Maladie artérielle périphérique (MAP) 2025

Aspects pharmacologiques

OBJECTIFS

1. Concilier les consensus canadien 2022, américain et européen 2024 avec les nouveautés 2025
2. Appliquer la meilleure stratégie anti-thrombotique
3. Intégrer les nouvelles interventions médicamenteuses

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

CANADIAN SOCIETY OF VASCULAR MEDICINE

Thrombosis Canada
Thrombose Canada

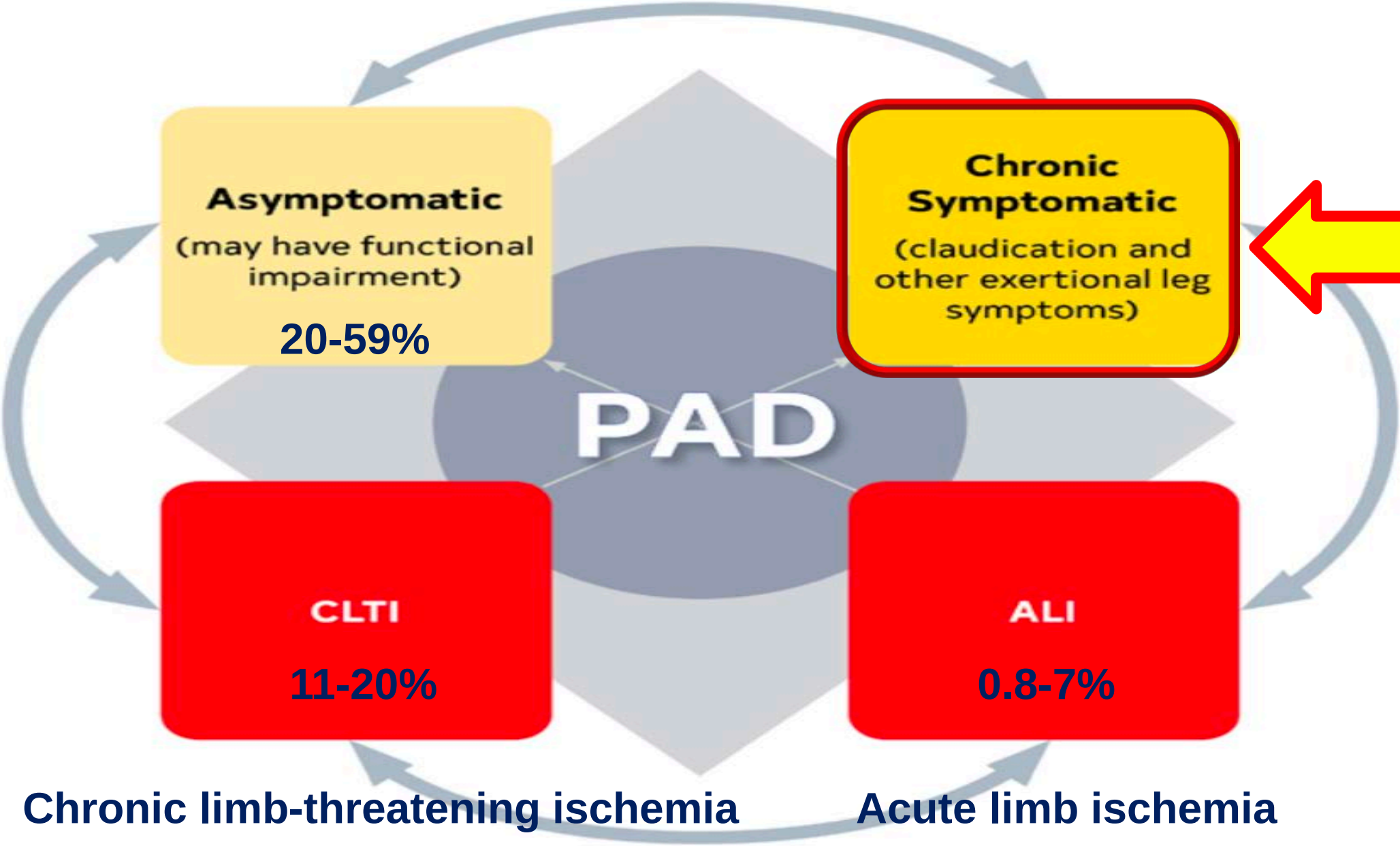
SSVQ
Société des sciences vasculaires du Québec

Déclaration de conflits d’intérêt potentiels

- Aucun conflit d‘intérêts
- Aucun honoraire pour cette conférence

A Roussin

MAP: classification, dont AHA 2024

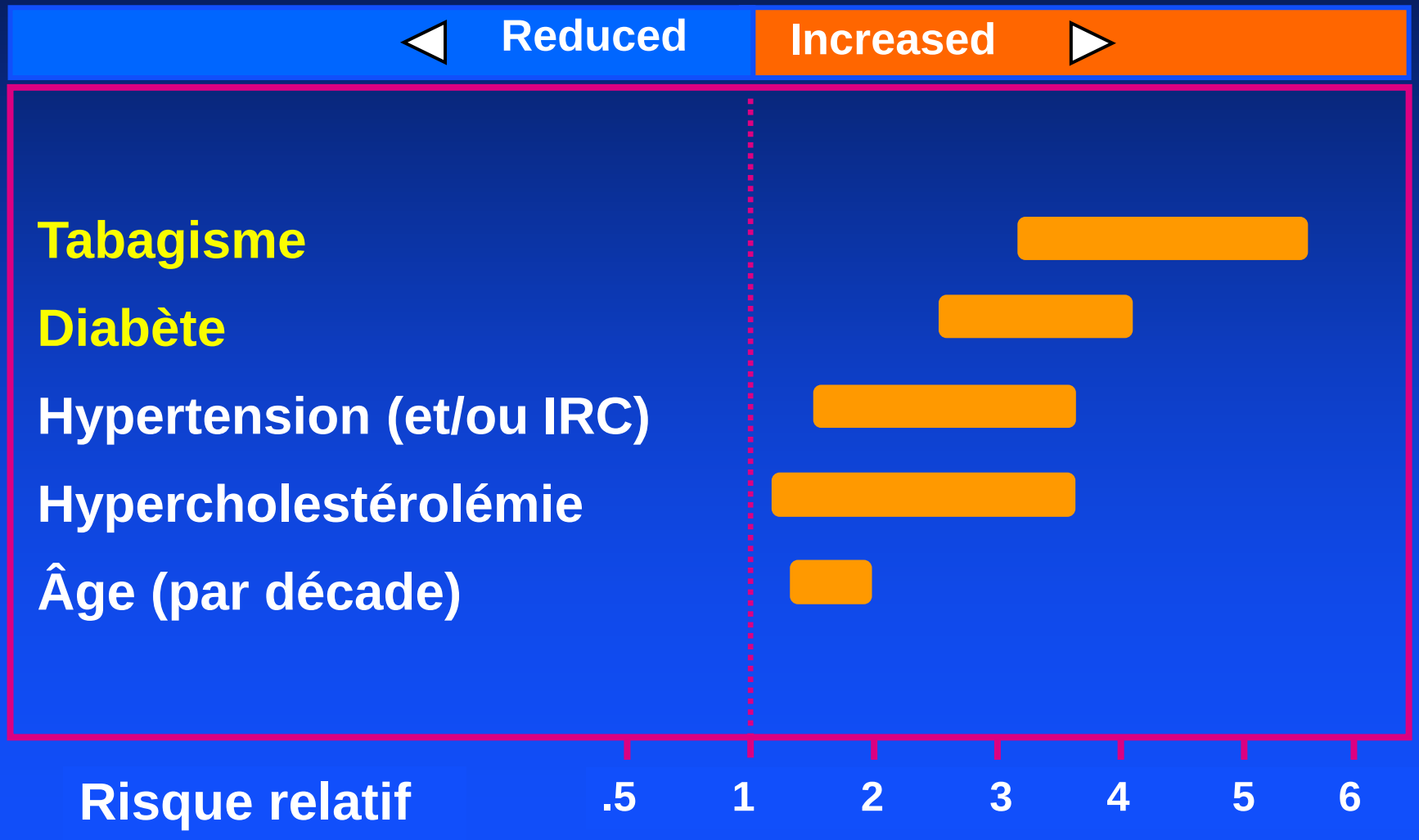


Chronic limb-threatening ischemia

Acute limb ischemia

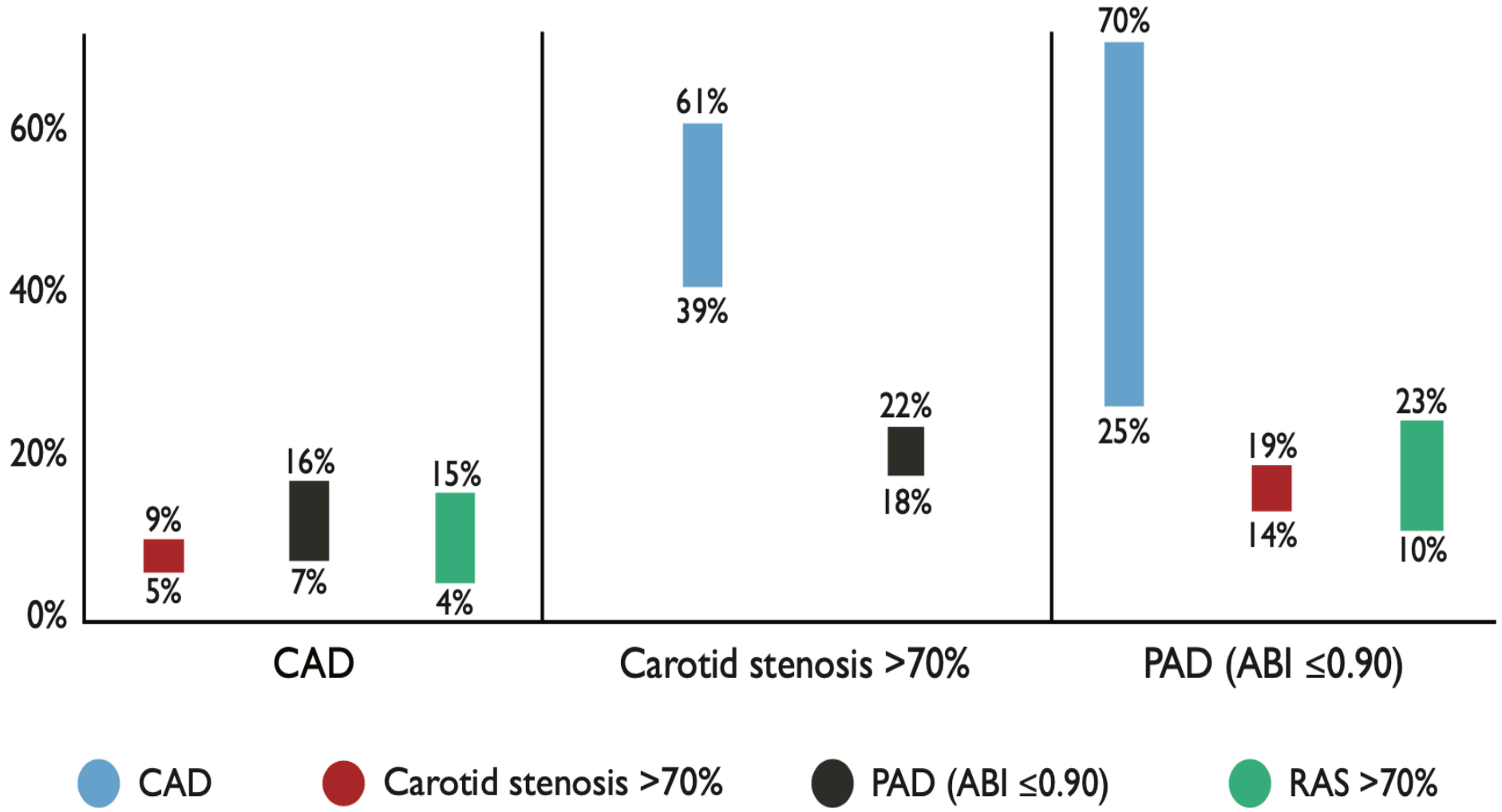
MAP

Facteurs de risque principaux



A Roussin

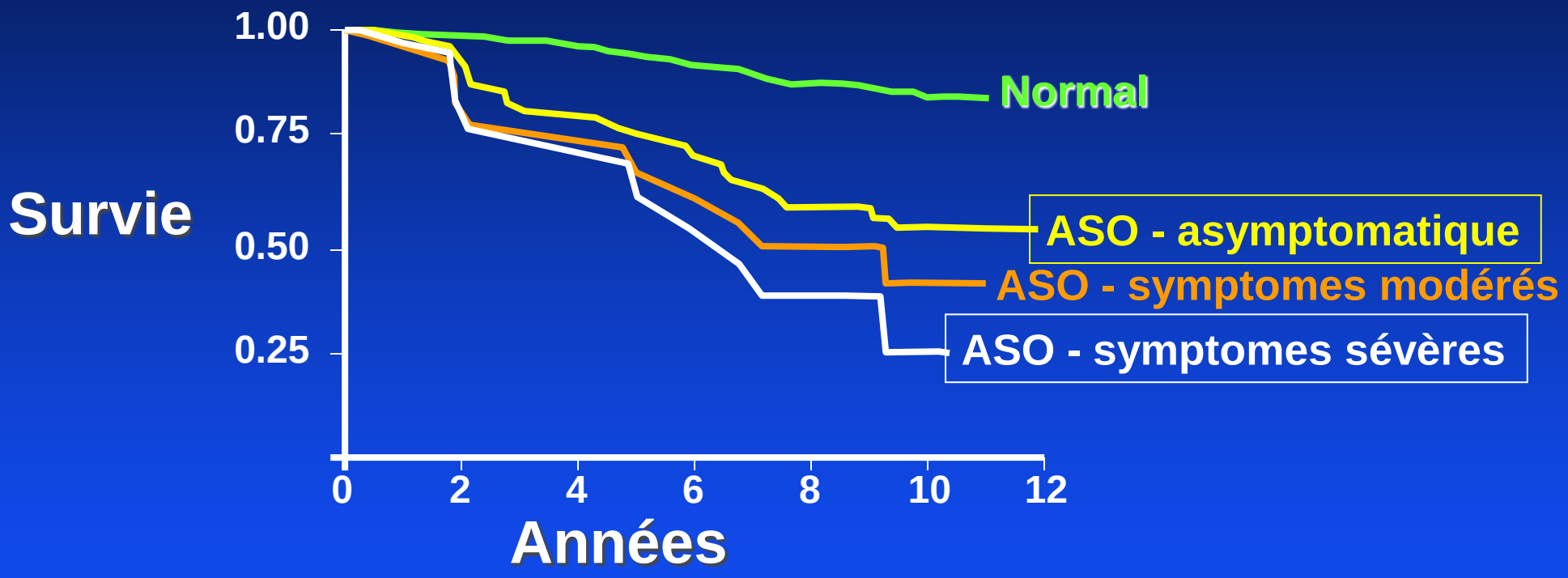
MAP, MCAS et ASO carotidienne



ESC

MAP: Survie long terme *(mortalité totale)*

San Diego Artery Study



RR mortalité: 3.1

Criqui MH et al.

A Roussin

MAP symptomatique: Claudication
Questionnaire d'Edinburgh

- Avez-vous une douleur ou incomfort de la (les) jambe(s) en marchant ? O
- Cette douleur débute en position assise ou debout immobile ? N
- Cette douleur est-elle provoquée en accélérant ou montant une côte ? O
- L'avez-vous en marchant normalement en terrain plat ? N /O
- Qu'arrive-t-il si vous vous arrêtez ?
  - La douleur dure plus de 10 minutes N
  - La douleur disparait en 10 minutes ou moins O
- Où ressentez-vous la douleur ou incomfort ? Désignez l'endroit

A Roussin

MAP: Méthodes diagnostiques

- ITH = index tibio-huméral (ABI en anglais)
- Duplex couleur = échographie avec Doppler
- *Tapis roulant*

Si atteinte fonctionnelle malgré approche médicale complète et revasculatisatioin considérée:

- Angio-CT = angiographie par SCAN injecté
- Angio-RMN = angiographie par RMN avec gadolinium
- Angiographie conventionnelle

Évaluation non-invasive

Index tibio-huméral (ITH)

ANKLE-BRACHIAL INDEX



HIGHEST OF the ankle pressure --> **NUMERATOR**

$$\frac{\text{NUMERATOR}}{\text{DENOMINATOR}}$$



HIGHEST OF the brachial pressure --> **DENOMINATOR**

- **0.9 TO 1.4** --> **normal** limit
- **0.8 TO 0.9** --> **some** arterial disease
- **0.5 TO 0.8** --> **moderate** arterial disease
- **LESS THAN 0.5** --> **severe** arterial disease
- **GREATHER THAN 1.4** --> **calcification** of the arteries

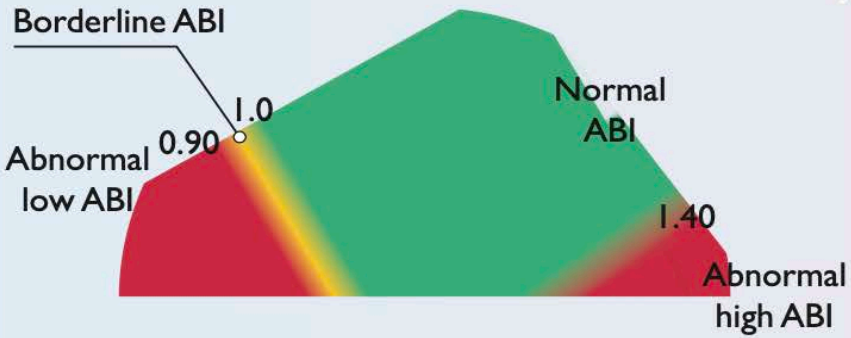


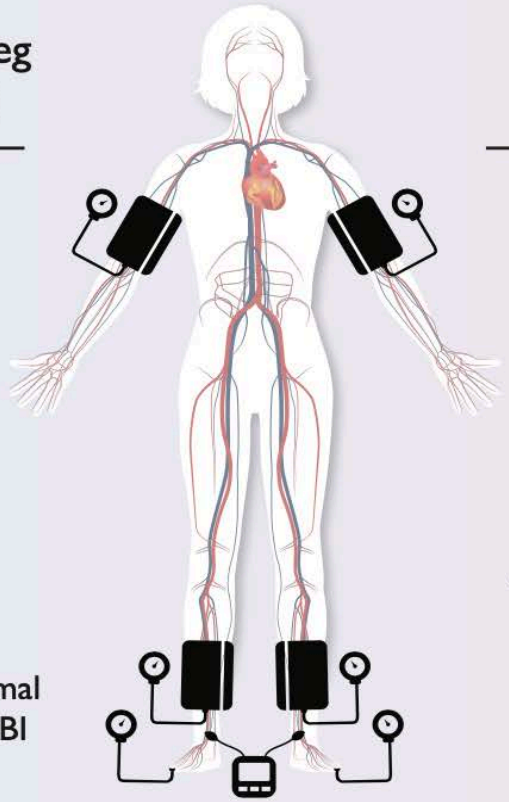
SSVQ

Haemodynamic criteria for PAD

Higher systolic **ankle pressure** of target leg (posterior tibial or dorsalis pedis artery)

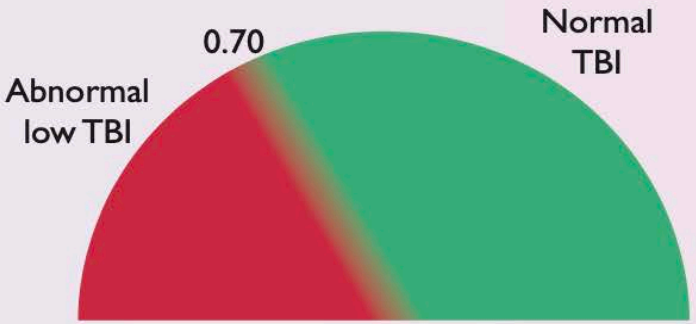
Higher systolic **brachial pressure**, irrespective of target leg





Toe pressure of target leg

Higher systolic **brachial pressure**, irrespective of target leg



Haemodynamic criteria for CLTI

Ankle pressure <50 mmHg

Toe pressure <30 mmHg

Transcutaneous oxygen partial pressure ($TcPO_2$)

$TcPO_2$ <30 mmHg

EHJ 2024

Exercice pour la claudication: “comment”

Training characteristics

Supervised hospital-based exercise programmes



Supervised group sessions



Different training modes





At least three times per week



Session duration of at least 30 min. Programmes duration of at least 12 weeks.



Low-to-moderate exercise intensity (or high if tolerated)



Different levels of elicited pain

Supervised home-based exercise programmes



Remote monitoring, logbook and connected devices

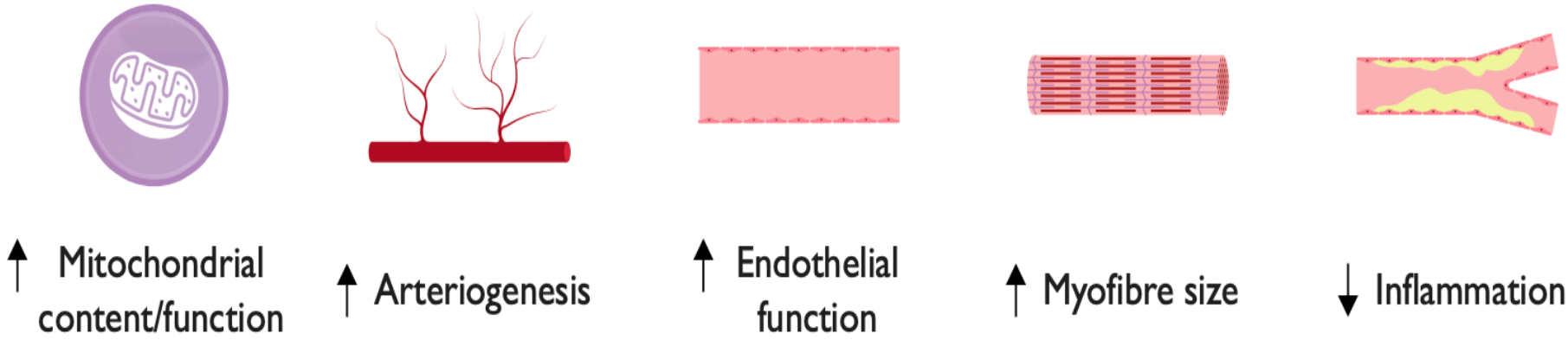


Exercice pour la claudication
Bénéfices et mécanismes

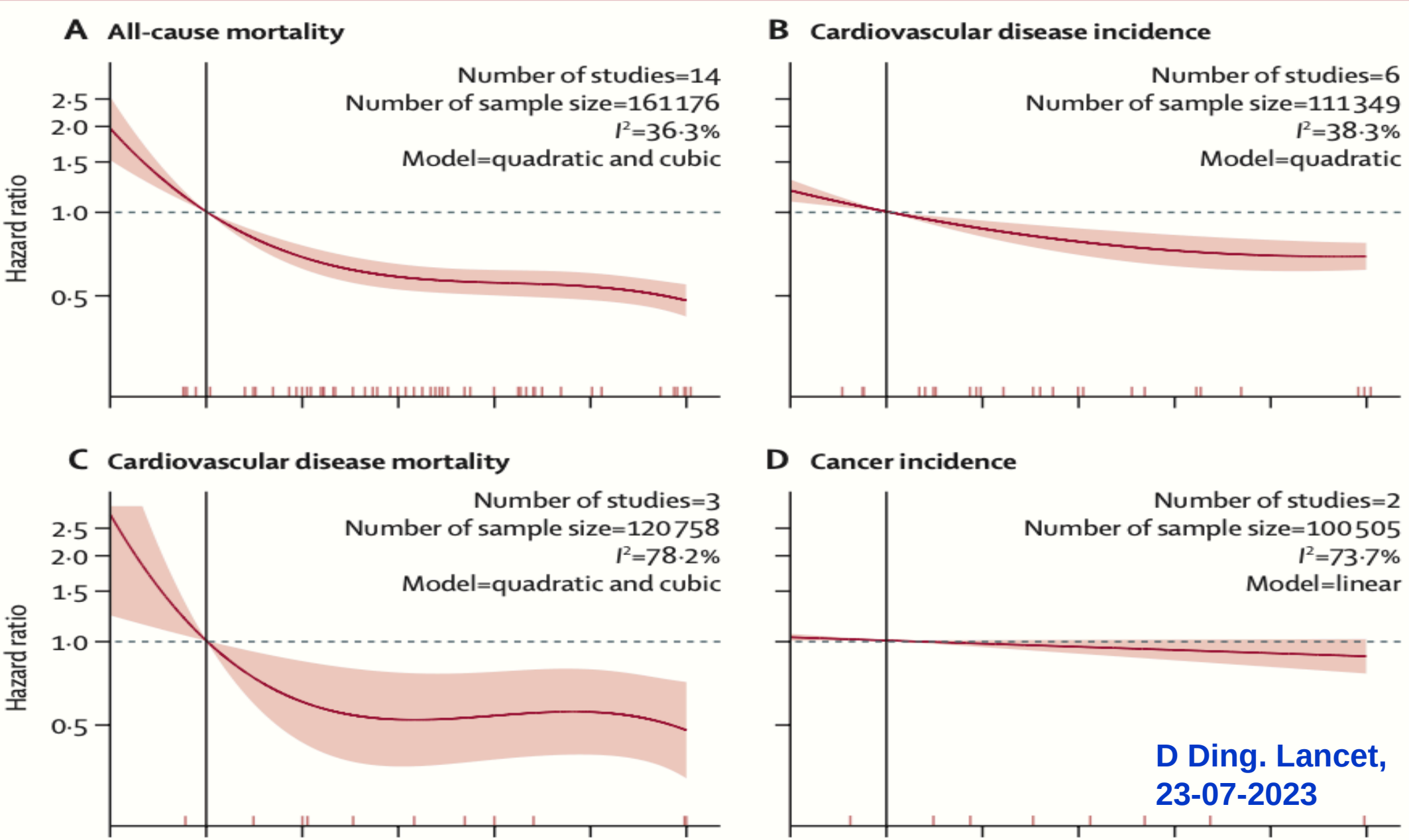
Training benefits



Potential involved mechanisms



Le nouveau 10,000 pas: « 7000 pas »



Traitements pharmacologiques pour la MAP

Recommandations CCS, AHA, ESC* et autres 2025

CLASSES

Statines haute intensité, avec EZ ou iPCSK9* si LDL demeure > 1.7 voir > 1.4*

IECA ou BRA si hypertension > 130 mmHg et même sans HTA*

iSGLT-2 ou aGLP-1* ou inh. DPP-4 (avec metformine)

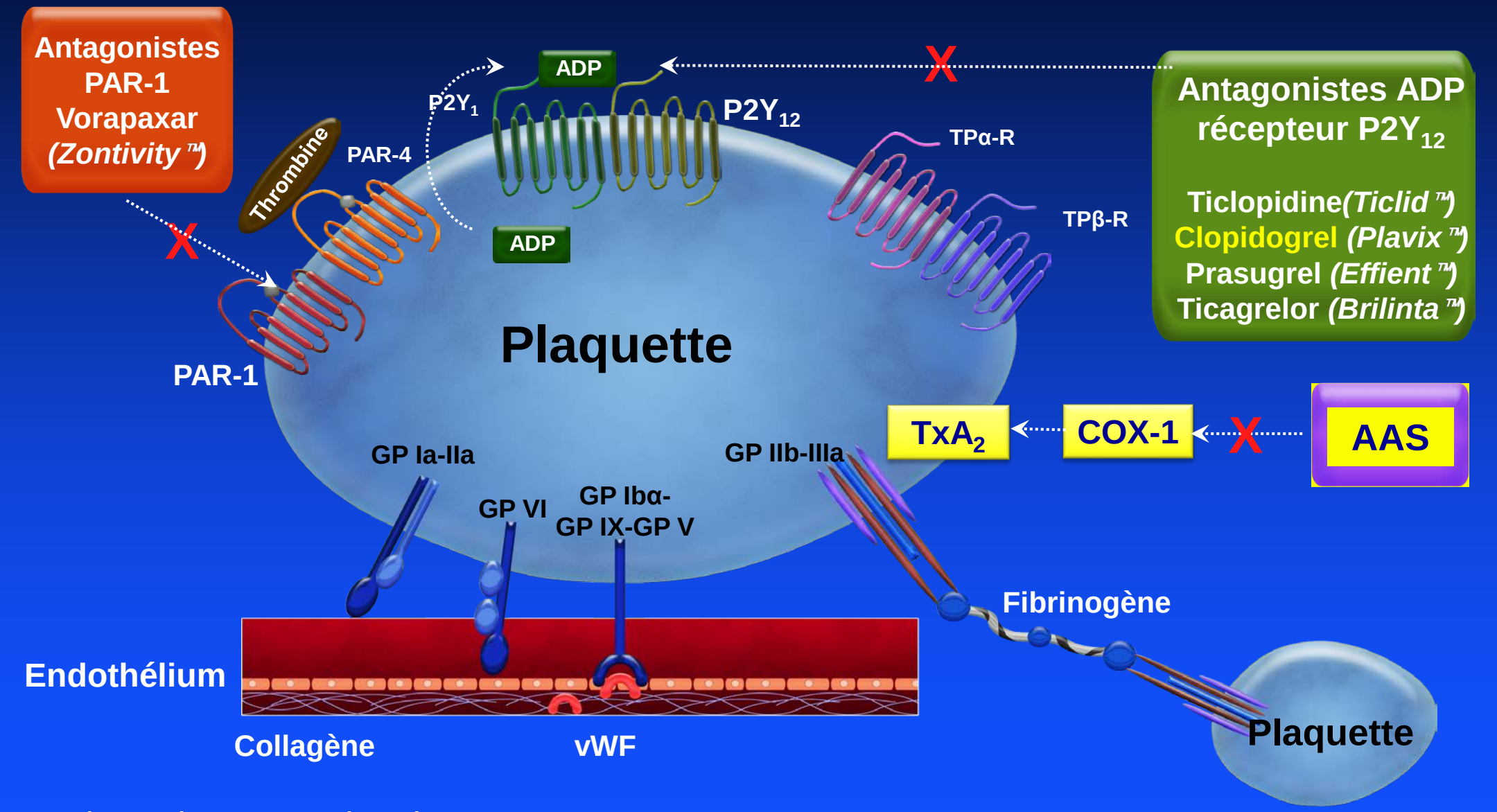
Antiplaquettaire ou AAS/Rivaroxaban si symptomatique*

Médicaments anti-tabagiques

Cilostazol (USA) ? en l'absence d'insuffisance cardiaque: 25-76% amelioration distance maximale de marche

Antiplaquettaires oraux 2025

Bloqueurs TxA2, ADP ($P2Y_{12}$) et PAR-1



Adapté, modifié, traduit et mis-à-jour à partir de: Angiolillo DJ et al. European Heart Journal (2010) 31, 17–28

A Roussin

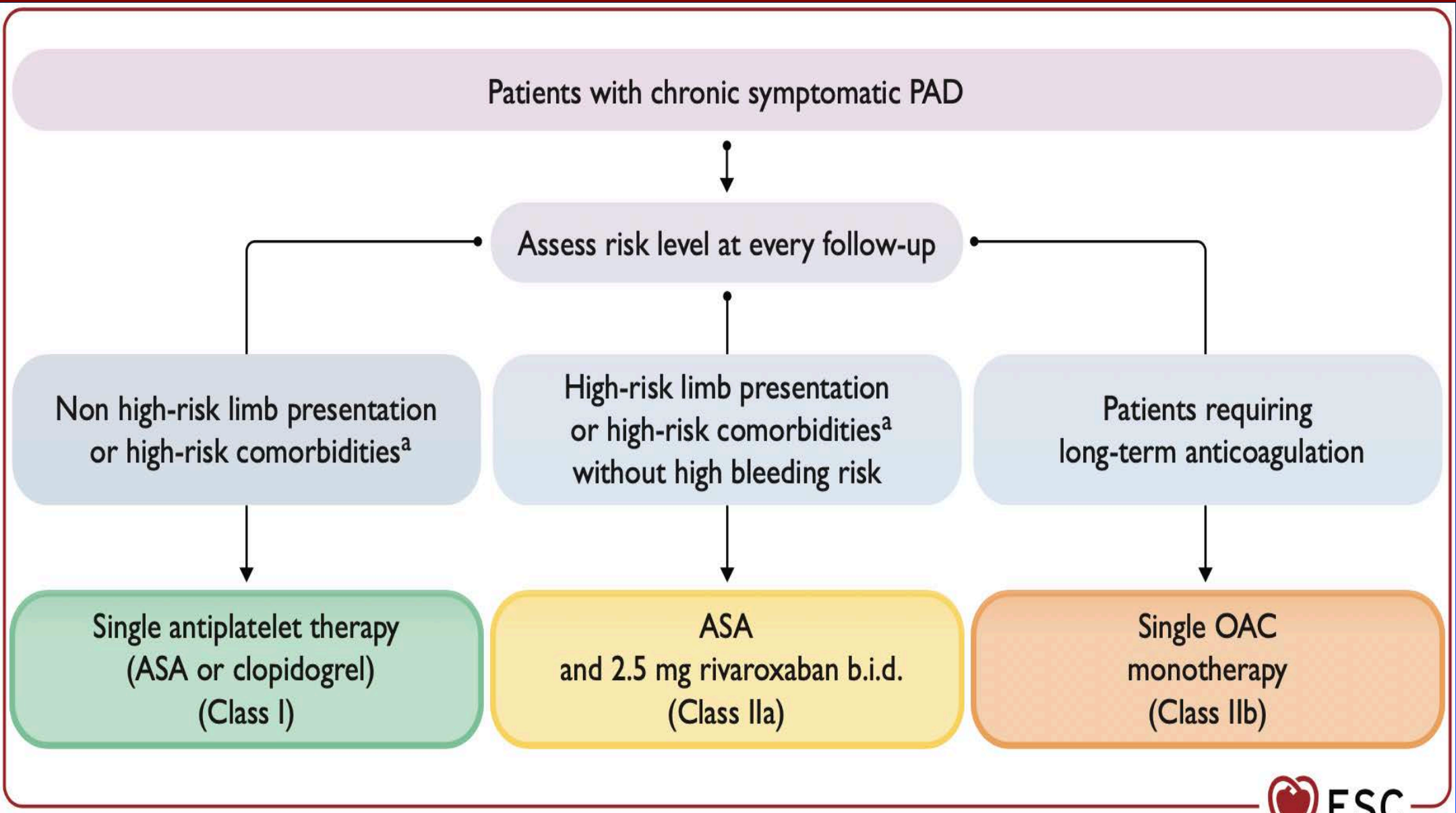
Thérapie antithrombotique (CCS, AHA, ESC*)

Patients avec MAP *asymptomatique* isolée

AAS ou anticoagulations déconseillés, pour la MAP isolée *asymptomatique, car le risque de saignement contrebalance en bonne partie la réduction du risque d'infarctus du myocarde**

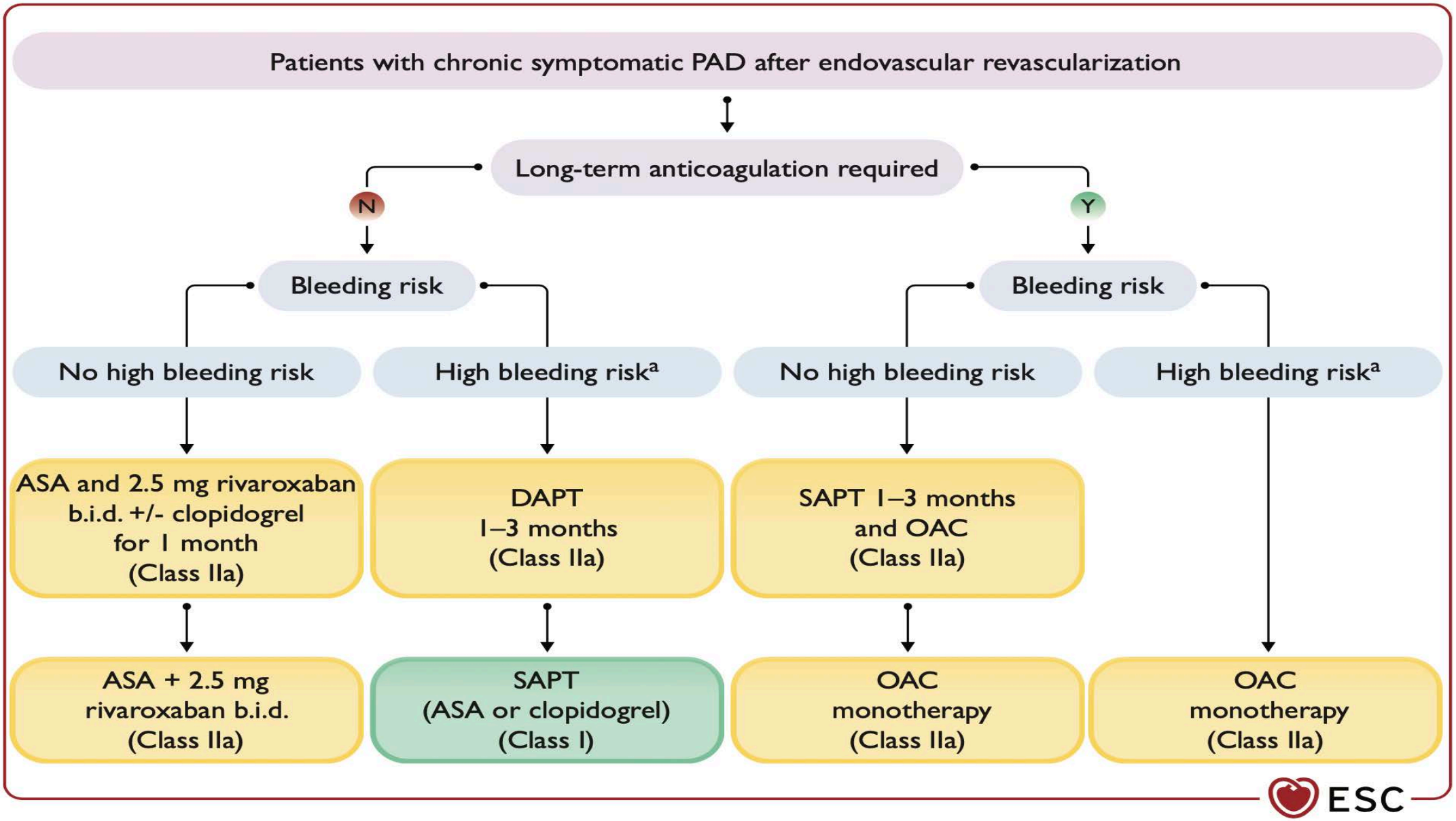
A Roussin

MAP chronique symptomatique



ESC

Thérapie antithrombotique
Après une intervention endovasculaire



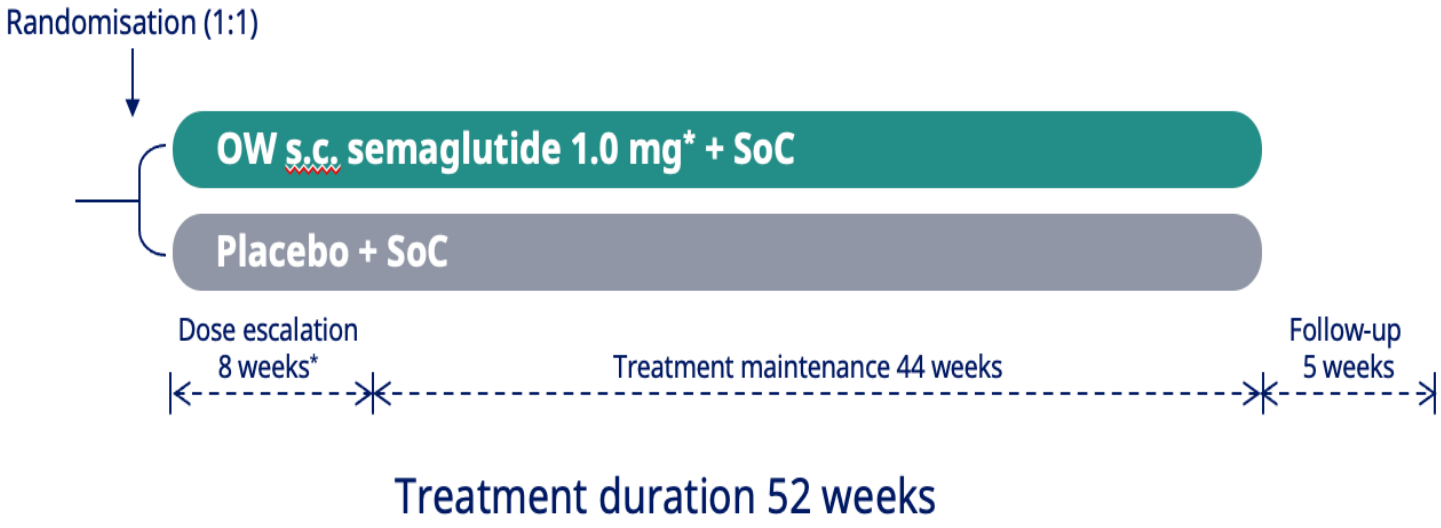
STRIDE: devis de l'étude

Trial design

Functional outcomes in people with PAD and T2D

792 people with T2D

- Age ≥18 years
- T2D diagnosis ≥180 days prior to screening
- HbA_{1c} ≤10%
- PAD with intermittent claudication (Fontaine stage IIa) ≥3 months and:
  - Pain-free walking distance >200 m on flat treadmill test (3.2 km/h (2 mph))
  - Maximum walking distance ≤600 m on a constant load treadmill test†
  - ABI ≤0.90 or TBI ≤0.70



Trial information

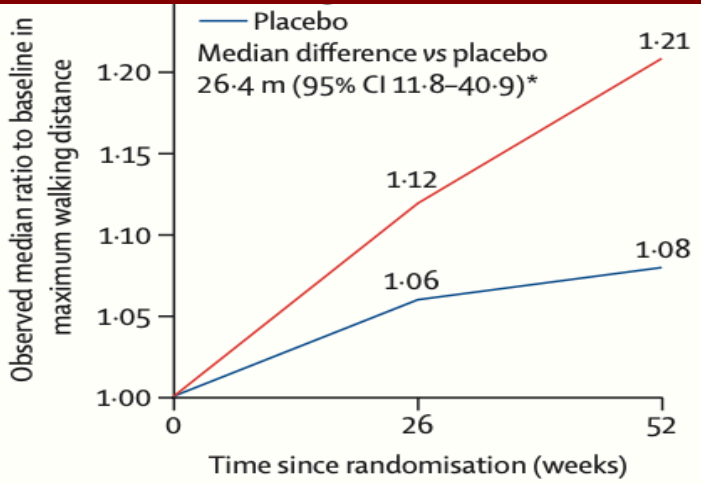
- **Trial objective:** to compare the effect of OW s.c. semaglutide on functional capacity in terms of maximum walking distance in people with PAD and T2D vs placebo
- Randomised, phase 3b, double-blind, parallel-group trial

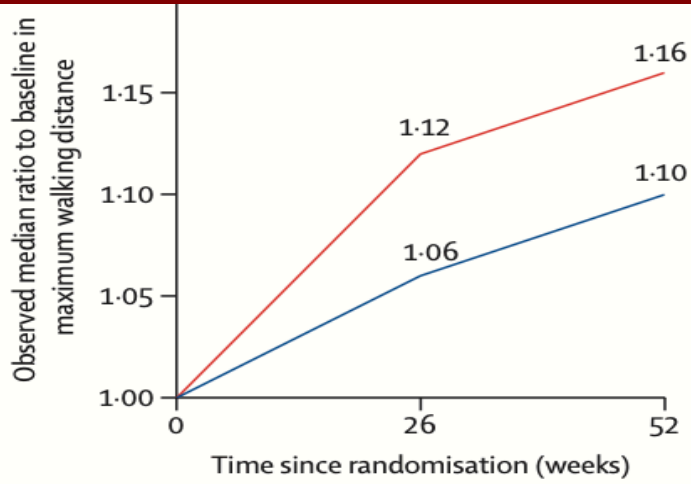
Primary endpoint

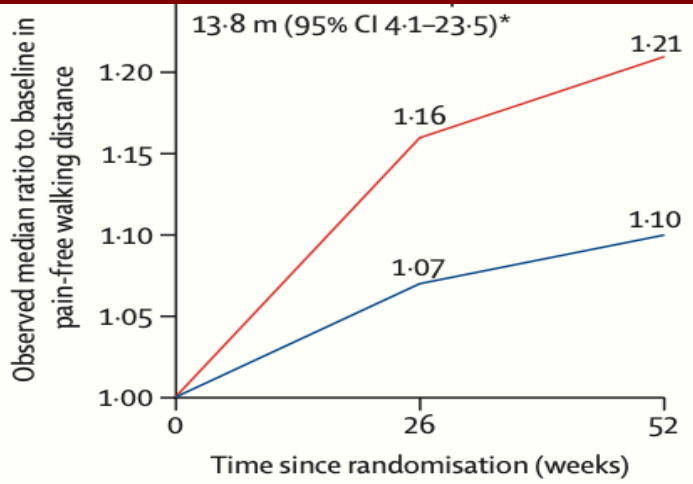
- Change from baseline in maximum walking distance on a constant load treadmill test† at week 52

M P Bonacca et al. Lancet 2025, 29 mars

STRIDE: sémaglutide et distance de marche

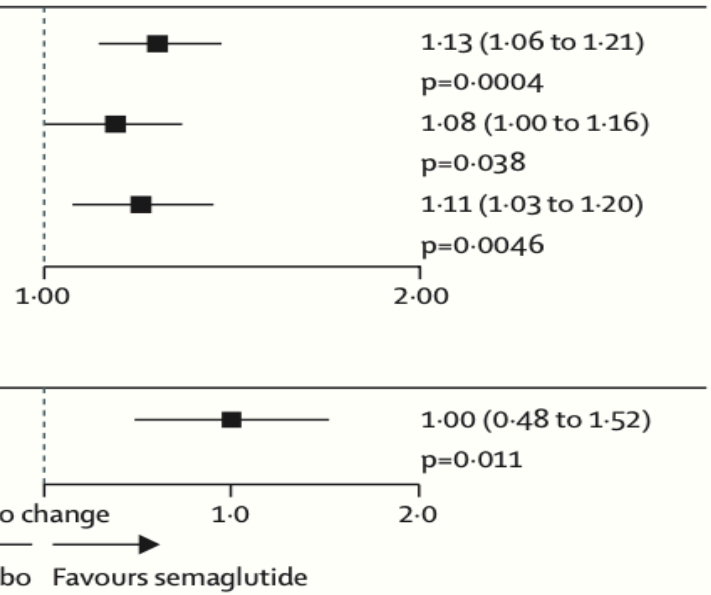






D

	Semaglutide (n=396)		Placebo (n=396)		ETR (95% CI) semaglutide *vs* placebo
	Number of participants	Median (IQR) ratio to baseline	Number of participants	Median (IQR) ratio to baseline	
Maximum walking distance at week 52	338	1·21 (0·95 to 1·55)	345	1·08 (0·86 to 1·36)	1·13 (1·06 to 1·21) p=0·0004
Maximum walking distance at week 57	329	1·16 (0·92 to 1·48)	333	1·10 (0·87 to 1·40)	1·08 (1·00 to 1·16) p=0·038
Pain-free walking distance at week 52	338	1·21 (0·92 to 1·52)	334	1·10 (0·86 to 1·44)	1·11 (1·03 to 1·20) p=0·0046
	Total (IQR) change from baseline				
VascuQoL-6 total score at week 52	362	2·0 (0·0 to 4·0)	362	1·0 (–1·0 to 4·0)	1·00 (0·48 to 1·52) p=0·011



M P Bonacca et al. Lancet 2025, 29 mars

STRIDE: sémaglutide et distance de marche

OW Semaglutide improved MWD by 13% compared to placebo

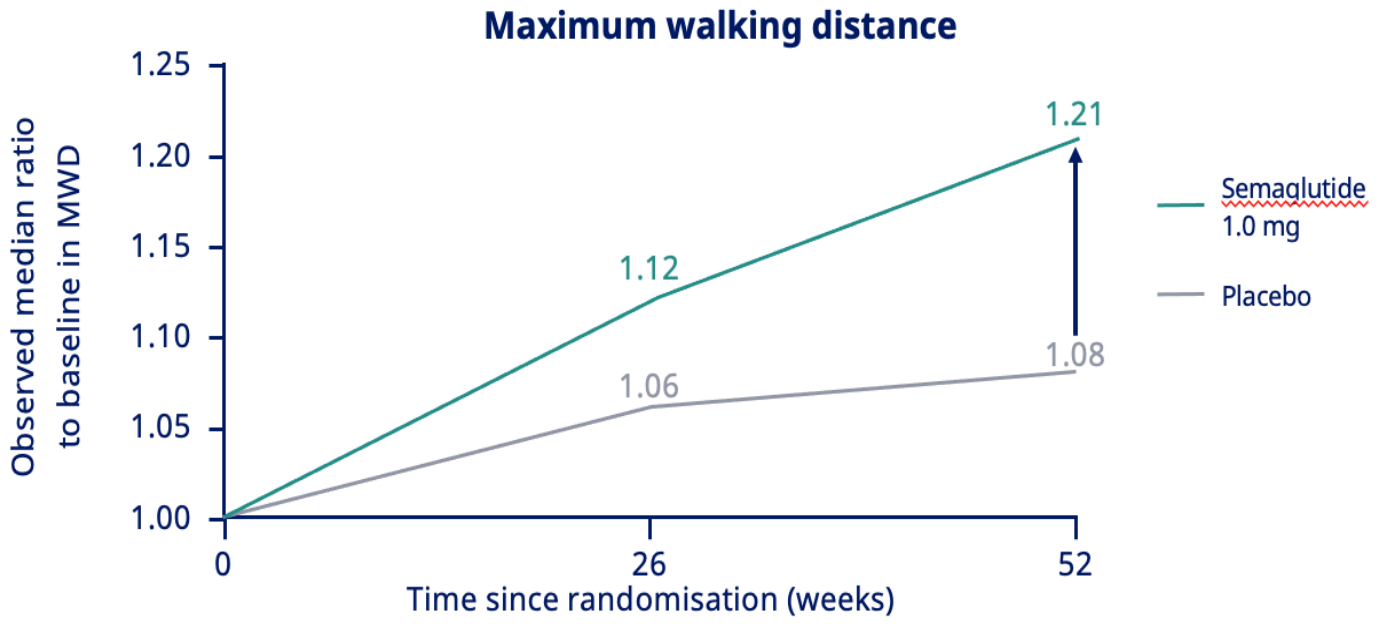
Ratio to baseline at week 52

Donc 303.7 sec. plutôt que 253.7 sec. = Δ 50 secondes

Semaglutide demonstrated a **13% MWD improvement** compared to placebo on top of SoC [ETR **1.13** (95% CI, 1.06–1.21; p=0.0004)]

Median improvement*
26.4 m (95% CI, 11.8–40.9)

Mean improvement*
39.9 m (95% CI, 13.9–66.0)



*Median differences in MWD for semaglutide versus placebo were derived from an analysis using the trial product estimand.
CI, confidence interval; ETR, estimated treatment ratio; MWD, maximum walking distance; SoC, standard of care
NN data on file; Marc, B. et. al. Lancet 2025: https://www.thelancet.com/journals/lancet/article/PIIS0140-6736(25)00509-4/fulltext

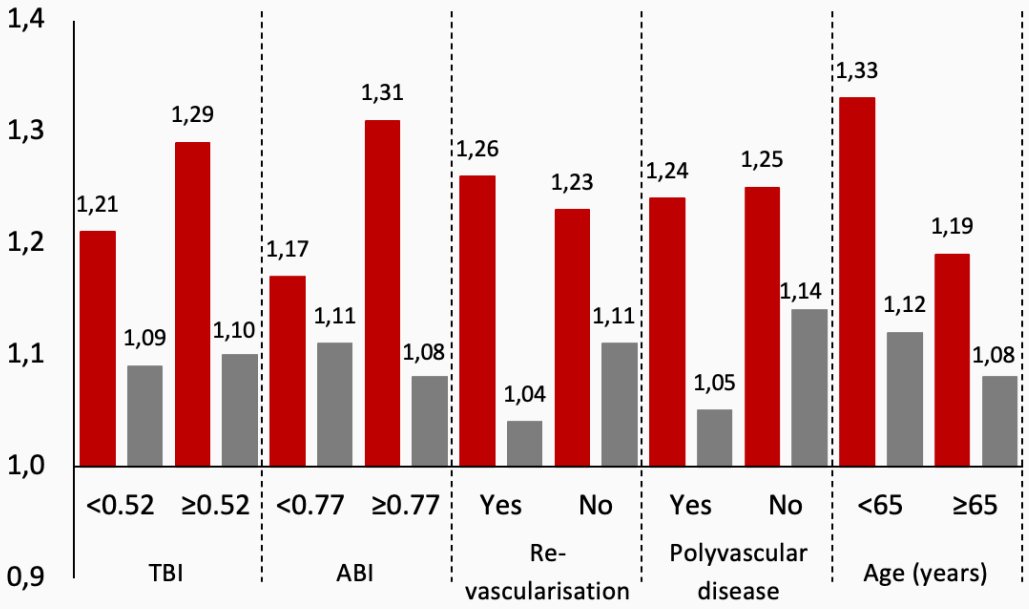
M P Bonacca et al. Lancet 2025, 29 mars

STRIDE: sémaglutide et distance de marche

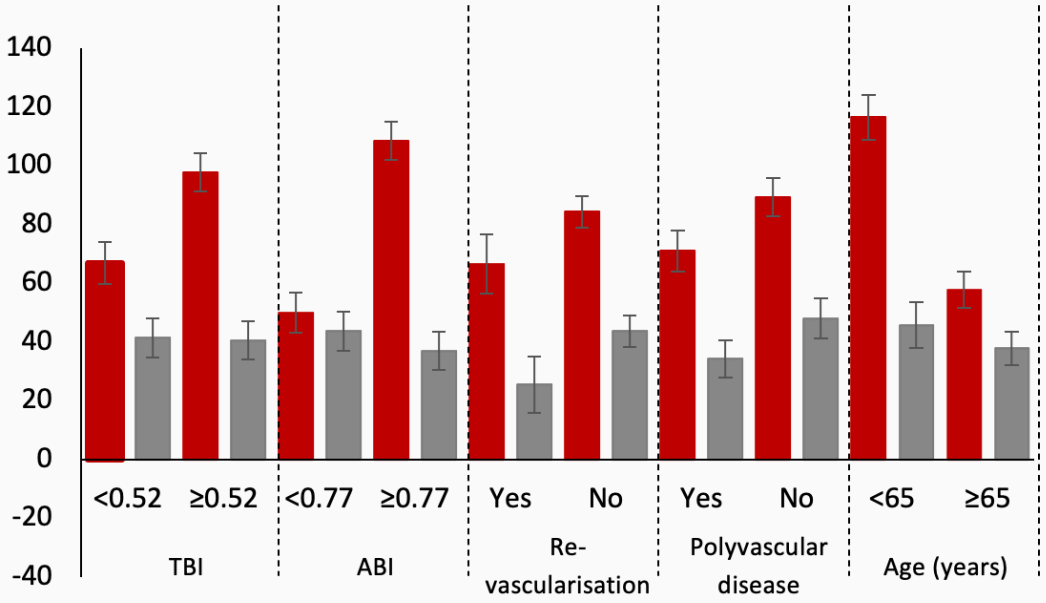
En function de ITH(ABI) et conditions de base

Maximum walking distance (MWD)

Geometric mean **ratio to baseline** at week 52



Mean change from baseline at week 52 (meters)

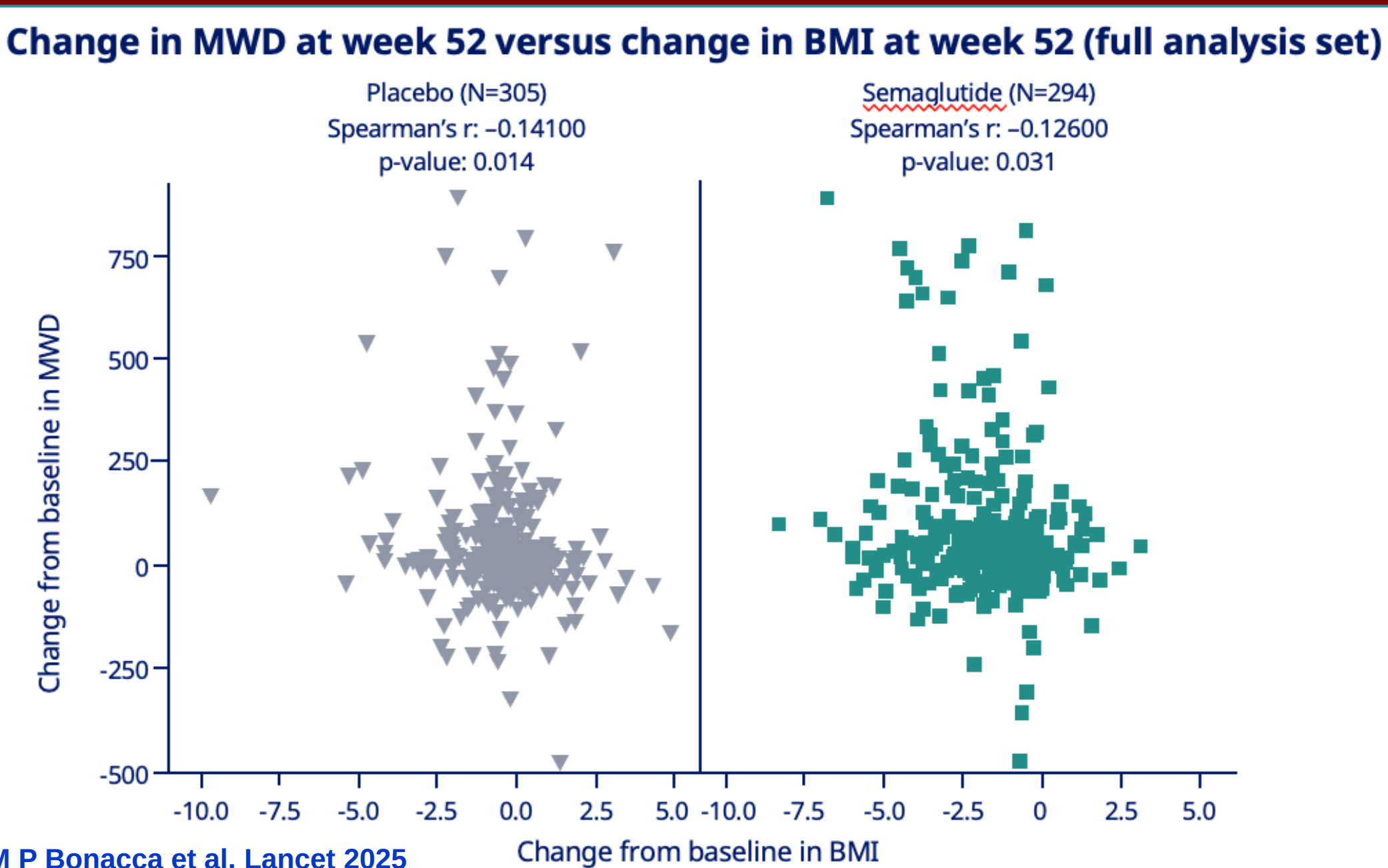


Semaglutide 1.0 mg Placebo

ESC Congress 2025 Madrid
TOGETHER WITH World Congress of Cardiology

ABI, ankle-brachial index; MWD, maximum walking distance; TBI, toe-brachial index

STRIDE: effet indépendant de la perte de poids



M P Bonacca et al. Lancet 2025

SOUL: sémaglutide et bénéfices

SOUL primary objective

- To demonstrate that oral semaglutide lowers the risk of 3-point MACE vs placebo

SOUL study design (N=9650)

- International, double-blind, randomized (1:1), placebo-controlled, event-driven, phase 3b CVOT across >30 countries
- Eligible participants were:
  - Aged ≥50 years with T2D (A1c 6.5–10.0%) + established ASCVD and/or CKD
  - Randomized to oral semaglutide (up to 14 mg once daily) vs placebo, as an adjunct to SoC
- Dose escalation: 3 mg → 7 mg → 14 mg, adjusted based on tolerability

This SOUL *post hoc* analysis

- Assessed CV outcomes by participant A1c levels, BMI and body weight at baseline
- CV outcomes were also analyzed by change in these variables at week 52 of the trial

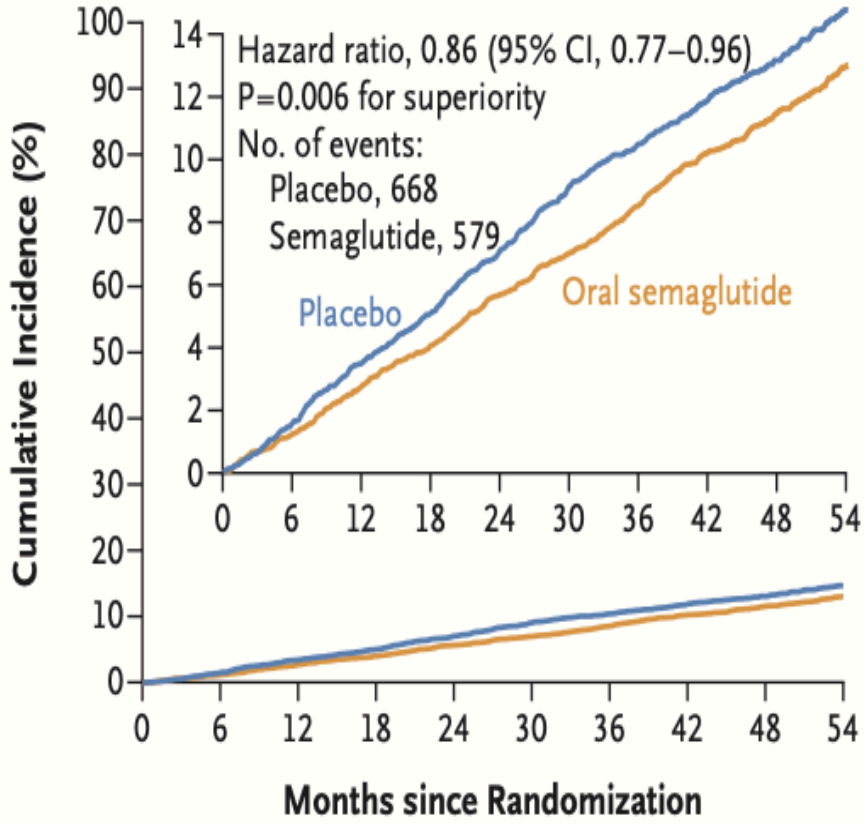
- **Statistical approaches**:
  - Cox regression for time-to-event subgroup analyses
  - Cumulative incidence estimates based on Aalen-Johansen estimator with non-CV death modeled as competing risk
  - Quadratic spline models for assessment of baseline measures as *continuous* variables

DK McGuire et al. NEJM 2025 29 mars

A Roussin

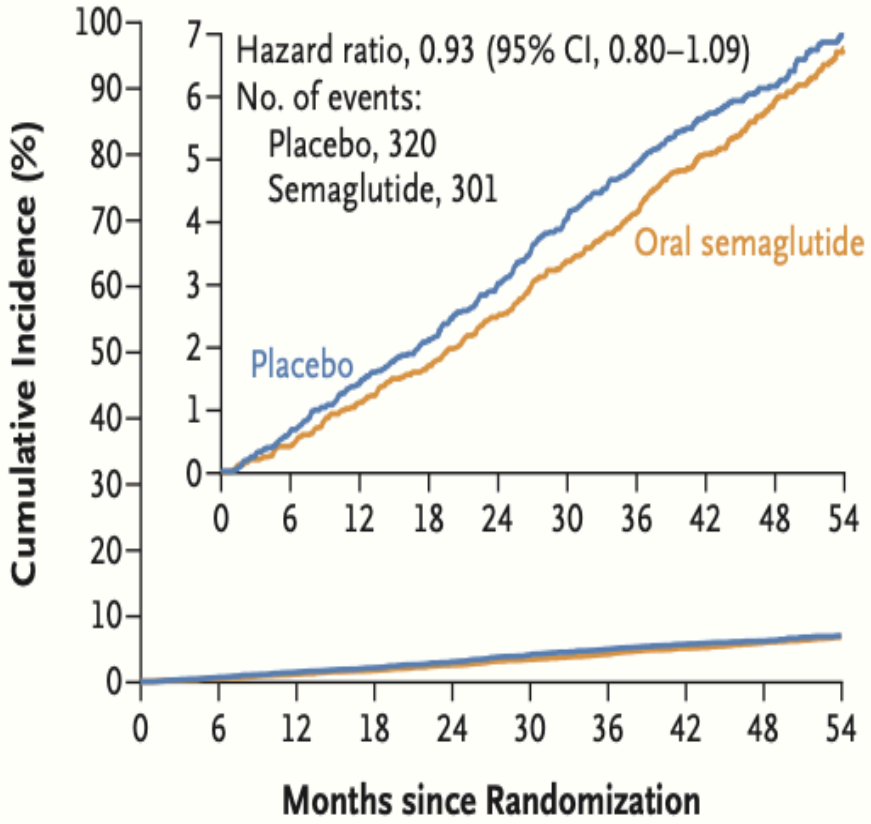
SOUL: sémaglutude et bénéfices CV

A Major Adverse Cardiovascular Events



No. at Risk										
Placebo	4825	4718	4583	4455	4322	4194	4101	3727	2517	1346
Oral semaglutide	4825	4743	4635	4542	4438	4346	4239	3831	2555	1346

B Death from Cardiovascular Causes

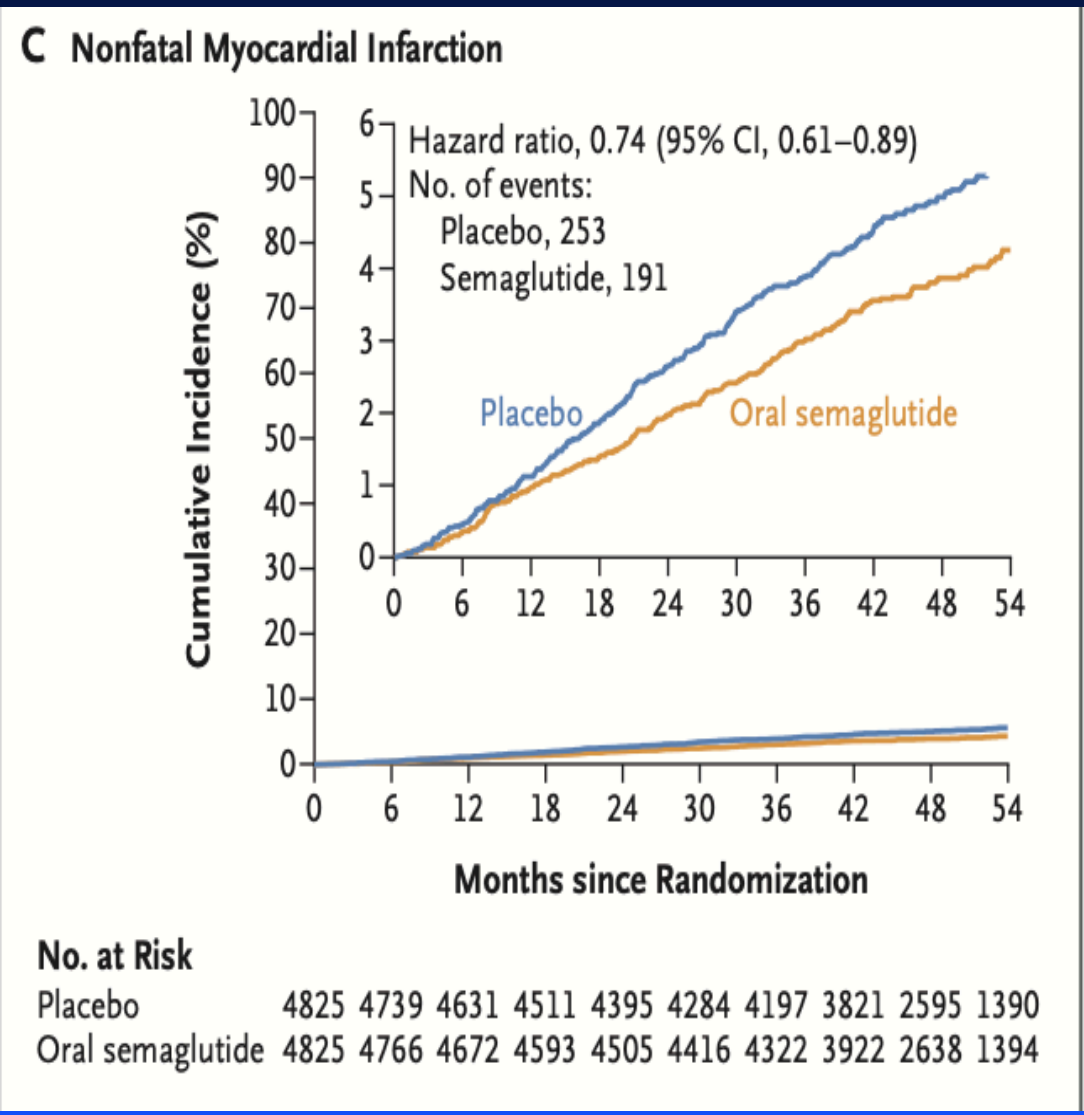


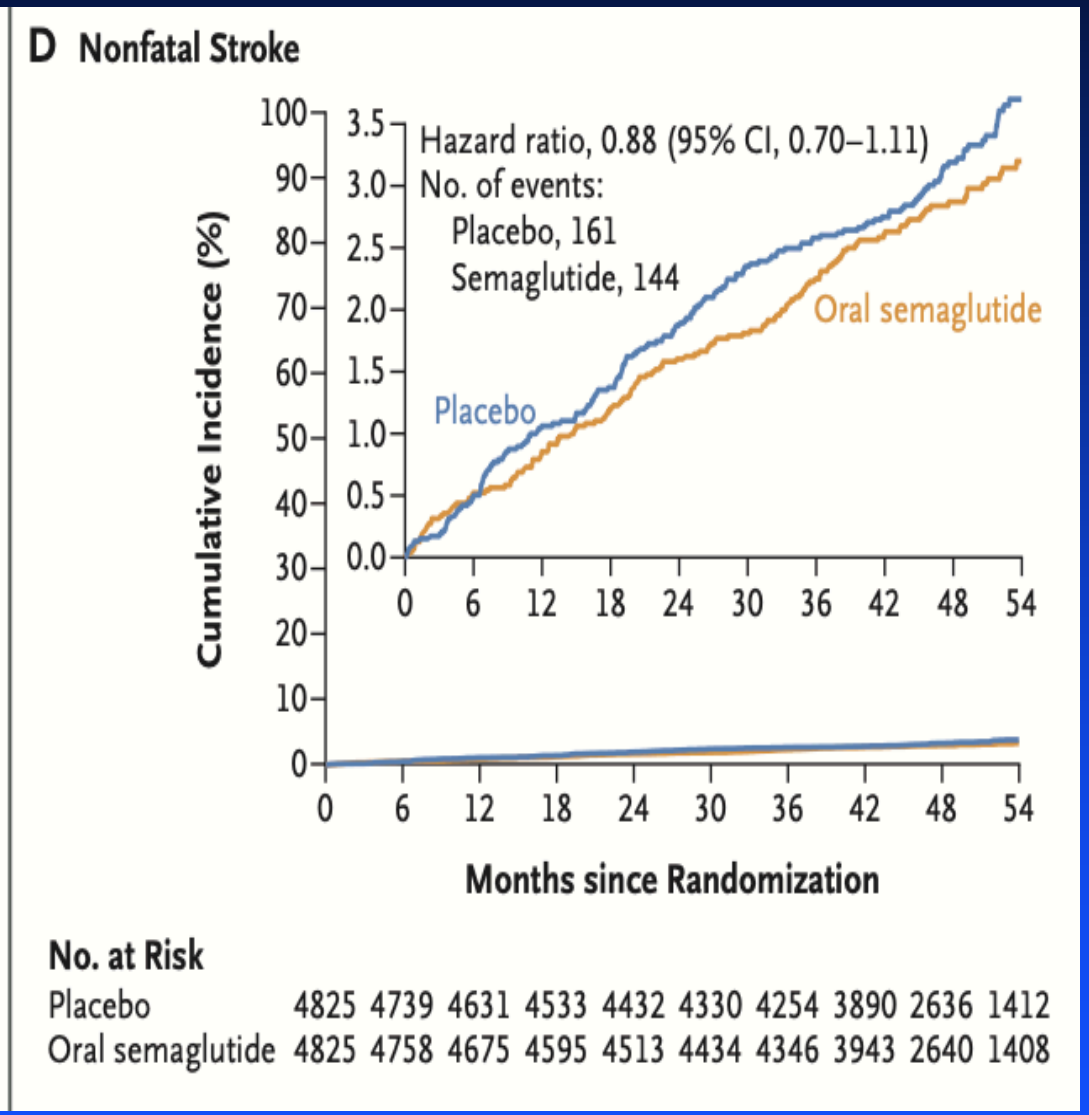
No. at Risk										
Placebo	4825	4760	4680	4594	4511	4427	4355	3991	2721	1460
Oral semaglutide	4825	4781	4712	4648	4583	4509	4436	4040	2727	1460

DK McGuire et al. NEJM 2025 29 mars

A Roussin

SOUL: sémaglutude et bénéfices IM + AVC



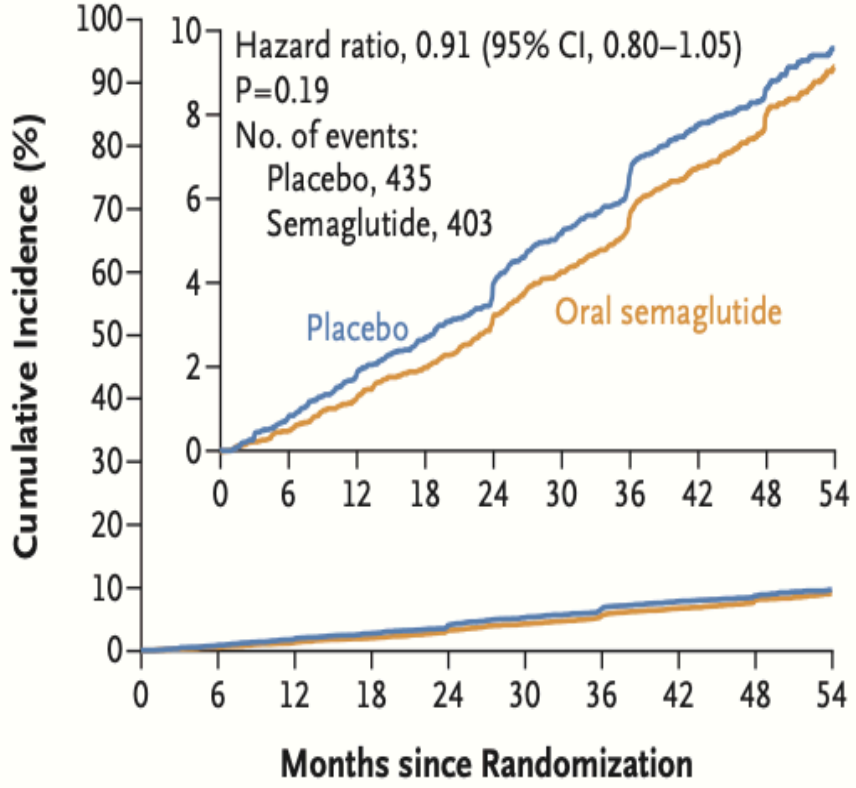


DK McGuire et al. NEJM 2025 29 mars

A Roussin

SOUL: sémaglutide et bénéfices rénaux + jambiers

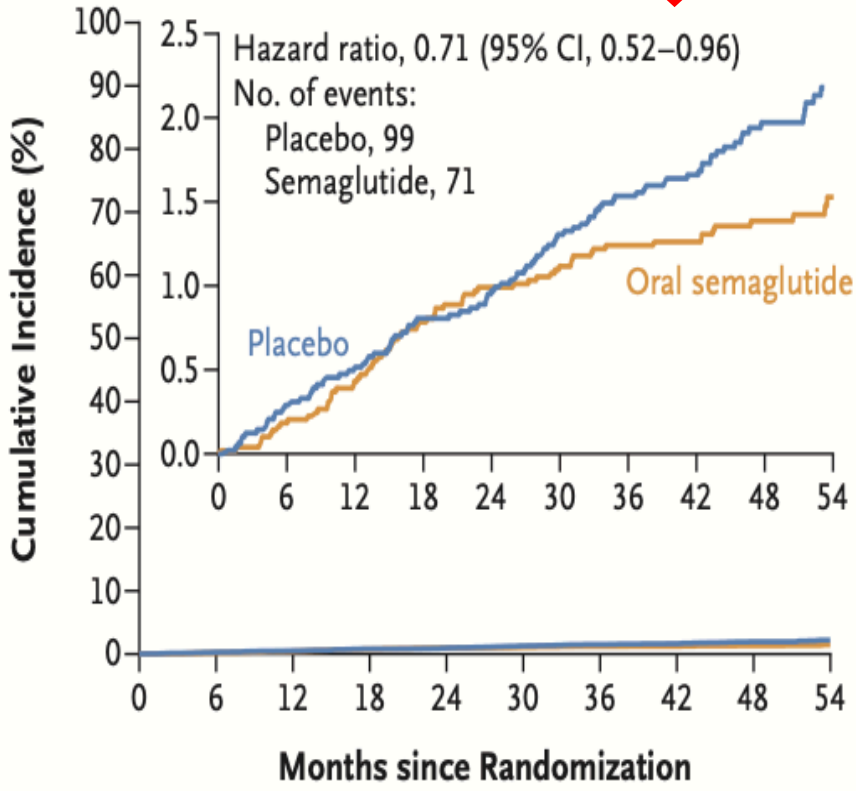
E Major Kidney Disease Events



No. at Risk

Placebo	4825	4753	4661	4570	4469	4378	4282	3911	2658	1429
Oral semaglutide	4825	4778	4704	4636	4551	4469	4372	3973	2681	1430

F Major Adverse Limb Events



No. at Risk

Placebo	4825	4746	4655	4459	4470	4376	4296	3940	2678	1436
Oral semaglutide	4825	4772	4691	4612	4540	4463	4388	3999	2696	1439

DK McGuire et al. NEJM 2025 29 mars

A Roussin

SOUL: sémaglutide bénéfices hiérarchisés

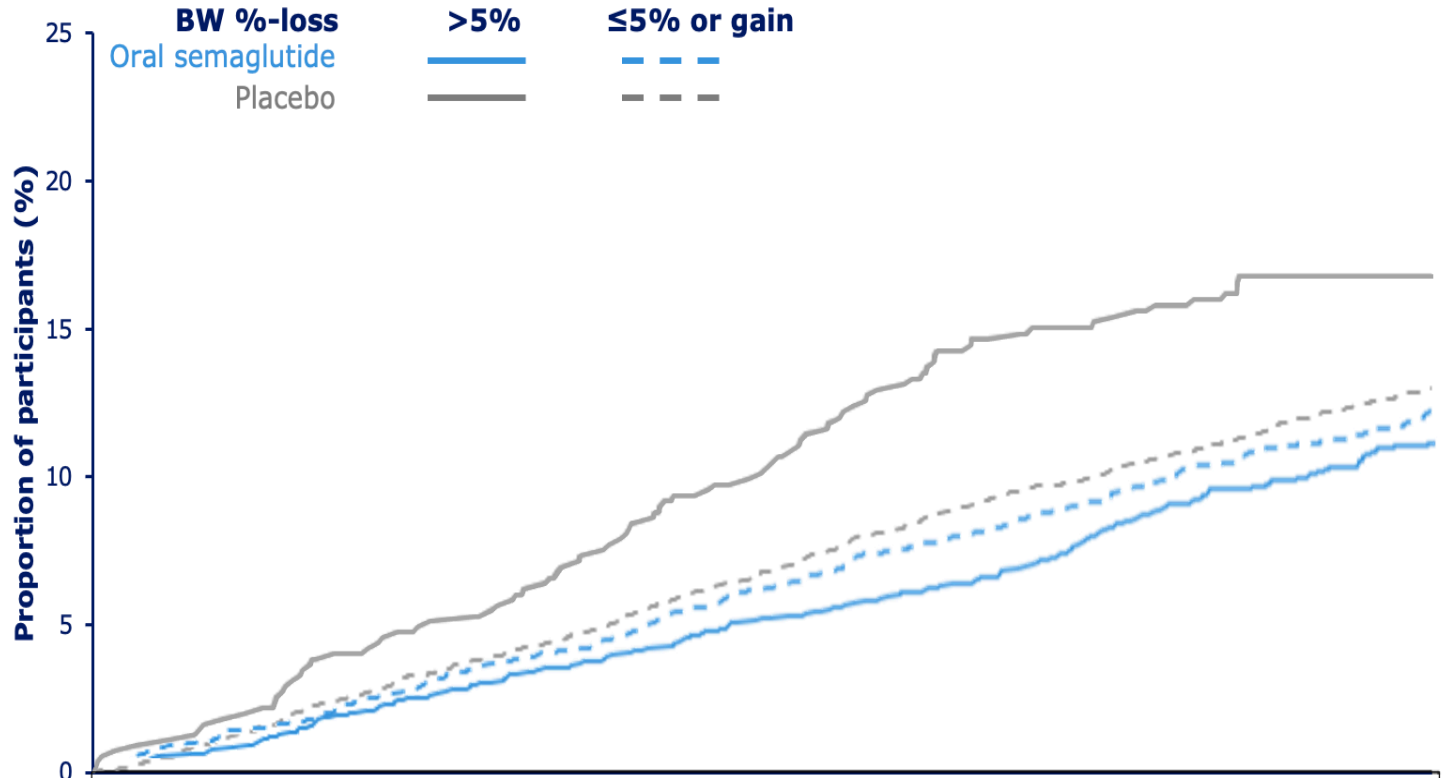
Table 2. Primary and Secondary Efficacy Outcomes.*

Outcome	Oral Semaglutide (N=4825)		Placebo (N=4825)		Hazard Ratio (95% CI)	P Value†
	no. of participants with event (%)	*no. of events per 100 person-yr*	*no. of participants with event (%)*	*no. of events per 100 person-yr*		
Primary outcome						
Major adverse cardiovascular events, three-point composite‡	579 (12.0)	3.1	668 (13.8)	3.7	0.86 (0.77–0.96)	0.006
Confirmatory secondary outcomes						
Major kidney disease events, five-point composite§	403 (8.4)	2.1	435 (9.0)	2.3	0.91 (0.80–1.05)	0.19
Death from cardiovascular causes	301 (6.2)	1.6	320 (6.6)	1.7	0.93 (0.80–1.09)	—
Major adverse limb events, two-point composite¶	71 (1.5)	0.4	99 (2.1)	0.5	0.71 (0.52–0.96)	—
Supportive secondary outcomes						
Major adverse cardiovascular events, five-point composite‖	670 (13.9)	3.6	777 (16.1)	4.3	0.84 (0.76–0.93)	—
Nonfatal myocardial infarction	191 (4.0)	1.0	253 (5.2)	1.4	0.74 (0.61–0.89)	—
Fatal or nonfatal myocardial infarction	200 (4.1)	1.1	268 (5.6)	1.4	0.73 (0.61–0.88)	—
Nonfatal stroke	144 (3.0)	0.8	161 (3.3)	0.9	0.88 (0.70–1.11)	—
Fatal or nonfatal stroke	164 (3.4)	0.9	171 (3.5)	0.9	0.95 (0.76–1.17)	—

SOUL: effet indépendant de la perte de poids

Time to first MACE by change in body weight @week 52

(> or ≤5% change in body weight)



No. at risk									
Oral semaglutide	BW %-loss ≤5% or gain	3008	2963	2883	2823	2755	2692	2629	2375	1594
	BW %-loss >5%	1800	1786	1741	1707	1669	1641	1599	1462	998
Placebo	BW %-loss ≤5% or gain	4261	4195	4056	3945	3839	3730	3652	3337	2287
	BW %-loss >5%	550	541	518	501	477	455	440	405	257
		0	20	52	78	104	130	156	182	208

Time since randomization (weeks)

Sémaglutide: étude FLOW

Patients diabétiques avec Néphropathie chronique

Table 2. Efficacy and Safety Outcomes.*

Outcome	Semaglutide (N=1767)	Placebo (N=1766)	Hazard Ratio (95% CI)	Estimated Difference (95% CI)	P Value
Primary outcome: major kidney disease events — no. (%)†	331 (18.7)	410 (23.2)	0.76 (0.66 to 0.88)	—	0.0003
Components of primary outcome — no. (%)					
Persistent ≥50% reduction from baseline in eGFR	165 (9.3)	213 (12.1)	0.73 (0.59 to 0.89)	—	—
Persistent eGFR <15 ml/min/1.73 m^2	92 (5.2)	110 (6.2)	0.80 (0.61 to 1.06)	—	—
Initiation of kidney-replacement therapy	87 (4.9)	100 (5.7)	0.84 (0.63 to 1.12)	—	—
Death from kidney-related causes	5 (0.3)	5 (0.3)	0.97 (0.27 to 3.49)	—	—
Death from cardiovascular causes	123 (7.0)	169 (9.6)	0.71 (0.56 to 0.89)	—	—
Confirmatory secondary outcomes					
Mean annual rate of change in eGFR — ml/min/1.73 m^2	−2.19	−3.36	—	1.16 (0.86 to 1.47)	<0.001
Major cardiovascular events — no. (%)	212 (12.0)	254 (14.4)	0.82 (0.68 to 0.98)	—	0.029
Death from cardiovascular causes	123 (7.0)	169 (9.6)	0.71 (0.56 to 0.89)	—	—
Nonfatal myocardial infarction	52 (2.9)	64 (3.6)	0.80 (0.55 to 1.15)	—	—
Nonfatal stroke	63 (3.6)	51 (2.9)	1.22 (0.84 to 1.77)	—	—
Death from any cause — no. (%)	227 (12.8)	279 (15.8)	0.80 (0.67 to 0.95)	—	0.01
Supportive secondary outcomes					
Major adverse limb event in a time-to-first-event analysis — no. of events	16	28	0.56 (0.30 to 1.02)	—	—

McGuire D et al. *N Engl J Med* 2025;392:2001–2012

Sémaglutide: analyse groupée de 3 études

MALE

Semaglutide and Risk Reduction of Major Adverse Limb Events in Diabetes: A Pooled Analysis of 13,975 Participants from the SOUL, FLOW and STRIDE Randomised Trials

Subodh Verma, Marc P. Bonaca, Joakim Nordanstig, John B. Buse, Matthew A. Cavender, Kenneth W. Mahaffey, Richard Pratley, Peter Rossing, Alex Videmark, Andrei-Mircea Catarig, Søren Rasmussen, Florian M. M. Baeres, Mads D. M. Engelmann, Darren K. McGuire

On behalf of the SOUL, FLOW, and STRIDE investigator groups

Professor Subodh Verma

Division of Cardiac Surgery, Li Ka Shing Knowledge Institute of St Michael's Hospital, Unity Health Toronto, University of Toronto, Toronto, ON, Canada

EASD 2025 VIENNA #EASD2025

61ST ANNUAL MEETING

EUROPEAN ASSOCIATION FOR THE STUDY OF DIABETES

15 - 19 September 2025 Vienna - Austria easd.org

Sémaglutide: comparaison de 3 études

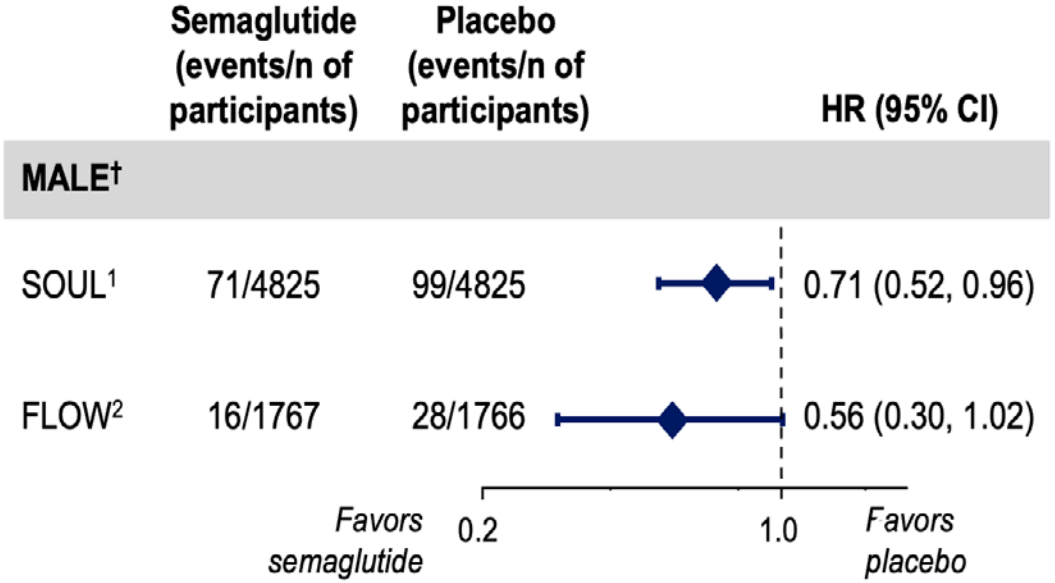
MALE

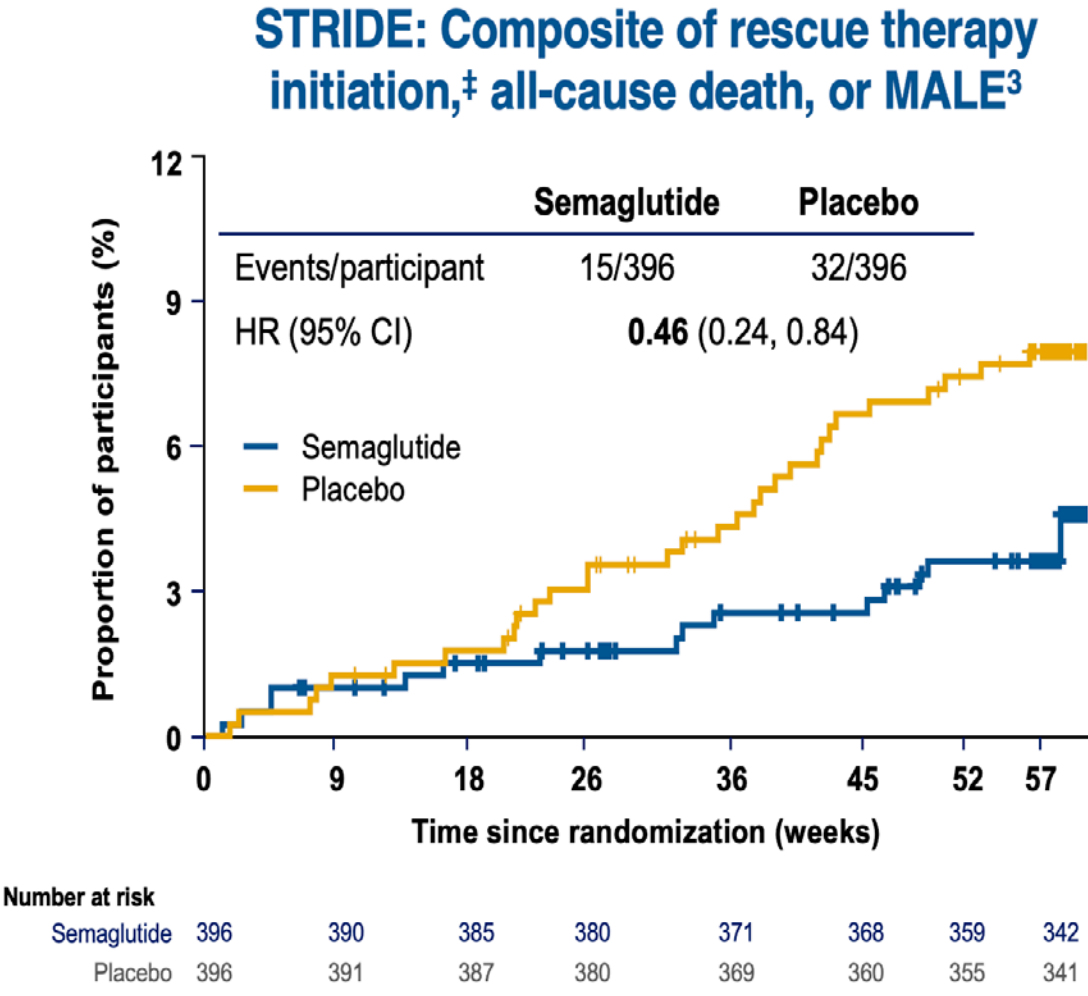
	SOUL[1]	FLOW[2]	STRIDE[3]
Participants	≥50 years T2D ASCVD and/or CKD	≥18 years T2D CKD	≥18 years T2D Symptomatic PAD
Study size and dosages	N=9650 14.0 mg, p.o., once daily	N=3533 1.0 mg, s.c., once weekly	N=792 1.0 mg, s.c., once weekly
Proportion with PAD	16%	17%	100%
Primary outcome	**14%** reduction in MACE† with semaglutide p=0.006	**24%** reduction in major kidney disease events‡ with semaglutide p=0.0003	MWD increased by **13%** **(40 m)**¶ with semaglutide p=0.0004
MALE§ outcome	Confirmatory secondary	Supportive secondary	Exploratory

1. McGuire D et al. *N Engl J Med* 2025;392:2001–2012
2. 2. Perkovic V et al. *N Engl J Med* 2024;391:109–121
3. 3. Bonaca MP et al. *Lancet* 2025;405:1580–1593.

Sémaglutide: comparaison de 3 études

MALE



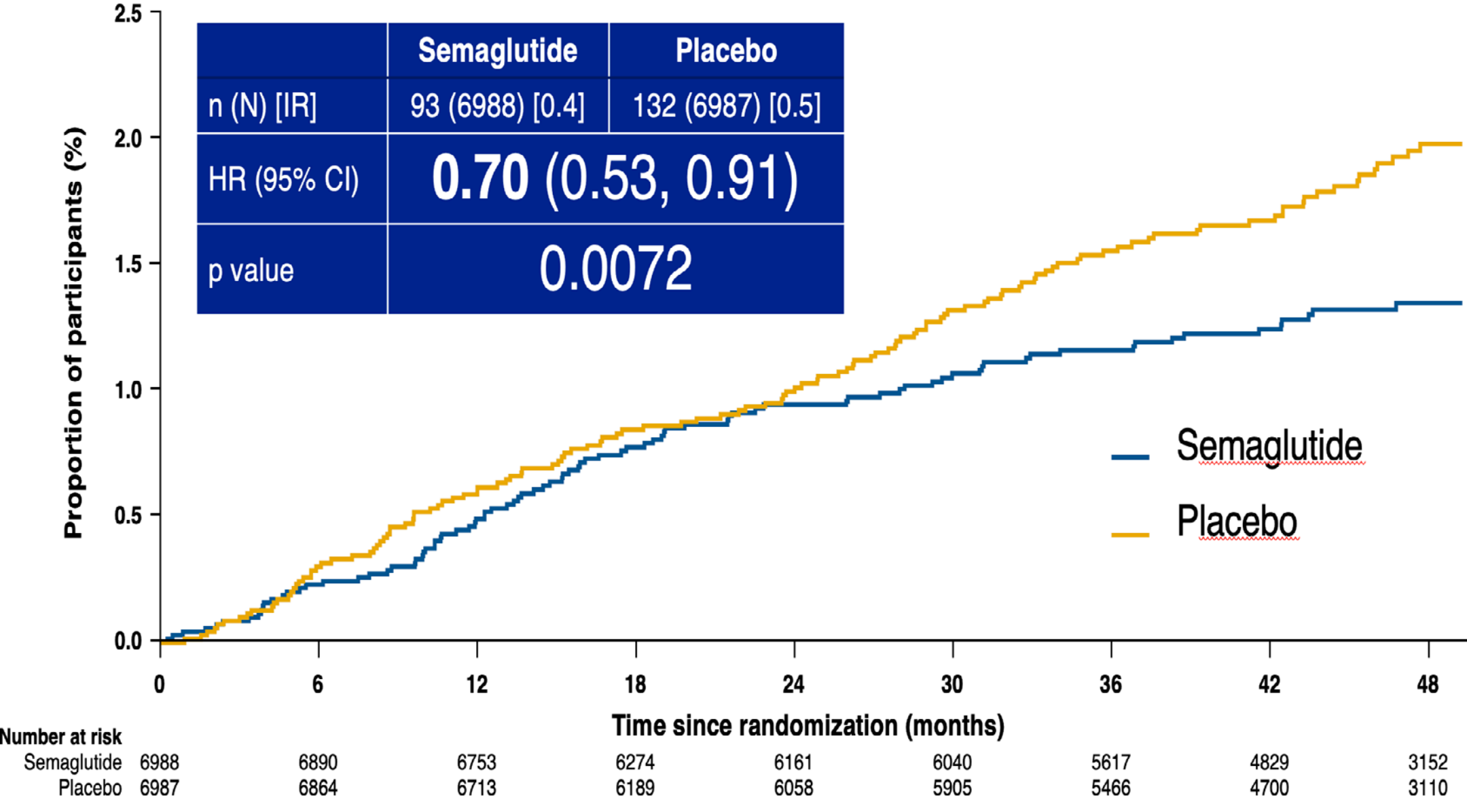


1. McGuire D et al. *N Engl J Med* 2025;392:2001–2012
2. 2. Perkovic V et al. *N Engl J Med* 2024;391:109–121
3. 3. Bonaca MP et al. *Lancet* 2025;405:1580–1593.

A Roussin

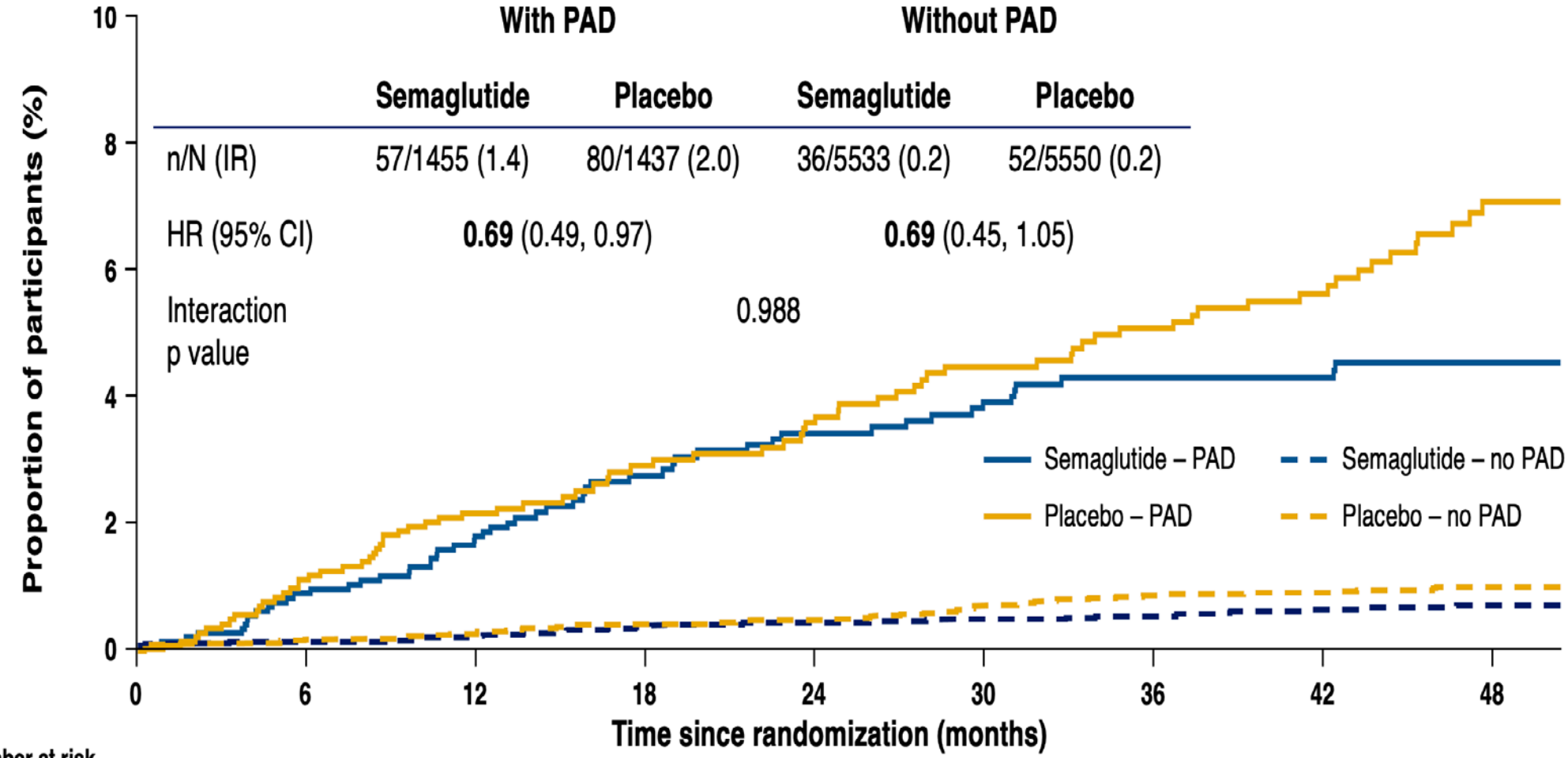
Sémaglutide: analyse groupée

MALE



Sémaglutide: analyse groupée

MALE selon la présence ou non de MAP au départ

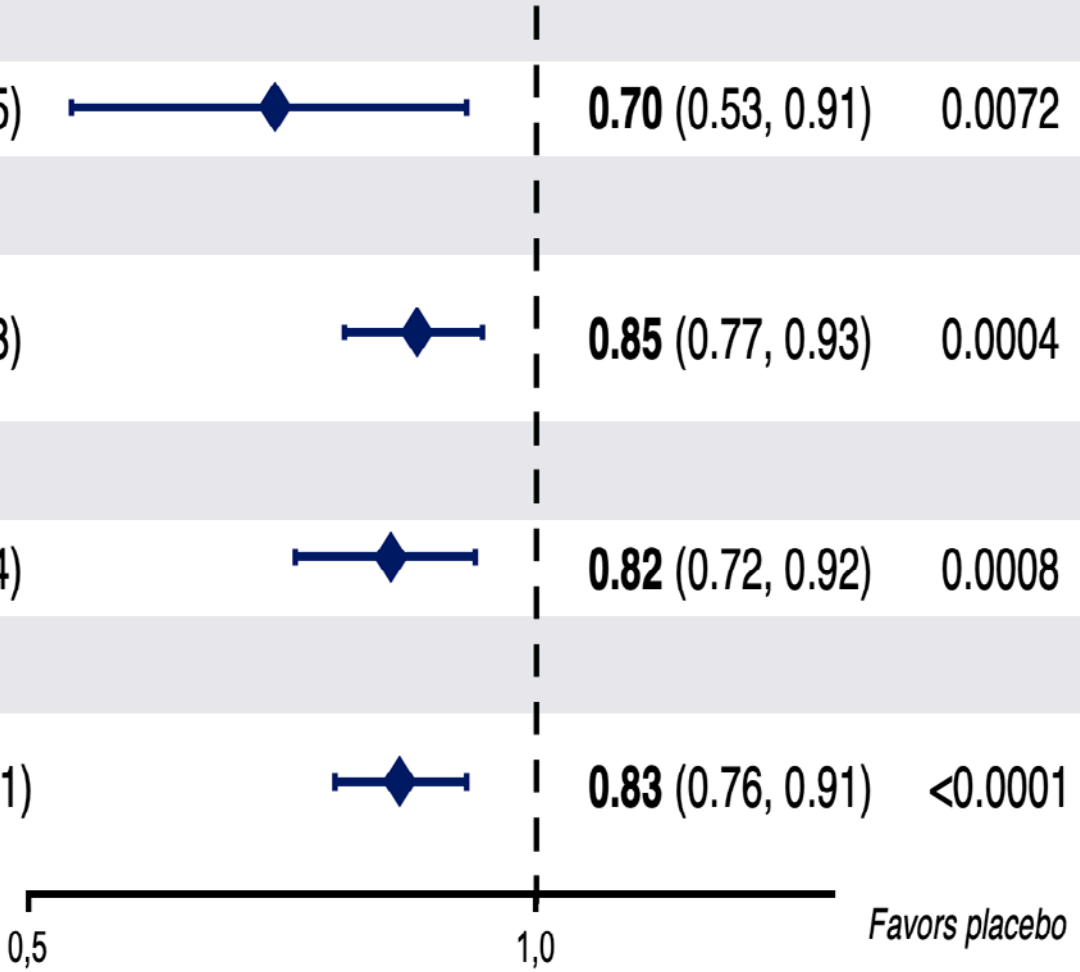


Number at risk									
Semaglutide – PAD	1455	1408	1358	959	929	908	829	698	443
Semaglutide – no PAD	5533	5482	5395	5315	5232	5132	4788	4131	2709
Placebo – PAD	1437	1393	1344	930	895	856	778	647	418
Placebo – no PAD	5550	5471	5369	5259	5163	5049	4688	4053	2692

Sémaglutide: analyse groupée

MALE et autres issues

Pooled (SOUL, FLOW, and STRIDE)	Semaglutide n/N (IR)	Placebo n/N (IR)	HR (95% CI)	p value
MALE	93/6988 (0.4)	132/6987 (0.5)	**0.70** (0.53, 0.91)	0.0072
MALE or all-cause death	825/6988 (3.2)	959/6987 (3.8)	**0.85** (0.77, 0.93)	0.0004
MALE or CV death	498/6988 (2.0)	600/6987 (2.4)	**0.82** (0.72, 0.92)	0.0008
MALE or MACE	867/6988 (3.4)	1024/6987 (4.1)	**0.83** (0.76, 0.91)	<0.0001



Effet de classe possible des aGLP-1

Étude rétrospective sur 858,750 patients avec MAP

ITH 0.4 – 0.9

What's New

- GLP-1 receptor agonists (GLP-1RAs), like tirzepatide and semaglutide, were studied in patients with moderate peripheral arterial disease (PAD).
- The study compared patients with PAD who started GLP-1RAs to those who did not, using a large, matched dataset.

Key Findings

- GLP-1RA use was linked to:
  - Lower mortality (1.7% vs 4.4% at 1 year)
  - Fewer major adverse cardiac events (MACEs: 25.4% vs 29.3%)
  - Fewer major adverse limb events (MALEs: 0.8% vs 1.5%)
  - Fewer inpatient hospitalizations (17.9% vs 26.8%)
- Statistically significant reductions in risk for:
  - MACEs (HR 0.87)
  - MALEs (HR 0.57)
  - Hospital admissions and complications

MAIS, très importantes différences entre le groupe aGLP-1 (plus malade) et le groupe placebo. PAS généralisable pour l'instant

J Vasc Surg 2025 Sep; 82(3): 1024-1032

A Roussin

CONCLUSION 1

Approche minimale pour la MAP en 2025

- Questionnaire d'Edimburgh, facteurs de risque et examen ciblé
- Investigation : ITH puis imagerie Duplex
- Programme de marche et habitudes de vie
- AAS **ou** clopidogrel **ou** AAS/Rivaroxaban, **si** symptomatique*

A Roussin

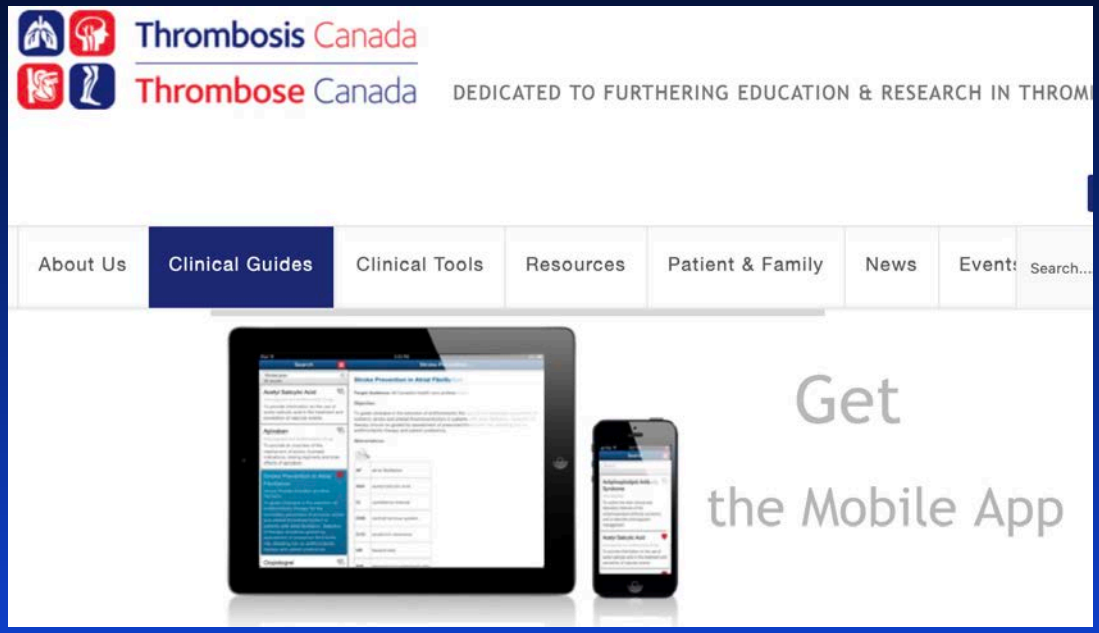
CONCLUSION 2

Approche minimale pour la MAP en 2025

- Statines haute intensité avec EZ ou iPCSK9 si LDL demeure > 1.7
  - Ou si LDL > 1.4 en Europe*
  - Icosapent ethyl et acide bempedoique à considérer
- IECA ou BRA en priorité si TA > 130 et même si TA normale*
- aGLP2 ou Semaglutide* à considérer si diabète* (UE 2025)
- Les approches endovasculaires et chirurgicales dépendent du degré d'atteinte fonctionnelle

A Roussin

Références principales







SSVQ Société des sciences vasculaires du Québec
Chef de file en santé vasculaire.

ESC European Society of Cardiology

CANADIAN SOCIETY OF VASCULAR MEDICINE

American Heart Association®

A Roussin