patients.[660, 661] Second, female patients with AF have been shown to have a relatively greater burden of atrial fibrosis using delayed-enhancement MRI imaging.[662] Third, male patients with AF have greater expression of repolarizing ion-channel subunits, which could favor re-entry.[660, 663] Fourth, the contribution of sex hormones has been explored in several studies: with testosterone deficiency having been linked to increased atrial arrhythmogenicity;[664] progesterone associated with shortened action potential;[665] and estrogen has been postulated to play a central role in arrhythmogenesis due to prolongation in conduction time, action potential duration, and the atrial effective refractory period.[666]

10.2. Presentation

Female patients with AF are more likely to have underlying hypertension and valvular disease, while male patients with AF are more likely to have CAD and abnormal LV function. Female patients with AF report more atypical symptoms, with a relatively greater symptom burden and lower QOL compared to male patients.[667, 668] As a result, women are more likely to seek care for AF symptoms and are more likely to experience depression related to AF.[669]

10.3. Outcomes

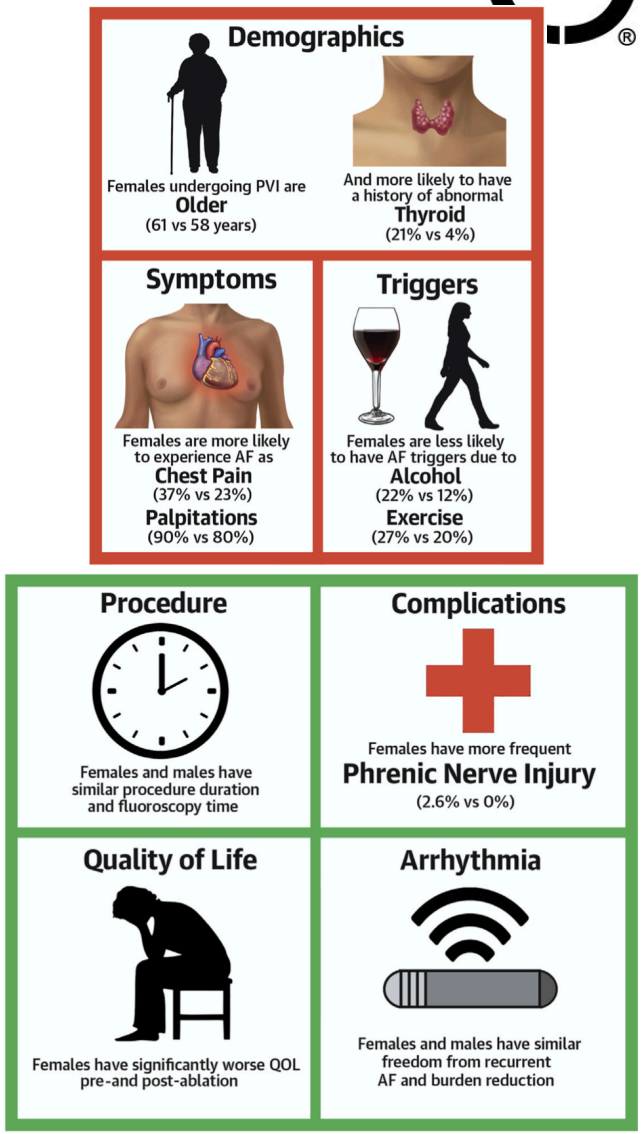
Important sex-specific differences in cardiovascular outcomes have been described. AF in female patients is associated with a greater all-cause mortality relative to male patients (RR 1.12, 95%CI 1.07-1.17).[670] Compared to male patients with AF, strokes experienced by female patients tend to be larger, and are associated with poorer functional outcomes and greater need for institutionalization.[671]

10.4. Stroke Prevention

Sex-specific differences in antithrombotic therapy have been observed: female patients with AF are more likely to be prescribed antiplatelet agents; when OACs are prescribed, they are more likely to receive a DOAC and, are more likely to be inappropriately-prescribed the lower approved dose.[672-675] In terms of efficacy, female patients with AF have a greater residual risk of stroke despite VKA-therapy, which may reflect sex-specific differences in VKA metabolism or underlying risk factor control.[676, 677] While no sex-specific difference in DOAC efficacy has been observed, there is a significant reduction in major and CRNM bleeding in female patients with AF treated with a DOAC.[21-23, 25, 52, 677]

10.5. Rate and Rhythm Management

Female patients with AF are more likely to receive rate-control, when compared with male patients with AF.[678, 679] In those receiving rhythm-control, female patients with AF are preferentially managed with pharmacologic antiarrhythmic therapy, and are less likely to undergo ablation (OR 0.5-0.8 when compared to men).[680, 681] Moreover, those female patients that do undergo ablation tend to be older, have more comorbidities, have more advanced AF (e.g. longer duration of AF, more likely to be persistent), and failed a larger number of antiarrhythmics.[395, 663, 682, 683] Despite their more complex clinical profile before ablation, female patients undergoing ablation have comparable acute and longer-term success rates compared to male patients.[668, 682, 683]



J Am Coll Cardiol EP 2020;6:945

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Special Populations

AF management in populations with:

- Device Detected AF
- Hypertrophic Cardiomyopathy
- Athletes
- Adult Congenital Heart Disease
- Secondary AF
- Post-Operative AF
- AF in patients with SVT and WPW

OAC management in populations with:

- Chronic Kidney Disease
- Coronary Artery Disease
- Liver Disease
- Cancer
- Amyloidosis
- Frail Elderly
- Obesity

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Other Aspects of AF Care

Quality of Life

Instrument	Type	Domains	Administration	Comments
SF-36[876]	Generic QOL	Vitality Physical functioning Bodily pain General health perceptions Physical role functioning Emotional role functioning Social role functioning Mental health	Patient	Extensive Validation Widespread clinical use Good for comparing between diseases Can be used to evaluate cost-effectiveness Insensitive AF
EQ-5D[877]	Generic QOL	Mobility Self-care Usual activities Pain/discomfort Anxiety/depression	Patient	
AFEQT[878]	Specific QOL	Symptoms Daily activities Treatment concerns Treatment satisfaction	Patient	Good reliability Good validity Fair responsiveness (sensitive to change)
AFQOL[879]	Specific QOL	Physical Psychological Sexual activity	Patient	Poor reliability Good validity Poor responsiveness
AFSS[880]	Symptom	Symptom frequency, duration and severity	Patient	
AFS/B[881]	Symptom	Symptom severity and burden	Patient and Caregiver	
EHRA[882]	Classification	Impact of AF on ability to complete daily activities	Caregiver	Simple classification
CCS-SAF[77]	Classification	Impact of AF on ability to complete daily activities	Caregiver	Detailed classification Impact of symptoms on QOL

We recommend that patient-reported AF-related symptoms and quality-of-life be assessed with validated instruments as part of the longitudinal management of patients with AF (Strong Recommendation Low-Quality Evidence).

- ***Values and Preferences*** *- This recommendation places a high value on the recognition that symptom control has a powerful influence on disability and healthcare resource utilization. The assessment of patient-reported outcomes with validated multi-dimensional instruments offers a relevant and complementary means to evaluate the impact of therapeutic interventions.*

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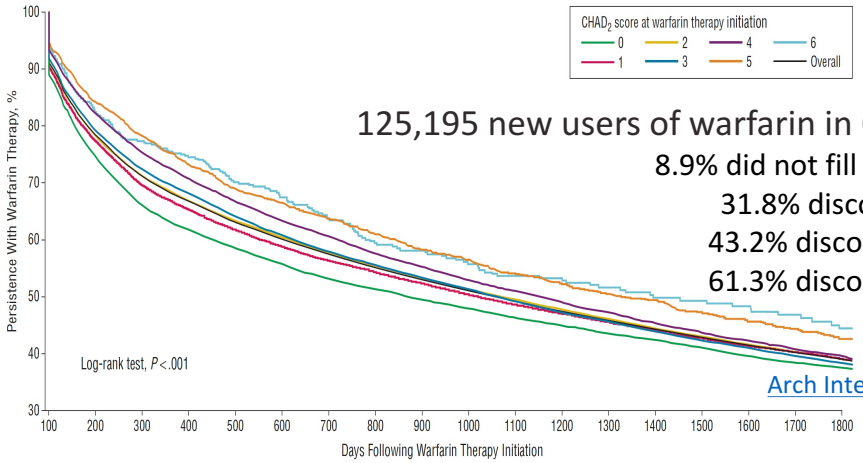
Other Aspects of AF Care

We recommend that adherence and persistence to pharmacotherapy be regularly assessed at each clinical encounter and supported using patient-centered strategies. (Strong Recommendation; Low-Quality Evidence).

- ***Values and Preferences*** *– This recommendation puts high value on the evidence indicating poor long-term persistence and adherence with OAC, as well as the recognition that strategies to improve persistence and adherence can substantially reduce the risk of stroke/systemic embolism.*

Medication Adherence & Persistence

- Establishment of a "blame-free" healthcare environment (e.g. recognising that adherence is not exclusively the responsibility of the patient)
- Assess health literacy and provide tailored education
- Employ motivational strategies and focus the interventions on behavioural strategies
- Address rational non-adherence
- Modify care delivery (e.g. provide more convenient care such as telemedicine; employ structured follow-up)
- Simplify dosing regimens (e.g. reducing the number of daily doses)
- Consider medication delivery (e.g. blister packs)



125,195 new users of warfarin in Ontario >65 years with AF
8.9% did not fill a second warfarin prescription
31.8% discontinued therapy within 1 year
43.2% discontinued therapy within 2 years
61.3% discontinued therapy within 5 years

Arch Intern Med. 2012 Nov 26;172(21):1687-9.

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Thank you!