ATHÉROSCLÉROSE

Approche intégrative des grands syndromes

- Grands syndromes et inter-relations
- Antithrombothérapie
- Approche non-pharmacologique

André Roussin MD, FRCP
Professeur agrégé
CHUM, Université de Montréal

SSVQ
Société des sciences vasculaires du Québec

Thrombosis Canada
Thrombose Canada

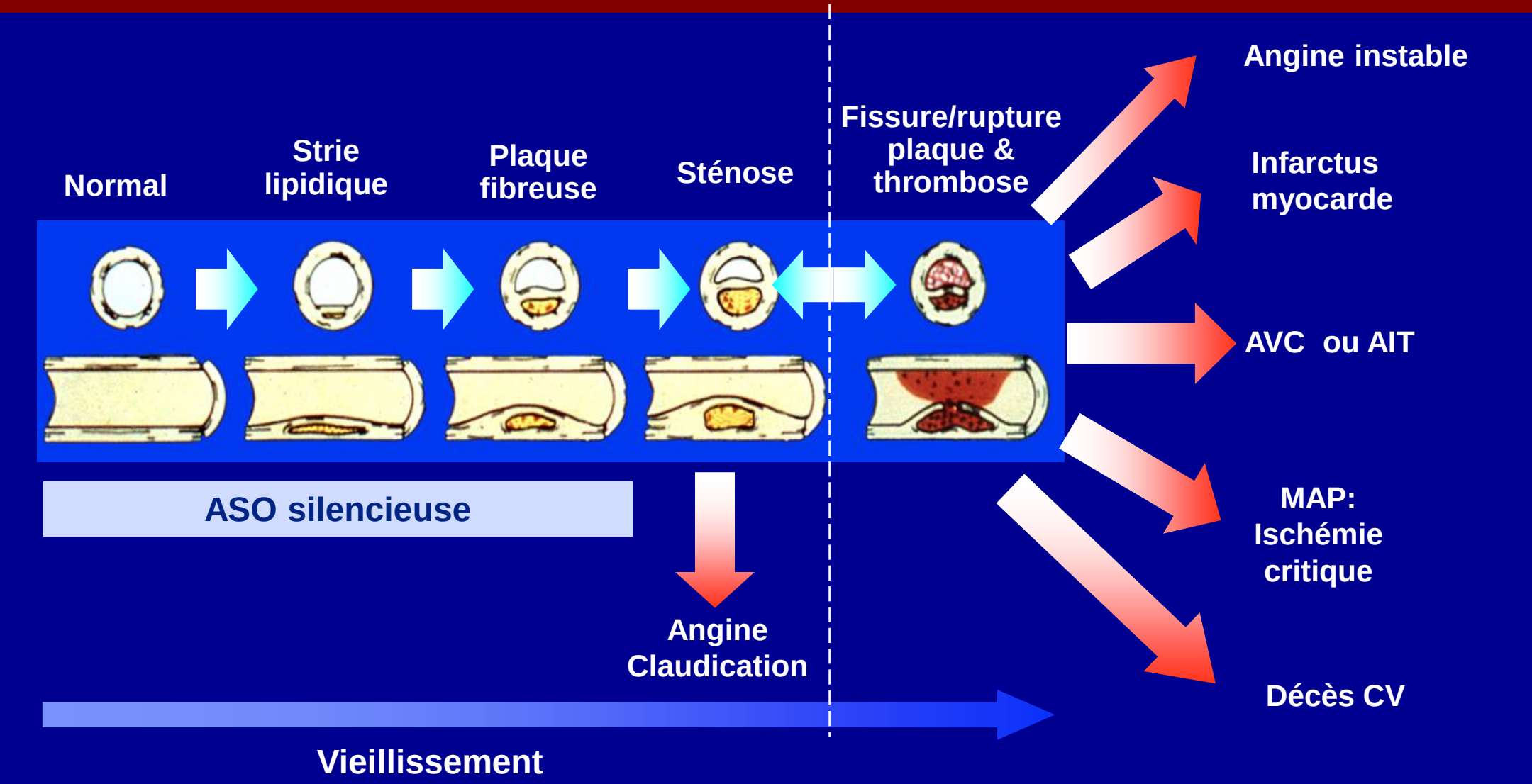
Athérosclérose 1 juin 2022

Conflits d'intérêts potentiels 2021-2022

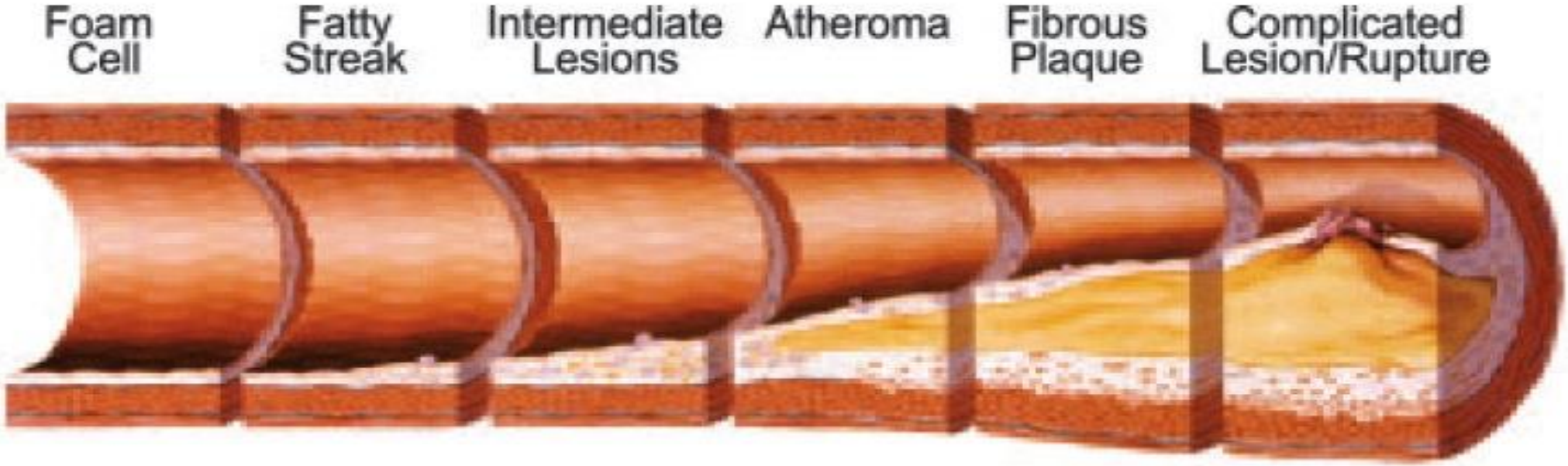
Aucun

Athérosclérose sur une vie

Une maladie endothéliale “lipidique”, “inflammatoire” et “thrombosante”



Marqueurs inflammatoires selon stade ASO



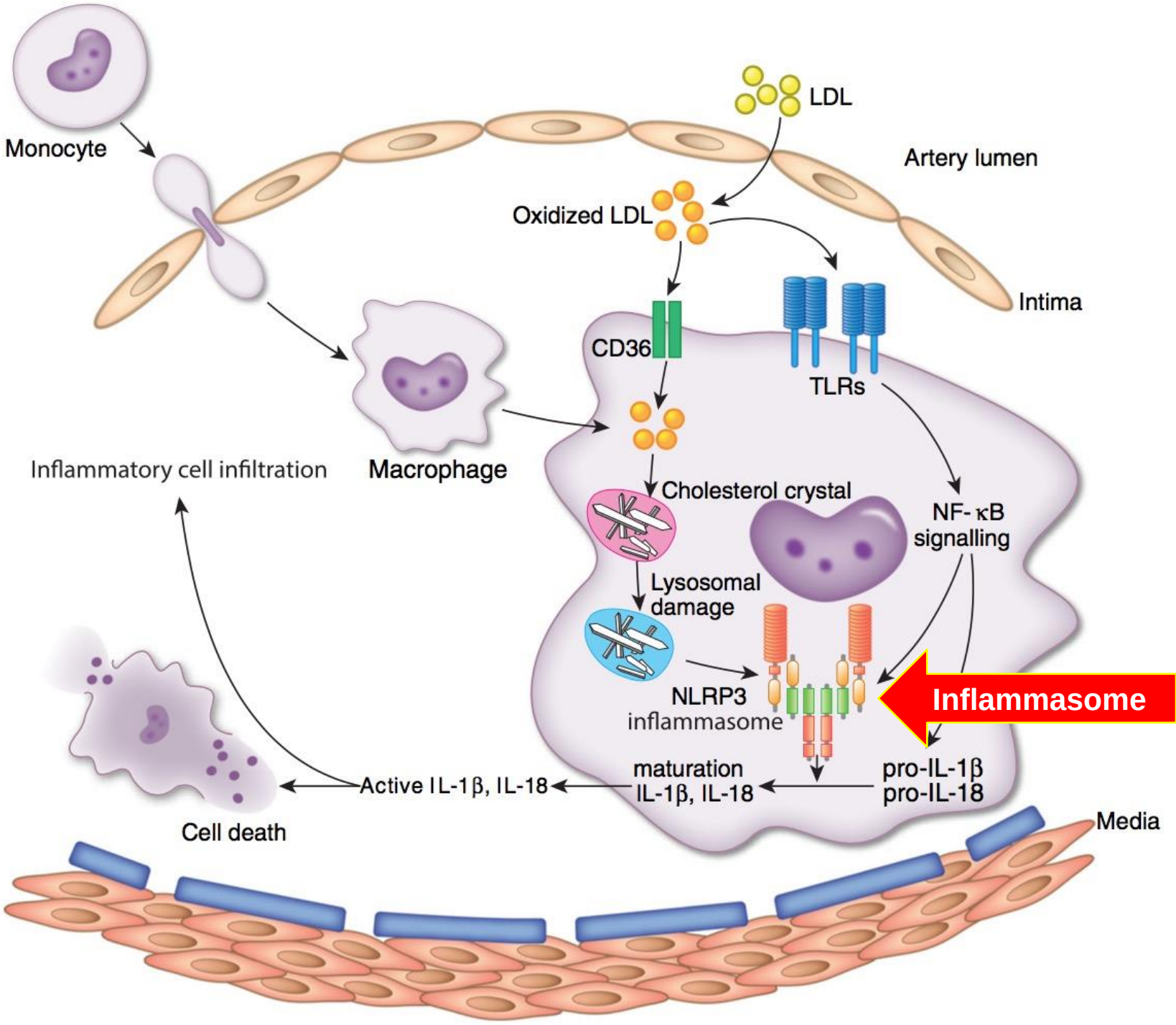
1°& Messenger Inflamm. Cyto/Chemokines		Cellular Adhesion Molecules	Plaque Destabilization		Plaque Rupture
IL-1	IL-6*	sICAM	IL-18*	MPO*	PAPP-A*
TNF-α	IL-18*	sVCAM	oxLDL*	MMPs *	sCD40L*
	MCP-1*	sSelectins	Lp-PLA$_2$*	MCP-1*	
			GPx-1*	PlGF*	

Acute Phase Reactants
CRP*, sPLA$_2$*, SAA, Fibrinogen, WBCC

Koenig W, Khuseyinova N. ATVB 2007; 27: 15-26

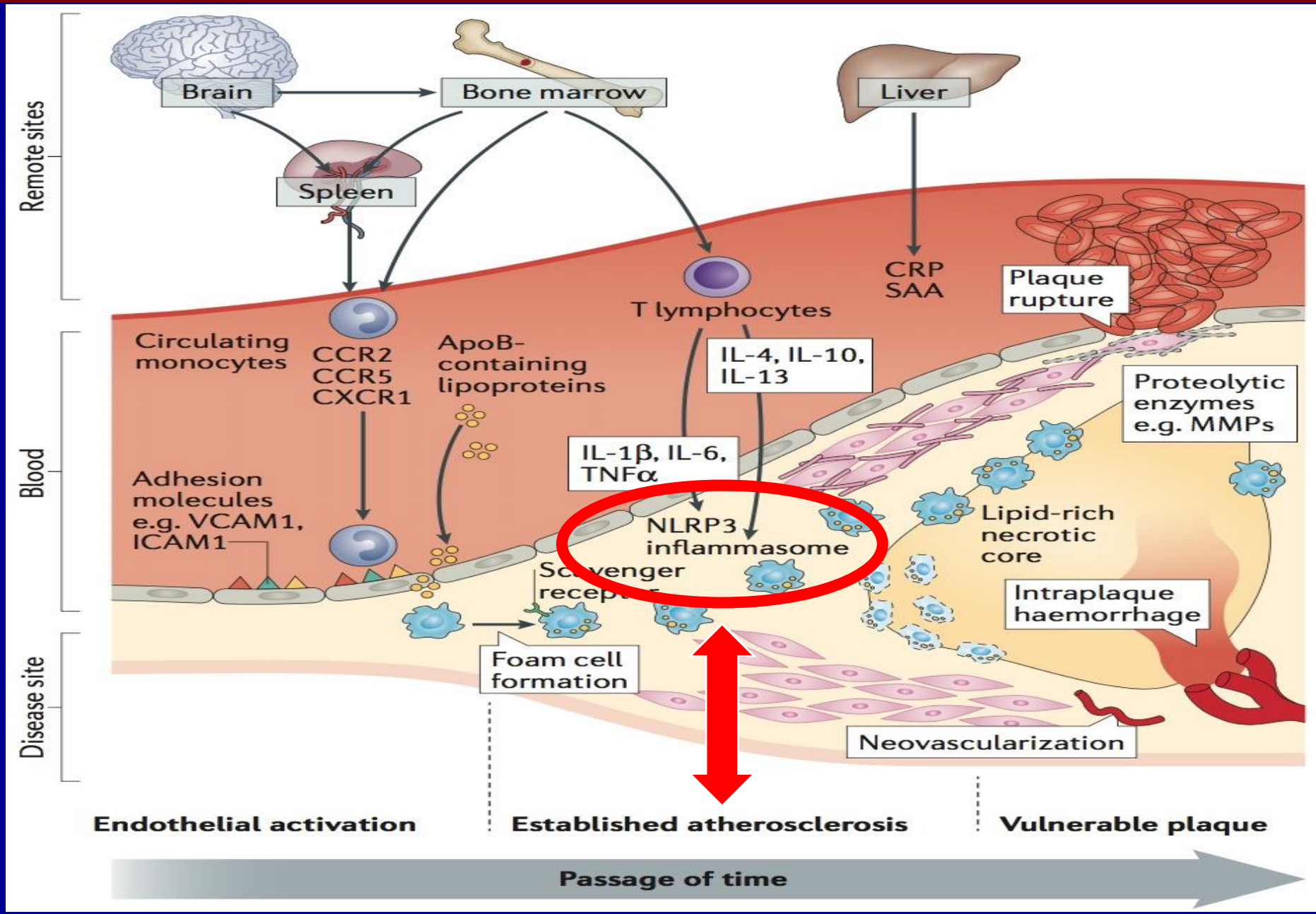
Inflammasome NLRP3 et ASO

Du LDL-C oxydé ou cristaux de cholestérol à IL-1β et IL-18



Guo H et al. Nature Medecine 2015; 21: 677-87

Inflammasome selon l'évolution de l'ASO



Ruparelia N et al. Nat. Rev. Cardiol 2017

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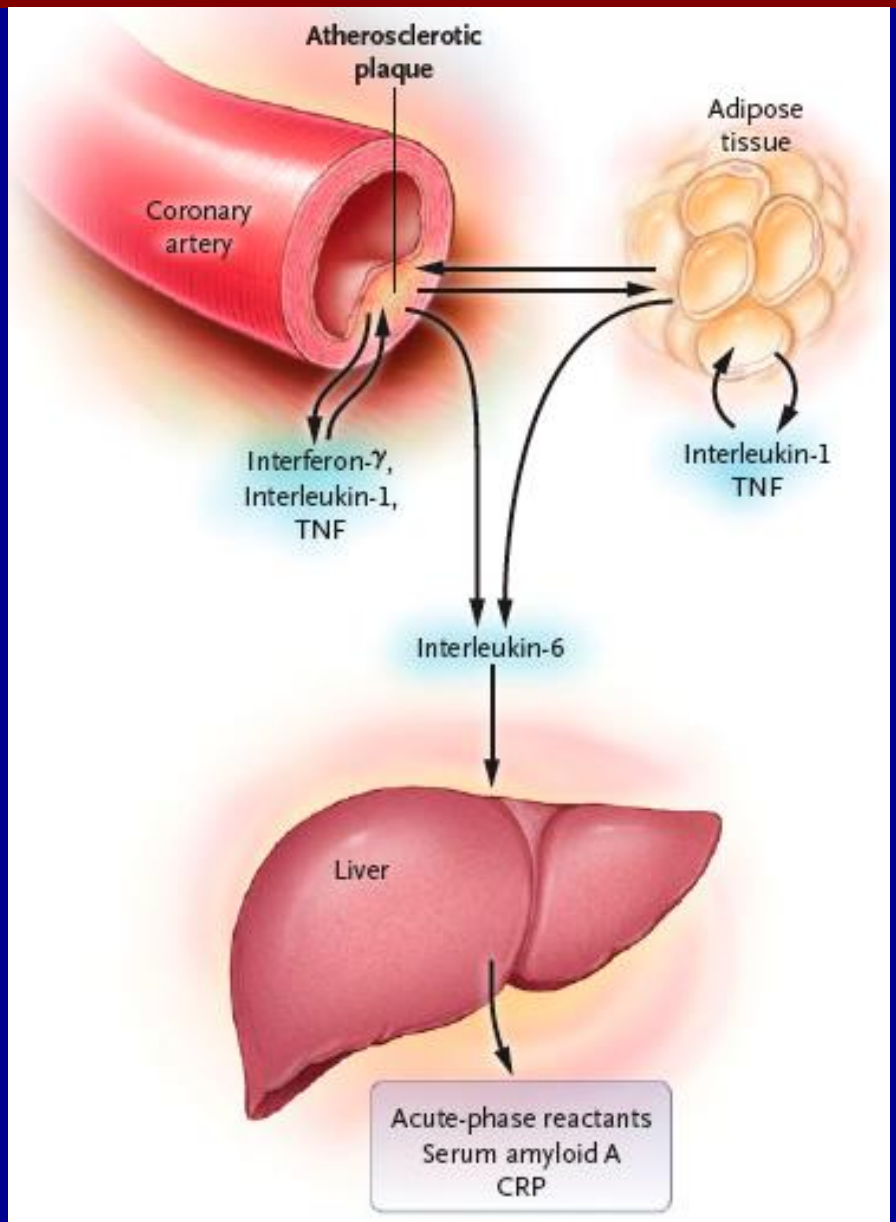
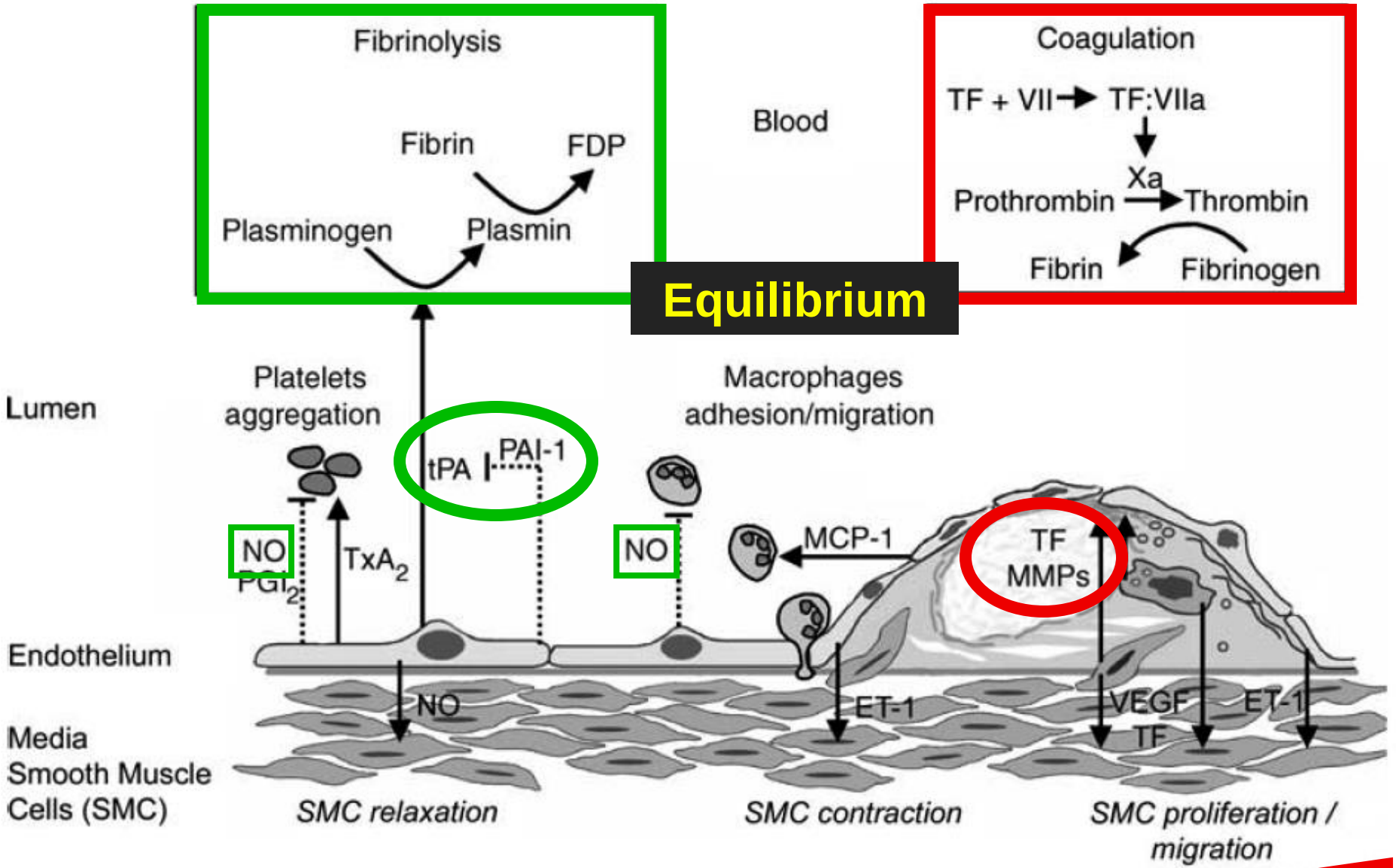
Athérosclérose: Cytokines et CRP

Hansson G K. NEJM 2005;352:1685-95



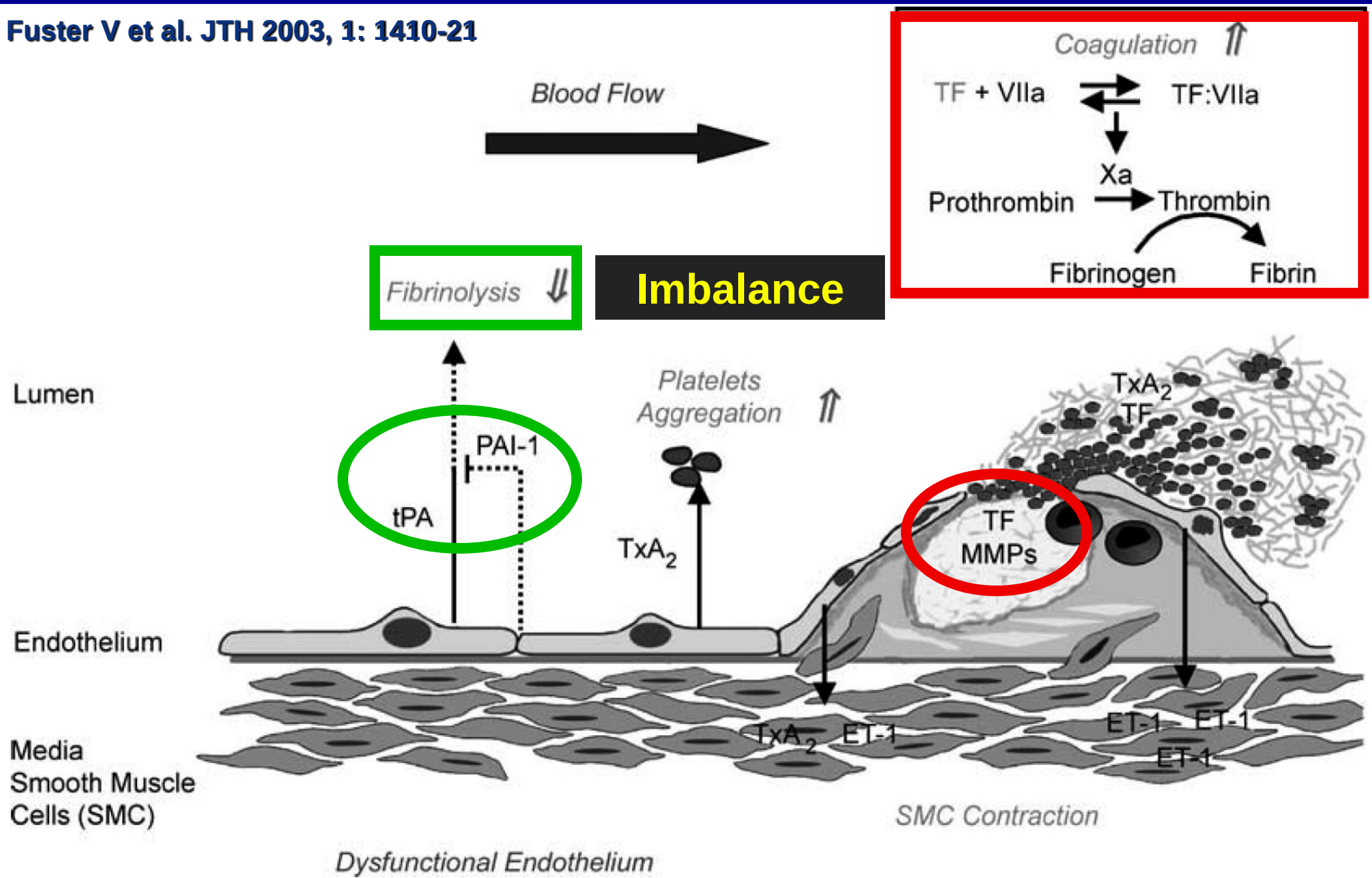
Athérosclérose stable: Fibrinolyse ≥ Coagulation



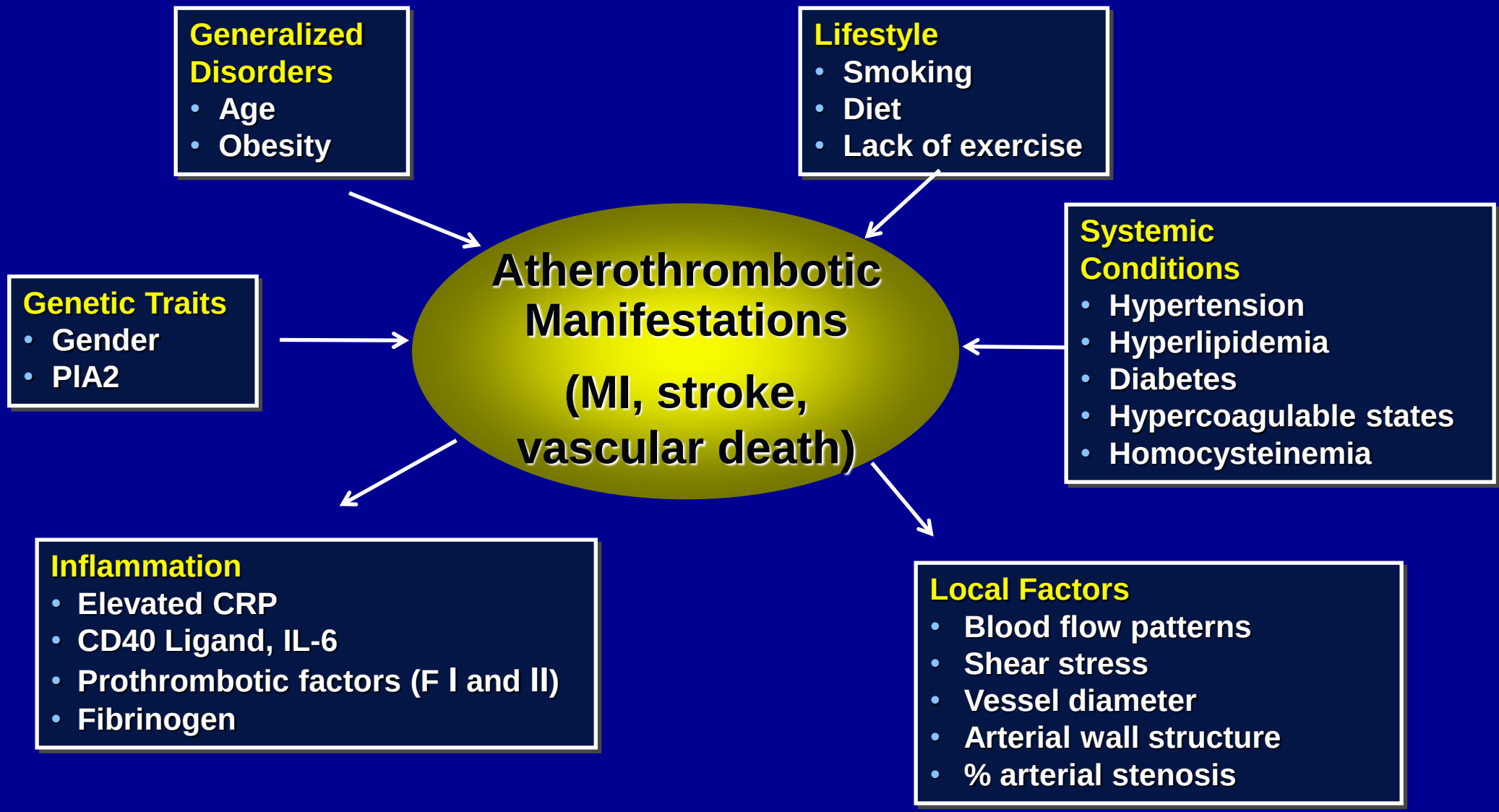
Fuster V et al. JTH 2003, 1: 1410-21

Athérothrombose: Fibrinolyse < Coagulation

Fuster V et al. JTH 2003, 1: 1410-21

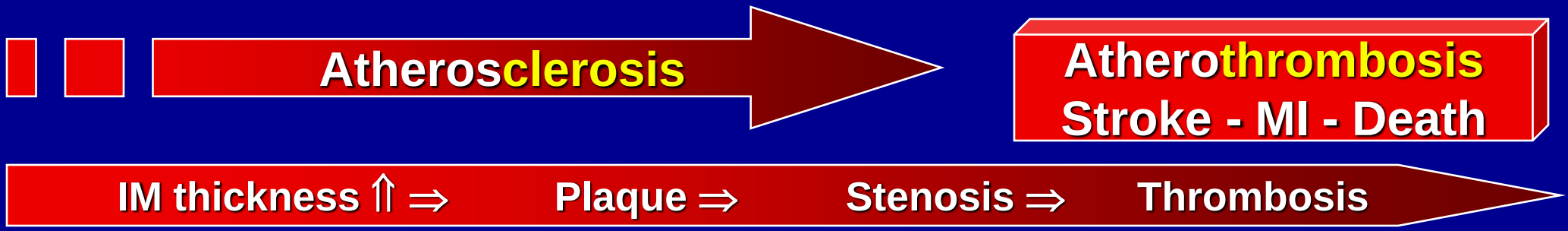


Facteurs de risqué CV: Vue d'ensemble



Adapted from Yusuf S, et al. *Circulation.* 2001;104:2746-2753.
Drouet L. *Cerebrovasc Dis.* 2002;13(suppl 1):1-6.

Facteurs de risque: séquence clinique



Traditional Factors

- Triggerring factors : AgII/AT1, Shear stress, Diabetes, LDL/oxLDL
- Genetic (fixed or modifiable) and acquired

Endothelial Factors

Inflammation Factors

Cells, Intercellular + intracellular signaling, proteins-enz. actions

Procoagulant Factors

TF, PAI-1 / tPA and TxA_2 / Prostacycline imbalances

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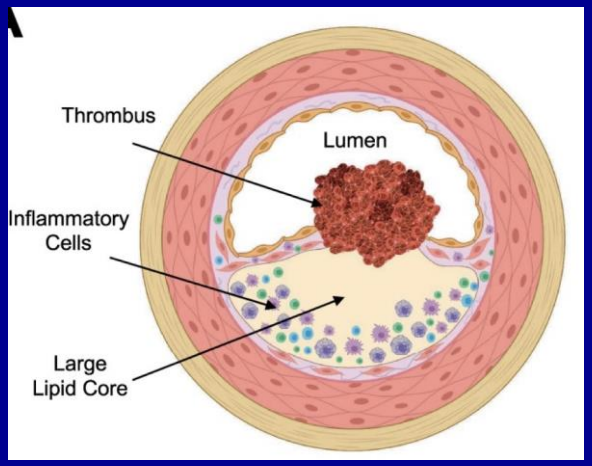
Les grands syndromes
Modes principaux de présentation clinique

ASO



3 composantes principales

MAP

. Asymptomatique
. Claudication
. Ischémie critique

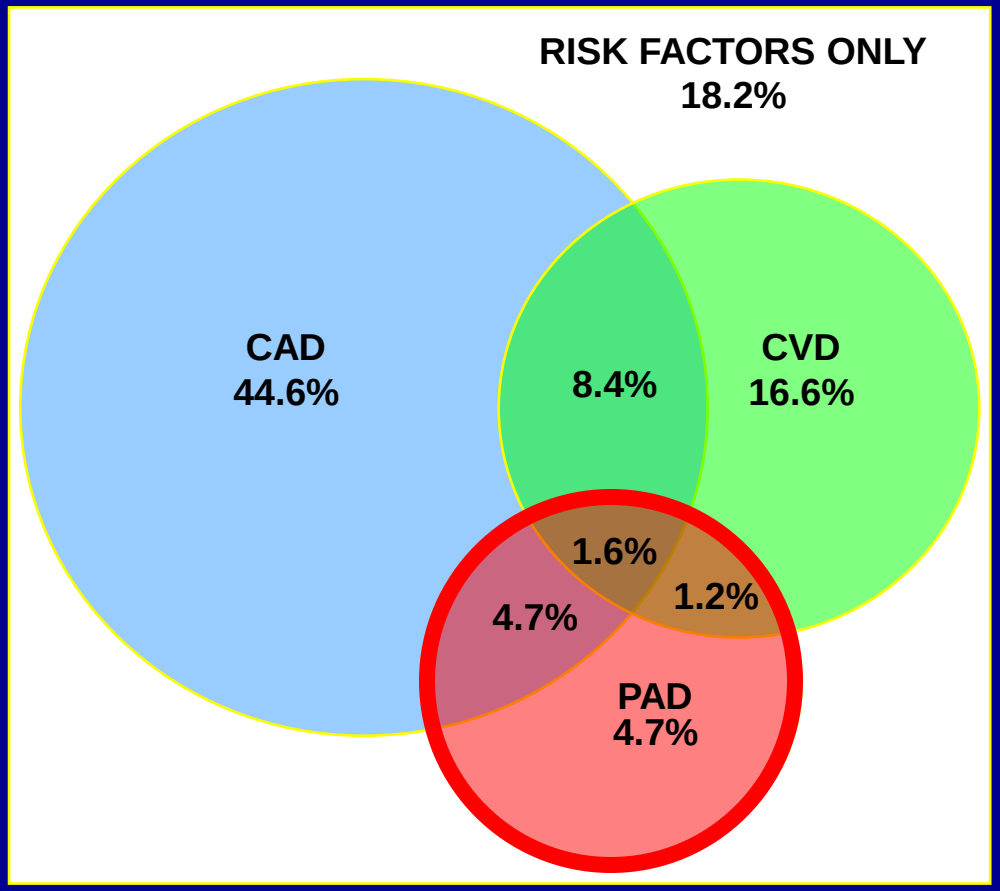
MCAS

. Asymptomatique
. Angine stable
. Angine instable
. Infarctus

MCV

. Asymptomatique
. AIT ischémique
. AVC ischémique

REACH
Cohorte prospective



CAD= Stable angina
Unstable angina
MI
Angioplasty/stenting
CABG

CVD= TIA
Stroke

PAD= history or current intermittent claudication with:
- ABI < 0.9
- Angioplasty/stenting
- Amputation

RISK FACTORS ONLY: at least 3 risk factors and no manifestation of symptomatic atherothrombosis

Worldwide distribution

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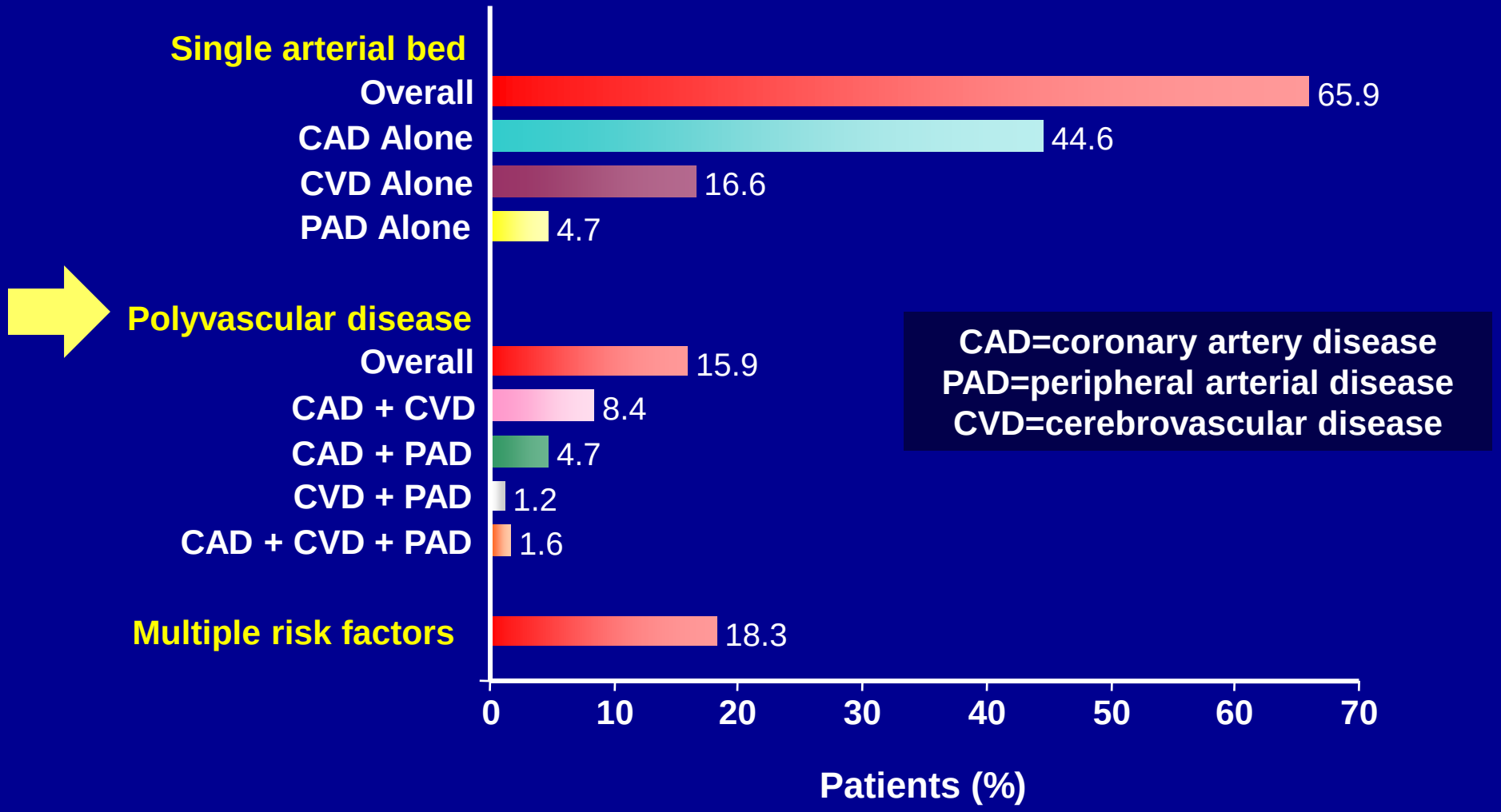
Population at Baseline REACH Registry

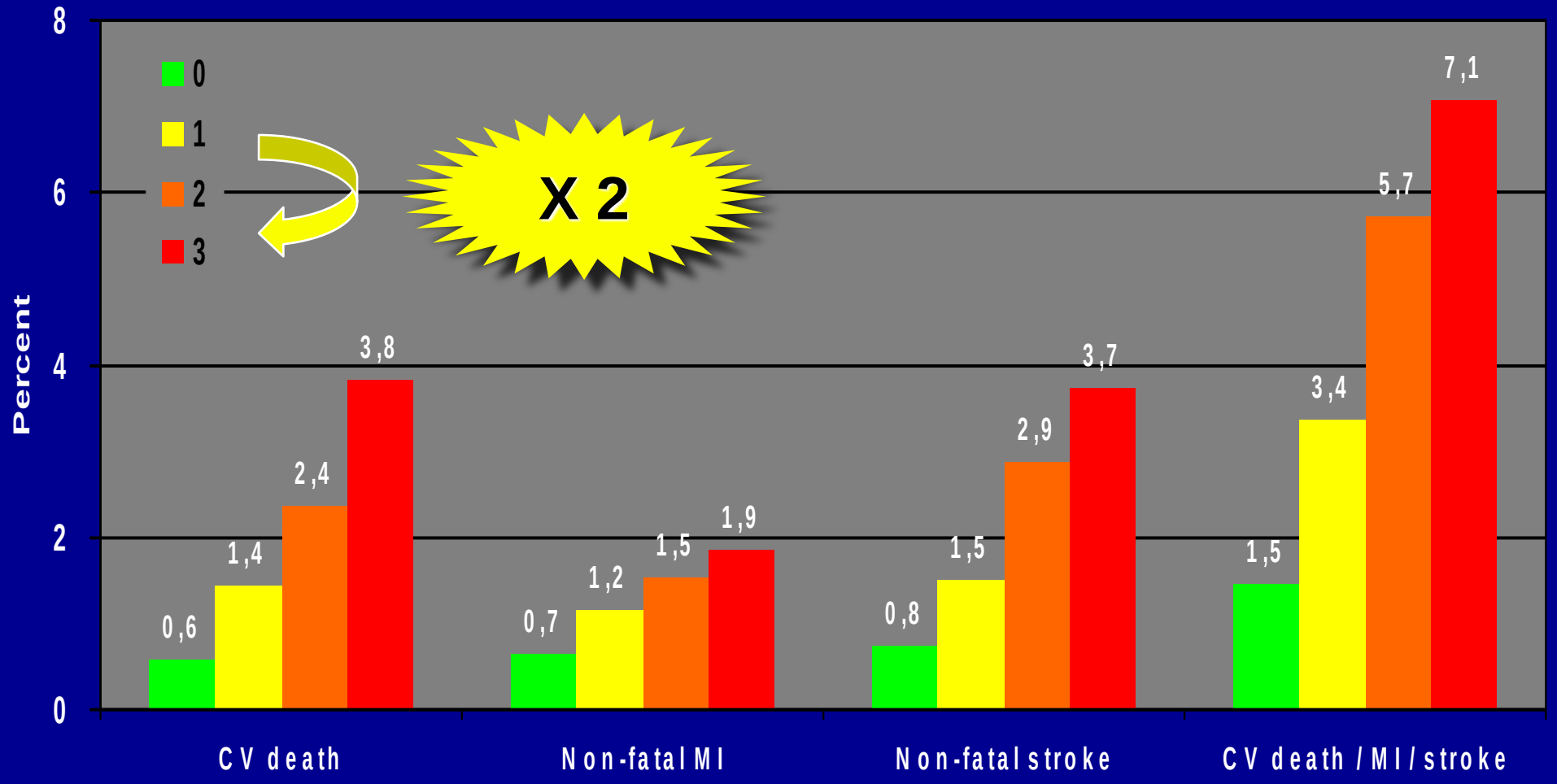
Prevalence of disease in arterial beds (% of total)



Bhatt DL et al, on behalf of the REACH Registry Investigators. *JAMA* 2006;295(2):180-189.

REACH: 1-year cardiovascular event rates

According to number of symptomatic disease locations*



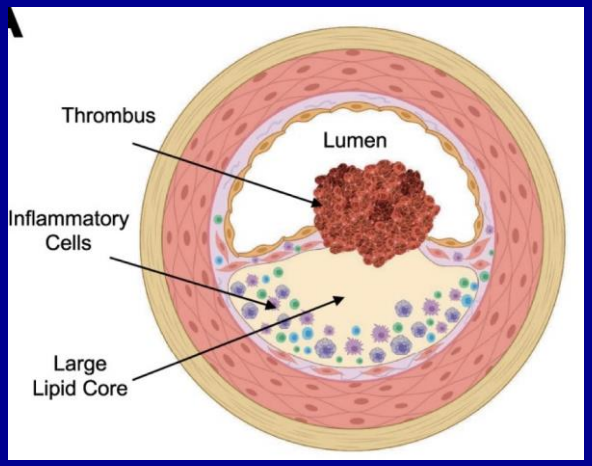
All p values <0.001

*Pts with ≥3 risk factors but no symptoms are counted as 0, even in the presence of asymptomatic carotid plaque or reduced ABI

**TIA, unstable angina, other ischemic arterial event including worsening of peripheral arterial disease

Les grands syndromes
Approche anti-thrombotique

ASO



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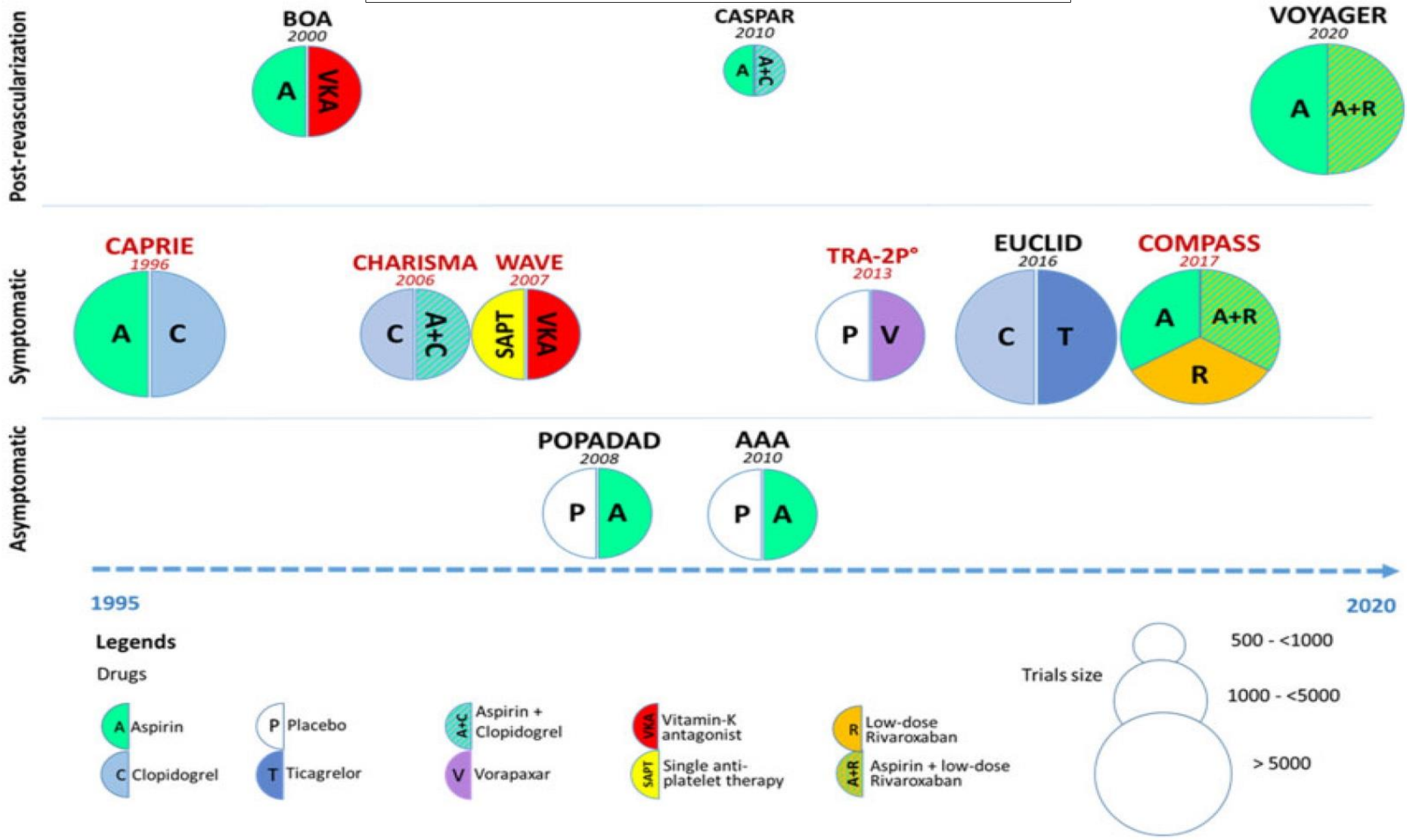
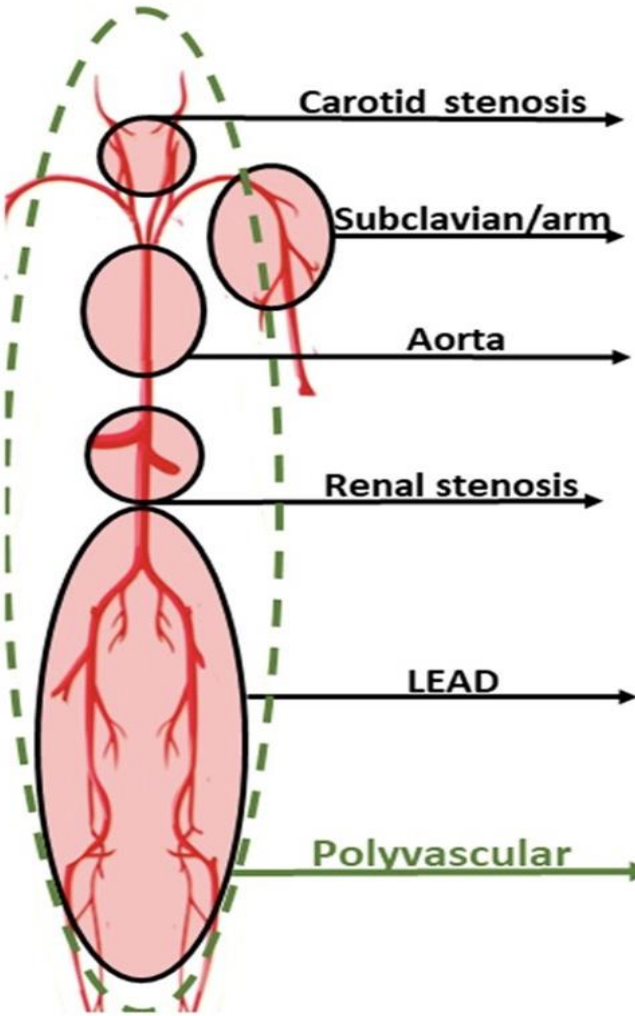
- . AIT ischémique
- . AVC ischémique


Post-revascularization
Symptomatic
Asymptomatic
BOA
2000
A
VKA
CASPAR
2010
A
A+C
VOYAGER
2020
A
A+R
CAPRIE
1996
A
C
CHARISMA
2006
C
A+C
WAVE
2007
SAPT
VKA
TRA-2P°
2013
P
V
EUCLID
2016
C
T
COMPASS
2017
A
A+R
R
POPADAD
2008
P
A
AAA
2010
P
A
1995
2020
Legends
Drugs
A Aspirin
C Clopidogrel
P Placebo
T Ticagrelor
A+C Aspirin + Clopidogrel
V Vorapaxar
VKA Vitamin-K antagonist
SAPT Single anti-platelet therapy
R Low-dose Rivaroxaban
A+R Aspirin + low-dose Rivaroxaban
Trials size
500 - <1000
1000 - <5000
> 5000



	Chronic disease (long-term) Default strategy (or alternative) (or if high bleeding risk)		Post-revascularization Period (1-3 months)	
	Symptomatic	***Asymptomatic***	***Surgery***	***Endovascular***
Carotid stenosis	**A** (or C) *A*	**A** (or C) *N*	**A** (or C)	**A+C**
Subclavian/arm	**A** (or C) *A*	**A** (or C) *N*	**A**	**A+C**
Aorta	**A** (or C) *N*	**A** (or N) *N*	**A**	**A+C**
Renal stenosis	**A** (or C) *N*	**A** (or N) *N*	**A**	**A+C**
LEAD	**R+A** *C (or A)*	**N**[a]	**R+A** *C (or A)*	**R+A±C*** (or A+C) *C (or A)*
Polyvascular	**R+A** *C (or A)*			

[a]only if isolated

Abbreviations: ***A***: aspirin; ***C***: Clopidogrel; ***N***: no antithrombotic therapy; ***R***: low-dose rivaroxaban (2.5 mg bid)

MAP 2022

Méthodologie:
PICO
MERST
GRADE

Les grands syndromes: MAP

Approche anti-thrombotique simplifiée: options principales

MAP

- . Asymptomatique / sub-clinique
- . MAP symptomatique
- . Haut risque de saignement
- . Monothérapie

. **Asymptomatique**: Pas d'antithrombotique

. **MAP et haut risque de saignement:** Monothérapie

. **Monothérapie**: Clopidogrel est l'agent de choix

Adapté du Consensus Canadien 2022

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Les grands syndromes: MAP

Approche anti-thrombotique simplifiée: options principales

MAP

- **MAP haut risque**
- **MAP non à haut risque**
- **Contre-indication au rivaroxaban**

. MAP à haut risque CV ou M. inf. + bas risque saignement:
AAS + Rivaroxaban 2.5 mg BID

. MAP non à haut risque CV ou M. inf. + bas risque saignement :
AAS + Rivaroxaban 2.5 mg BID *ou* monothérapie

. MAP à haut risque et contre-indication au rivaroxaban:
AAS + Clopidogrel *ou* AAS + Ticagrelor

Adapté du Consensus Canadien 2022

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Les grands syndromes: MCAS

Approche anti-thrombotique simplifiée: options principales

MCAS

. Asymptomatique / sub-clinique
. Angine stable
. Angine instable / NSTEMI / STEMI

. Asymptomatique: Pas d'antithrombotique

. Angine stable: AAS *ou* Clopidogrel *ou* AAS + Rivaroxaban 2.5 mg BID

. Angine instable ou NSTEMI: AAS + Ticagrelor ou Clopidogrel, pour 1 mois à 1 an (puis 3 ans) selon risques CV et de saignement, puis AAS *ou* AAS + Rivaroxaban 2.5 mg BID

. Infarctus STEMI: Après revascularisation: AAS *ou* Clopidogrel *ou* AAS + Rivaroxaban 2.5 mg BID

Adapté des Consensus Canadiens 2011-2013-2018

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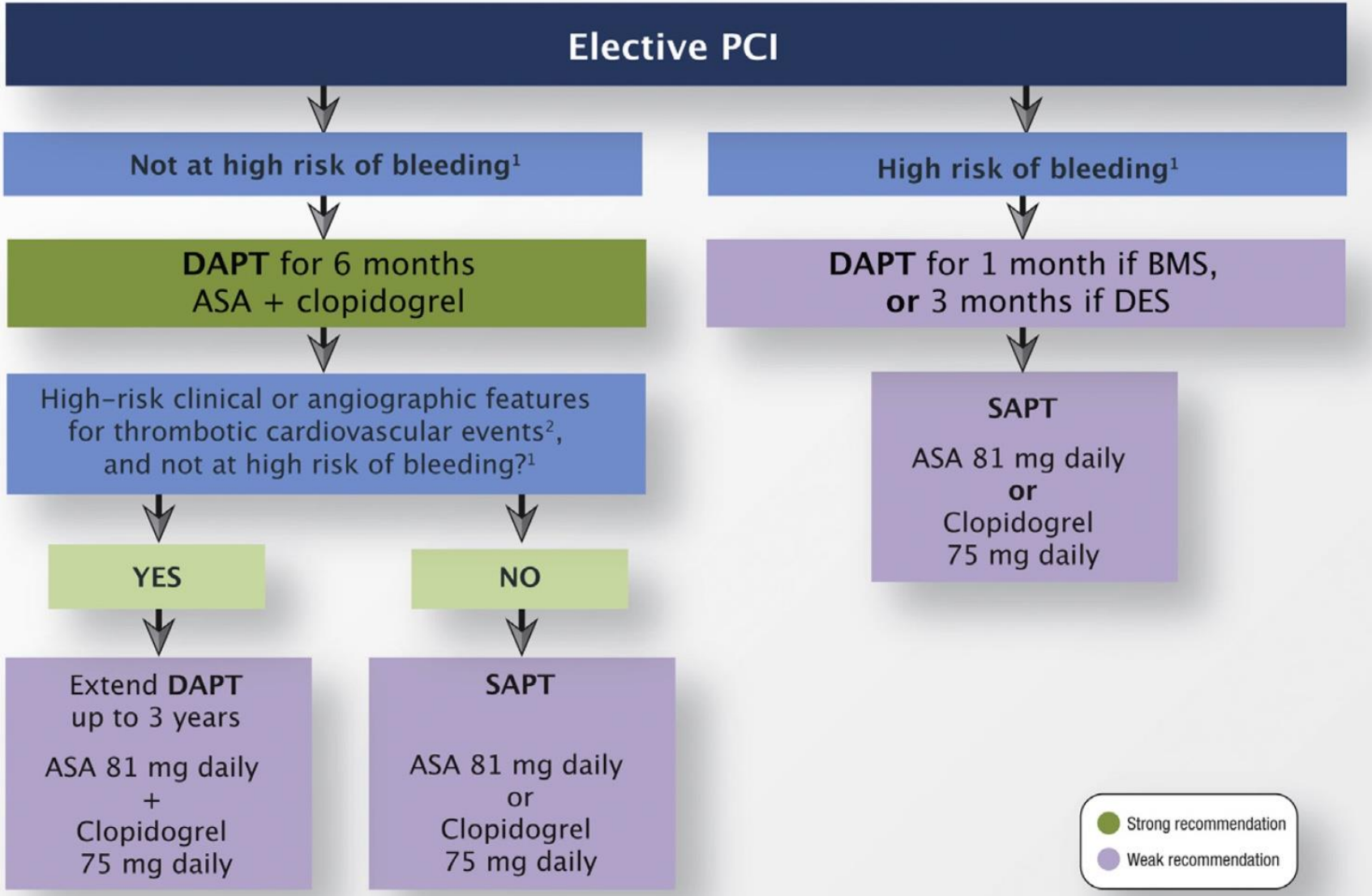
Consensus Canadien 2018 (n'incluant pas COMPASS)



1 Factors associated with increased bleeding risk include: need for OAC in addition to DAPT, advanced age (> 75 years), frailty, anemia with hemoglobin < 110 g/dL, chronic renal failure (creatinine clearance < 40 mL/min), low body weight (< 60 kg), hospitalization for bleeding within last year, prior stroke/intracranical bleed, regular need for NSAIDS or prednisone

2 Clinical and angiographic features associated with increased risk of thrombotic events include: age > 65, diabetes mellitus, prior myocardial infarction, chronic renal dysfunction (creatinine clearance < 60 mL/min), multi-vessel disease, multiple stents implanted, complex bifurcation lesion, total stent length > 60 mm, chronic total occlusion intervention or bioabsorbable vascular scaffold (BVS) implantation.

DAPT=dual antiplatelet therapy SAPT=single antiplatelet therapy BMS=bare metal stent DES=drug eluting stent

Consensus Canadien 2018 (n'incluant pas COMPASS)

Les grands syndromes: MCV

Approche anti-thrombotique simplifiée: options principales

MCV ← **. Asymptomatique**
. AIT ischémique
. AVC ischémique

. Asymptomatique: Pas d'antithrombotique

. AIT ischémique bas risque: AAS *ou* Clopidogrel *ou* AAS + Dipyridamole 25/200 BID

. AVC ischémique et AIT haut risque: AAS et Clopidogrel pour 3 semaines *ou* Ticagrelor pour 4 semaines *puis* AAS *ou* Clopidogrel *ou* AAS/Dip.

. Si MCAS ou MAP associée: AAS + Rivaroxaban 2.5 mg BID après le 1er mois

Adapté du nouveau Consensus Canadien 2020

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Les grands syndromes
Approche anti-thrombotique intégrée

MAP

+

MCAS

+

MCV

Lorsqu'il y a co-existence, il s'agit de patients à plus haut risque:

Prioriser, comme choix de Rx, la condition la plus récente, c'est-à-dire de moins de 1 an

Considérer double thérapie après la phase aigue, principalement AAS et Rivaroxaban 2.5 mg BID

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RÉFÉRENCES