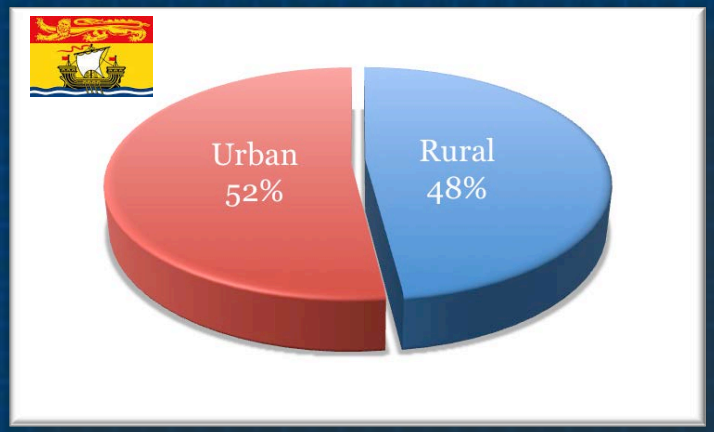
Atlantic Canada Population Demographics

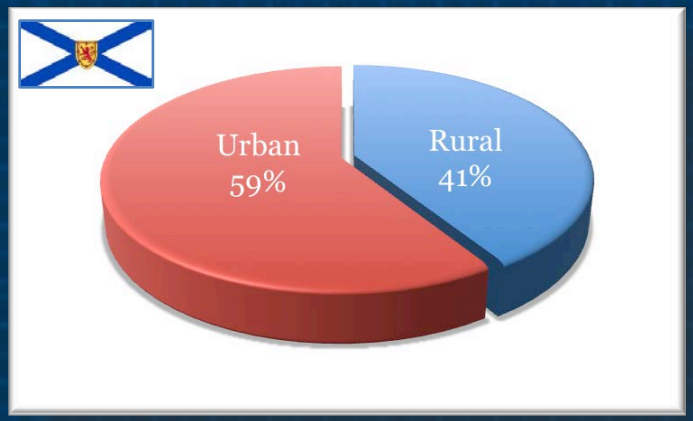
Atlantic Cardiovascular Society

2011 Atlantic Population Distribution

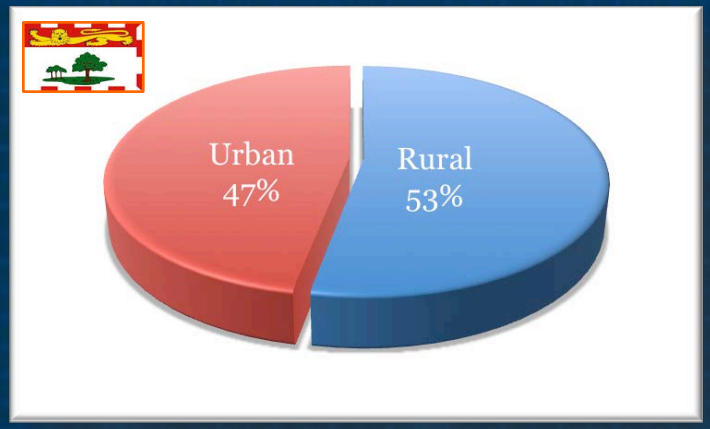
Population: 751 171



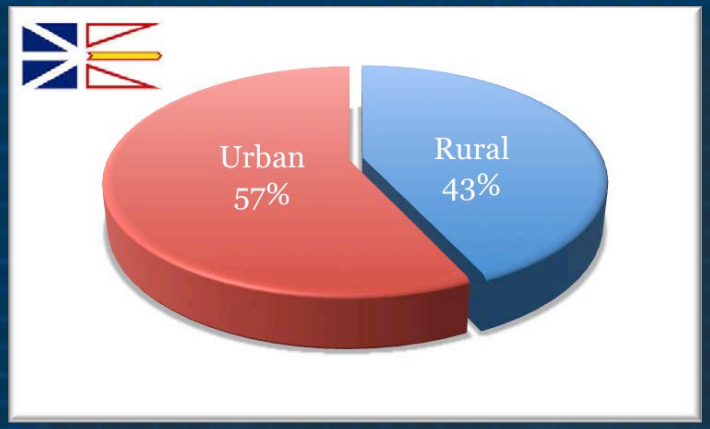
Population: 921 730



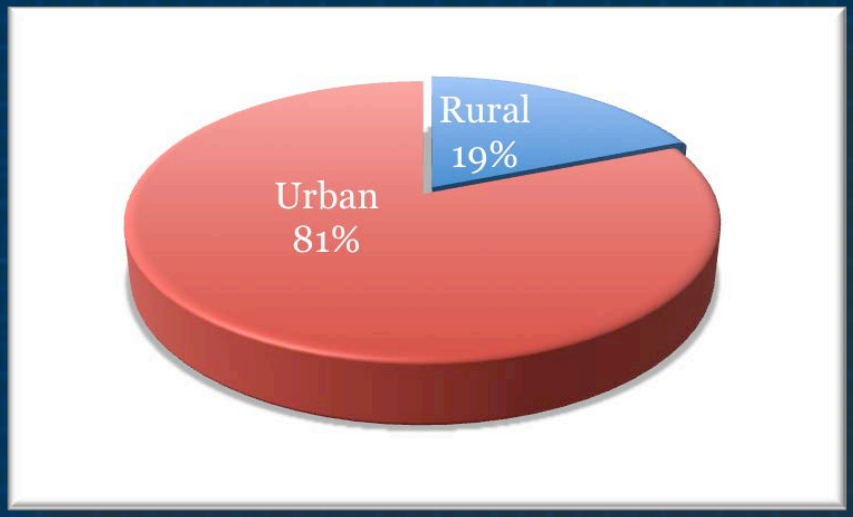
Population: 140 205



Population: 514 536

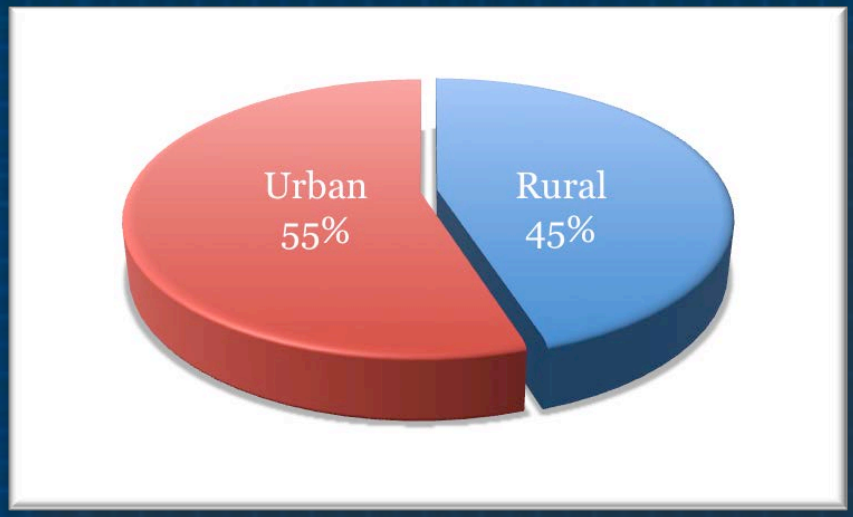


2011 Atlantic Population Distribution



Canadian Population

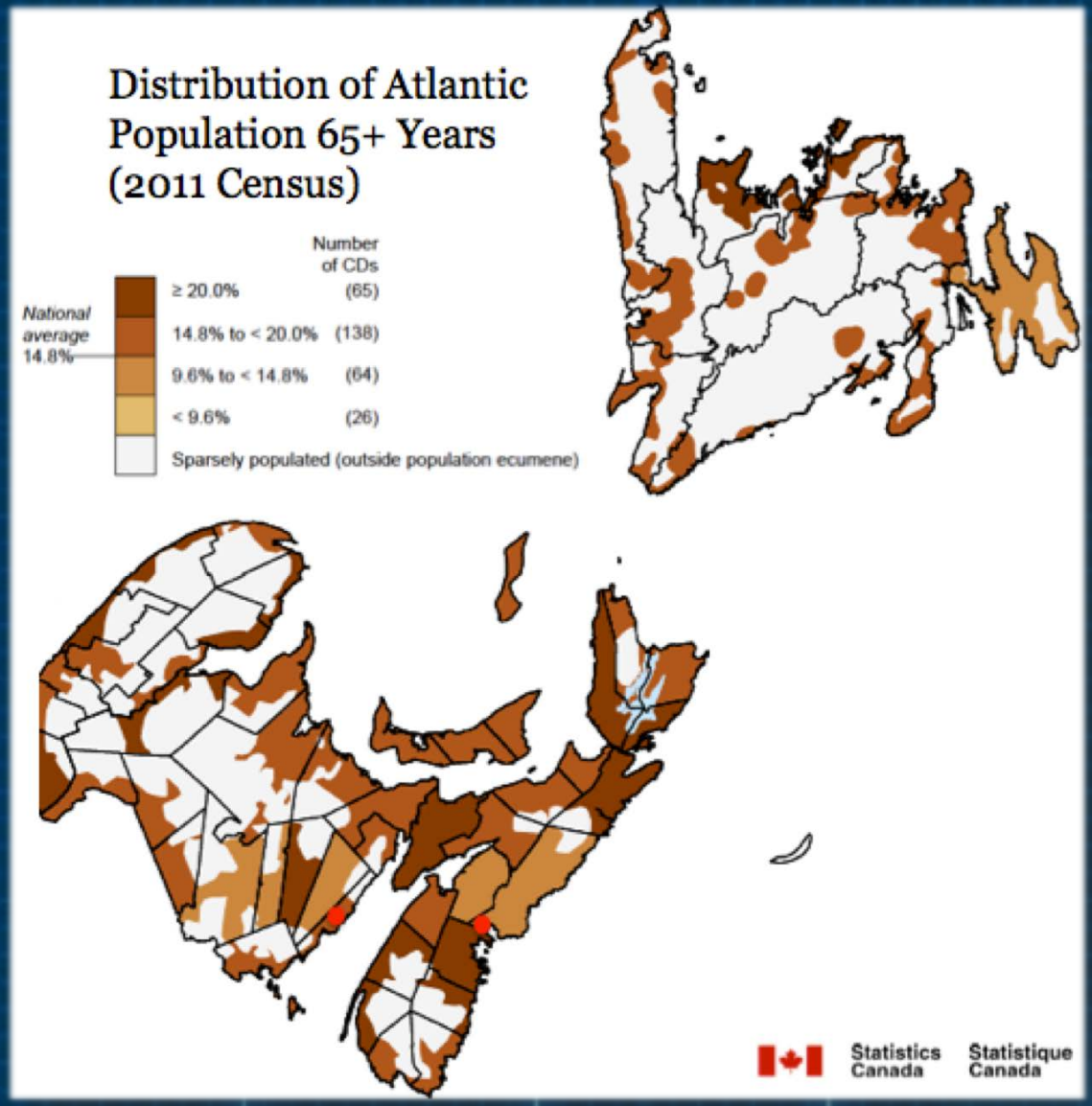
33 476 688



Atlantic Population

2 327 638

2011 Atlantic Population Distribution



2011 Nova Scotia Population Demographics

Broad age groups by sex	Population			
	2011	2006	change	% change
Both sexes				
Total	921,730	913,465	8,265	0.9
0 to 14	138,215	146,435	-8,220	-5.6
15 to 64	630,140	628,815	1,325	0.2
65 and over	153,375	138,215	15,160	11.0

Statistics Canada Statistique Canada

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2011 Newfoundland Population Demographics

Broad age groups by sex	Population			
	2011	2006	change	% change
Both sexes				
Total	514,540	505,465	9,075	1.8
0 to 14	76,630	78,225	-1,595	-2.0
15 to 64	355,800	356,975	-1,175	-0.3
65 and over	82,110	70,265	11,845	16.9

Statistics Canada Statistique Canada

2011 PEI Population Demographics

Broad age groups by sex	Population			
	2011	2006	change	% change
Both sexes				
Total	140,205	135,855	4,350	3.2
0 to 14	23,060	23,985	-925	-3.9
15 to 64	94,360	91,685	2,675	2.9
65 and over	22,785	20,185	2,600	12.9

Statistics Canada Statistique Canada

2011 New Brunswick Population Demographics

Broad age groups by sex	Population			
	2011	2006	change	% change
Both sexes				
Total	751,170	730,000	21,170	2.9
0 to 14	113,575	118,255	-4,680	-4.0
15 to 64	513,960	504,105	9,855	2.0
65 and over	123,630	107,635	15,995	14.9

Statistics Canada Statistique Canada

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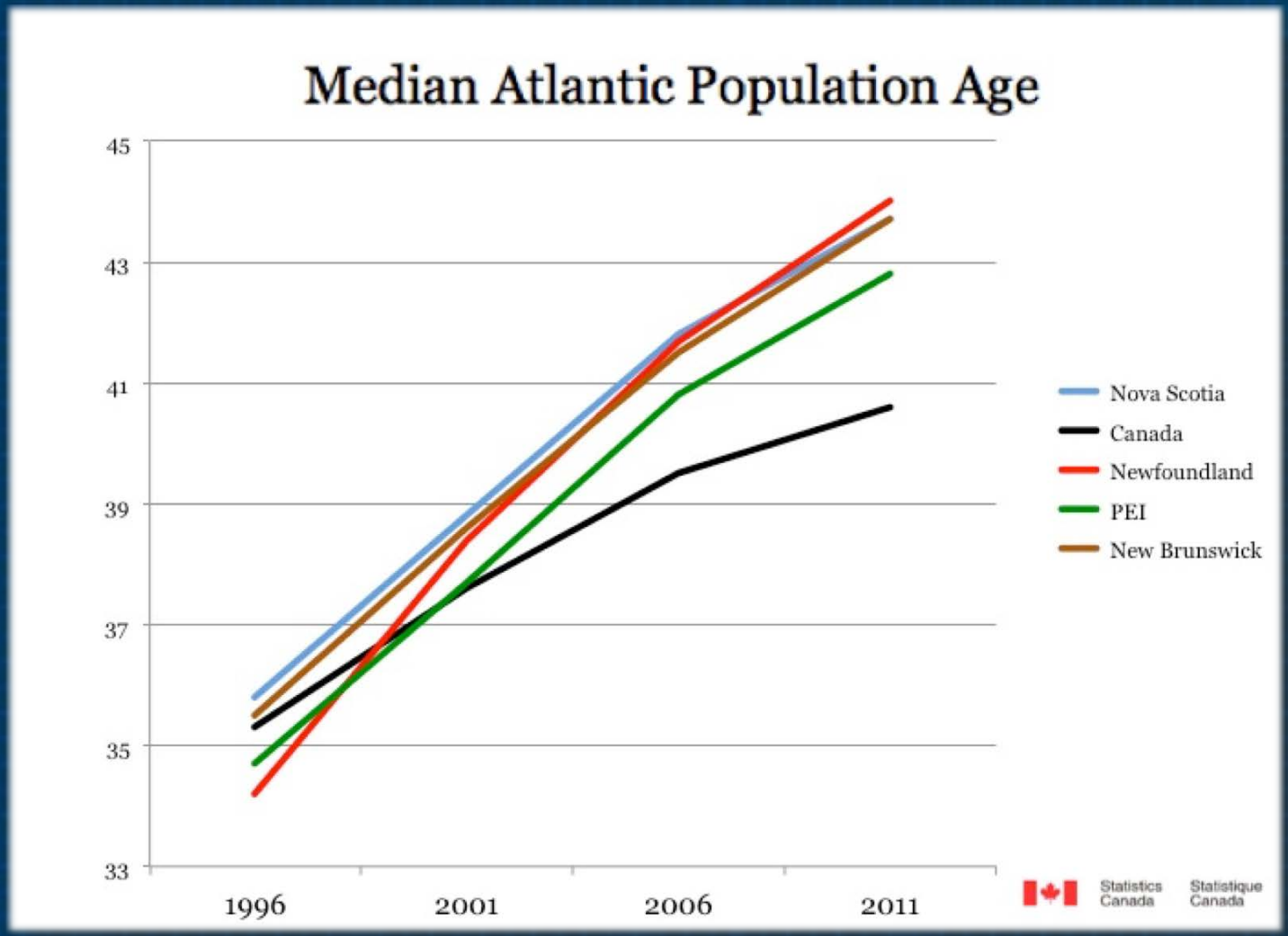
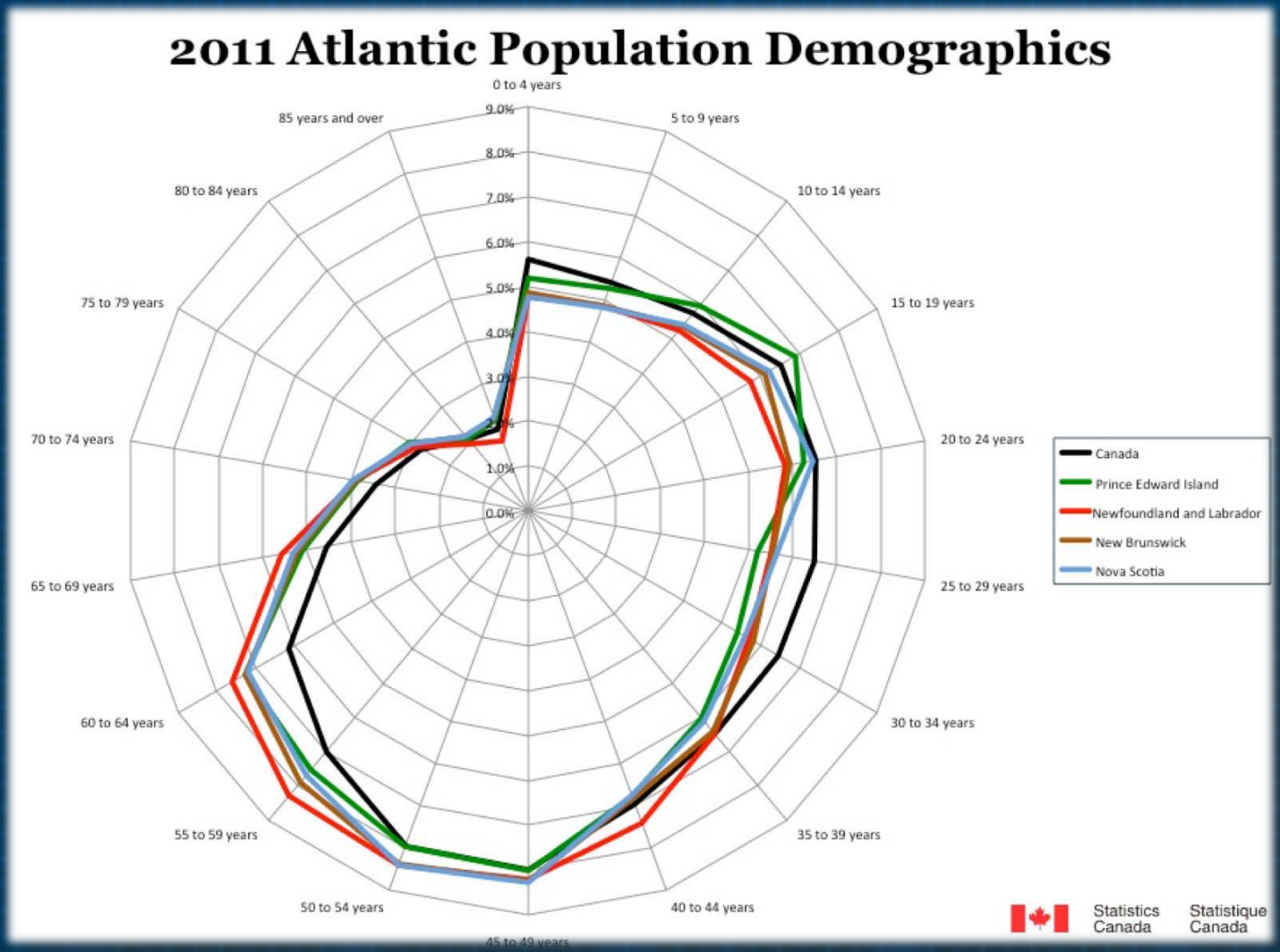
Atlantic Population Realities



Atlantic Population Realities



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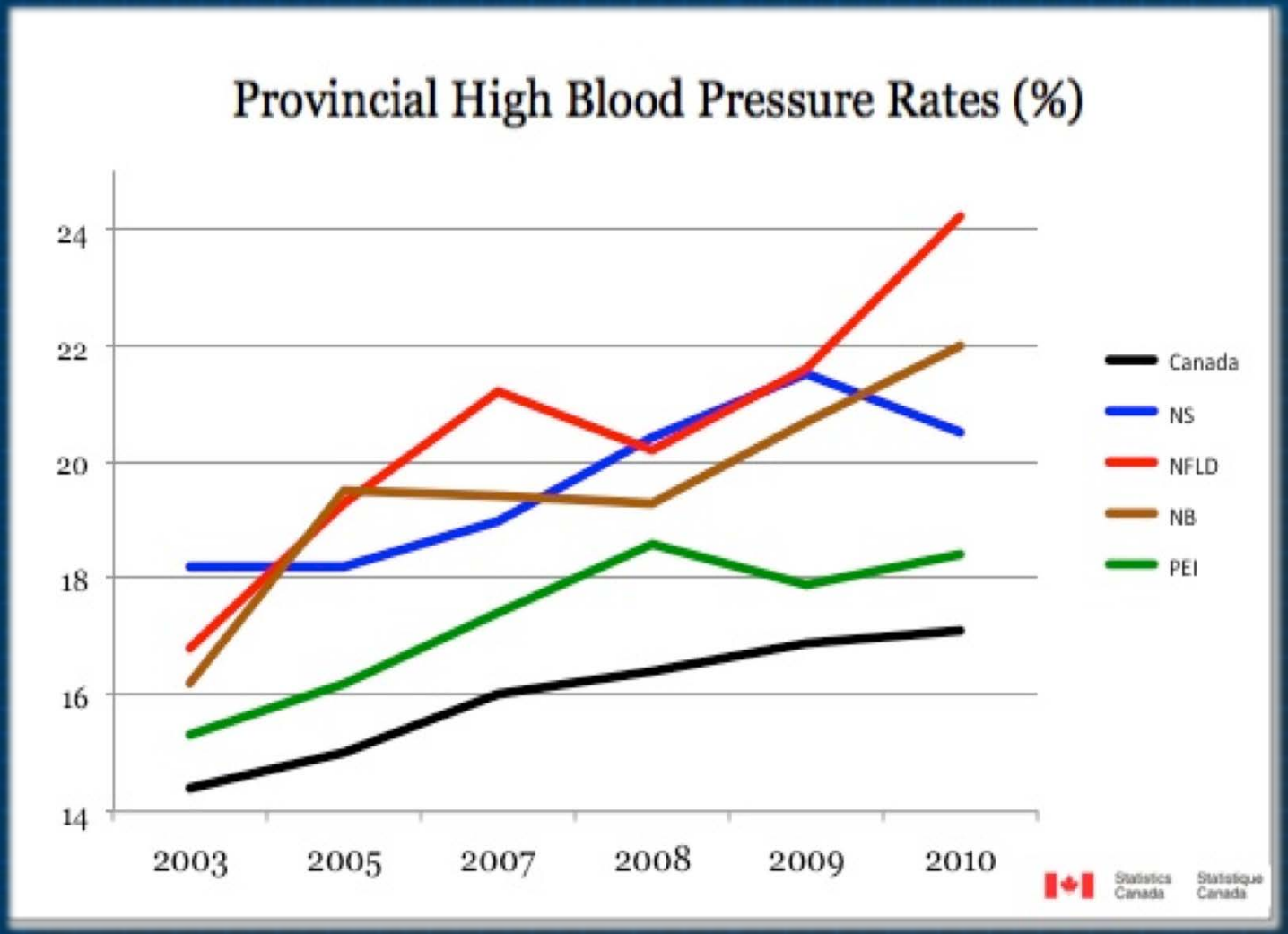
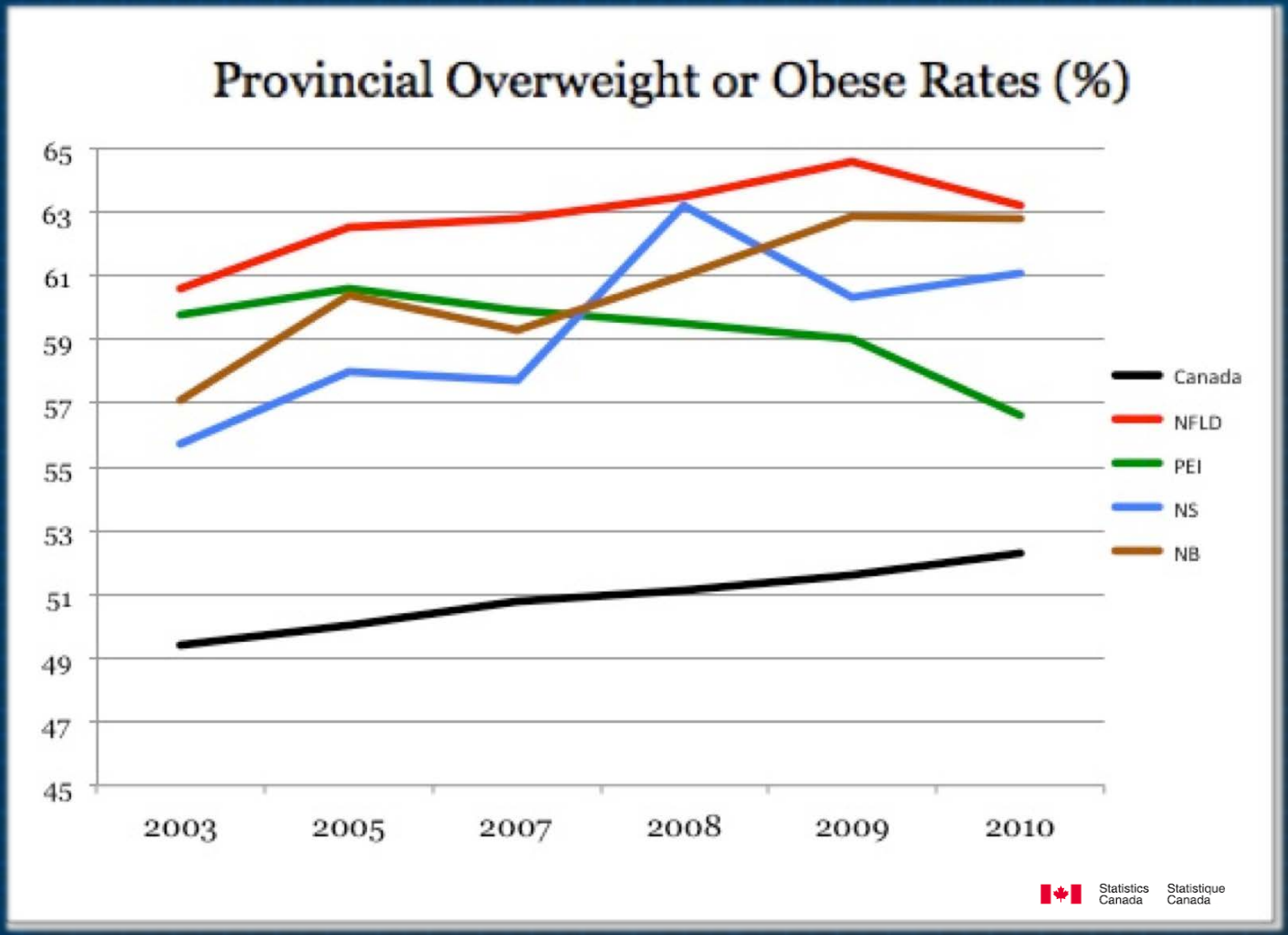
Atlantic Population Realities



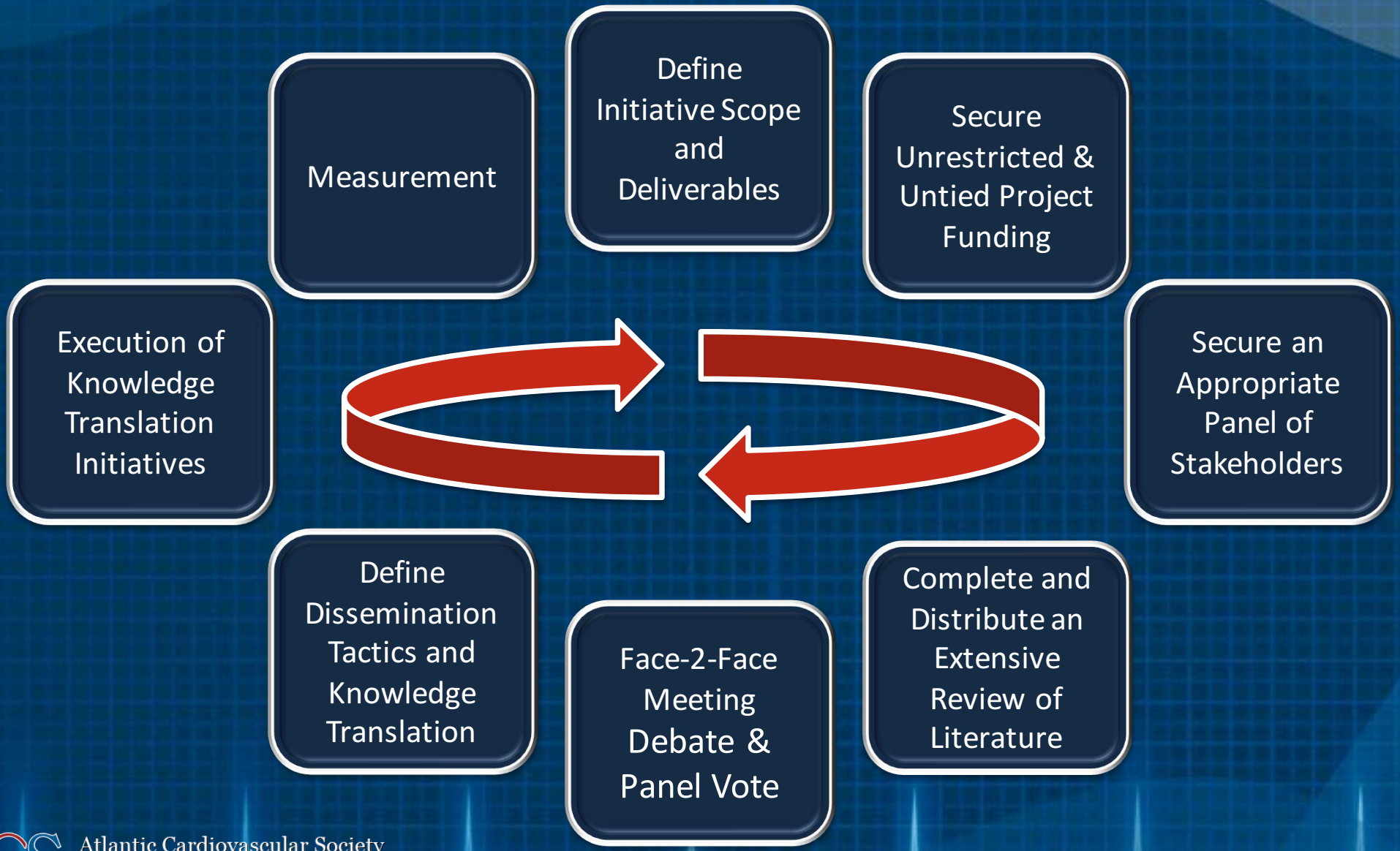
Atlantic Population Realities



Practical & Appropriate Oral Anticoagulant Use Initiative

This initiative represents an opportunity to standardize care for non-valvular AF patients throughout Atlantic Canada

Recommendation Creation Process



Atlantic Cardiovascular Society

OAC Initiative Overview

Unrestricted/untied grants were received from……

No Industry partners participated in or influenced Panel decision-making.

OAC Initiative Panel

Dr. David Marr	Cardiology	N.B.
Dr. Jafna Cox	Cardiology	N.S.
Dr. Sean Connors	Cardiology	N.L.
Dr. Ron Bourgeois	Cardiology	N.B.
Dr. Lenley Adams	Cardiology	P.E.I
Dr. Gregg McLean	Neurology	N.B.
Dr. Martin MacKinnon	Nephrology	N.B.
Dr. David Anderson	Hematology	N.S.
Dr. Tara Rector	Emergency Medicine	N.L.
Dr. Mohamed Ravalia	Primary Care	N.L
Rachel Harris (Pharm.D)	Pharmacy	N.B.
Dr. Gord Gubitz	Heart & Stroke	Atlantic
Dr. Carl Abbott	Patient Representative	N.S.
Kathy Harrigan	CVHNS	N.S.
Michel Boucher	CADTH	National

GRADE Recommendation Levels

Grade of Recommendation	Clarity of risk/benefit	Implications
Strong recommendation. High quality evidence	Benefits clearly outweigh risk and burdens, or vice versa	Strong recommendation, can apply to most patients in most circumstances without reservation
Strong recommendation. Moderate quality evidence	Benefits clearly outweigh risk and burdens, or vice versa	Strong recommendation, likely to apply to most patients
Strong recommendation. Low quality evidence	Benefits appear to outweigh risk and burdens, or vice versa	Relatively strong recommendation; might change when higher quality evidence becomes available
Weak recommendation. High quality evidence	Benefits closely balanced with risks and burdens	Weak recommendation, best action may differ depending on circumstance or patients or societal values
Weak recommendation. Moderate quality evidence	Benefits closely balanced with risks and burdens, some uncertainty in the estimates of benefits, risks and burdens	Weak recommendation, alternative approaches likely to be better for some patients under some circumstances
Weak recommendation. Low quality evidence	Uncertainty in the estimates of benefits, risks and burdens; benefits may be closely balanced with risks and burdens	Very weak recommendation; other alternatives may be equally reasonable

AF Screening & Risk Stratification

We recommend that Atlantic clinicians proactively screen all patients aged ≥ 65 years for AF via pulse palpation and/or cardiac auscultation; clinicians should then explore positive pulse diagnoses by ECG.

Screening for the co-morbidities of hypertension, hyperthyroidism (via Serum TSH) and diabetes is also recommended for patients exhibiting a positive pulse diagnosis

AF Screening & Risk Stratification

We recommend that the risk stratification tool CHA_2DS_2-VASc should be preferentially used (versus $CHADS_2$) to predict the need for OAC therapy for stroke prophylaxis in Atlantic patients with AF.

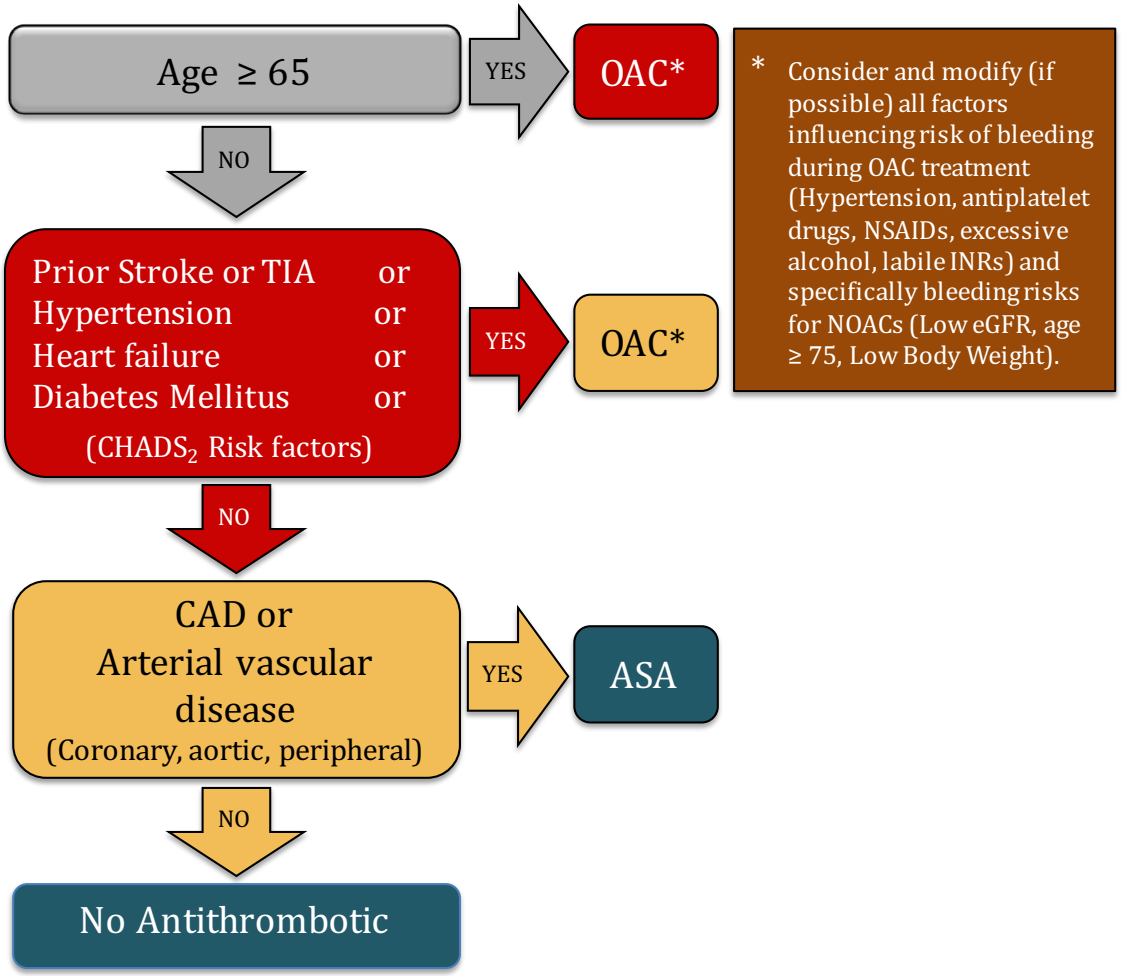
In addition, the new CCS algorithm CHADS-65 is an efficient and easy means through which a physician can simply determine a patient's eligibility for oral anticoagulant therapy. (Verma 2014)

CHA_2DS_2-VASc	Score
Congestive Heart Failure / Left Ventricular Dysfunction (EF<40%)	1
Hypertension	1
Age ≥ 75 Years	2
Diabetes Mellitus	1
Prior Stroke or TIA or Systemic Embolism	2
Vascular Disease (prior MI, PAD, aortic plaque)	1
Age > 65 but < 75	1
Sex category – Female	1

CHA_2DS_2-VASc Score	Stroke Rate Per Year (%/yr.)
0	0.0
1	1.3
2	2.2
3	3.2
4	4.0
5	6.7
6	9.8
7	9.6
8	6.7
9	15.2

Yip GB, *et al* Chest 2010; 137:263-72

CCS Algorithm for OAC Therapy in AF



Verma et. al., 2014 Focused Update of the Canadian Cardiovascular Society Guidelines for the Management of Atrial Fibrillation, Canadian Journal of Cardiology, Volume 30, Issue 10, October 2014.

Atlantic Cardiovascular Society

AF Screening & Risk Stratification

Score	Recommendation	Strength
0	**We recommend** that no OAC therapy be prescribed. (Skanes 2012, Camm 2012) Depending upon the clinical situation, a patient with CHA_2D_2S-VASC = 0 can receive ASA or no therapy (Skanes 2012, Lindsay 2012)	Strong Recommendation; Moderate Quality Evidence
1	**We suggest** prescribing treatment with an OAC based on the assessment of bleeding risk complications and patient preferences. (Camm 2012). **EXCEPTIONS:** – Patients at low risk of stroke (age <65 years, whether male or female) should not be considered for OAC therapy – In patients whose only risk factor is vascular disease, ASA should be considered.	Weak Recommendation; High Quality Evidence
≥ 2	**We recommend** treatment with an OAC. (Camm 2012) **We suggest** that if patients refuse OAC therapy the clinician can consider prescribing combination therapy including ASA 81mg plus clopidogrel 75mg daily* (where there is a low risk of bleeding) or ASA 75 – 325mg daily* (Recognizing that ASA alone is less efficacious). (Camm 2012, Olesen 2012, Connelly 2009) This treatment strategy should **NOT** be considered a routine alternative to OAC therapy. * If dual antiplatelet therapy is prescribed in the scenario above, consider gastric protection with a PPI to modify GI bleeding risk	Strong Recommendation; High Quality Evidence Weak Recommendation; Moderate Quality Evidence

AF Screening & Risk Stratification

We recommend using a bleeding risk scoring system to assess bleeding risk prior to prescribing OAC therapy.

We suggest that the HAS-BLED bleeding risk assessment score be used preferentially due to its validation and ease of use.

HAS-BLED Score for major bleeding risk

Risk Factor	Score
Hypertension	1
Abnormal renal/hepatic function	1 (each)
Stroke	1
Bleeding	1
Labile INRs	1
Elderly (≥ 65 years)	1
Drugs or Alcohol use	1 (each)

HAS-BLED Score	Bleeding rate (%/year)
0	1.13
1	1.02
2	1.88
3	3.74
4	8.70
≥ 5	Insufficient data

AF Screening & Risk Stratification

We recommend using a bleeding risk scoring system to assess bleeding risk prior to prescribing OAC therapy.

We suggest that the HAS-BLED bleeding risk assessment score be used preferentially due to its validation and ease of use.

PRACTICAL TIPS:

① Employing the ESC management process for patients with non-valvular AF places the initial emphasis on stroke reduction then bleeding risk:

   A. Establish the patient's risk of stroke via CHA_2DS_2-VASc

   B. Select the appropriate OAC therapy

   C. Calculate a HAS-BLED risk score; define & modify the patient's bleeding risk factors

② The HAS-BLED bleeding risk assessment tool should not be used to deny required therapy.

Selecting OAC Therapy

We suggest that one of the DOACs (dabigatran, rivaroxaban, or apixaban) should be prescribed preferentially over a VKA based on the DOAC's ease of use and superior clinical benefit, particularly related to ICH.

VALUES & PREFERENCES:

The Panel endorses the OAC prescribing recommendations published in the CCS Atrial Fibrillation guidelines (Skanes 2012), Canadian Best Practice Recommendations for Stroke Care (Lindsay 2012) and ESC Atrial Fibrillation Guidelines (Camm 2012). In addition, the Panel agrees with the recommendation that the preference for DOACs over VKAs is less relevant for patients on VKAs who have stable INRs (greater than 65% TTR) and no bleeding complications.

Chronic Kidney Disease

We suggest that NO DOAC be used in patients with a CrCl < 30 ml/min as there are no RCT data available. (This is a standardized and conservative approach for all DOAC's)

We suggest prescribing a VKA for patients with severe renal insufficiency who are not on dialysis (CrCl = 15 – 30 ml/min) and a VKA or nothing for patients with CrCl < 15 ml/min who are on dialysis, according to physician and patient preferences.

Chronic Kidney Disease

Monitor frequency of kidney function as defined in the table below.

A minimum of every **12** months[1]	Hemoglobin, renal and liver function
A minimum of every **6** months	If CrCl (eGFR) = 30 – 60 ml/min If prescribed dabigatran & > 75 years
A minimum of every **3** months	If CrCl = 15 – 30 ml/min
On indication	If the patient develops a medical condition which may impact renal or hepatic function

[1]CCS Grade - Strong Recommendation, Moderate Quality Evidence

Perioperative Management for Planned Procedures

Assessment

We suggest that a patient's bleeding risk (HAS-BLED) and stroke risk (CHA_2DS_2-VASc) should be assessed and documented prior to a planned surgical procedure.

In assessing risk, clinicians should consider kidney function, age, hypertension, history of bleeding complications, and concomitant medications. Physicians should proactively manage any modifiable risk factors. Thereafter, consider the procedural bleeding risk and manage OAC therapy accordingly.

Perioperative Management for Planned Procedures

Assessment

Planned Surgical Interventions & Bleeding Risk	Examples
Interventions not necessarily requiring the discontinuation of anticoagulation therapy	Dental Procedures Dental extractions (1 - 3 teeth) Periodontal surgery Incision of abscess Implant positioning Cataract or glaucoma intervention Endoscopy without surgery Superficial surgery (e.g. abscess incision small dermatologic excisions)
Interventions with LOW bleeding risk 2 day risk of major bleed 0% - 2%	Endoscopy with biopsy Electrophysiological study Radiofrequency catheter ablation for supraventricular tachycardia (including left-sided ablation via single transeptal puncture) Angiography Pacemaker or ICD implantation (Unless complex anatomical setting such as congenital heart disease)
Interventions with HIGH bleeding risk 2 day risk of major bleed 2% - 4%	Complex left-sided ablation (Pulmonary vein isolation; VT ablation) Spinal or epidural anesthesia; lumbar puncture Thoracic surgery Abdominal surgery Major orthopedic surgery Liver biopsy Prostate or bladder biopsy Transurethral prostate resection Kidney biopsy

Adapted from Heidbuchel et. al., Europace (2013) 15, 625–651

Perioperative Management for Planned Procedures
Management (DOAC)

We suggest that perioperative patients with AF who are prescribed DOAC therapy be managed according to the strategies below. DOAC therapy should reach trough concentrations (occurring 12 - 24 hours after the last dose depending upon *bid* or *OD* regimen) for planned surgical procedures that may not necessarily require discontinuation (Heidbuchel 2013)

Timing the Withdrawal of DOAC Therapy Preoperatively

	Dabigatran		Rivaroxaban		Apixaban	
	LOW bleeding risk procedure	HIGH bleeding risk procedure	LOW bleeding risk procedure	HIGH bleeding risk procedure	LOW bleeding risk procedure	HIGH bleeding risk procedure
CrCl ≥ 80 mL/min	≥ 24 h	≥ 48 h	≥ 24 h	≥ 48 h	≥ 24 h	≥ 48 h
CrCl ≥ 50 - ≤ 80 mL/min	≥ 36 h	≥ 72 h	≥ 24 h	≥ 48 h	≥ 24 h	≥ 48 h
CrCl ≥ 30 - ≤ 50 mL/min	≥ 48 h	≥ 96 h	≥ 24 h	≥ 48 h	≥ 24 h	≥ 48 h

* Refer to Table 5 for a categorization of bleeding risk associated with procedural type
* Stopping DOAC therapy is ultimately based on the physician's clinical judgment
* Data is referenced from each DOAC's Canadian Product Monograph

Assess Creatinine Clearance

Perioperative Management for Planned Procedures
Management (DOAC)

Bridging therapy may not be necessary for non-valvular AF patients who are prescribed DOAC therapy due to the speed of offset & onset. Short-term cessation and reinitiating therapy must be synchronized with the procedure.

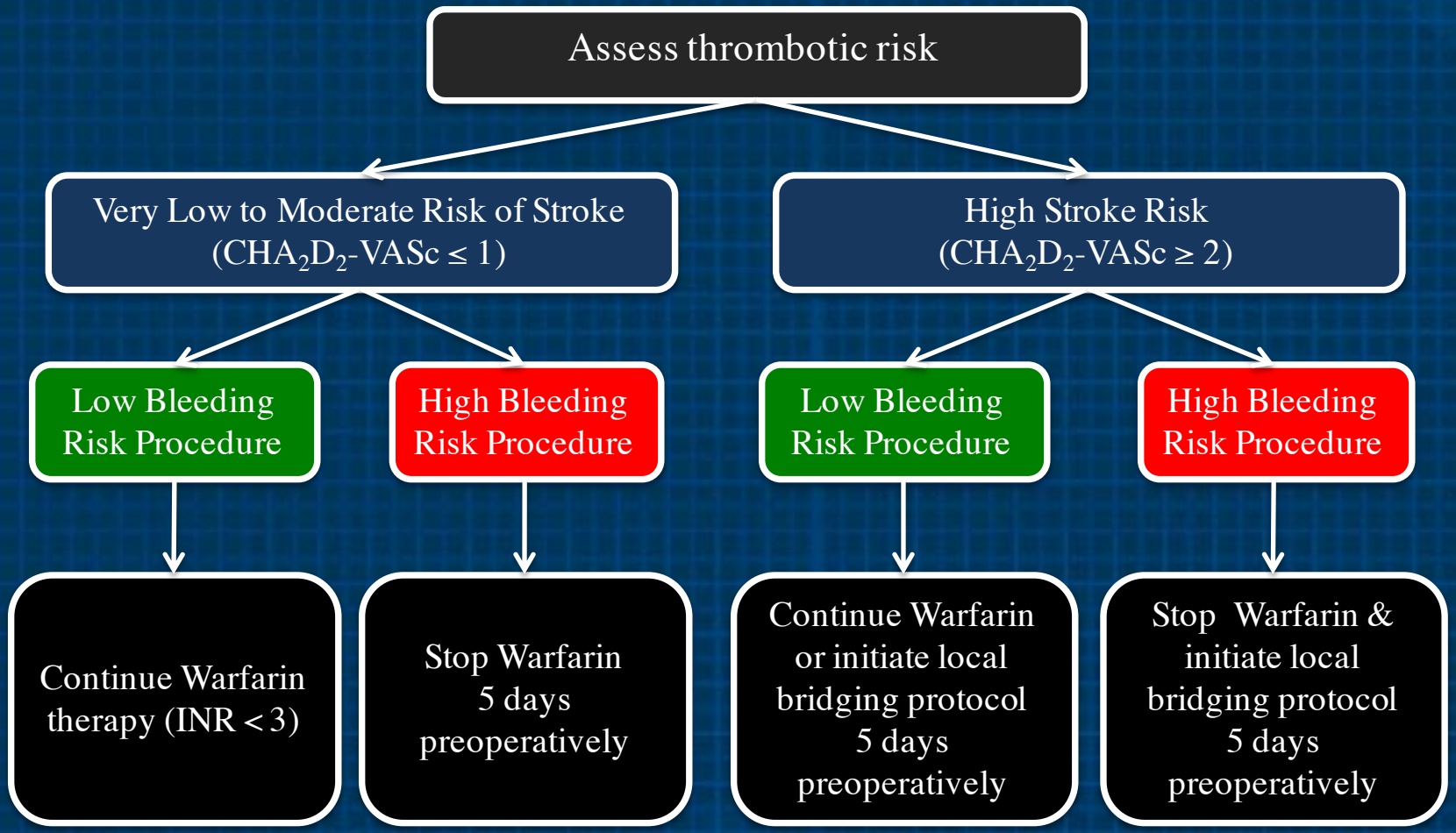
Renal function should be reassessed after surgery prior to restarting therapy as the dose or even suitability of using a DOAC will depend on the actual CrCl.

If the patient is at low bleeding risk, DOAC therapy can be reinitiated within 24 hours post-operatively. Patient's at higher bleeding risk can be reinitiated 48 - 72 hours post-operatively unless still actively bleeding.

Consider bridging therapy in ANY post-operative patient who's OAC therapy can not be reinitiated within 72 hours based on undue delay.

Perioperative Management for Planned Procedures

Management (VKA)



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The BRIDGE Study, published in June 2015 (Douketis, 2015), was not reviewed by the Primary Panel. This study addresses the need for bridging anticoagulation during warfarin interruption; clinicians will need to consider how to incorporate study findings into their practices.

Managing non life-threatening bleeding on an DOAC

Time is the most important DOAC antidote; therefore, it is important to establish both the dosing regimen and last dose taken to determine peak and trough plasma concentrations.

We suggest that the clinician estimate the normalization of hemostasis at 12 to 48 hours for dabigatran (depending on renal function) and 12 to 24 hours for rivaroxaban and apixaban.

Normalization Estimate of Hemostasis			
Dabigatran		Rivaroxaban	Apixaban
CrCl ≥ 80 ml/min	12 - 24 hours	12 - 24 hours	12 - 24 hours
CrCl ≥ 50 ≤ 80 ml/min	24 - 36 hours		
CrCl ≥ 30 ≤ 50 ml/min	36 - 48 hours		

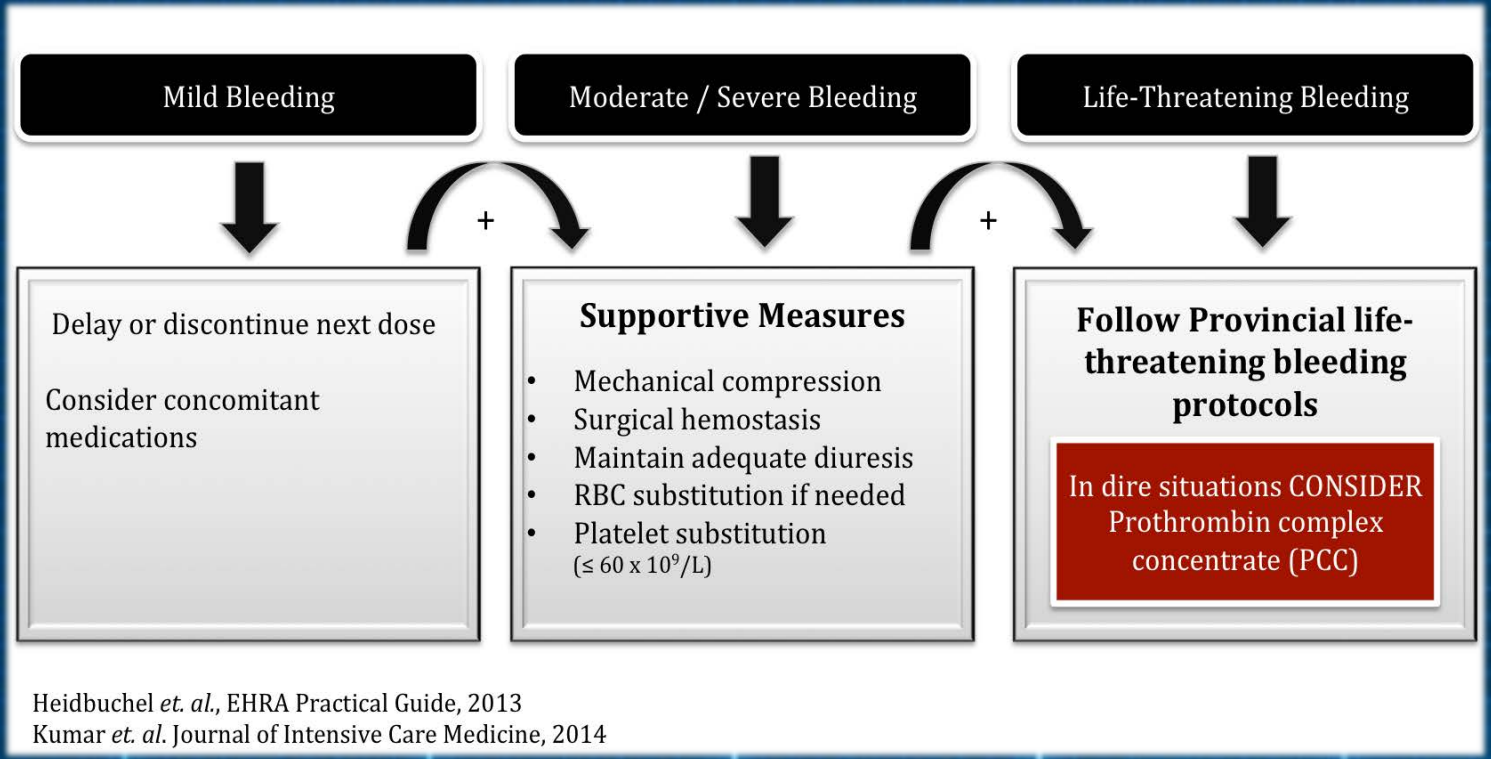
H. Heidbuchel et al. European Heart Journal, 2013

Managing non life-threatening bleeding on an DOAC

We suggest that an aPTT assay be used to qualitatively determine if dabigatran is actively circulating, a PT assay can be used for rivaroxaban. There is no clear method for apixaban; however, the Rotachrom anti-FXa assay may be of value.

Managing life-threatening bleeding on an DOAC

We suggest that clinicians follow Provincial life-threatening bleeding protocols until antidotes for DOACs are available. Despite the absence of any clinical trial evidence, PCC may be CONSIDERED to control life threatening bleeding.



Heidbuchel *et. al.*, EHRA Practical Guide, 2013
Kumar *et. al.* Journal of Intensive Care Medicine, 2014

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Acute management of patients with non-valvular AF who are already established on OAC therapy presenting with a definite ACS

GENERAL PRINCIPLES

Administration of fibrinolytic, antiplatelet and antithrombin therapy to ACS patients currently taking anticoagulant therapy should **ONLY** be considered if the ischemic-reducing benefits are felt likely to outweigh the bleeding risks.

DOAC and warfarin therapy should generally be withheld during the acute in-patient phase of ACS management while patients are receiving usual ACS antiplatelet and antithrombin therapies.

Anticoagulant therapy should generally be restarted prior to discharge; the timing and type of therapy will depend upon many factors but in particular the timing and outcome of cardiac catheterization.

Acute management of patients with non-valvular AF who are already established on OAC therapy presenting with a definite ACS

ORAL ANTIPLATELET THERAPY

In the absence of allergy or active bleeding, the majority of patients with definite ACS (STEMI or NSTEACS) should receive an immediate combination of oral antiplatelet therapy with ASA (at least 162mg if ASA naïve then 81mg once daily) and clopidogrel (300mg oral loading dose if clopidogrel naïve then 75mg once daily). {*Clopidogrel loading dose should generally be omitted in STEMI patients >75 years receiving fibrinolytic therapy and in other patients felt to be at increased risk of intracranial hemorrhage*}

Clopidogrel is the preferred $P2Y_{12}$ receptor for acute administration to ACS patients currently receiving DOAC or VKA therapy; ticagrelor and prasugrel are generally not recommended in the acute phase management.

Acute management of patients with non-valvular AF who are already established on OAC therapy presenting with a definite ACS

FIBRINOLYTIC THERAPY IN PATIENTS WITH NON-VALVULAR AF AND STEMI

STEMI patients taking **maintenance DOAC therapy** who do not have access to timely primary PCI should generally receive immediate fibrinolytic therapy and usual adjunctive antithrombin therapy.

STEMI patients taking **maintenance VKA therapy** who do not have access to timely primary PCI should have their INR checked urgently. The INR result and overall risk of bleeding should be factored into the decision whether or not to administer fibrinolytic and adjunctive antithrombin therapy. *{Excessive anticoagulation with warfarin is strongly associated with an increased risk of ICH in STEMI patients receiving fibrinolytic therapy, especially in older patients with an INR ≥ 4. (Brass, 2000)}*

Fibrinolytic therapy should ***not*** be administered to STEMI patients taking maintenance DOAC or VKA therapy in whom the bleeding risks are felt to be prohibitive; transfer for primary PCI should be considered even if a longer than normal treatment delay is anticipated.

Acute management of patients with non-valvular AF who are already established on OAC therapy presenting with a definite ACS

PRIMARY PCI IN PATIENTS WITH NON-VALVULAR AF AND STEMI

STEMI patients taking **maintenance DOAC therapy** who have access to timely cardiac catheterization should general be referred for urgent primary PCI; radial artery access is strongly preferred. The recent administration of DOAC therapy should be taken into account when choosing appropriate adjunctive antiplatelet and antithrombin therapy.

STEMI patients taking **maintenance VKA therapy** who have access to timely cardiac catheterization should generally be referred for urgent primary PCI. The INR should be checked urgently but this should not delay PCI; radial access is strongly preferred. The INR result should be taken into account when choosing appropriate adjunctive antiplatelet and antithrombin therapy.

Management of patients with non-valvular AF on OAC therapy who are undergoing PCI post-ACS or for stable CAD

Patients with non-valvular AF who cannot discontinue OAC after undergoing PCI following an ACS or for stable CAD will require a period of treatment with both OAC and oral antiplatelet therapy. The optimal combination and duration of treatment should be individualized and take account of the risk of stroke, bleeding and ischemia/stent thrombosis. Discussion should preferably commence before PCI and involve the Interventional Cardiologist who performs the procedure.

Managing OAC therapy and thrombolysis for acute ischemic stroke

We suggest that AF patients on a VKA and diagnosed with an acute ischemic stroke NOT be thrombolyzed if INR > 1.7

We recommend that until such time when there is a commercially available and validated assessment tool to establish circulating DOAC levels, and until such time it is reliably known what these levels mean clinically, tPA should not routinely be administered to patients on DOACs presenting with acute ischemic stroke.

Reinitiating OAC therapy after a TIA or acute ischemic stroke

We recommend that patients with transient ischemic attack and atrial fibrillation should begin oral anticoagulation (dabigatran, or rivaroxaban, or apixaban, or warfarin) immediately after brain imaging has excluded intracranial hemorrhage or large infarct.

For patients with an acute ischemic stroke, **we suggest** that the optimal timing to reinitiate OAC therapy is unclear; common practice is to wait 2 to 14 days and repeat brain imaging (CT or MRI) to rule out asymptomatic ICH before reinitiating OAC therapy. Infarct size and other clinical circumstances will factor when anticoagulation is reinitiated.

Switching OAC therapy after an acute ischemic stroke

We recommend switching to a DOAC if a patient's INR remains outside of the acceptable TTR.

If a stroke or TIA is diagnosed while a patient is on a VKA and their INR is consistently documented within therapeutic levels in the previous months, **we suggest** switching therapy from the VKA to a DOAC.

If a patient is diagnosed with a cardioembolic stroke while prescribed a DOAC, **we suggest** that medication adherence be assessed; relevant risk factors explored (e.g., hypertension, diabetes, dyslipidemia, smoking, obesity, sleep apnea) and non-cardioembolic mechanisms excluded before considering a switch to a VKA.

DOAC use in children

The safety and efficacy of DOACs have not been established in children (< 18 years) and no indication currently exists. We recommended that DOACs NOT be used.

OAC use during pregnancy

Thrombolytic and anticoagulant agents can induce teratogenic effects, placental hemorrhage, prematurity and potential fetal loss. We recommended that DOACs NOT be prescribed during pregnancy.

Please register with the Atlantic Cardiovascular Society to receive updates regarding this and subsequent projects that will be of clinical value.

www.ac-society.org

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