

# Nouveautés dans l'usage des NACOs

Lignes directrices de la société canadienne de cardiologie en matière de fibrillation auriculaire



**Laurent Macle, MD, FHRS**

Cardiologue, Électrophysiologiste

Professeur titulaire de Médecine, Université de Montréal

Chef du service d'électrophysiologie, Institut de Cardiologie de Montréal

# Objectifs

- Comparer les différents NACOs en fibrillation auriculaire.
- Revoir l'utilité et les dangers de l'AAS (en monothérapie ou en association).
- Connaitre l'utilité possible des NACOs en MCAS stable et maladie artérielle périphérique.

# **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

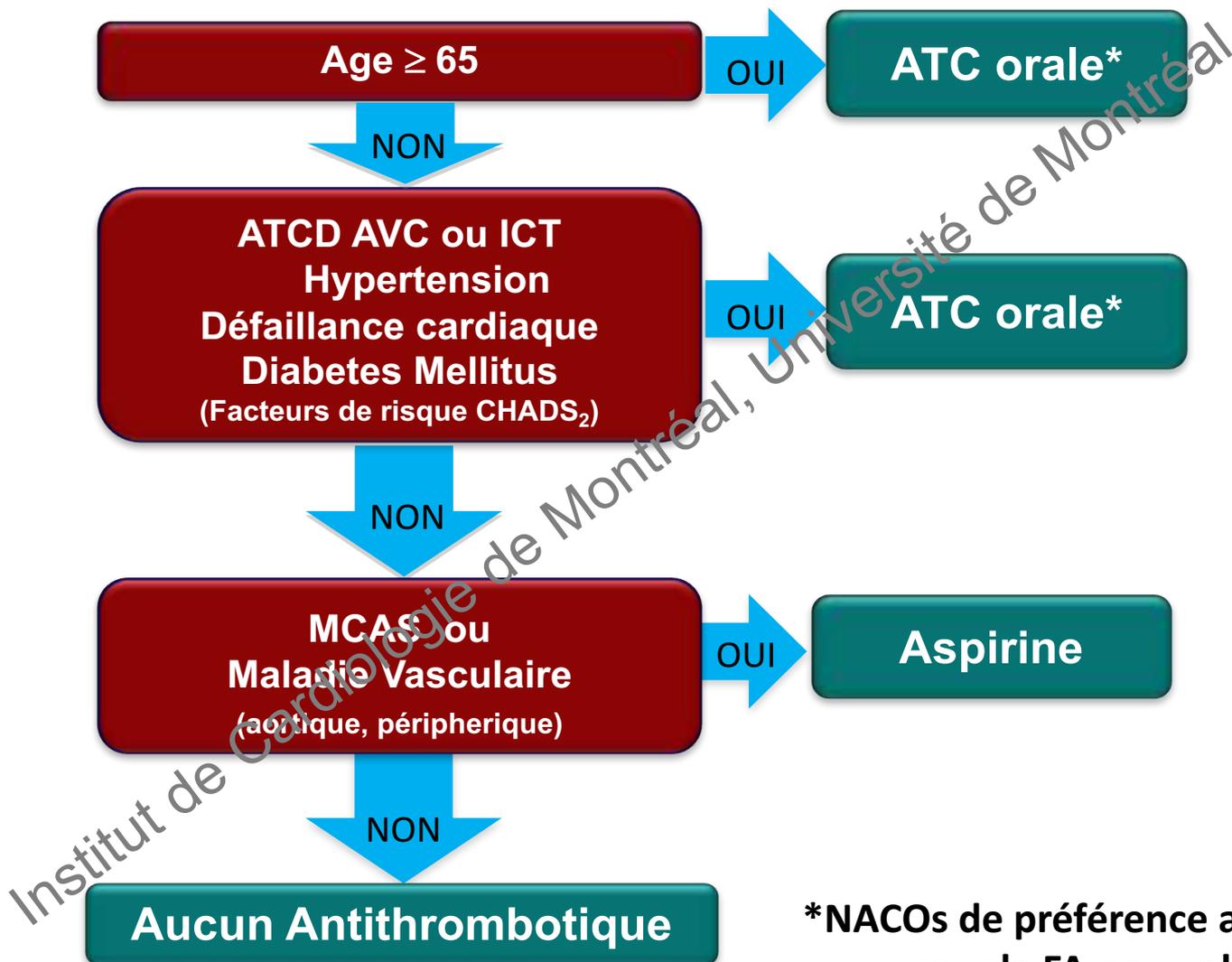
## **The 2014 Atrial Fibrillation Guidelines Companion: A Practical Approach to the Use of the Canadian Cardiovascular Society Guidelines**

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

# Algorithme CCS pour le traitement antithrombotique (CHADS65)



**\*NACOs de préférence au Coumadin pour la FA non-valvulaire**

# Risque Thrombo-embolique: Scores CHADS<sub>2</sub> et CHA<sub>2</sub>DS<sub>2</sub>-VASc

Rates of Ischemic Stroke According to Both CHADS<sub>2</sub> and CHA<sub>2</sub>DS<sub>2</sub>-VASc Scores

Score CHADS <sub>2</sub>	Risque annuel d'AVC
0	1.9 %
1	2.8 %
2	4.0 %
3	5.9 %
4	8.5 %
5	12.5 %
6	18.2 %

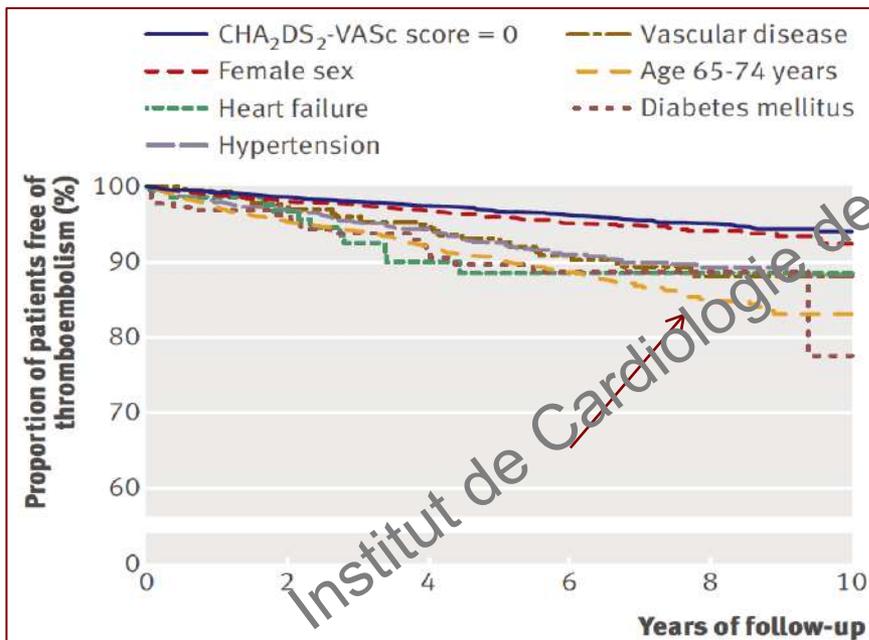
Gage et al. JAMA 2001; 285:2864-2870

Score	Adjusted stroke rate (%/year) based on CHA <sub>2</sub> DS <sub>2</sub> -VASc score
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

ESC 2012

# Validation of risk stratification schemes for predicting stroke and thromboembolism in patients with AF: a nationwide cohort study

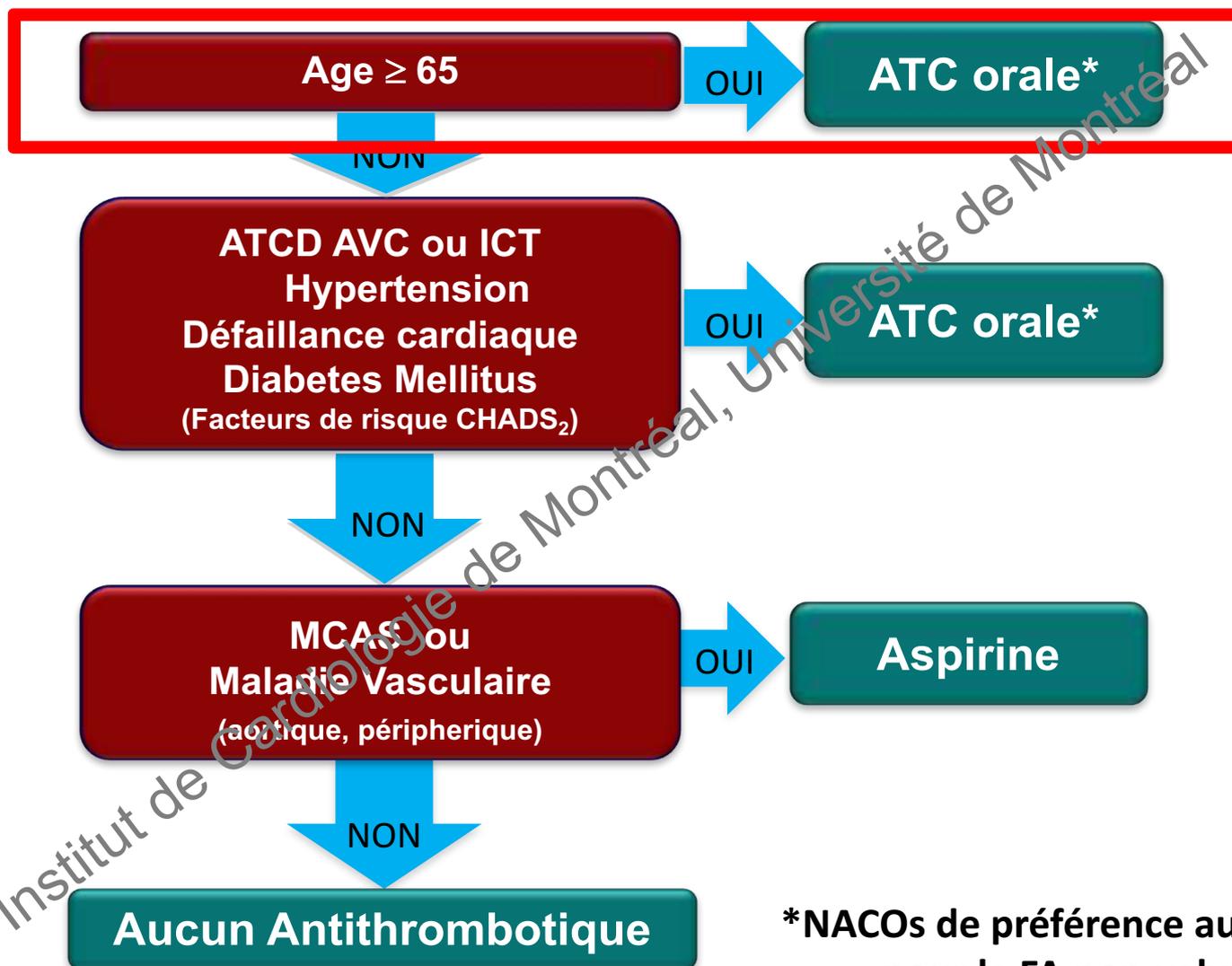
Cohorte Danoise; 73 538 patients, FA non-valvulaire, Non anticoagulés



## Hospital admission and death due to thromboembolism (5yr Follow-up)

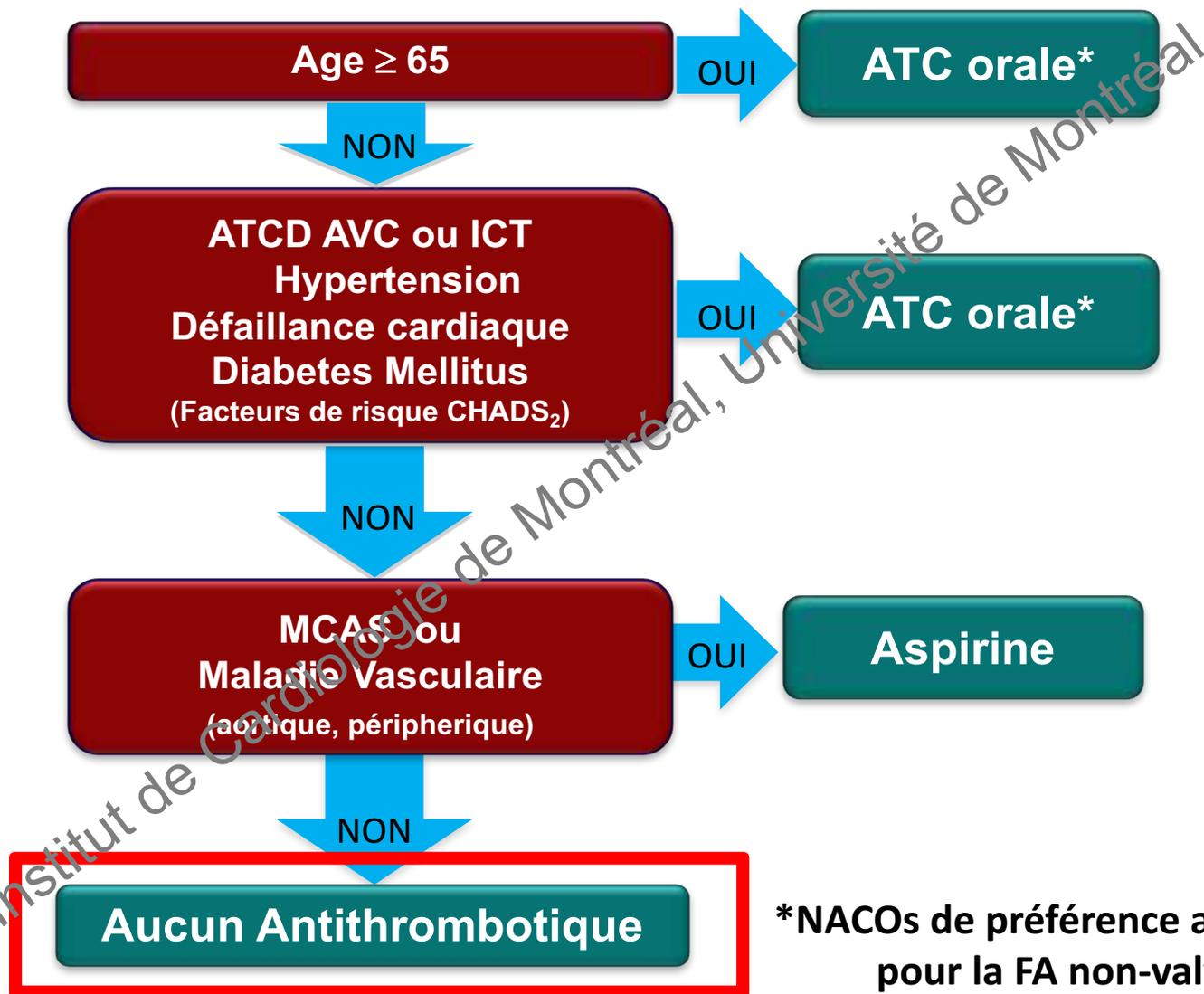
Risk factor	Annual risk	HR (95% CI)	P value
CHA <sub>2</sub> DS <sub>2</sub> -VASc = 0	0.69 %	1.0	
<b>CHA<sub>2</sub>DS<sub>2</sub>-VASc = 1</b>			
Heart Failure	2.35 %	3.39 (1.84-6.26)	<0.0001
Diabetes Mellitus	2.28 %	3.31 (2.00-5.46)	<0.0001
Hypertension	1.60 %	2.32 (1.75-3.07)	<0.0001
Age 65-74	2.13 %	3.07 (2.48-3.80)	<0.0001
Vascular disease	1.40 %	2.04 (1.29-3.22)	0.002
Female sex	0.86 %	1.25 (0.96-1.63)	0.10

# Algorithme CCS pour le traitement antithrombotique (CHADS65)



**\*NACOs de préférence au Coumadin pour la FA non-valvulaire**

# Algorithme CCS pour le traitement antithrombotique (CHADS65)

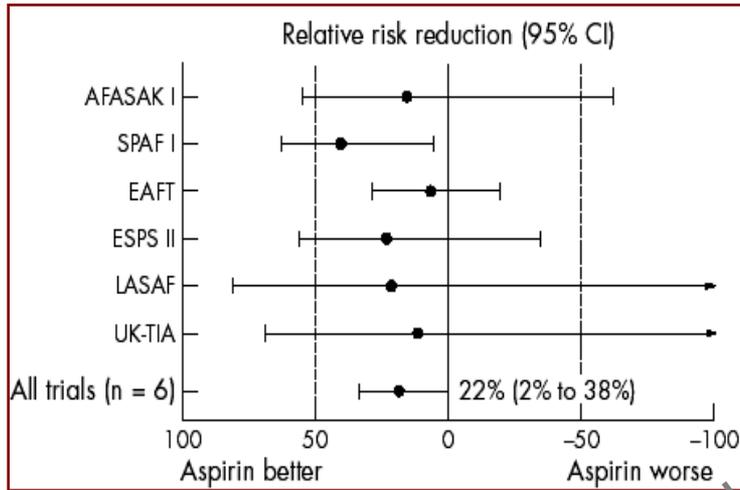


**\*NACOs de préférence au Coumadin pour la FA non-valvulaire**

# Aspirine vs Aucun Traitement Antithrombotique

## Méta-analyse

6 études, 3119 patients



Hart et al. Ann Int med 1999; 131:492-501

## Registre Danois (132,372 pts) Hazard Ratio vs Warfarin

	HR Stroke	HR Bleeding
ASA	1.81 (1.73-1.90)	0.93 (0.89-0.97)
No Treatment	1.86 (1.78-1.95)	0.84 (0.81-0.88)

Adapted from Olesen et al  
Thromb Haemost 2011;106:739-749

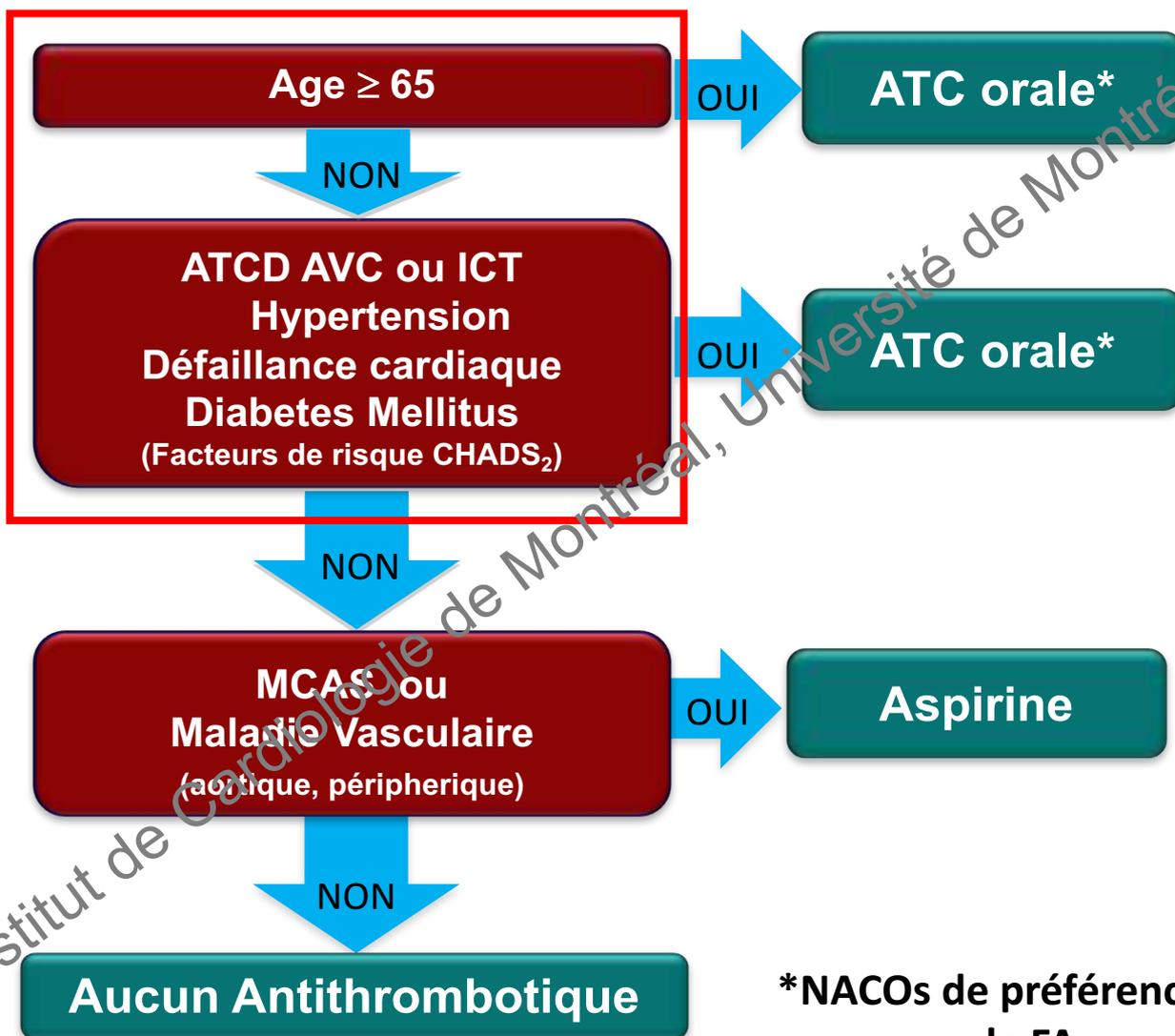
## Registre Suédois (115 185 pts)

Annualized incidence (95% CI) of outcome events according to propensity score matching

	ASA	No antithrombotic treatment	P
Ischaemic stroke	7.37% (7.11–7.63)	6.61% (6.37–6.86)	<0.001
Thrombo-embolic event	10.60% (10.29–10.92)	9.53% (9.24–9.83)	<0.001

« Our results suggest that patients with AF, who are not suitable for oral anticoagulation, may benefit more from abstaining from ASA, than from using it. »

# Algorithme CCS pour le traitement antithrombotique (CHADS65)

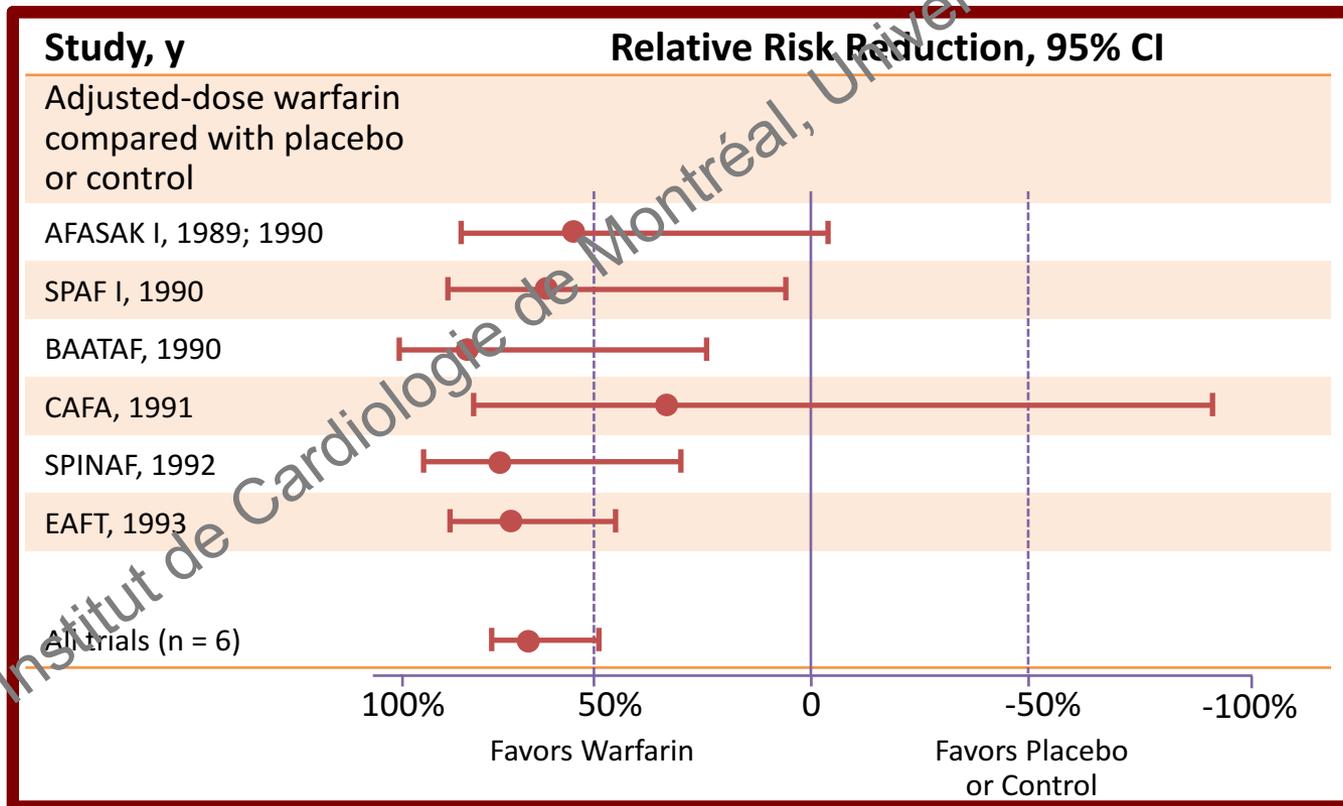


**\*NACOs de préférence au Coumadin pour la FA non-valvulaire**

# Anticoagulants: Coumadin

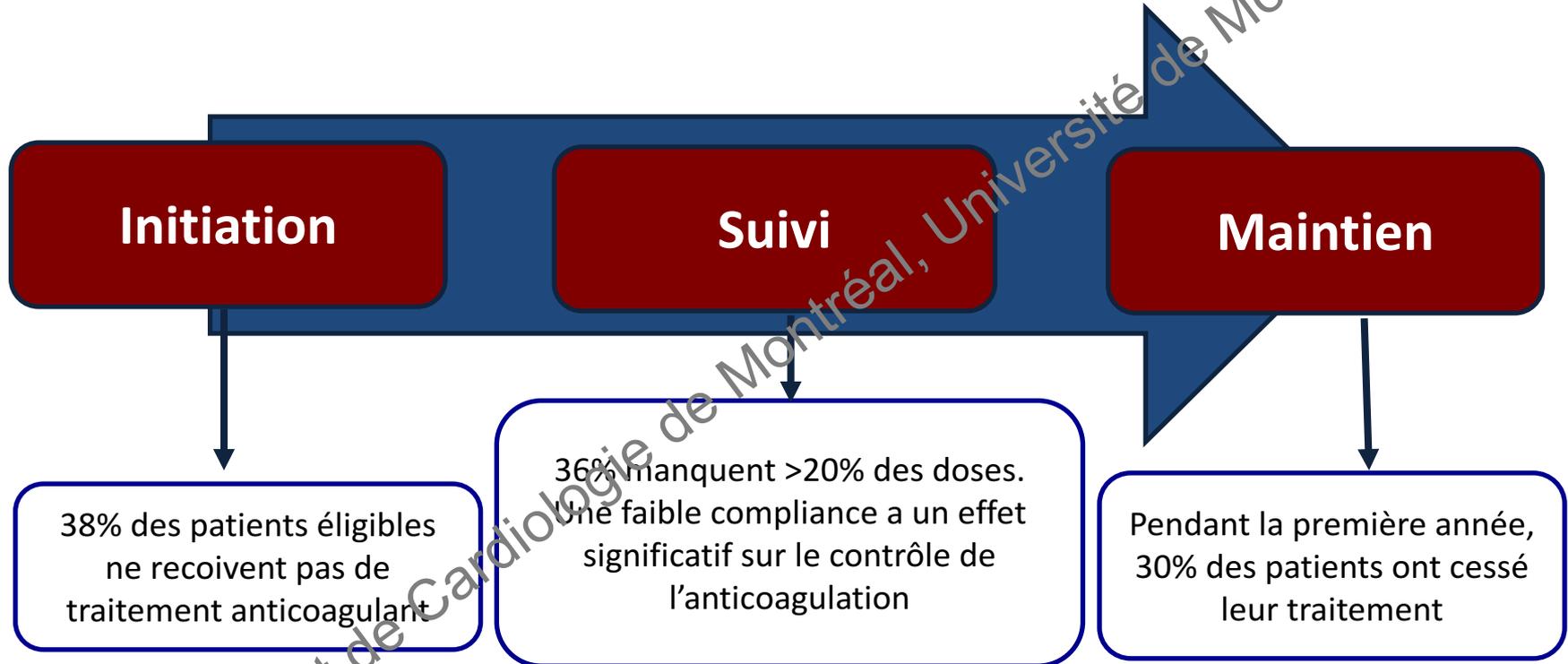
## Réduction du risque d'AVC en FA

Meta-analyses d'études cliniques randomisées avec Coumadin:  
Réduction de 64% des AVC chez les patients en FA



# Anticoagulants: Coumadin

## Problématique du traitement avec Coumadin



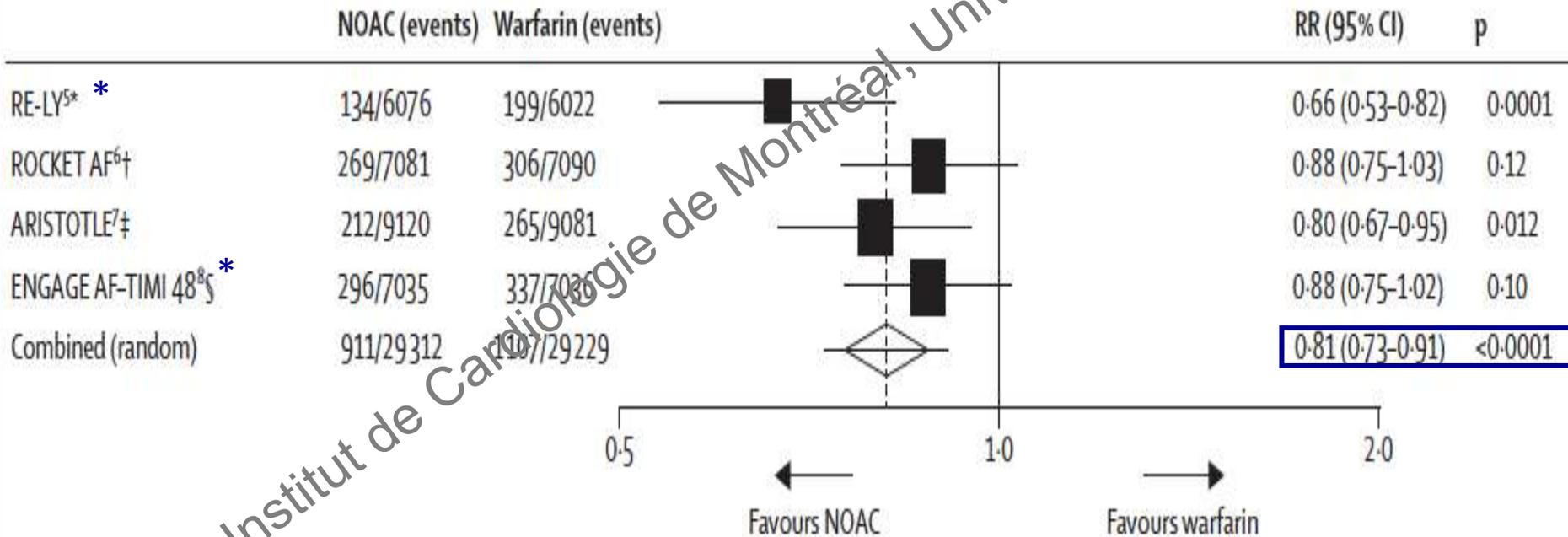
Institut de Cardiologie de Montréal, Université de Montréal

# Anticoagulants: NACOs

	RE-LY <sup>1</sup>	ROCKET AF <sup>2</sup>	ARISTOTLE <sup>3</sup>	ENGAGE-AF <sup>4</sup>
Number of patients	18 113	14 264	18 201	21 105
Primary goal	Non-inferiority	Non-inferiority	Non-inferiority	Non-inferiority
Study drug	Two dabigatran doses, double blind	Rivaroxaban, double blind	Apixaban, double blind	Two Edoxaban doses, double blind
Control	Warfarin, open label (INR : 2-3)	Warfarin, double blind (INR : 2-3)	Warfarin, double blind (INR : 2-3)	Warfarin, double blind (INR : 2-3)
Risk profile according to CHADS <sub>2</sub> score	<ul style="list-style-type: none"> <li>▪ ≤ 1 : 31,9 %</li> <li>▪ 2 : 35,6 %</li> <li>▪ ≥3 : 32,4 %</li> </ul> Mean = 2,1	<ul style="list-style-type: none"> <li>▪ ≤ 1 : &lt; 1 %</li> <li>▪ 2 : 13,0 %</li> <li>▪ ≥3 : 86,9 %</li> </ul> Mean = 3,5	<ul style="list-style-type: none"> <li>▪ ≤ 1 : 34,0 %</li> <li>▪ 2 : 35,8 %</li> <li>▪ ≥3 : 30,2 %</li> </ul> Mean = 2,1	<ul style="list-style-type: none"> <li>▪ ≤ 1 : &lt; 1%</li> <li>▪ 2 : 47%</li> <li>▪ ≥ 3: 53%</li> </ul> Mean = 2,8
Prior stroke	20%	55%	19%	28%
Median age	71,5 years	73 years	70 years	72 years
Median FU	2,0 years	1,9 year	1,8 year	2,8 years

# Comparison of the efficacy and safety of new oral anticoagulants with warfarin in patients with atrial fibrillation: a meta-analysis of randomised trials

## Prévention Thrombo-embolique (AVC et Embolies systémiques)

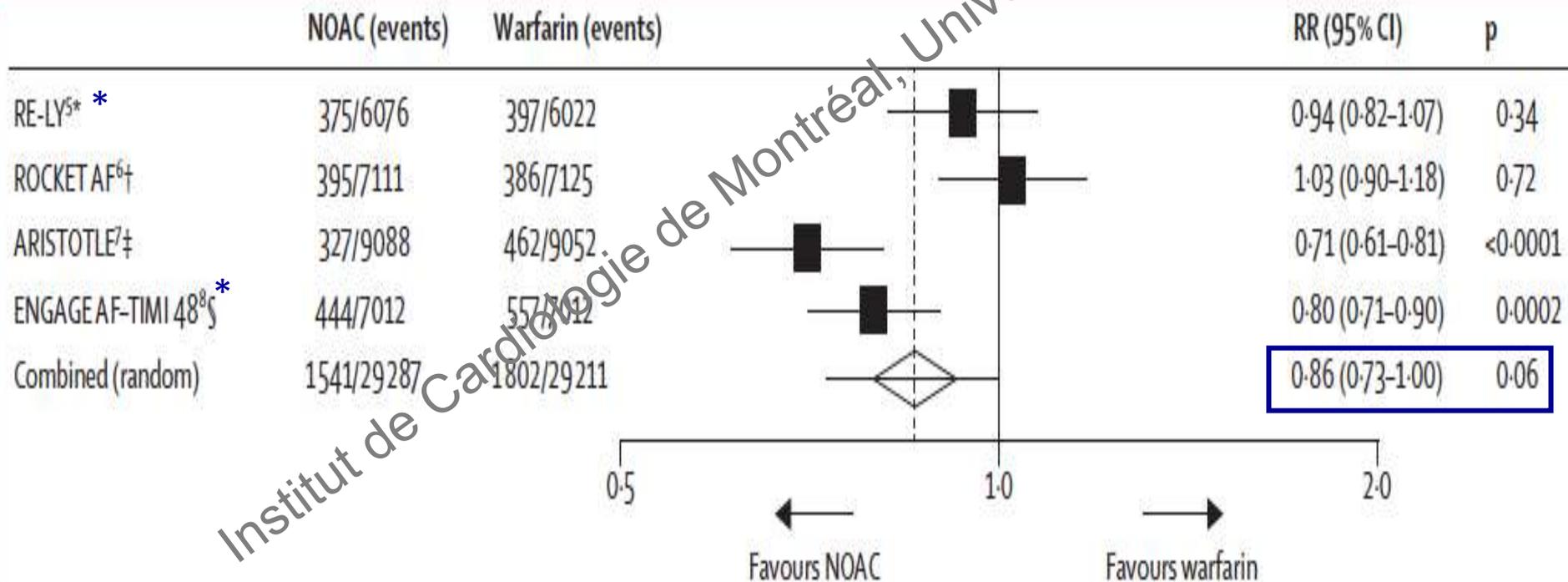


4 trials (\*using higher dose regimen)

N = 58,541 patients

# Comparison of the efficacy and safety of new oral anticoagulants with warfarin in patients with atrial fibrillation: a meta-analysis of randomised trials

## Hémorragies majeures

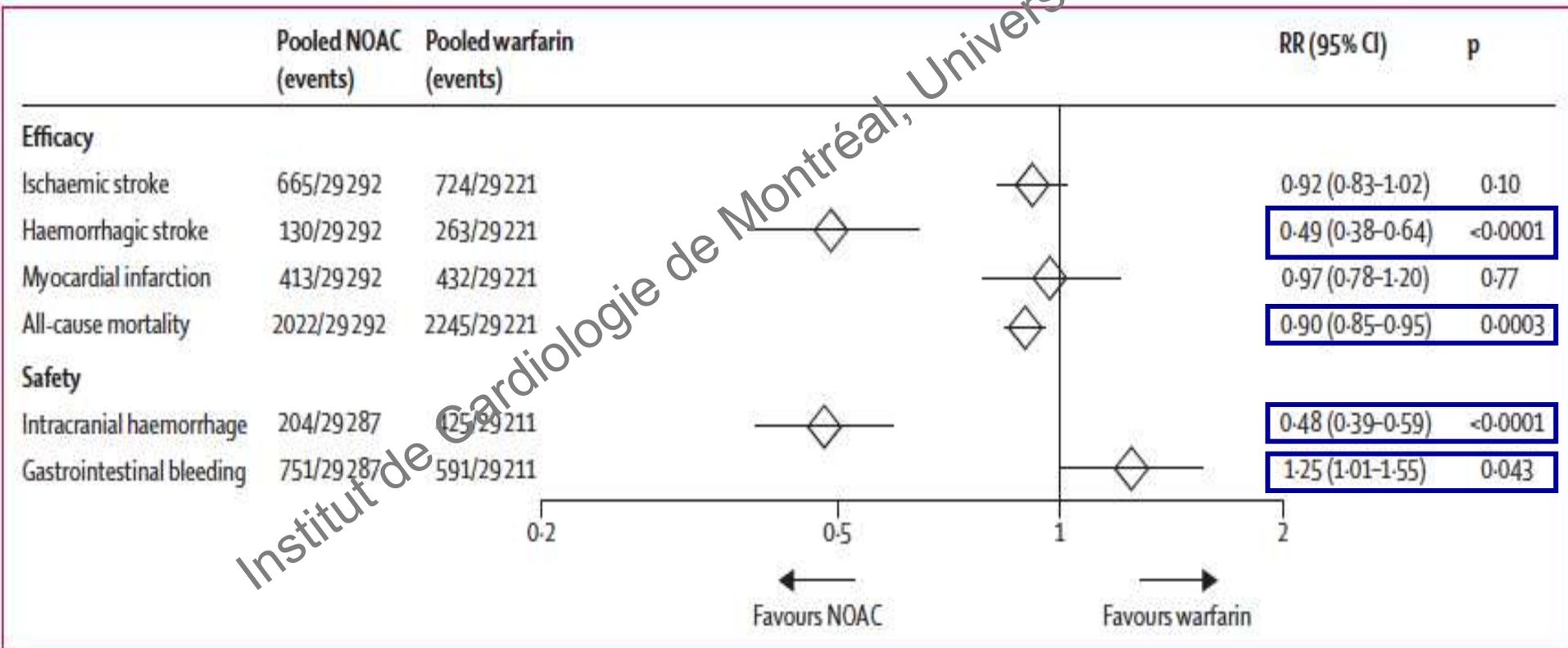


4 trials (\*using higher dose regimen)

N = 58,498 patients

# Comparison of the efficacy and safety of new oral anticoagulants with warfarin in patients with atrial fibrillation: a meta-analysis of randomised trials

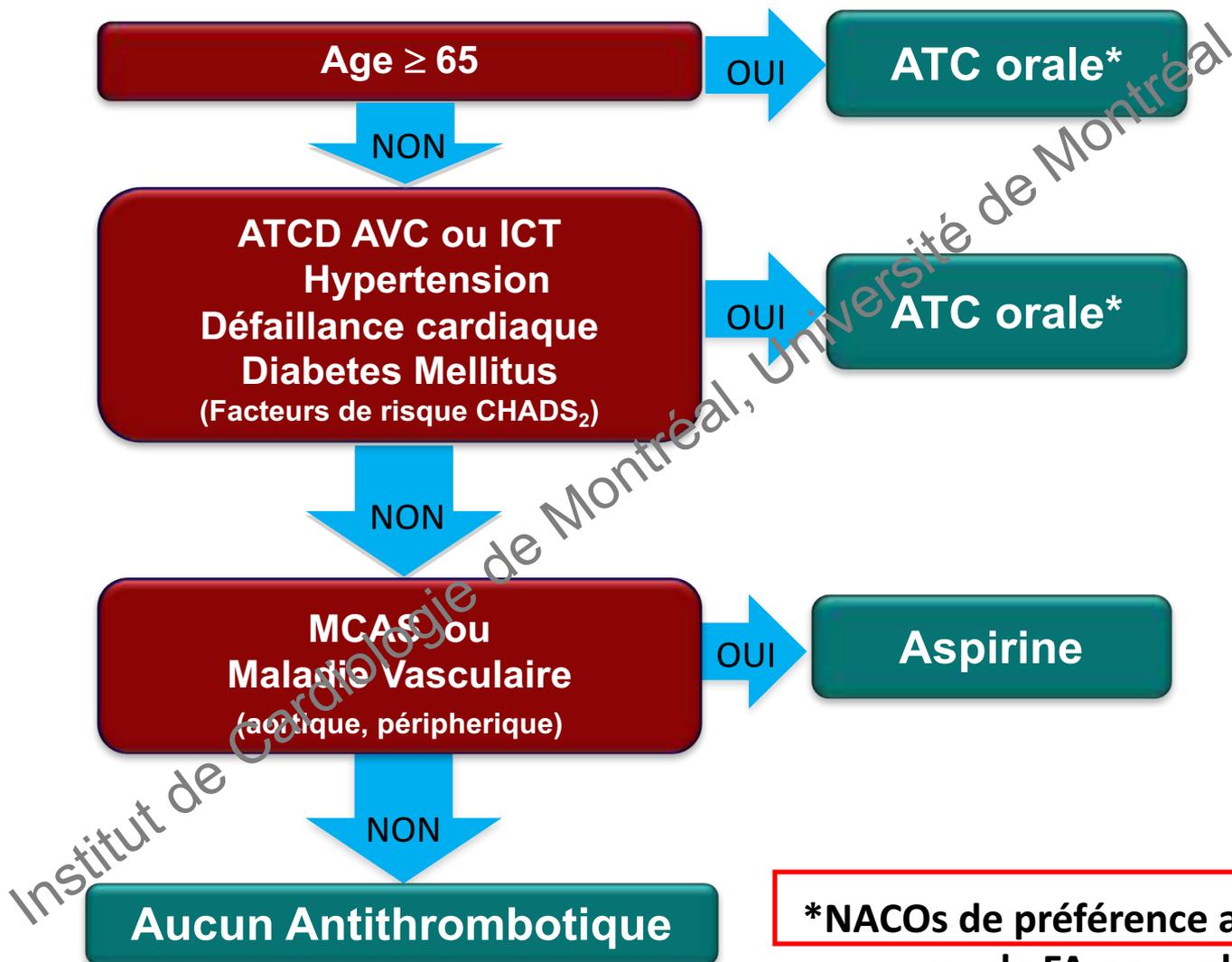
## Secondary efficacy and safety outcomes



4 trials (\*using higher dose regimen)

N = 58,498 patients

# Algorithme CCS pour le traitement antithrombotique (CHADS65)



**\*NACOs de préférence au Coumadin pour la FA non-valvulaire**

# 2016 ESC Guidelines for the management of atrial fibrillation developed in collaboration with EACTS

## Age $\geq 65$

Oral anticoagulation therapy to prevent thromboembolism should be considered in male AF patients with a CHA <sub>2</sub> DS <sub>2</sub> -VASc score of 1, considering individual characteristics and patient preferences.	IIa	B
Oral anticoagulation therapy to prevent thromboembolism should be considered in female AF patients with a CHA <sub>2</sub> DS <sub>2</sub> -VASc score of 2, considering individual characteristics and patient preferences.	IIa	B

« Importantly, age ( $\geq 65$  years) conveys a relatively high and continuously increasing stroke risk. »

## Aspirine

In male or female AF patients without additional stroke risk factors, anticoagulant or antiplatelet therapy is not recommended for stroke prevention.	III (harm)	B
Antiplatelet monotherapy is not recommended for stroke prevention in AF patients, regardless of stroke risk.	III (harm)	A

## NACO > Warfarin

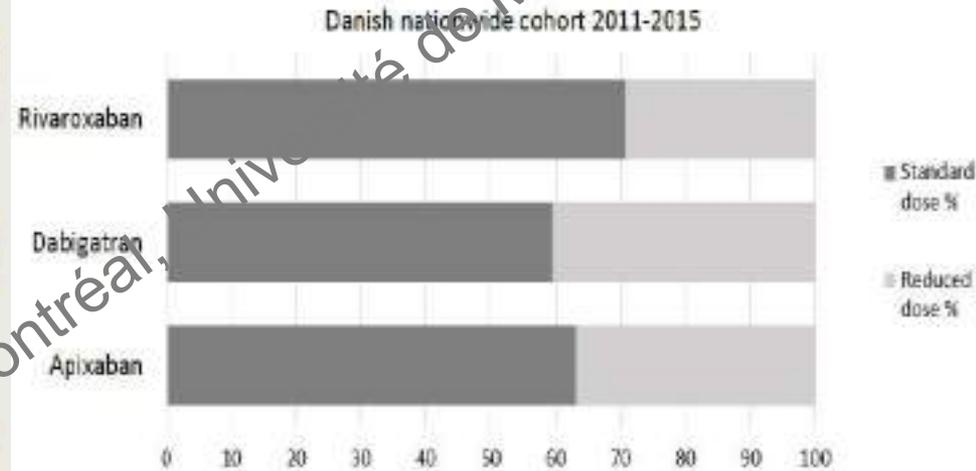
When oral anticoagulation is initiated in a patient with AF who is eligible for a NOAC (apixaban, dabigatran, edoxaban, or rivaroxaban), a NOAC is recommended in preference to a Vitamin K antagonist.	I	A
---	---	---

# Real Life Data with NOACs

## Utilisation des doses appropriées...



Fay et al. ESC 2016



Staerk et al. EHJ Oct 2016

### Revisit-US

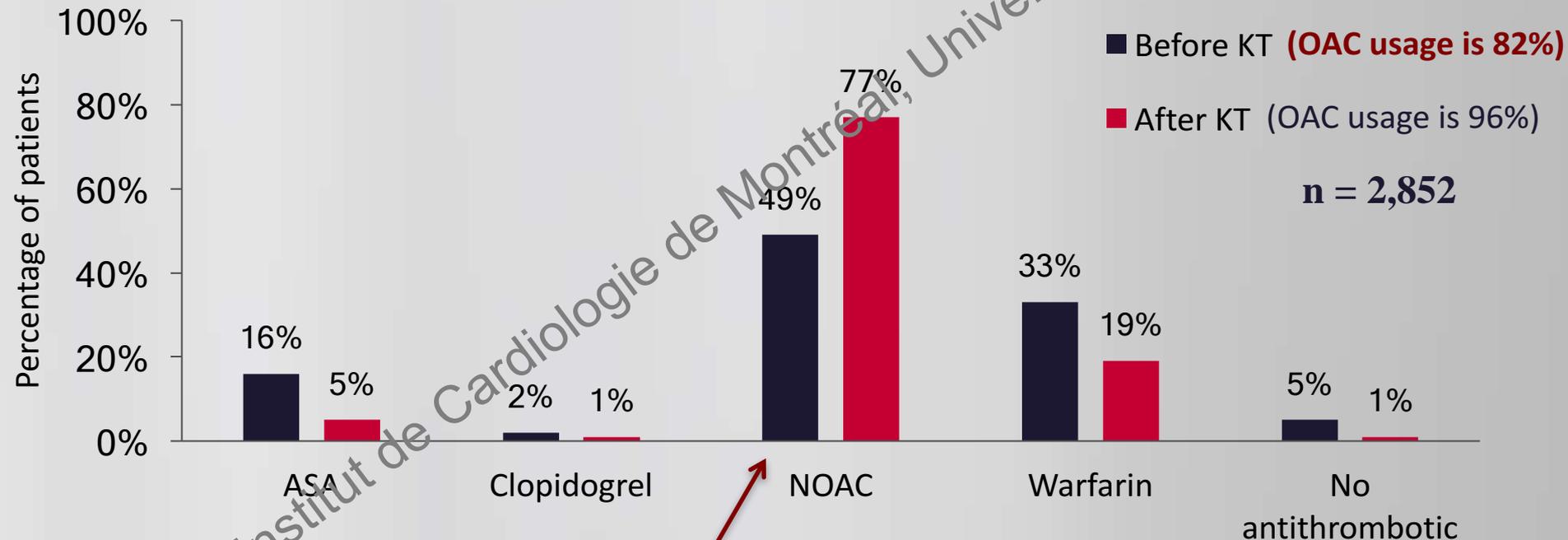
Apixaban 2.5 BID	15.5%
Dabigatran 75 BID	10.3%
Rivaroxaban 15 DIE	17.3%

Coleman et al. ESC 2016

# THE GUIDELINE CONNECT PROGRAM

## SONDAGE (EMC) : 77 CARDIOLOGUES ET 201 MDs FAMILLE

### PATIENTS AVEC RECOMMANDATION D'ACO POUR PREVENTION AVC



**20% des patients recevaient la petite dose de NACO de façon inappropriée**



GUIDELINE  
CONNECT

Implementing the 2014 Atrial  
Fibrillation Guidelines in Practice

Macle et al, CCC 2015

# RISQUE D'HÉMORRAGIE : SCORE HAS-BLED P/R AU RISQUE D'HÉMORRAGIE PERÇU PAR LE MÉDECIN

Score HAS-BLED (moyenne / n)

1,5 ± 1,1 / 1 463

- Chez 314 patients (21%), le score HAS-BLED ne correspondait pas au risque d'hémorragie perçu par le cardiologue :
  - **Le risque d'hémorragie était surestimé chez 283 patients (19 %).**
  - Le risque d'hémorragie était *sous-estimé* chez 31 patients (2 %).

Institut de Cardiologie de Montréal, Université de Montréal

# ÉCHELLE HAS-BLED POUR L'ÉVALUATION DU RISQUE D'HÉMORRAGIE

Facteur de risque	Score
Hypertension (non maîtrisée, tension systolique > 160 mm Hg)	1
Anomalie de la fonction rénale (+1) ou hépatique (+1)	2
Antécédents d'AVC ( <i>Stroke</i> )	1
Antécédents d'hémorragie majeure ou prédisposition aux hémorragies ( <i>Bleeding</i> )	1
INR Labile (INR instable/élevé)	1
Âge >65 ans ( <i>Elderly</i> )	1
Médicaments ( <i>Drugs</i> ), c.-à-d. antiagrégants plaquettaires, AINS (+1), ou consommation excessive d'alcool (≥ 8 consommations par semaine) (+1)	2
<b>Score maximal</b>	<b>9</b>

# Niveau d'évidence clinique pour les doses réduites

Trial	Drug	Dose	N (Total)	N (High dose)	N (Low dose)
RE-LY	Dabigatran	150 & 110 mg BID	18,113	150 mg <del>6076</del> <b>6076</b>	110 mg <b>6015</b>
ROCKET-AF	Rivaroxaban	20 / 15 mg QD	14,264	20 mg <b>7131</b>	(15 mg) <b>1474</b>
ARISTOTLE	Apixaban	5 / 2.5 mg BID	18,201	5 mg <b>9120</b>	(2.5mg) <b>428</b>
ENGAGE AF	Edoxaban	60 / 30 mg QD	21,105	60 mg <b>5251</b>	(30mg) <b>1784</b>

« À moins de raison spécifique, les patients doivent recevoir la dose normale »

	Dabigatran	Rivaroxaban	Apixaban	Edoxaban
Recommandations pour doses réduites	<p>“Age ≥75 yrs”</p> <p>Considérer si CrCL: 30-49 mL/min</p>	<p>CrCL: 30-49 mL/min</p>	<p>If ≥2 of the following:</p> <ul style="list-style-type: none"> <li>• Age ≥80 years,</li> <li>• Body weight ≤60 kg,</li> <li>• Creatinine ≥133 µmol/L</li> </ul>	<p>If any of the following:</p> <ul style="list-style-type: none"> <li>• CrCL: 30-49 mL/min</li> <li>• Body weight ≤60 kg</li> </ul>

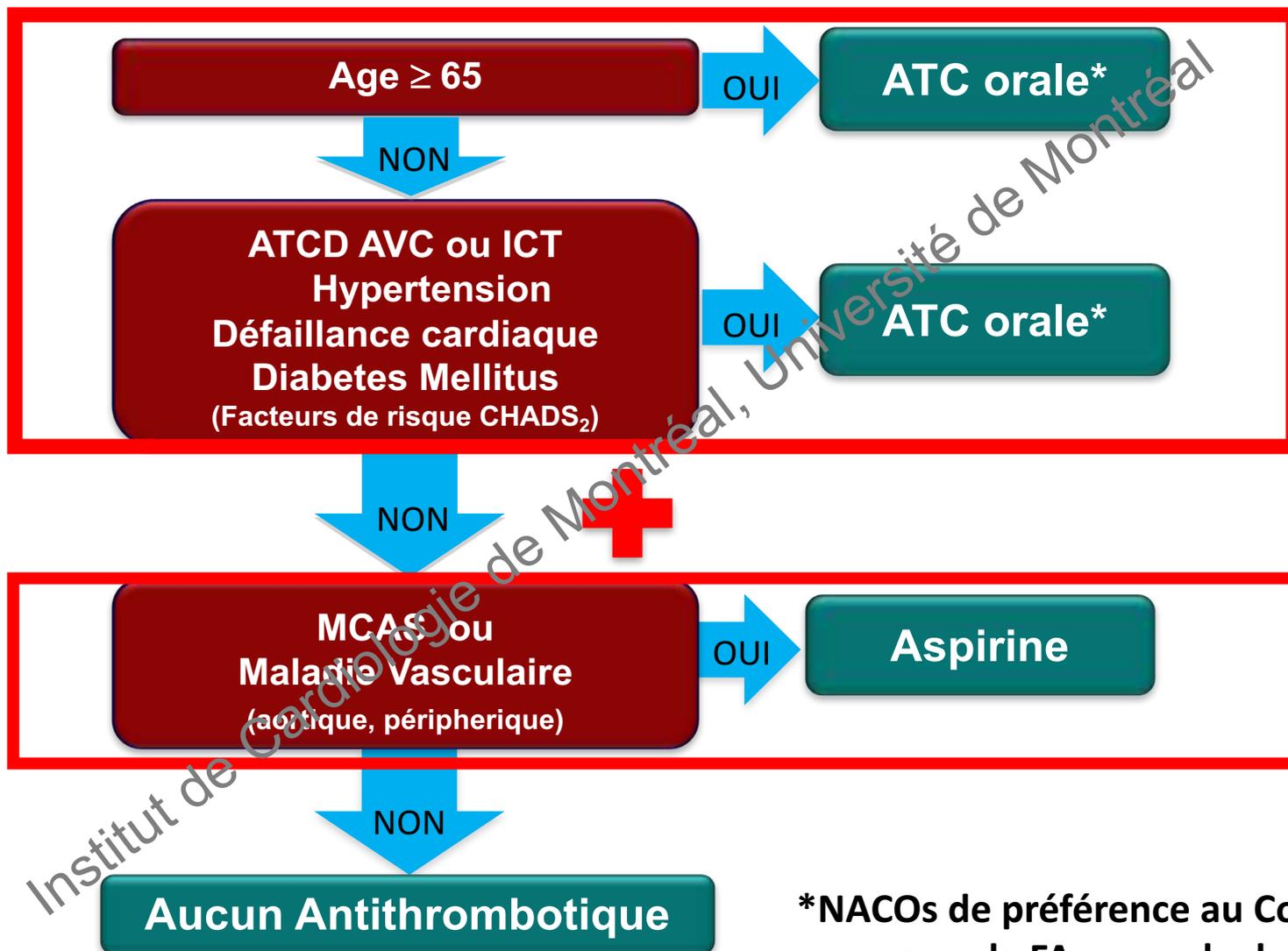
Connolly et al. NEJM. 2009; 361:1139–1151

Patel et al. NEJM. 2011; 365:883–891

Granger et al. NEJM. 2011; 365:981–992

Giugliano RP et al. NEJM 2013; 369:2093–2104

# Algorithme CCS pour le traitement antithrombotique (CHADS65)



**\*NACOs de préférence au Coumadin pour la FA non-valvulaire**

# FA et MCAS concomittante

- MCAS présente chez 20-30% des patients avec FA

## ■ FA+MCAS

- ↑Hospitalisations
- ↑Mortalité à 30jrs et à 1an<sup>4</sup>

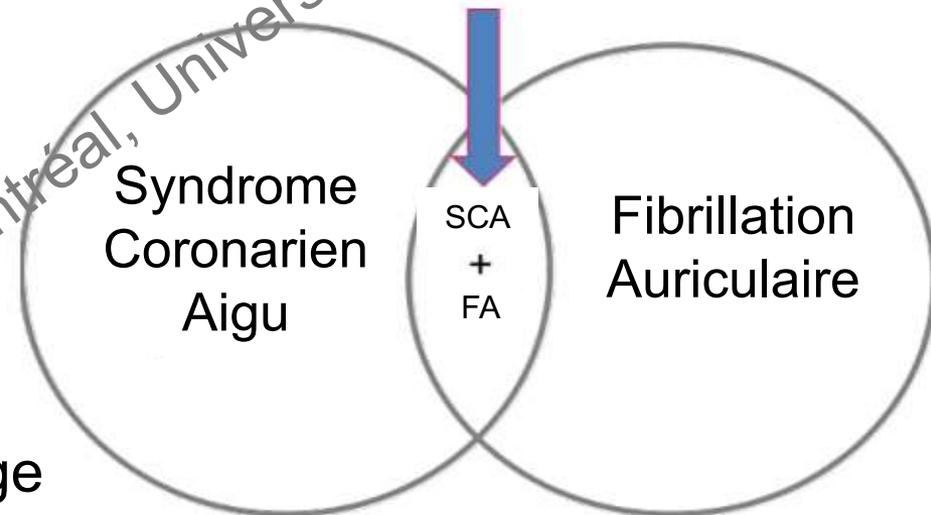
## ■ FA de novo chez MCAS

- ↑Mortalité Hospitalière (OR 5.2)
- ↑Mortalité à 30jrs (OR 3.9)
- ↑Mortalité à 1an (OR 3.1)<sup>4</sup>

## ■ ↑Prévalence FA et MCAS avec âge

- Antithrombotiques indiqués pour les 2 pathologies

Incidence FA lors SCA: 2-21% patients<sup>5</sup>



1. Nieuwlaat R, et al. *Eur Heart J.* 2005;26:2422-2434. 2. Nabauer M, et al. *Europace.* 2009;11:423-434.

3. Goette A, et al. *Eur Heart J.* 2009;30:1411-1420. 4. Hersi A, et al. *Angiology.* 2012;63:466-471. 5. Schmitt J, et al. *Eur Heart J.* 2009;30:1038-1045.

# Traitement Antithrombotique chez les Patients avec FA et MCAS

**Anticoagulants Oraux** pour  
prévention des ICT/AVC/embolies  
systémiques liés à la FA

**Antiplaquettaires** pour  
prévention des événements coronariens  
liés à la MCAS



**Combinaison ACO +Antiplaquettaires utilisée  
post Angioplastie et SCA chez les patients avec FA**

# Traitement Antithrombotique

## Patients avec FA

- ASA: Bénéfice marginal
  - Saignements

Danish Registry (132,372 pts)  
Hazard Ratio vs. Warfarin

	HR Stroke	HR Bleeding
ASA	1.81 (1.73-1.90)	0.93 (0.89-0.97)
No Treatment	1.86 (1.78-1.95)	0.84 (0.81-0.88)

Institut de Cardiologie de Montréal, Université de Montréal

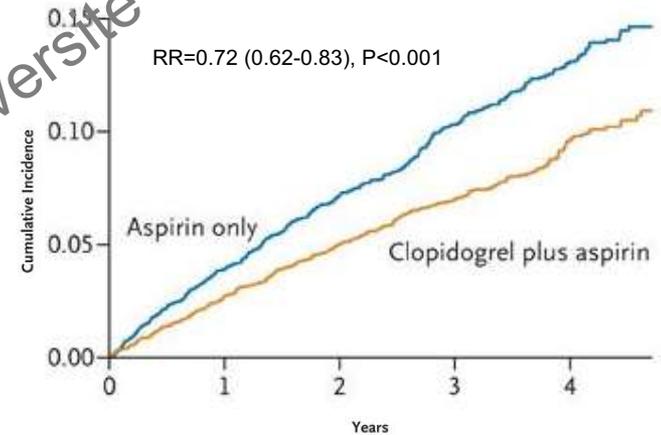
# Traitement Antithrombotique

## Patients avec FA

- ASA: Bénéfice marginal
  - Saignements
- ASA+Clopidogrel > ASA
  - Encore plus de saignements

Danish Registry (132,372 pts)  
Hazard Ratio vs. Warfarin

	HR Stroke	HR Bleeding
ASA	1.81 (1.73-1.90)	0.93 (0.89-0.97)
No Treatment	1.86 (1.78-1.95)	0.84 (0.81-0.88)



Institut de Cardiologie de Montréal, Université de Montréal

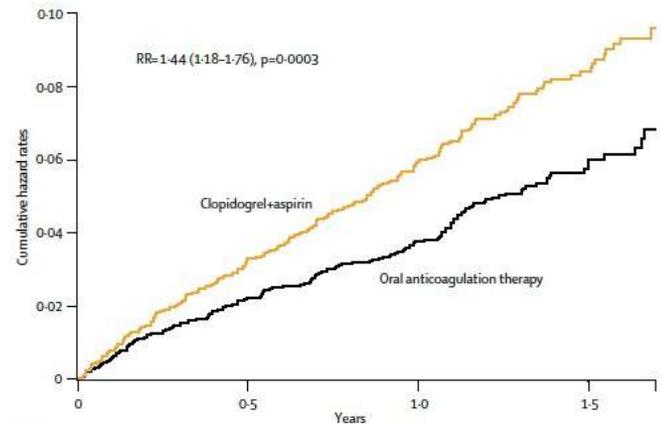
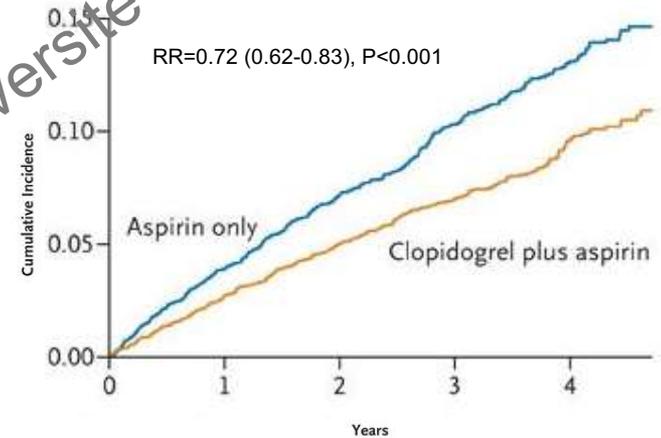
# Traitement Antithrombotique

## Patients avec FA

- ASA: Bénéfice marginal
  - Saignements
- ASA+Clopidogrel > ASA
  - Encore plus de saignements
- Coumadin > ASA+Clopidogrel

Danish Registry (132,372 pts)  
Hazard Ratio vs. Warfarin

	HR Stroke	HR Bleeding
ASA	1.81 (1.73-1.90)	0.93 (0.89-0.97)
No Treatment	1.86 (1.78-1.95)	0.84 (0.81-0.88)



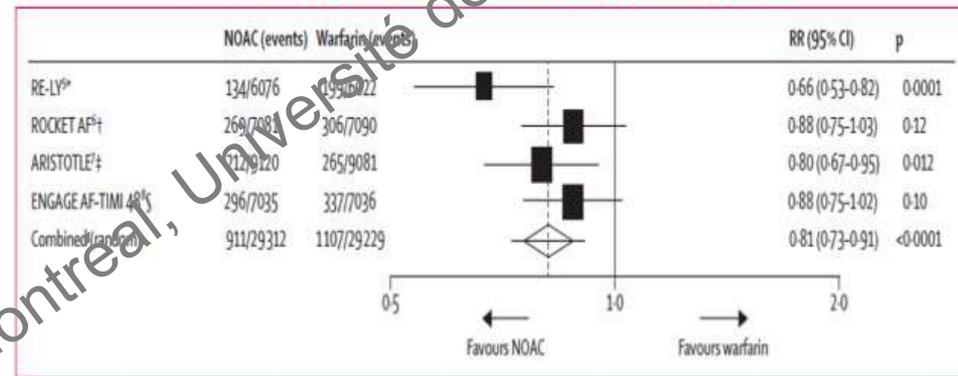
Institut de Cardiologie de Montréal, Université de Montréal

# Traitement Antithrombotique

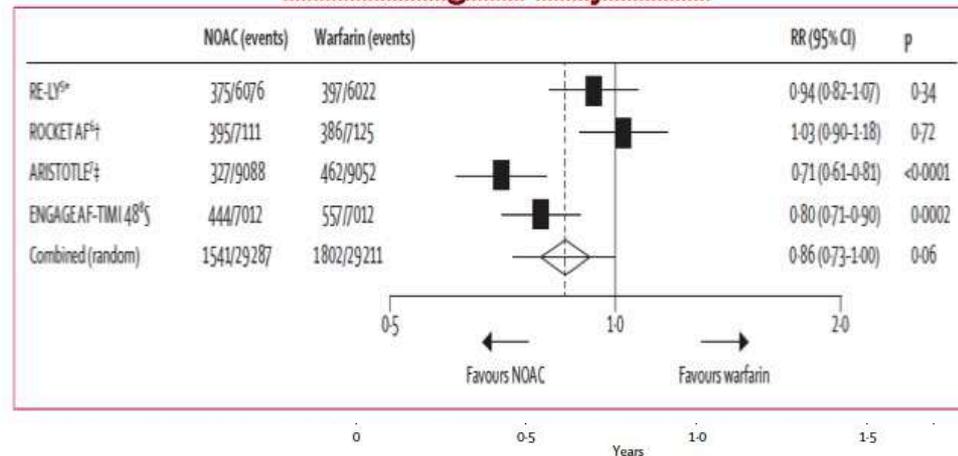
## Patients avec FA

- ASA: Bénéfice marginal
  - Saignements
- ASA+Clopidogrel > ASA
  - Encore plus de saignements
- Coumadin > ASA+Clopidogrel
- NACO ≥ Coumadin
  - Efficacité
  - Saignements
  - Mortalité

### Prévention Thrombo-embolique



### Hémorragies majeures



# Traitement Antithrombotique

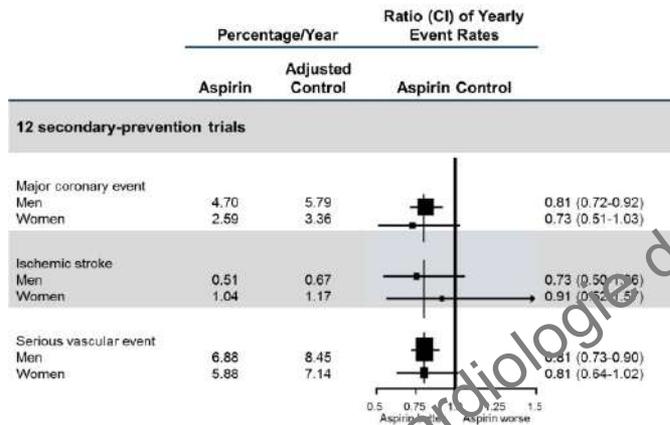
Study, Year (Reference)	Aspirin Dose, mg/d	Follow-up, mo	Population Description	RR (95% CI)
Herzfeldt 1981	100	43.2	Men and women with $\geq 1$ risk factor for CVD	0.69 (0.46-1.00)
HOPE, 1999 (24)	75	45.4	Men and women with hypertension	0.69 (0.45-0.95)
SPYD, 2008 (18)	100	32.1	Men and women with diabetes	1.25 (0.87-1.80)
JPPP, 2014 (30)	100	60.2	Men and women with $\geq 1$ risk factor for CVD	0.52 (0.21-0.91)
PHI, 1989 (30)	162.5	60.2	Men physicians	0.58 (0.47-0.74)
SAO, 1988 (36)	600	72	Men physicians	0.57 (0.47-1.11)
POPAD, 2008 (31)	100	60.1	Men and women with diabetes and CVD $\geq 0.89$	0.58 (0.49-1.00)
TYF, 1994 (34)	75	81.0	Men at high risk for ischemic heart disease	0.65 (0.45-0.95)
ASA, 2010 (32)	100	98.4	Men and women with AMI $\geq 0.55$	0.54 (0.45-1.00)
WHI, 2005 (37)	81	121.2	Women health professionals	1.04 (0.85-1.24)

Overall:  $I^2 = 61.9\%$ ;  $P = 0.002$

## Patients avec MCAS

### Bénéfice net de ASA

- Prévention Primaire si risque de MCAS > 1-2%/an
- Prévention Secondaire chez patients avec MCAS connue

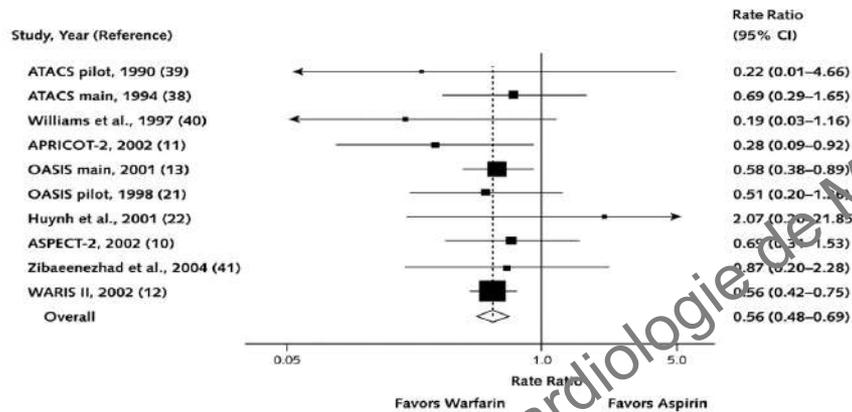


# Traitement Antithrombotique



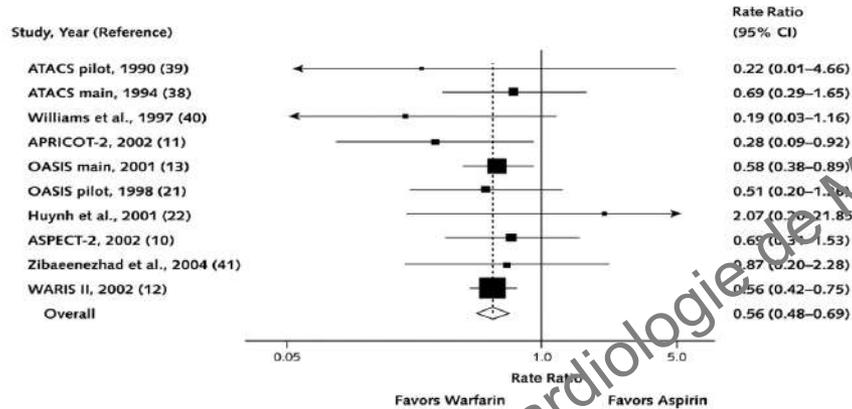
## Patients avec MCAS

- Bénéfice net de ASA
  - Prévention Primaire si risque de MCAS > 1-2%/an
  - Prévention Secondaire chez patients avec MCAS connue

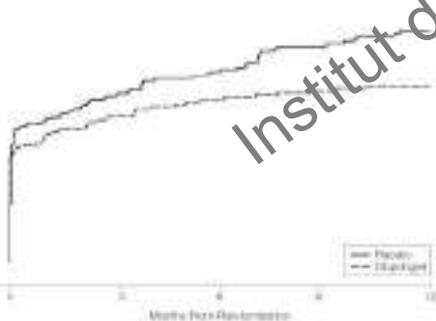


Coumadin aussi efficace que ASA pour prévention secondaire

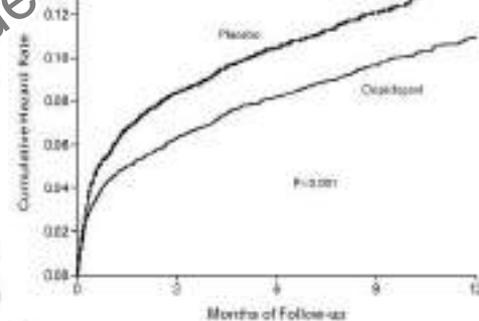
# Traitement Antithrombotique



CREDO – elective PCI



CURE - ACS



## Patients avec MCAS

- Bénéfice net de ASA
  - Prévention Primaire si risque de MCAS > 1-2%/an
  - Prévention Secondaire chez patients avec MCAS connue

- Coumadin aussi efficace que ASA pour prévention secondaire

Bénéfice net de DAPT chez patients haut-risque:

- SCA  $\geq 1$  an
- Angioplastie  $\geq 1$  mois post BMS et  $\geq 3-12$  mois post DES

# Traitement Antithrombotique chez les Patients avec FA et MCAS

## Patients avec FA

- ASA: Bénéfice marginal
  - Saignements
- ASA+Clopidogrel > ASA
  - Encore plus de saignements
- Coumadin > ASA+Clopidogrel
- NACO  $\geq$  Coumadin
  - Efficacité
  - Saignements
  - Mortalité

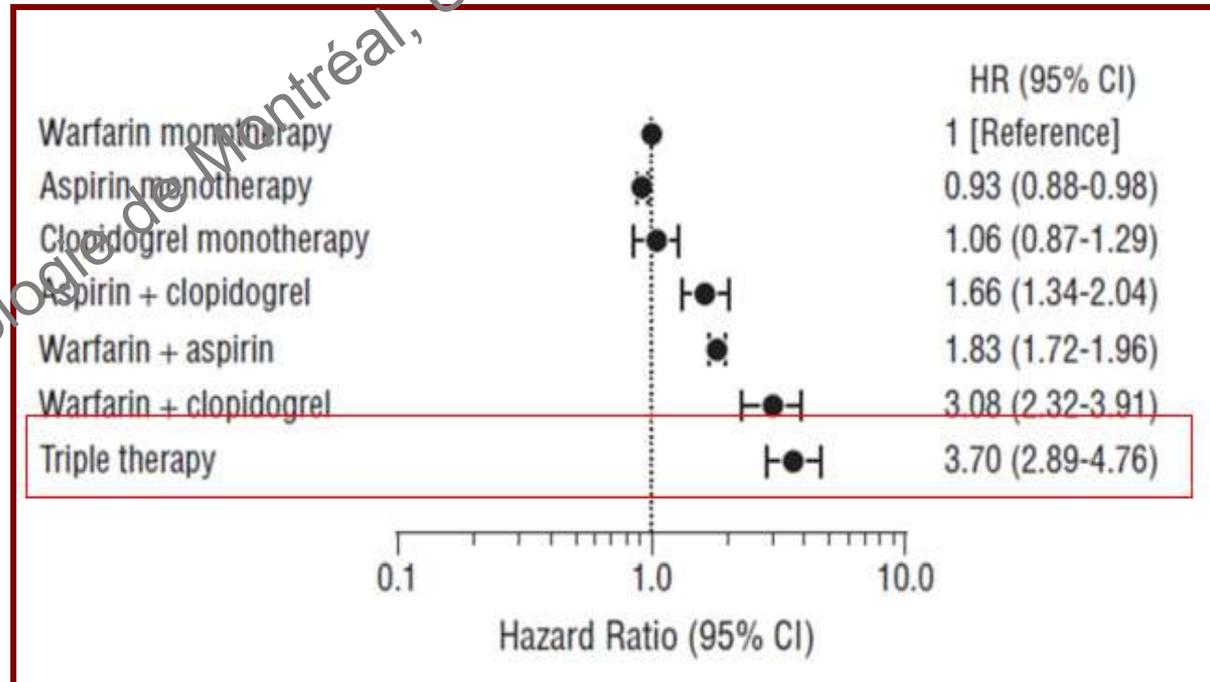
## Patients avec MCAS

- Bénéfice net de ASA
  - Prévention Primaire si risque de MCAS > 1-2%/an
  - Prévention Secondaire chez patients avec MCAS connue
- Coumadin aussi efficace que ASA pour prévention secondaire
- Bénéfice net de DAPT chez patients haut-risque:
  - SCA  $\geq$  1 an
  - Angioplastie  $\geq$  1 mois post BMS et  $\geq$  3-12 mois post DES

# Taux Annuels de Saignements Majeurs avec Combinaisons Traitement Antithrombotique

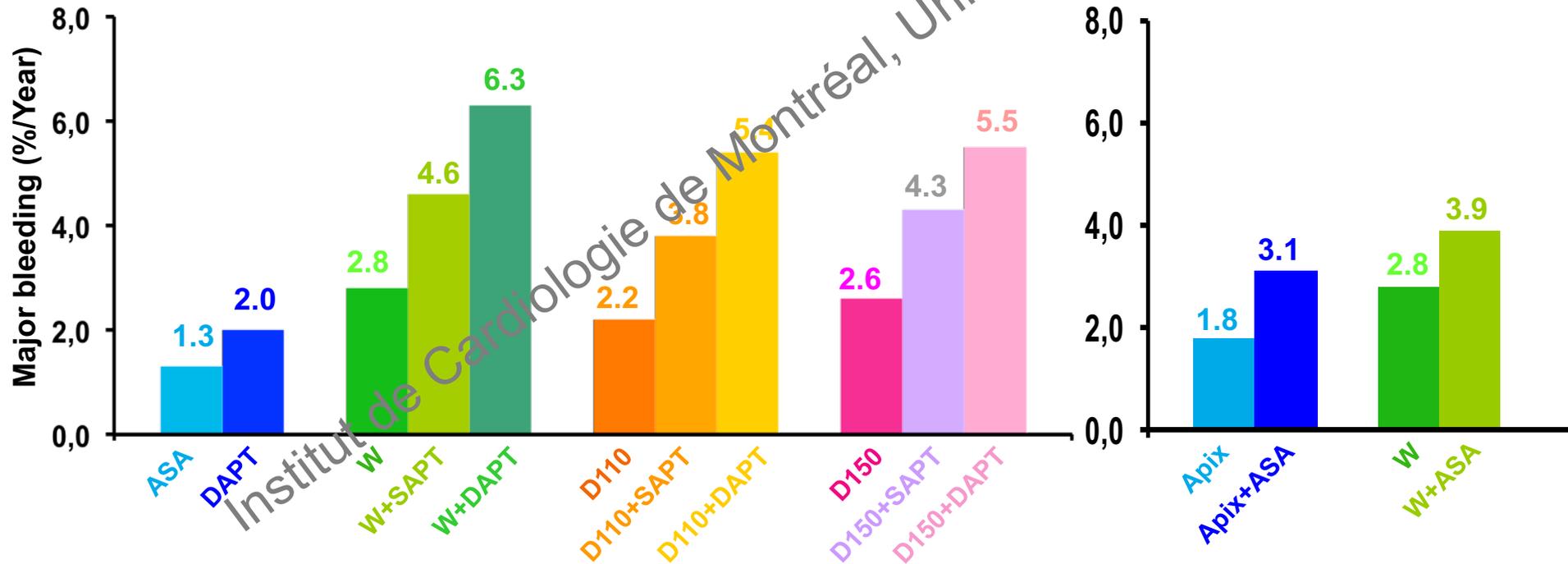
Risk of bleeding with single, dual, triple therapy with warfarin, aspirin, and clopidogrel

- Registre Danois
- 82k patients avec FA
- 1997-2006
- F-up moyen
  - 3.3 ans
- Incidence saignements  
(non-fatal ou fatal) 11.4%



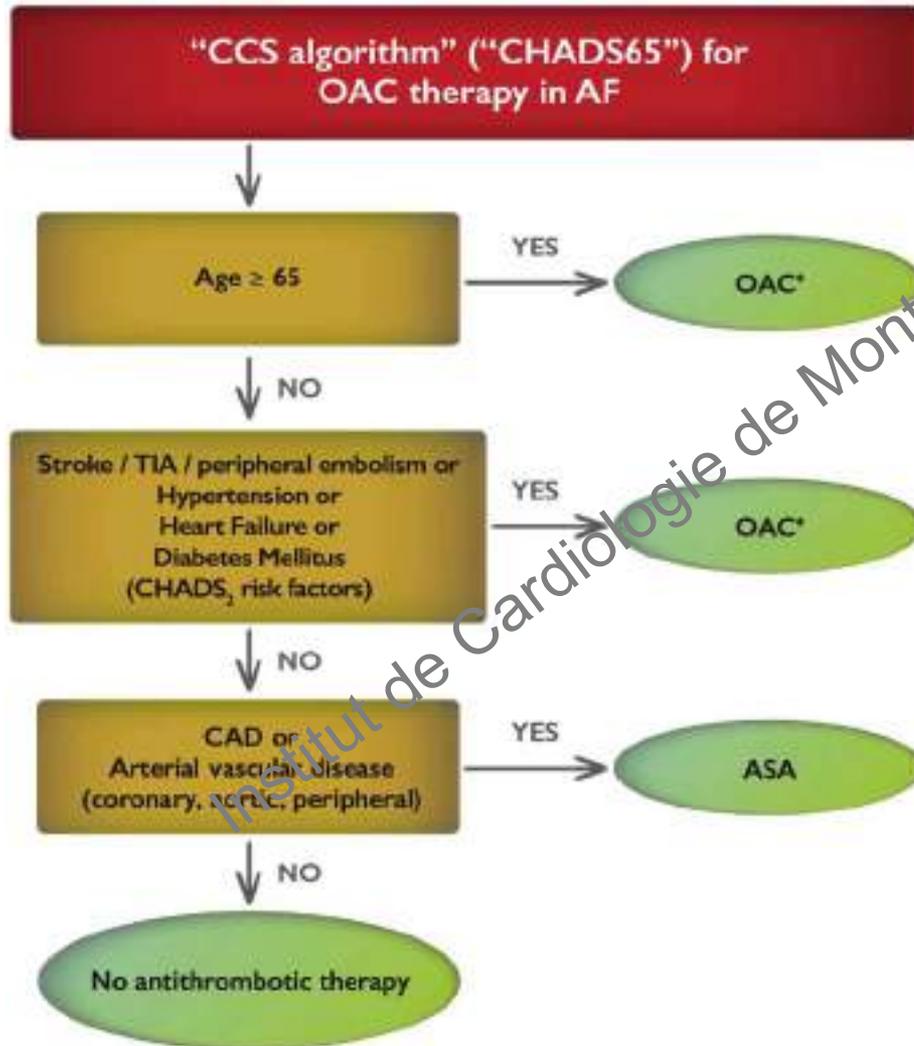
# Taux Annuels de Saignements Majeurs avec Combinaisons Traitement Antithrombotique

- ACTIVE-A (N=7554), RE-LY (N=18113), ARISTOTLE (N=18201)



# Traitement Antithrombotique chez les Patients avec FA et MCAS

## Risque Thrombo-embolique



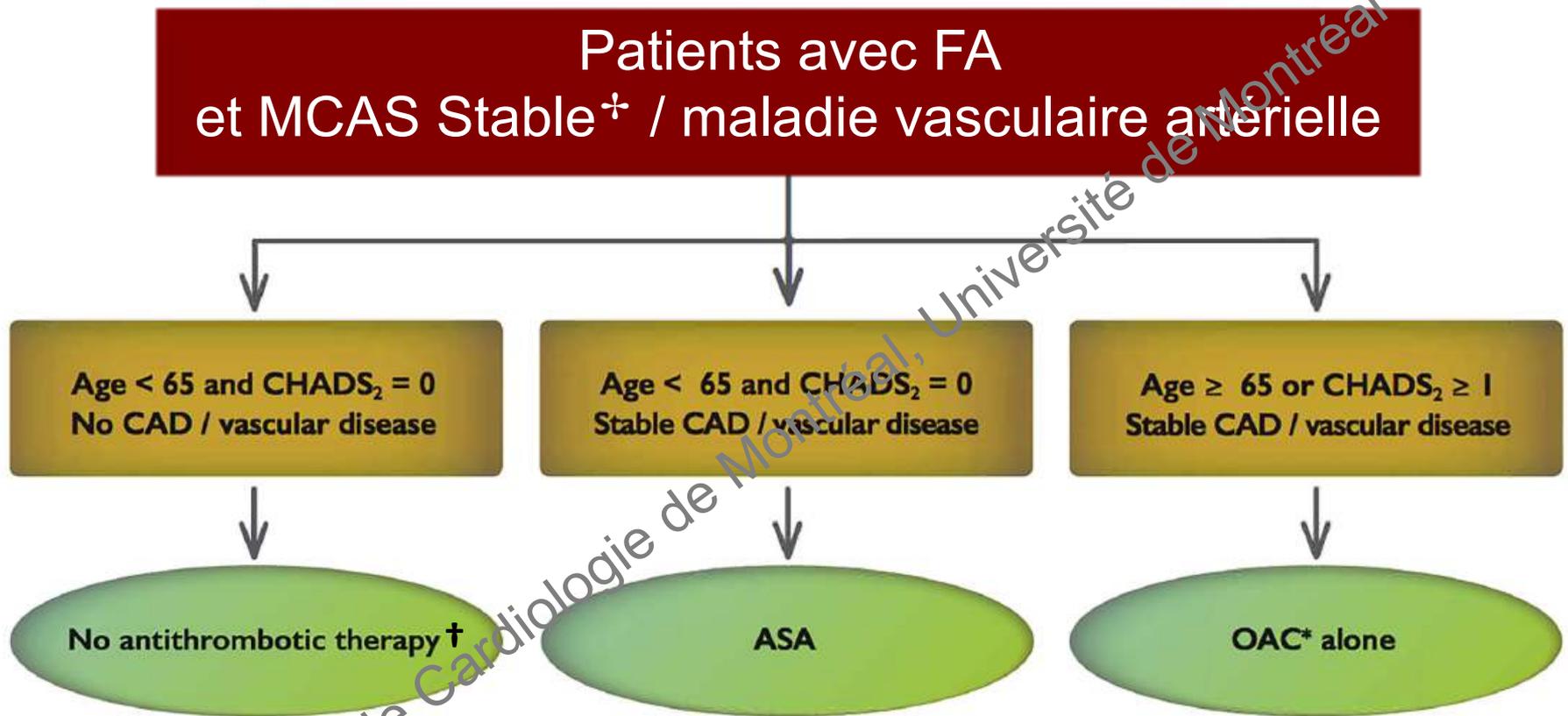
## Risque d'événements Coronariens

1. MCAS Stable

2. Angioplastie Elective

3. SCA

# Traitement Antithrombotique chez les Patients avec FA et MCAS Stable\* / maladie vasculaire artérielle



\*MCAS Stable: absence de syndrome coronarien aigu dans les derniers 12 mois.

† Primary CAD prevention with ASA may be considered in selected high-risk patients.

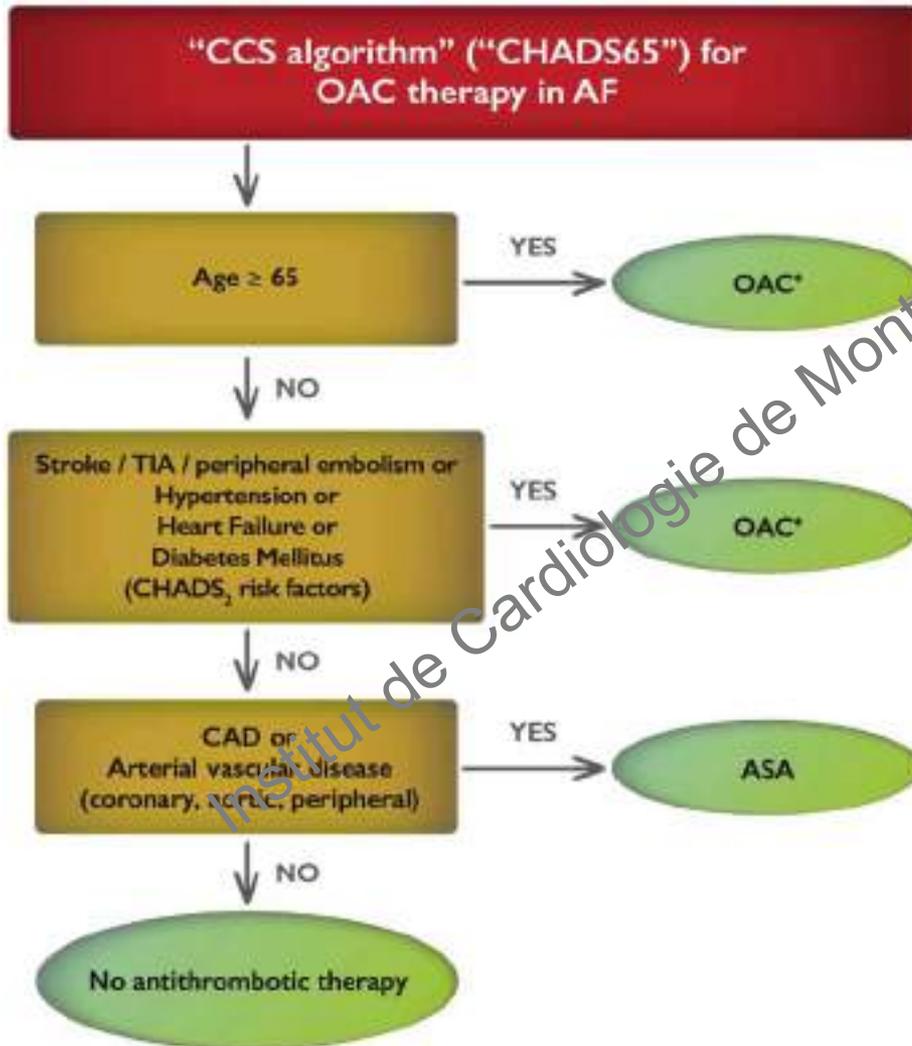
\*A NOAC is preferred over warfarin for non-valvular AF.

## Values and preferences:

The suggestion for use of a NOAC rather than warfarin places relatively greater weight on the ease of use of NOACs versus warfarin and on the data from RCTs of NOACs versus warfarin for NVAf, showing equal or greater reduction of stroke, equal or less major bleeding, less intracranial bleeding and no net increase in CAD outcomes. It places relatively less weight on the absence of long-term data on the effect of NOACs on coronary outcomes as opposed to the data for efficacy of warfarin

# Traitement Antithrombotique chez les Patients avec FA et MCAS

## Risque Thrombo-embolique



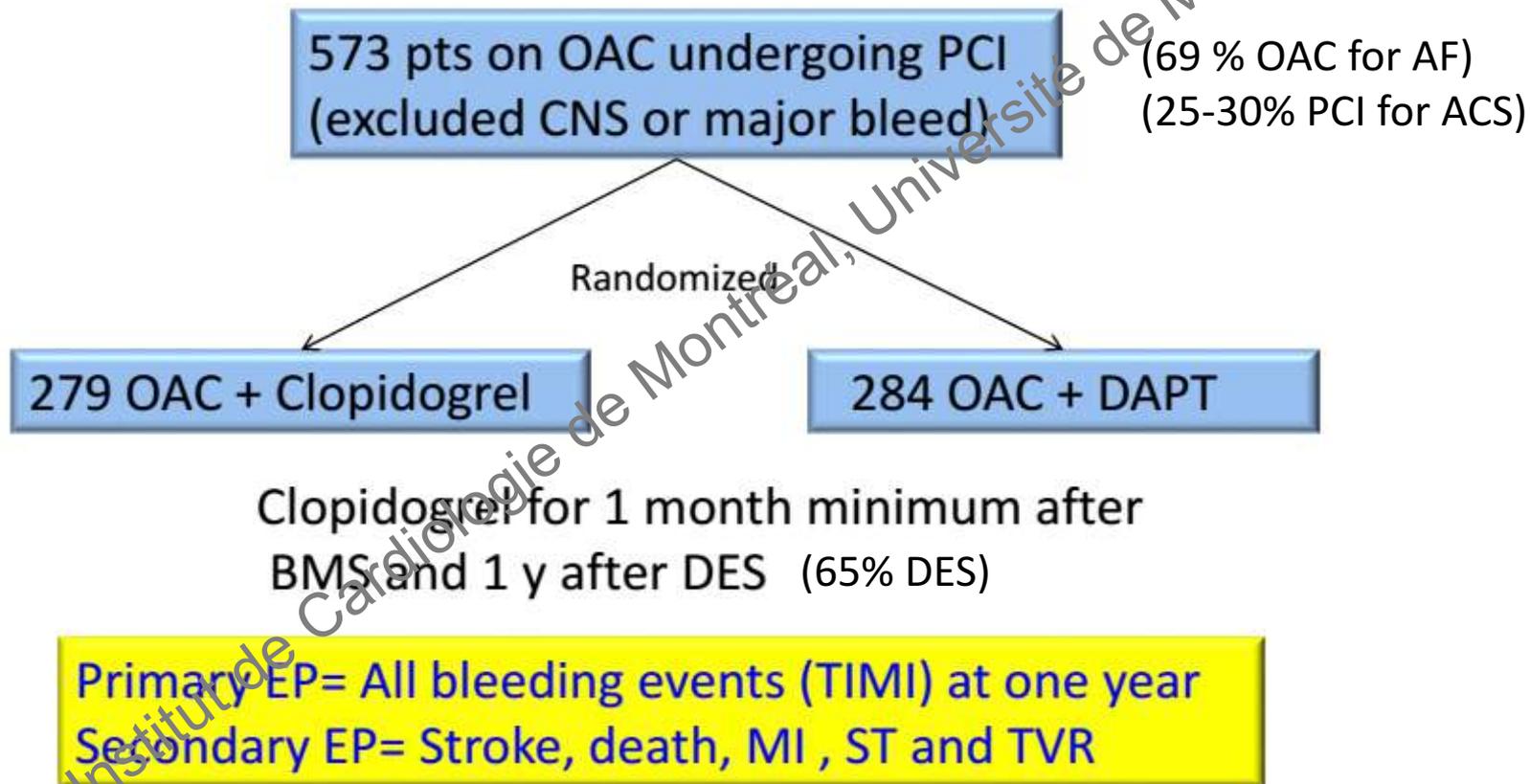
## Présentation Clinique de MCAS

1. MCAS Stable

2. Angioplastie Elective

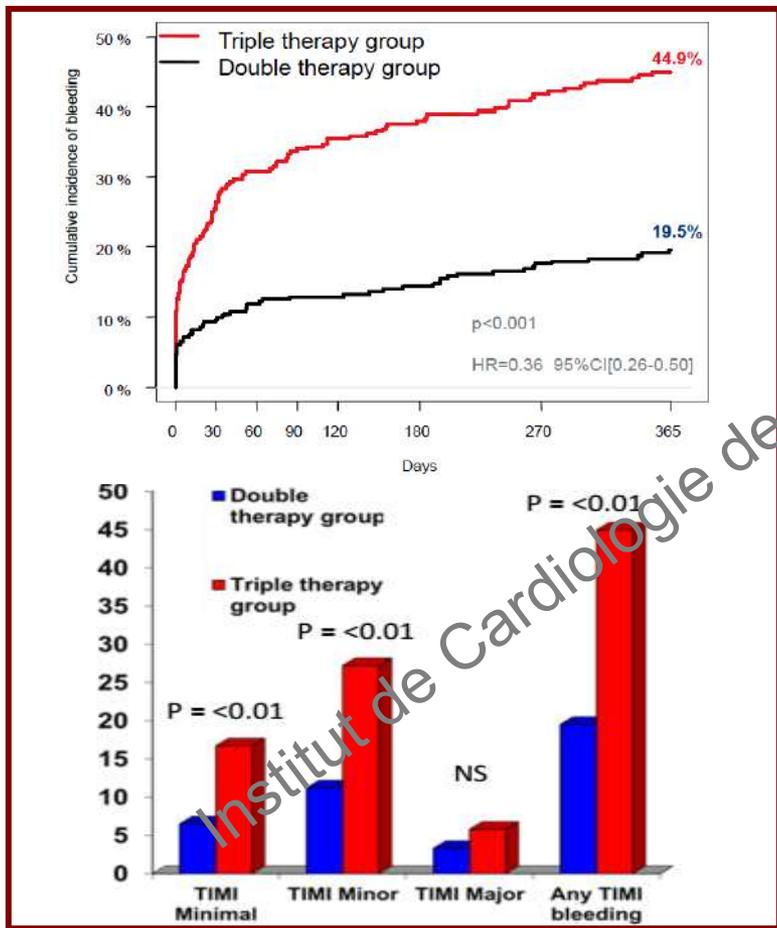
3. SCA

WOEST: Use of clopidogrel with or without aspirin in patients taking oral anticoagulant therapy and undergoing PCI: an open-label, randomised, controlled trial

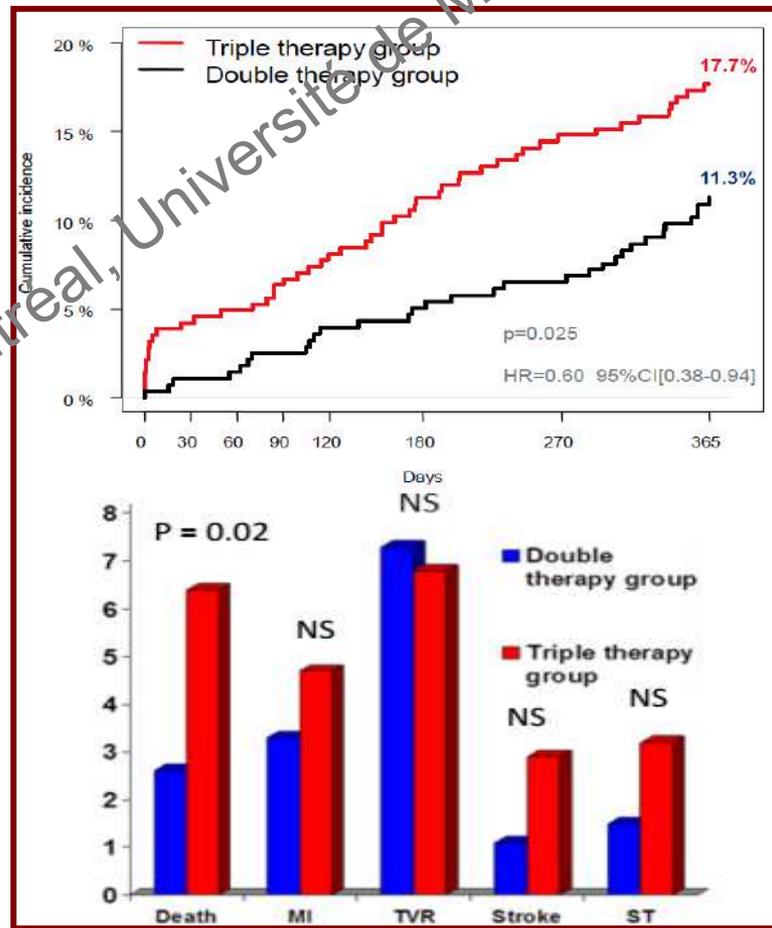


# WOEST: Use of clopidogrel with or without aspirin in patients taking oral anticoagulant therapy and undergoing PCI: an open-label, randomised, controlled trial

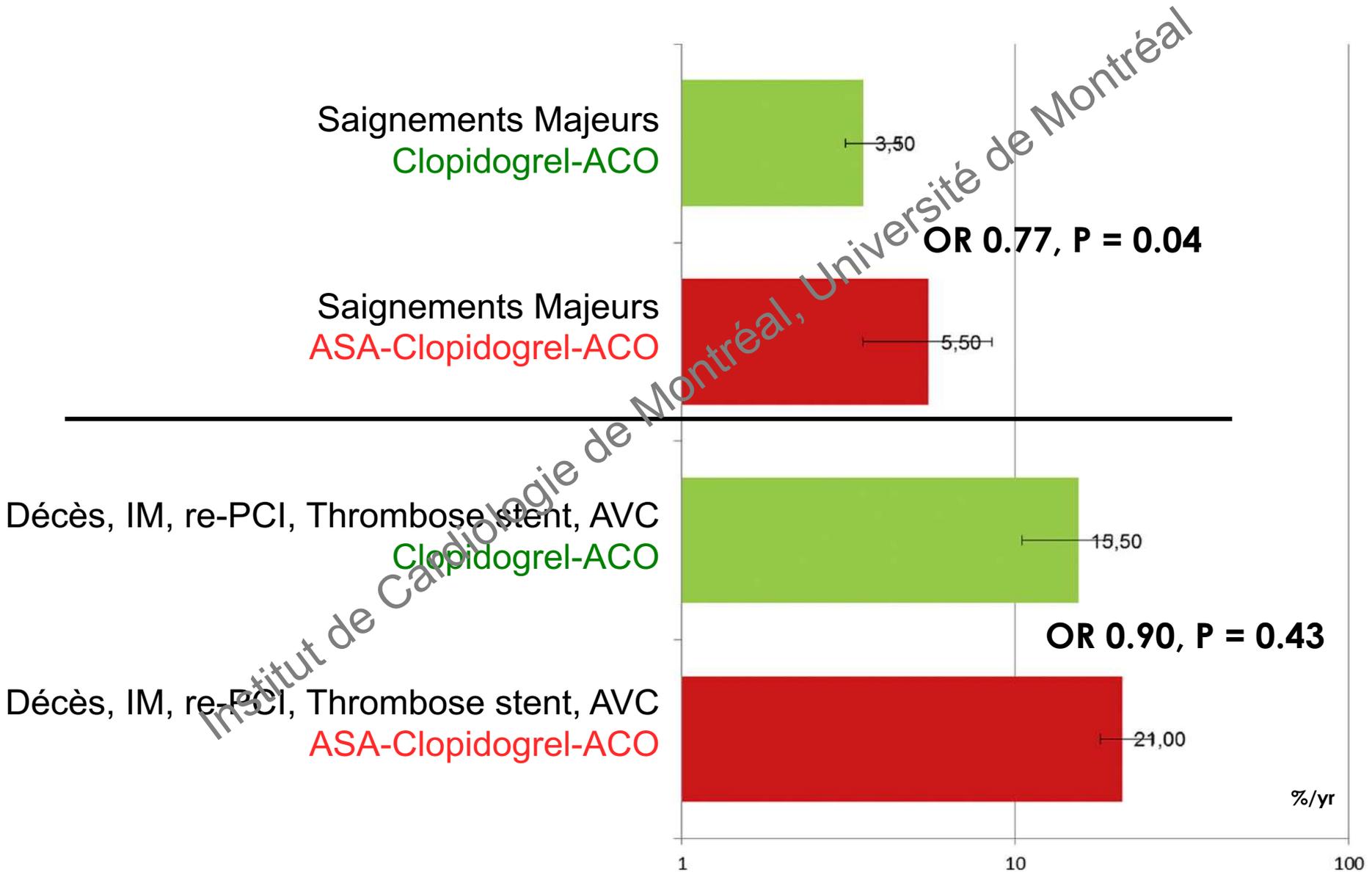
## Total number of Bleeding events



## Death, MI, TVR, Stroke, Stent thrombosis



# Meta-Analyse: Clopidogrel-ACO vs Triple thérapie (ASA/Clopidogrel/ACO) Saignements Majeurs et Évènements Coronariens post Angioplastie



# Pioneer-AF PCI

## Population:

Paroxysmal/persistent/permanent NVAF, undergoing PCI (with stent placement)

N=2,124

1:1:1

R

Rivaroxaban 15 mg od + (clopidogrel/ prasugrel/ ticagrelor)\*

Rivaroxaban 2.5 mg bid + DAPT

Rivaroxaban 15 mg od + low-dose ASA

\*\* Intended DAPT duration of 1, 6 or 12 months

VKA (INR 2.0–3.0) + DAPT

VKA + low-dose ASA

End of treatment (12 months)

- 44% Paroxysmal AF
- CHADSVASC
  - >50% 4 or more
- 66% DES
- Indication for PCI:
  - 12% STEMI; 40% NSTEMI/UA

\*\*Stratified by planned DAPT duration (MD decision)

- \*P2Y12: 93-96% Clopidogrel

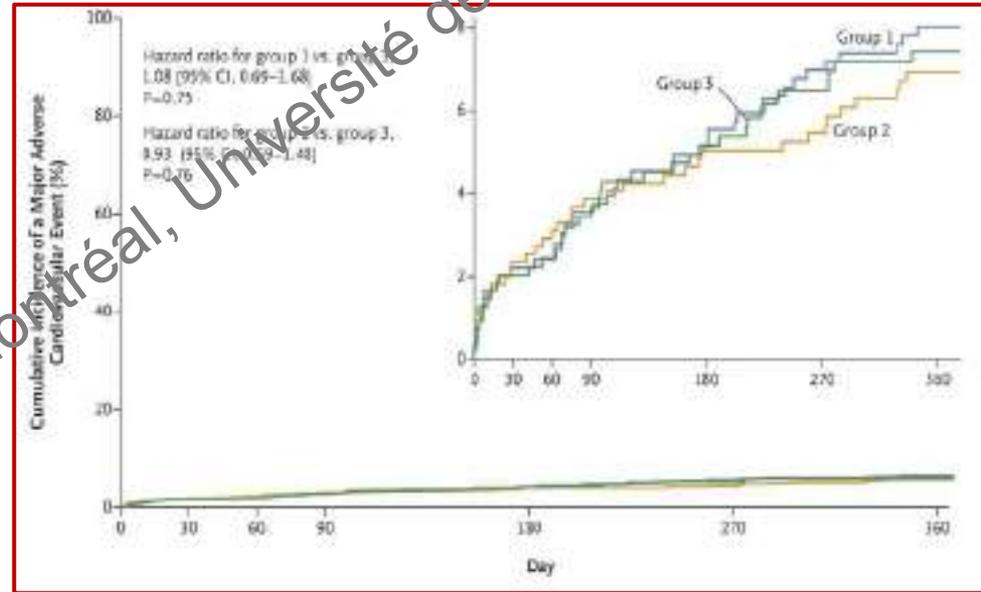
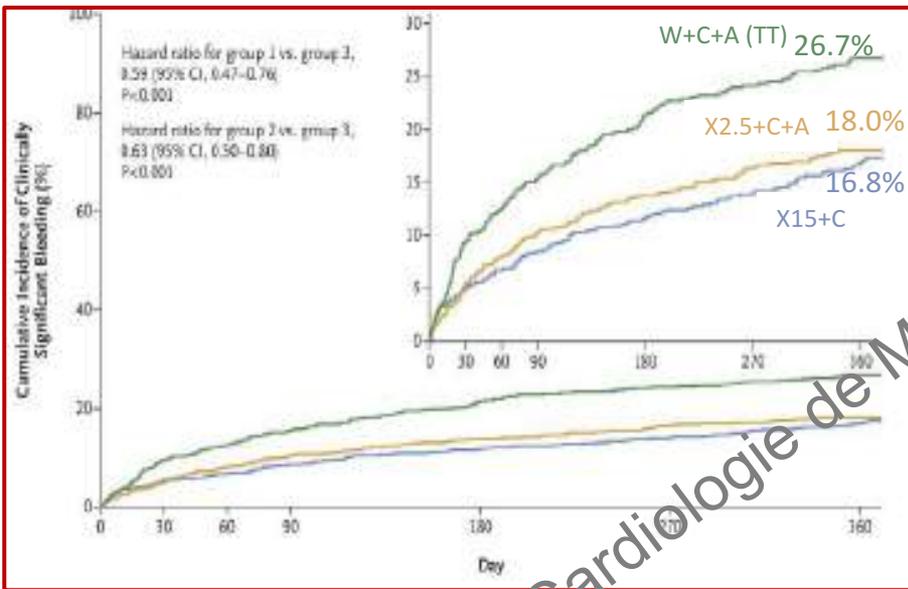
# Pioneer-AF PCI

## Primary safety end point

- **Clinically significant bleeding**
  - Composite of TIMI major bleeding, TIMI minor bleeding according, or bleeding requiring medical attention

## Secondary Efficacy end point

- **Composite of death from CV causes, MI, or stroke**



Cohort and End Point	Groups			
	Group 1	Group 2	Group 1 and 2	Group 3
	No. of Participants with Events (Kaplan–Meier Event Rate)			
<b>All participants — no.</b>	696	706	1402	697
Clinically significant bleeding	109 (16.8)	117 (18.0)	226 (17.4)	167 (26.7)
Major bleeding	14 (2.1)	12 (1.9)	26 (2.0)	20 (3.3)
Minor bleeding	7 (1.1)	7 (1.1)	14 (1.1)	13 (2.2)
Bleeding requiring medical attention	93 (14.6)	102 (15.8)	195 (15.2)	139 (22.6)

Cohort and End Point	Group 1 Group 2 Group 3		
	No. of Participants with Events (Kaplan–Meier Event Rate)		
<b>All participants — no.</b>	694	704	695
Major adverse cardiovascular event	41 (6.5)	36 (5.6)	36 (6.0)
Death from cardiovascular causes	15 (2.4)	14 (2.2)	11 (1.9)
Myocardial infarction	19 (3.0)	17 (2.7)	21 (3.5)
Stroke	8 (1.3)	10 (1.5)	7 (1.2)
Stent thrombosis	5 (0.8)	6 (0.9)	4 (0.7)
Major adverse cardiovascular event or stent thrombosis	41 (6.5)	36 (5.6)	36 (6.0)

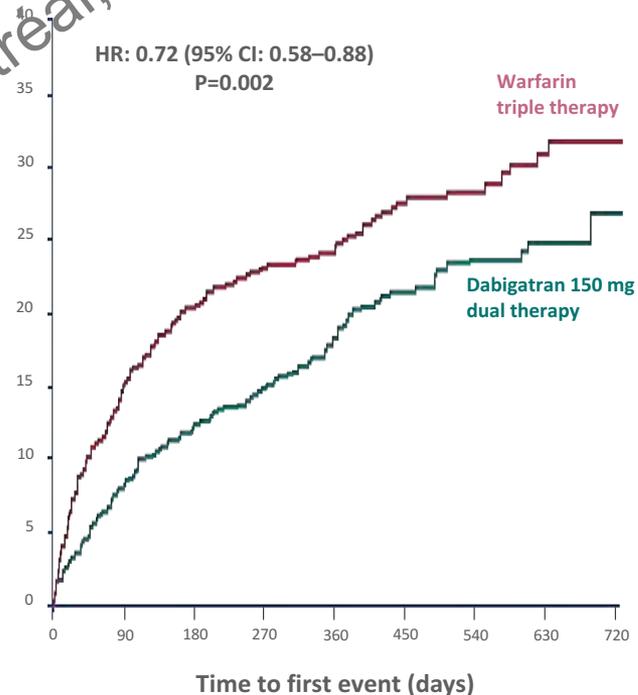
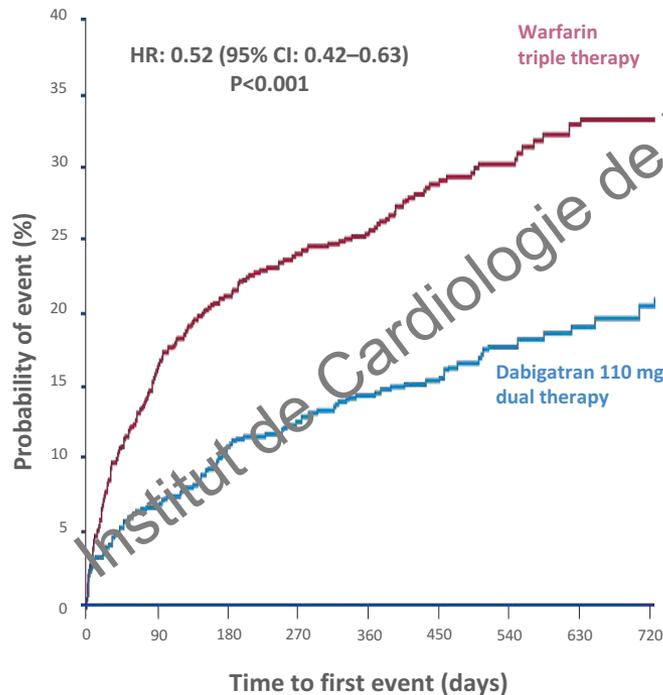
Group 1: X15+C, Group 2: X2.5+C+A, Group 3: W+C+A (TT)

# RE-DUAL PCI

- 2725 patients with AF undergoing PCI
- Dabi (110 or 150mg BID) + P2Y12 **VS** Triple therapy (W+P2Y12+ASA)

## Primary end point

- Major or Clinically relevant non-major bleeding

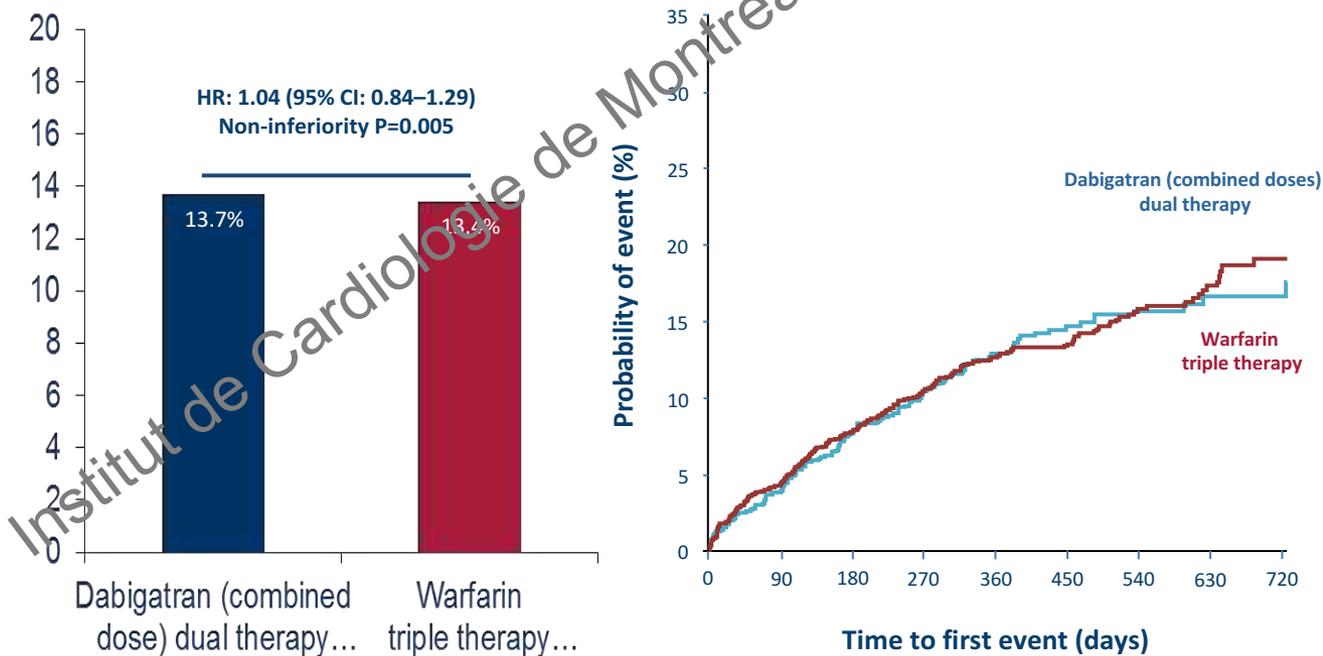


# RE-DUAL PCI

- 2725 patients with AF undergoing PCI
- Dabi 110 + P2Y12 vs Dabi 150 + P2Y12 vs Triple therapy (W+P2Y12+ASA)

## Efficacy end point

- Composite of thromboembolic events (myocardial infarction, stroke, or systemic embolism), death, or unplanned revascularization

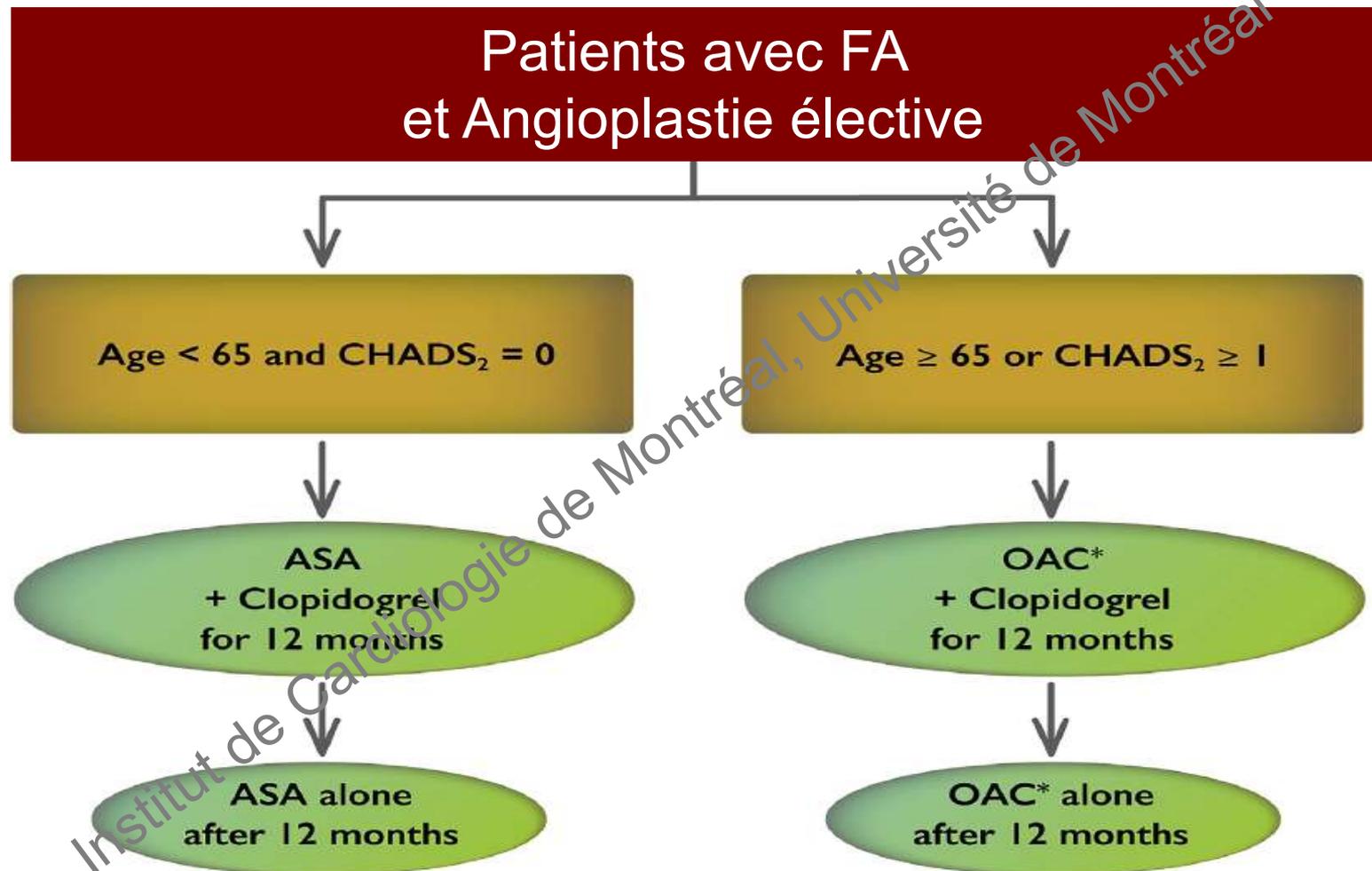


# Données pour le Traitement Antithrombotique après Angioplastie /SCA chez les Patients

trial	n	experimental arm	control arm	clinicaltrials.gov	primary endpoint
<b>PIONEER AF-PCI<sup>1</sup></b>	2,100	rivaroxaban P2Y12	warfarin P2Y12 aspirin	01830543	bleeding
<b>RE-DUAL PCI</b>	2,500	dabigatran* P2Y12	warfarin P2Y12 aspirin	02164864	bleeding
<b>AUGUSTUS**</b>	4,600	apixaban/warfarin P2Y12	warfarin P2Y12 aspirin	02415400	bleeding
<b>ENTRUST AF-PCI</b>	1,500	edoxaban P2Y12	warfarin P2Y12 aspirin	n.a.	bleeding
<b>MANJUSRI<sup>2</sup></b>	296	warfarin ticagrelor	warfarin clopidogrel aspirin	02206815	bleeding

<sup>1</sup>AHJ 2015;169:472-78, <sup>2</sup>Contemp Clin Trials 2015;40:166-71

# Traitement Antithrombotique chez les Patients avec FA et MCAS



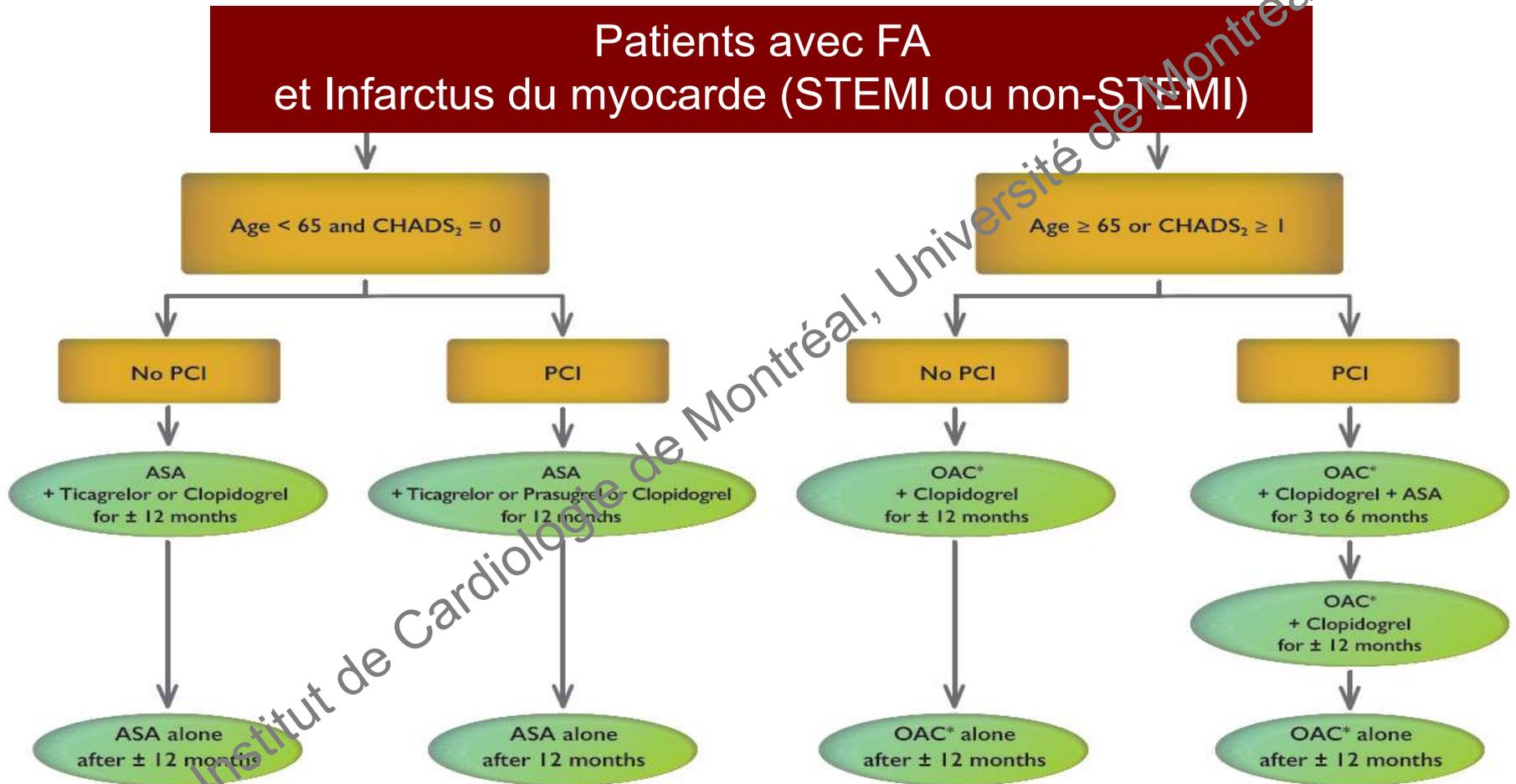
## Practical tips:

High risk of stent thrombosis and acceptable major bleeding risk :

1. May continue (ASA+Clopidogrel) or (OAC+Clopidogrel) >12 months.
2. Might prompt initial use of TT in selected patients.

High risk of major bleed: (ASA+Clopidogrel) or (OAC+Clopidogrel) converted to ASA alone or OAC alone <12 months.

# Traitement Antithrombotique chez les Patients avec FA et Infarctus du myocarde (STEMI ou non-STEMI)



## Practical tips:

**High risk of stent thrombosis and acceptable major bleeding risk:** may continue (C+ASA) or (C+OAC) >12 months.

**High risk of bleeding:** may have (C+ASA) or (C+OAC) converted to OAC alone <12 months.

**High risk of bleeding and ACS+PCI:** some clinicians may prefer C+OAC over TT

**High risk of coronary events and ACS+PCI** (at the lower end of the stroke risk spectrum): some clinicians may consider

ASA+ticagrelor, ASA+prasugrel, or ASA+clopidogrel over TT.

# Traitement Antithrombotique chez les Patients avec FA et MCAS

## **Practical tip:** Measures to reduce bleeding

- **Avoid prasugrel and ticagrelor** in conjunction with OAC
- Target the **lower end of the INR** range (warfarin)
- Consider the use of **lower effective NOAC** dose
- **Delay non-urgent catheterization** until there is clarity about coagulation and renal status
- Measures during **invasive procedures**
  - radial access, small-diameter sheaths, early removal from femoral site and minimized use of acute procedural anti-thrombotic therapies
- Consider routine **proton pump inhibitor (PPI)**

# Lignes directrices de la SCC en matière de FA

- **Mise à jour 2018...**

- Modification des facteurs de risque
- FA et MCAS
  - SCA / Angioplastie
- Anticoagulation peri-cardioversion
  - Timing, NACOs, ETO
- Ablation par cathéter
- Antidotes pour NOACs

Institut de Cardiologie de Montréal, Université de Montréal



# Merci !

Institut de Cardiologie de Montréal, Université de Montréal

