Revascularisation chirurgicale ou endovasculaire des sténoses carotidiennes

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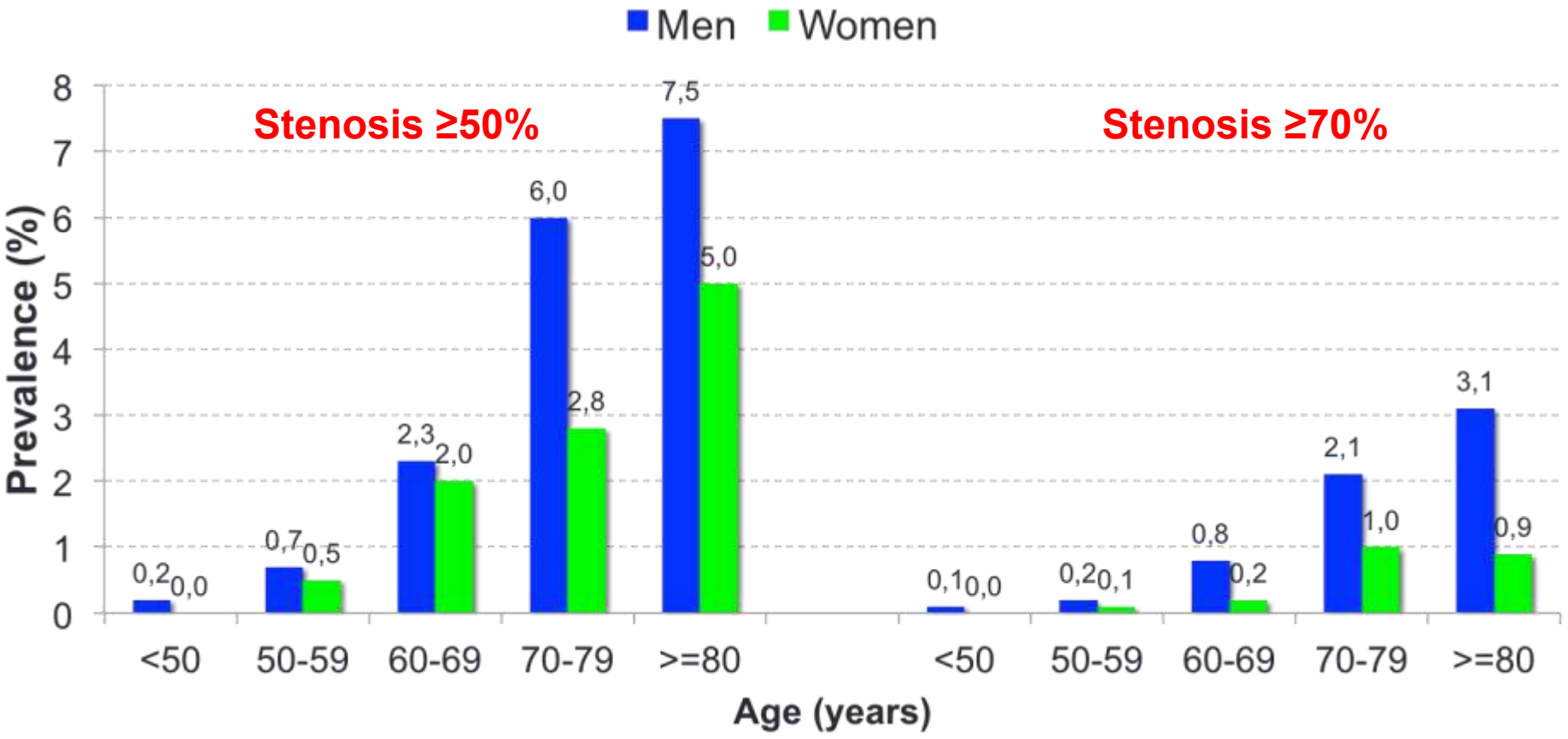
Prévalence en population générale

Meta-analyse sur données individuelles

4 population-based studies (23 706 participants)
Norway, Germany, The Netherlands



De Weerd et al. Stroke 2010;41:1294-97.

Circonstances du diagnostic

Patients sans symptômes dans le territoire de la sténose
=
STENOSE CAROTIDIENNE
ASYMPTOMATIQUE

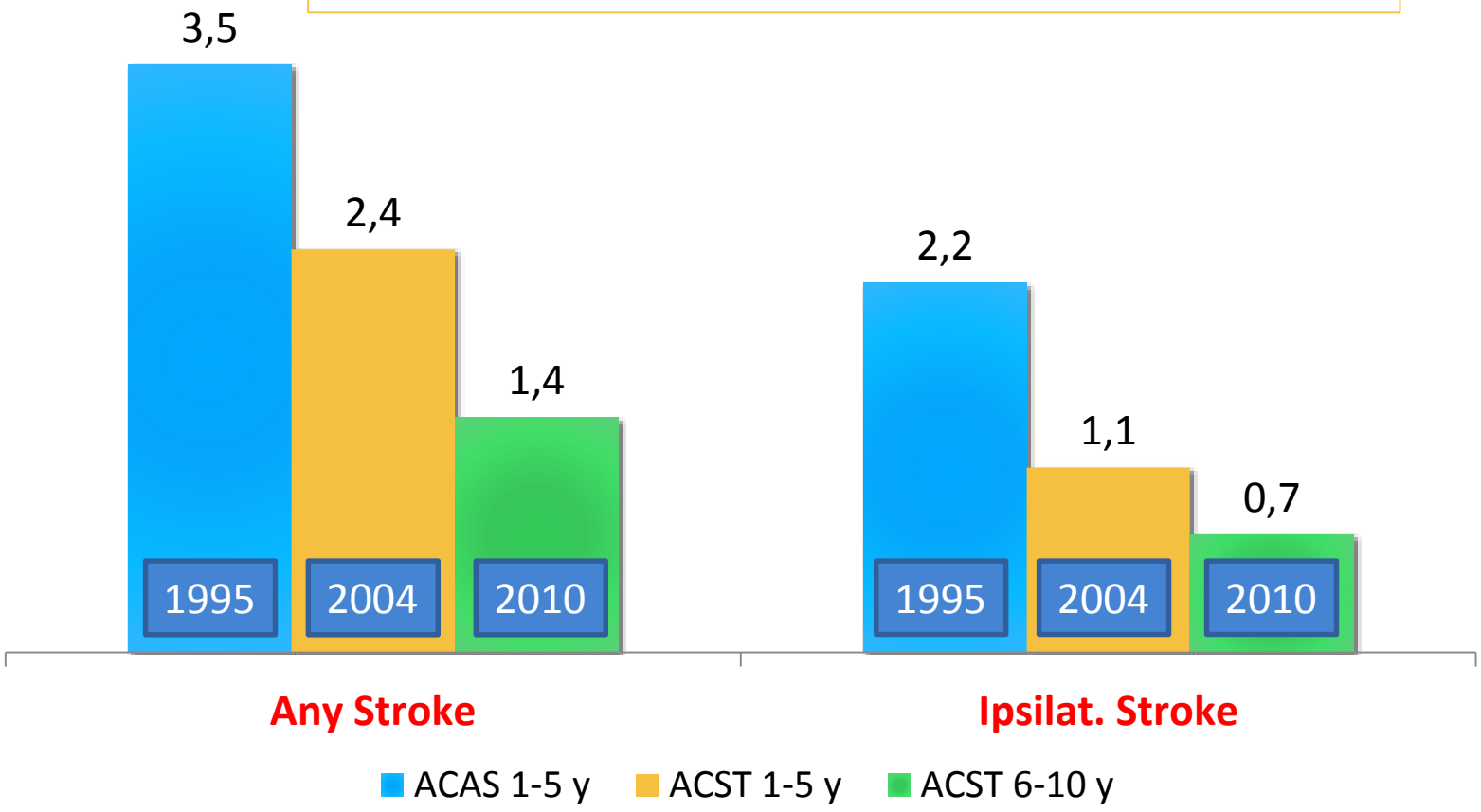
- Dépistage chez des patients ayant une maladie vasculaire: coronaires, membres inférieurs, aorte
- Dépistage chez les diabétiques
- Infarctus ou AIT dans un autre territoire

Patients avec des symptômes dans le territoire de la sténose
=
STENOSE CAROTIDIENNE
SYMPTOMATIQUE

- Infarctus cérébral ou AIT dans le territoire de la sténose <6-12 mois
- Infarctus cérébral ou AIT dans le territoire de la sténose >6-12 mois

Infarctus cérébral

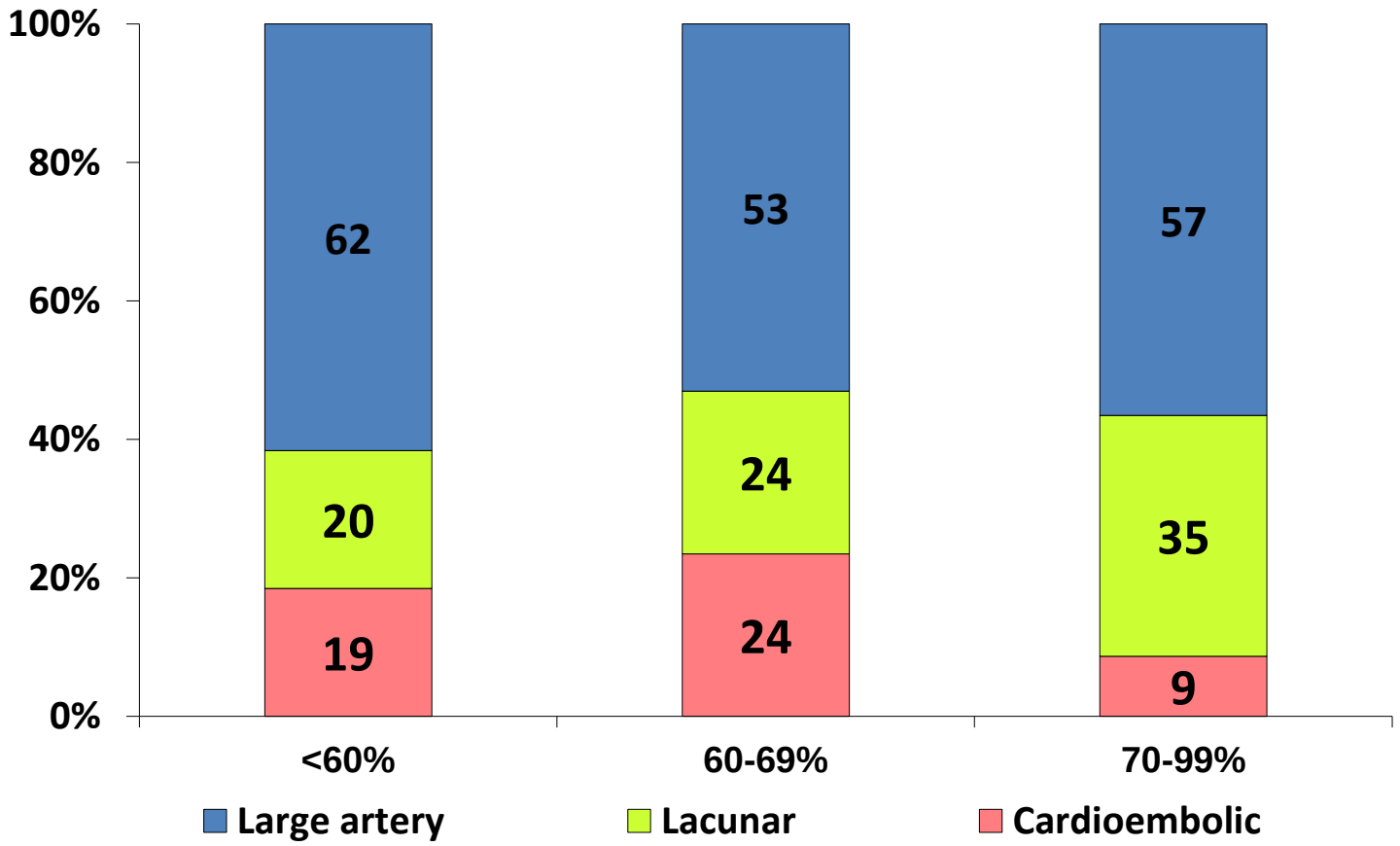
Risque annuel chez les patients traités médicalement dans les 2 grands essais thérapeutiques sur la chirurgie des sténoses asymptomatiques (%/an)



Naylor AR. Nature Reviews Cardiol 2012;9:116-124.

Sténose carotidienne asymptomatique

Mécanisme des infarctus cérébraux



Barnett et al. JAMA 2000;283:1429-36 – Inzitari et al. N Engl J Med 2000;342:1693-700.

Facteurs de risque d'accident ischémique ipsilatéral

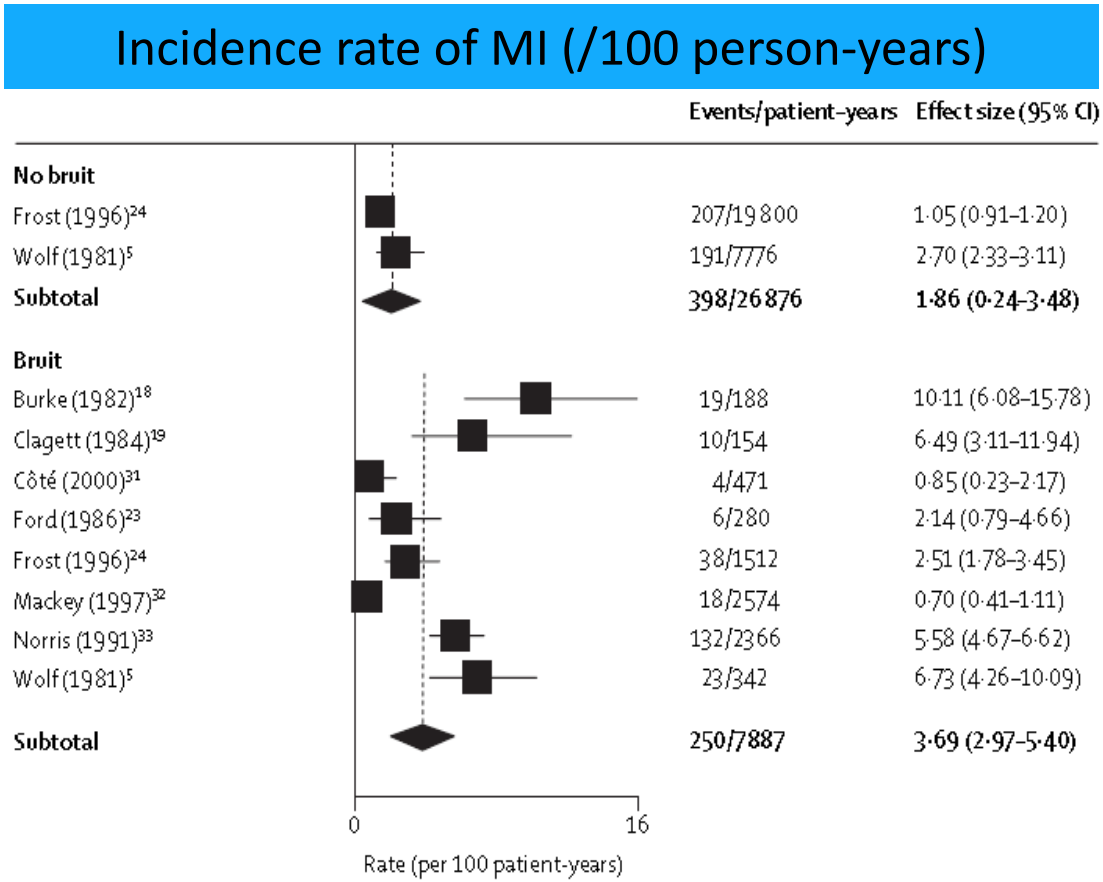
1. Degré de sténose ?
2. Progression de la sténose ?
3. Retentissement hémodynamique
4. Signaux microemboliques au Doppler transcrânien
5. Infarctus 'silencieux'
6. Composition de la plaque
7. Sexe

Evénements vasculaires non neurologiques

- Revue systématique
- 22 études
- 17295 patients

Risques (/100 py)

- IDM
  - 3.69% (2.97-5.40)
- Mort vasculaire
  - 2.27% (1.49-3.49)

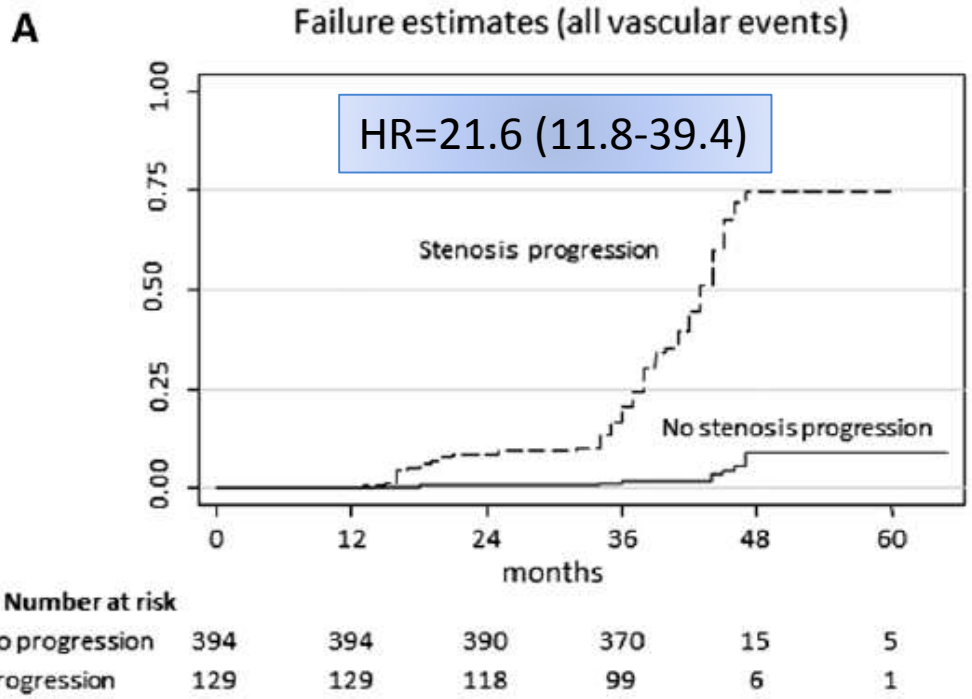


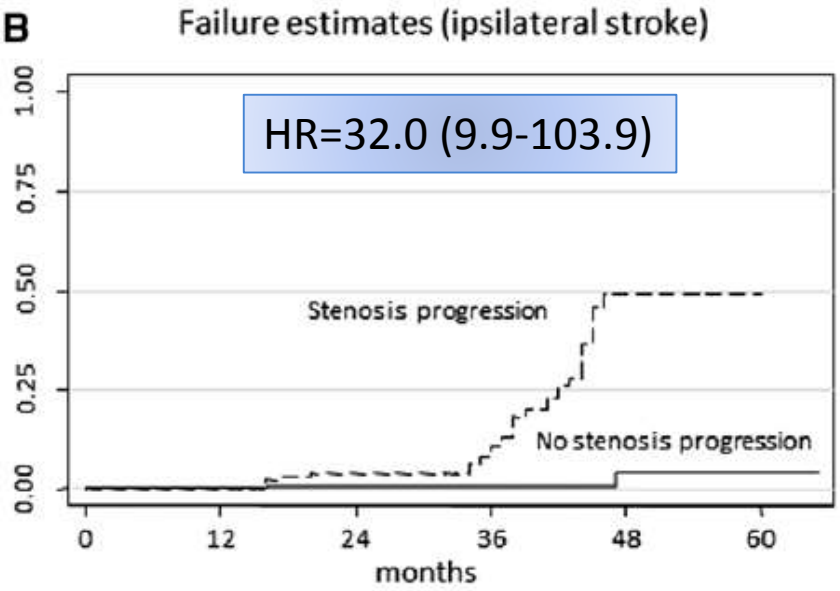
Pickett et al. Lancet 2008;371:1587-94.

Progression de la sténose

Un marqueur de risque vasculaire global ?

- Sténose 50-69% (523 patients – 2004 - 2009)
- Nouvelle évaluation Doppler ≤12 mois (med= 9mois)
- Progression définie par changement de catégorie (≥70%, near-occlusion, occlusion) ➔ 25% des patients
- Suivi clinique régulier (med = 42 mois)
- Critères d'évaluation: AIT, infarctus cérébral, IDM, décès



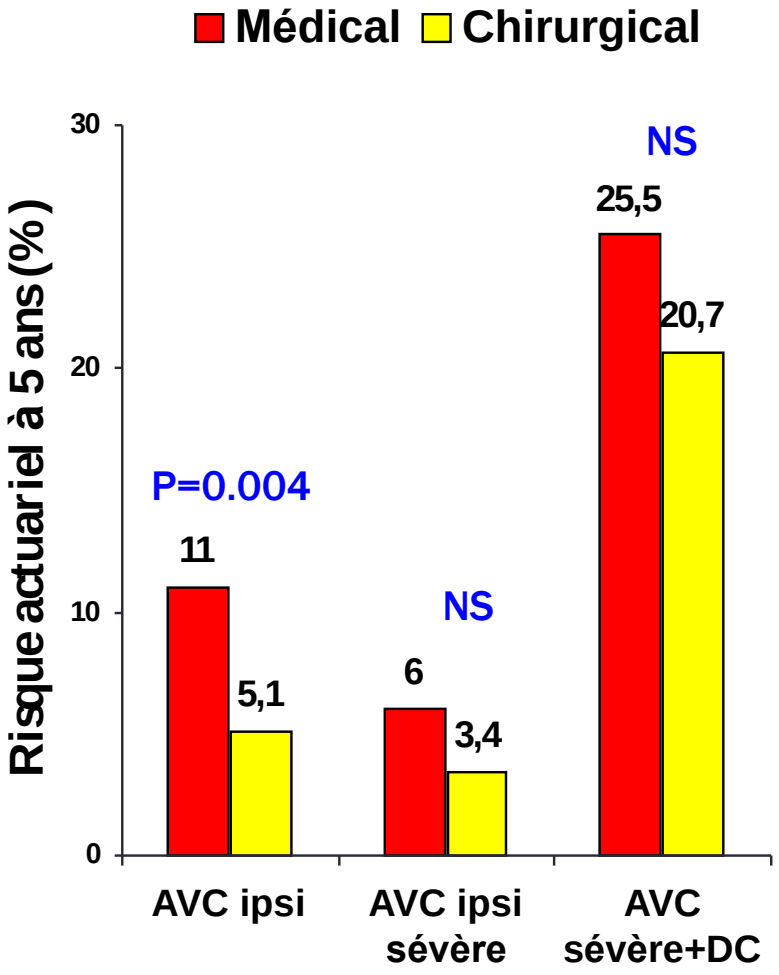


Balestrini et al. Stroke 2013;44:792-4.

Sténose carotidienne asymptomatique
Asymptomatic Carotid Atherosclerosis Study (ACAS)

- N=1662, 40 – 79 ans
- Sténose ≥ 60% (=NASCET)
- Arrêt prématuré à 2.7 ans
- Bénéfice
  - RRR 53%
  - RAR 6%
  - NNT (1 an) 85

Risque opératoire (AVC+DC) = 2.3% dont 1.2% par artériographie

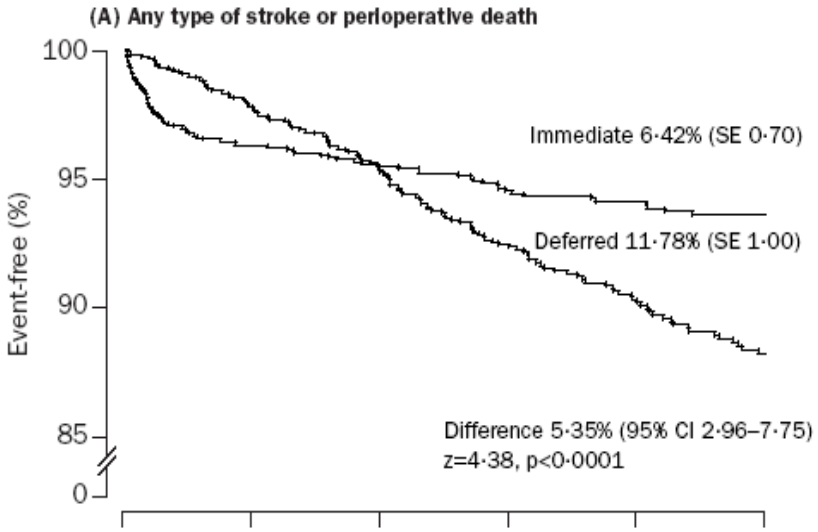


ACAS. JAMA 1995;273:1421-28

Sténose carotidienne asymptomatique

Asymptomatic Carotid Stenosis Trial (ACST)

- 3120 patients
  - Sténose ≥ 60% (échoDoppler)
  - Résultats à 5 ans
- RAR
  - AVC/DC
    5.3%
  - AVC fatal/invalidant/DC
    2.5%
- Risque opératoire = 3.1%



	Chirurgie (1560)	Médical (1560)
AVC ipsi	13	62
AVC contro	11	35
AVC côté ?	6	8
AVC VB+HIC	12	15
Total (5 ans)	**42 (3.8%)**	**120 (11.0%)**
AVC/DC op	40	11
	6.4%	**11.7%**

ACST. Lancet 2004;363:1491-502.

Sténose carotidienne asymptomatique
Asymptomatic Carotid Stenosis Trial (ACST)

10-year results

n=3120 patients

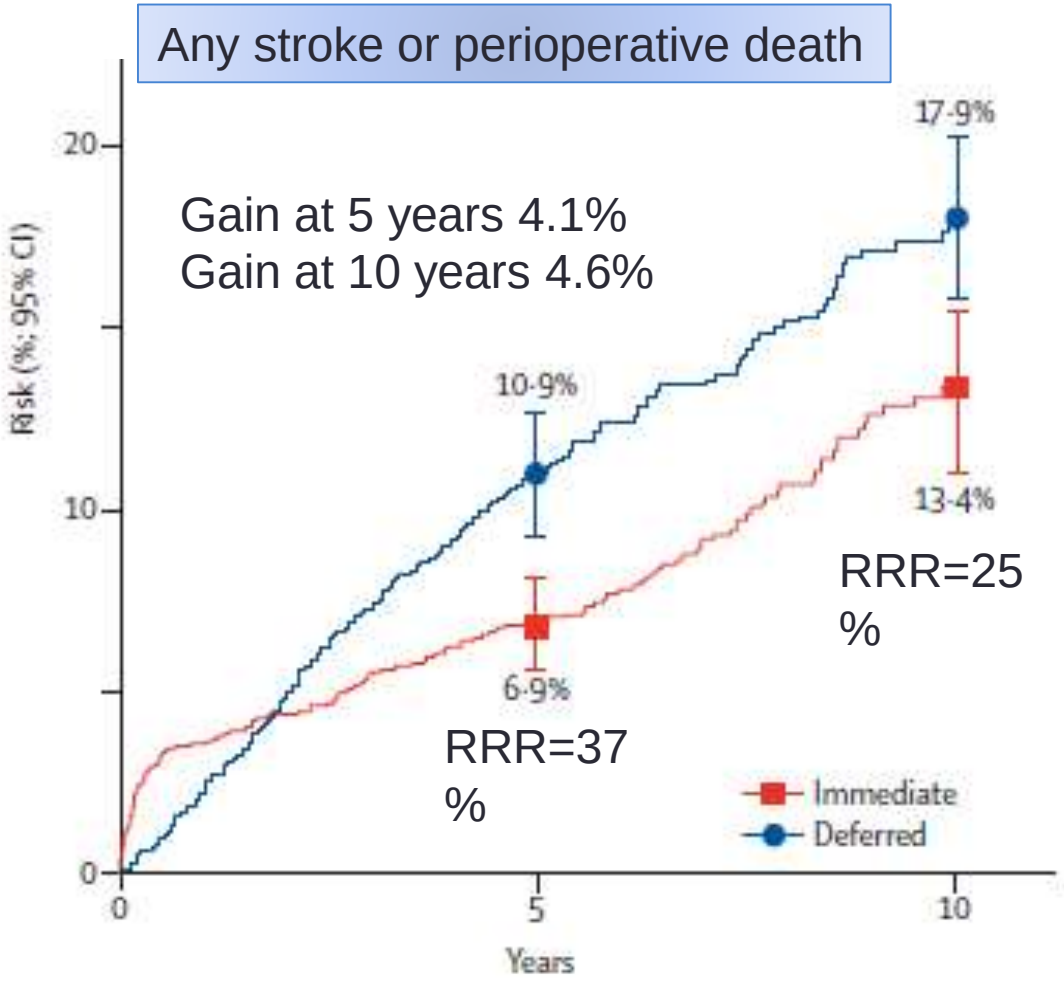
Recruited 1993-2003

Perioperative stroke-death=3.0%

NTT 5 y 25

NTT 10 y 22

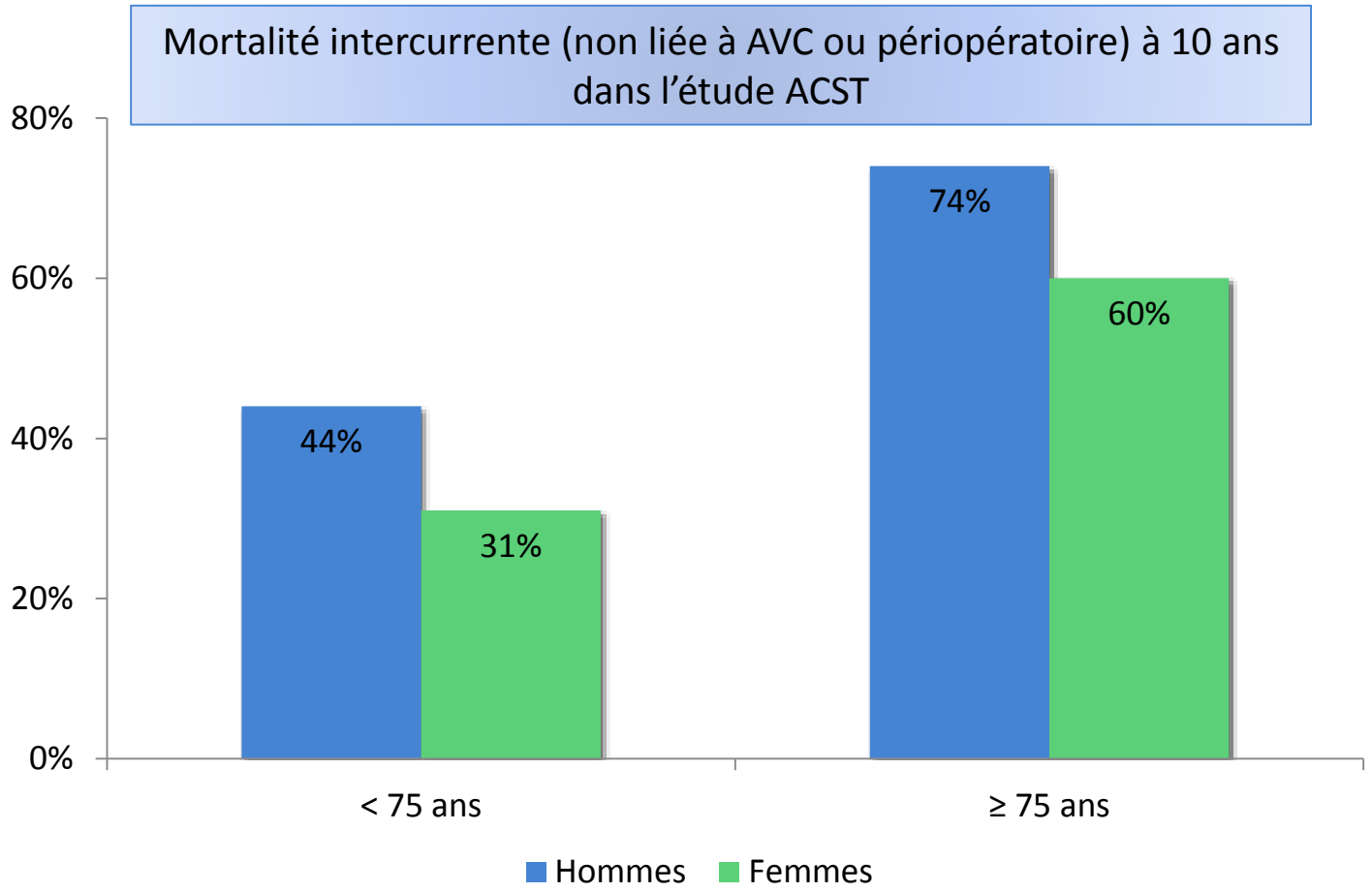
If the risk of death from another cause is >50% within 10 years, the benefit is reduced by half and does not offset the surgical risk



Halliday et al. ACST. Lancet 2010;376:1074-84.

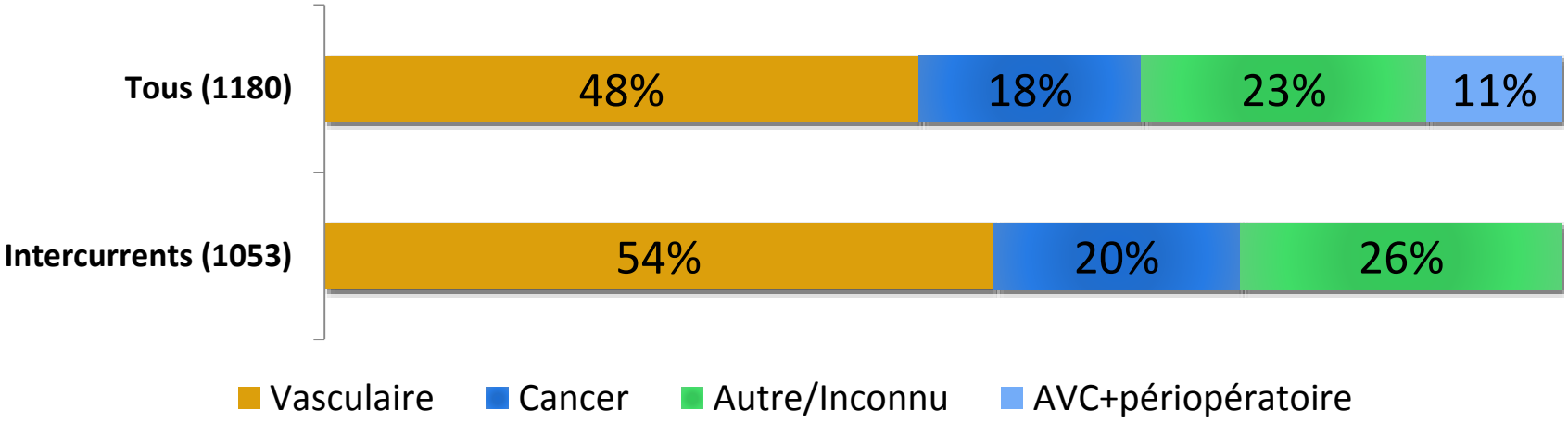
Décès

- En moyenne 5% par an dans les registres



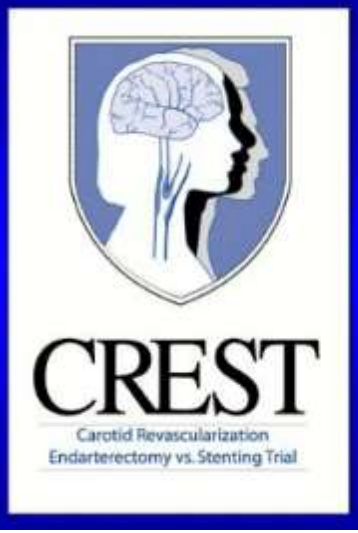
ACST. Lancet 2010;376:1074-84.

Causes de décès dans ACST



- Mortalité intercurrente=tout décès non lié à un AVC ou à une cause périopératoire

ACST. Lancet 2010;376:1074-84.



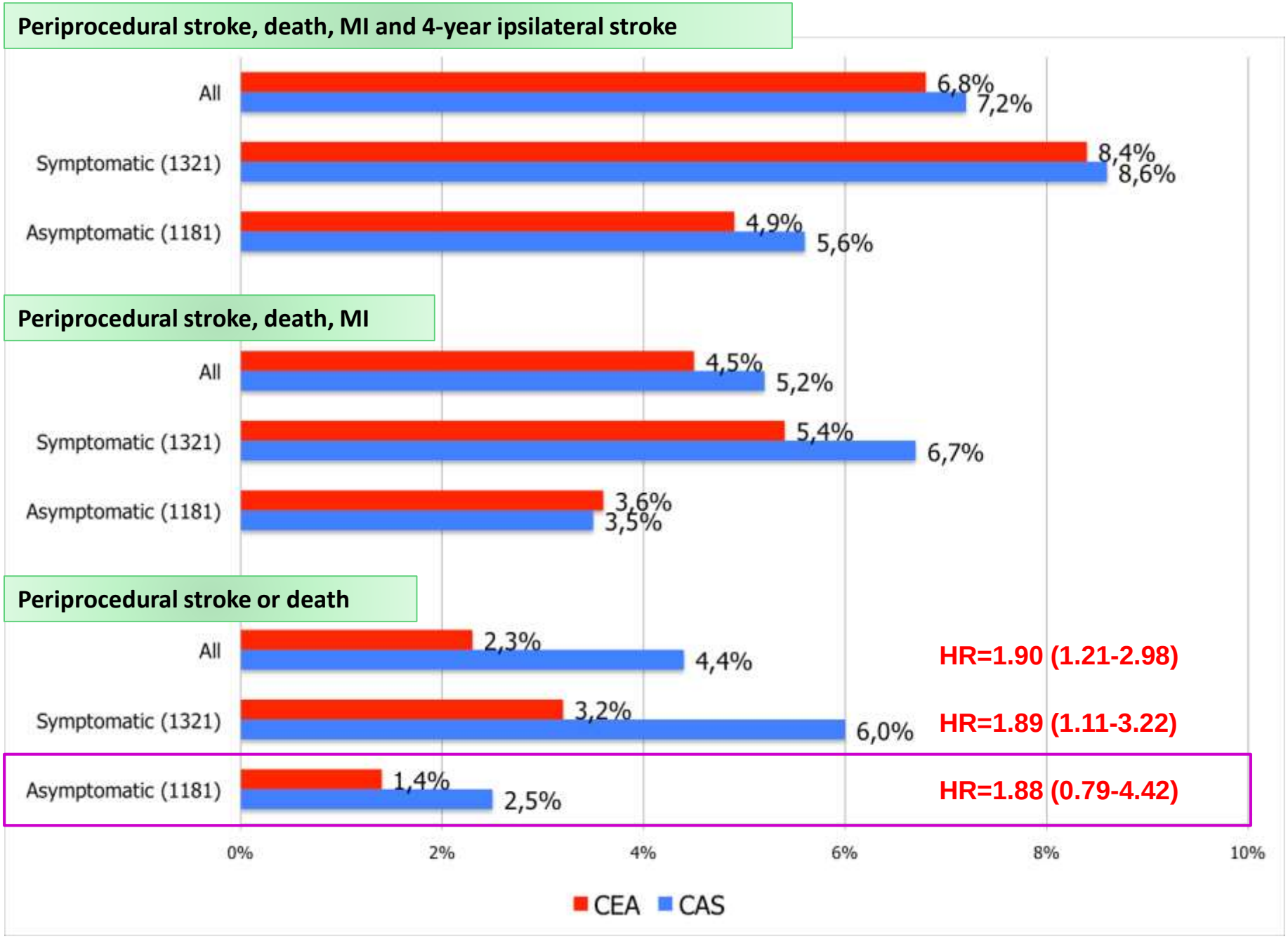
Carotid Revascularization Endarterectomy vs. Stenting Trial

Results according to symptomatic status

Stenting versus Endarterectomy for Treatment of Carotid-Artery Stenosis

Thomas G. Brott, M.D., Robert W. Hobson, II, M.D.,* George Howard, Dr.P.H., Gary S. Roubin, M.D., Ph.D., Wayne M. Clark, M.D., William Brooks, M.D., Ariane Mackey, M.D., Michael D. Hill, M.D., Pierre P. Leimgruber, M.D., Alice J. Sheffet, Ph.D., Virginia J. Howard, Ph.D., Wesley S. Moore, M.D., Jenifer H. Voeks, Ph.D., L. Nelson Hopkins, M.D., Donald E. Cutlip, M.D., David J. Cohen, M.D., Jeffrey J. Popma, M.D., Robert D. Ferguson, M.D., Stanley N. Cohen, M.D., Joseph L. Blackshear, M.D., Frank L. Silver, M.D., J.P. Mohr, M.D., Brajesh K. Lal, M.D., and James F. Meschia, M.D., for the CREST Investigators†

N Engl J Med 2010.


Periprocedural stroke, death, MI and 4-year ipsilateral stroke
All
6,8%
7,2%
Symptomatic (1321)
8,4%
8,6%
Asymptomatic (1181)
4,9%
5,6%
Periprocedural stroke, death, MI
All
4,5%
5,2%
Symptomatic (1321)
5,4%
6,7%
Asymptomatic (1181)
3,6%
3,5%
Periprocedural stroke or death
All
2,3%
4,4%
HR=1.90 (1.21-2.98)
Symptomatic (1321)
3,2%
6,0%
HR=1.89 (1.11-3.22)
Asymptomatic (1181)
1,4%
2,5%
HR=1.88 (0.79-4.42)
0%
2%
4%
6%
8%
10%
CEA
CAS

Importance du traitement médical

- Seule approche pouvant prévenir tous les événements vasculaires
- Peu de données spécifiques aux patients ayant de l'athérosclérose issues d'essais thérapeutiques
- Mais, nombreux arguments en faveur du bénéfice de:
  - Contrôle des facteurs de risque
  - Antiplaquettaires
  - Statines

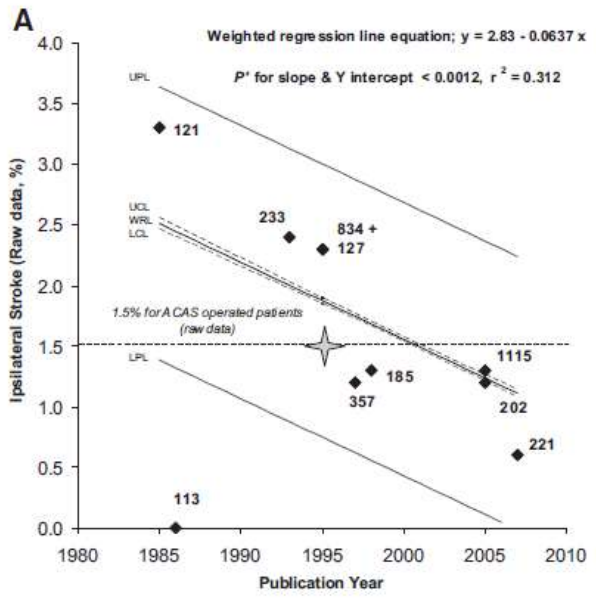
Bénéfice relatif globalement identique

quel que soit l'âge

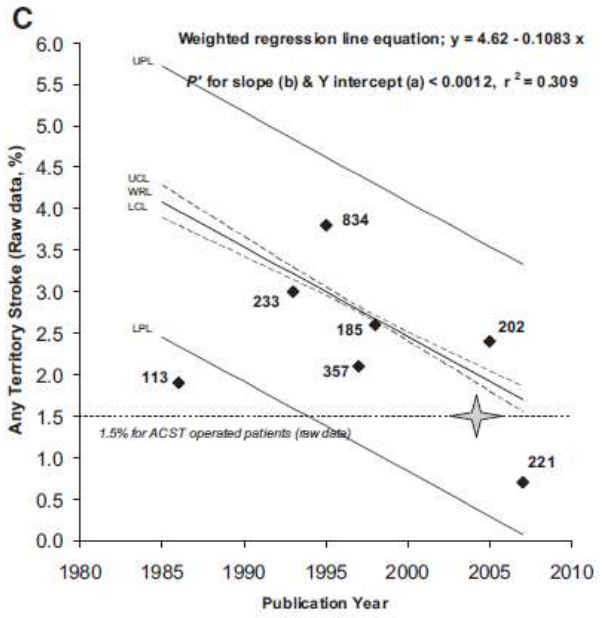
Brott et al. Circulation 2011;123:489-532.

Traitement médical

Ipsilateral stroke



Any territory stroke



<u>Falls coincide with:</u>

(1) Gains in vascular disease understanding

(2) Lowering or expansion of thresholds used to define and treat diabetes, hypertension, hyperlipidemia

(3) Progressive use of antiplatelet drugs, blood pressure-lowering drugs, and statins

Abbott et al. Stroke 2009;40:e573-e583.

Impact des statines sur les revascularisations carotidiennes

Study	Follow-up	Statin	Placebo	Relative Risk reduction
Heart Protection Study (simvastatine 40 mg/d)	4.6 yrs			
All patients		0.4%	0.8%	**50%**
Prior history of stroke		1.0%	2.3%	**56%**
SPARCL (atorvastatine 80 mg/d)	5 yrs			
Known carotid stenosis		3.2%	7.2%	**56%**

HPS. Lancet 2004;363:757-67 – Sillesen H et al. Stroke 2008;39:3297-3302.

Sténose asymptomatique

- La sténose carotide asymptomatique est avant tout un marqueur de risque d'événements vasculaire
  - IDM ~>2% par an ?
  - Mort vasculaire ~2.5% par an
  - Mort (non liée à AVC) ~5% par an
- Le risque d'accident ipsilatéral est faible dans les cohortes actuelles (<1%/an avec le traitement médical)
- Bénéfice faible de la chirurgie
- Intérêt d'identifier les patients à haut risque mais p eu de facteurs de risque d'accident ipsilatéral à la sténose connus

Sténose carotidienne symptomatique

Risque très élevé de récidive très précoce

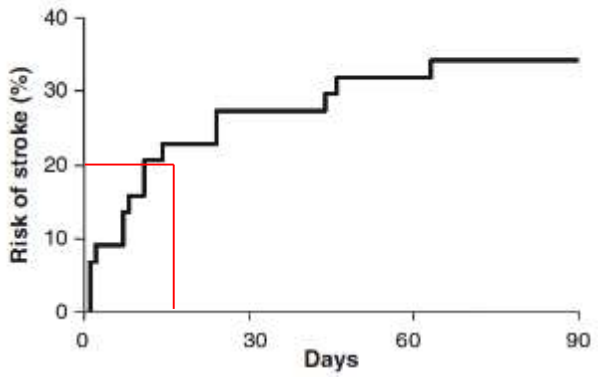
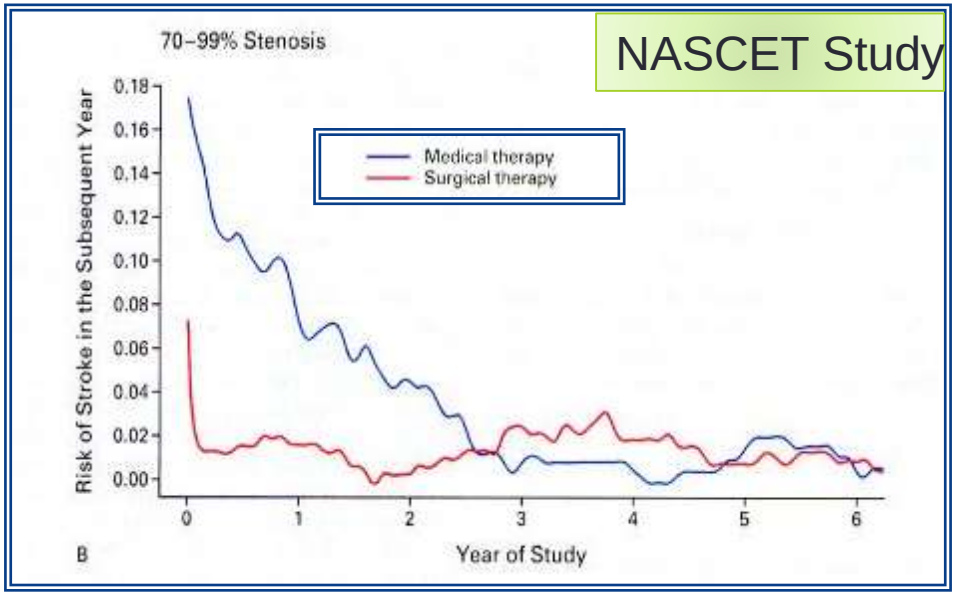


Fig. 1 Risk of recurrent stroke in all patients with TIA or nondisabling ischaemic stroke in the Oxford Vascular Study population who were found to have ≥50% symptomatic carotid stenosis. Analysis is censored before any endarterectomy (2).



NASCET. N Engl J Med 1998;339:1415-25.

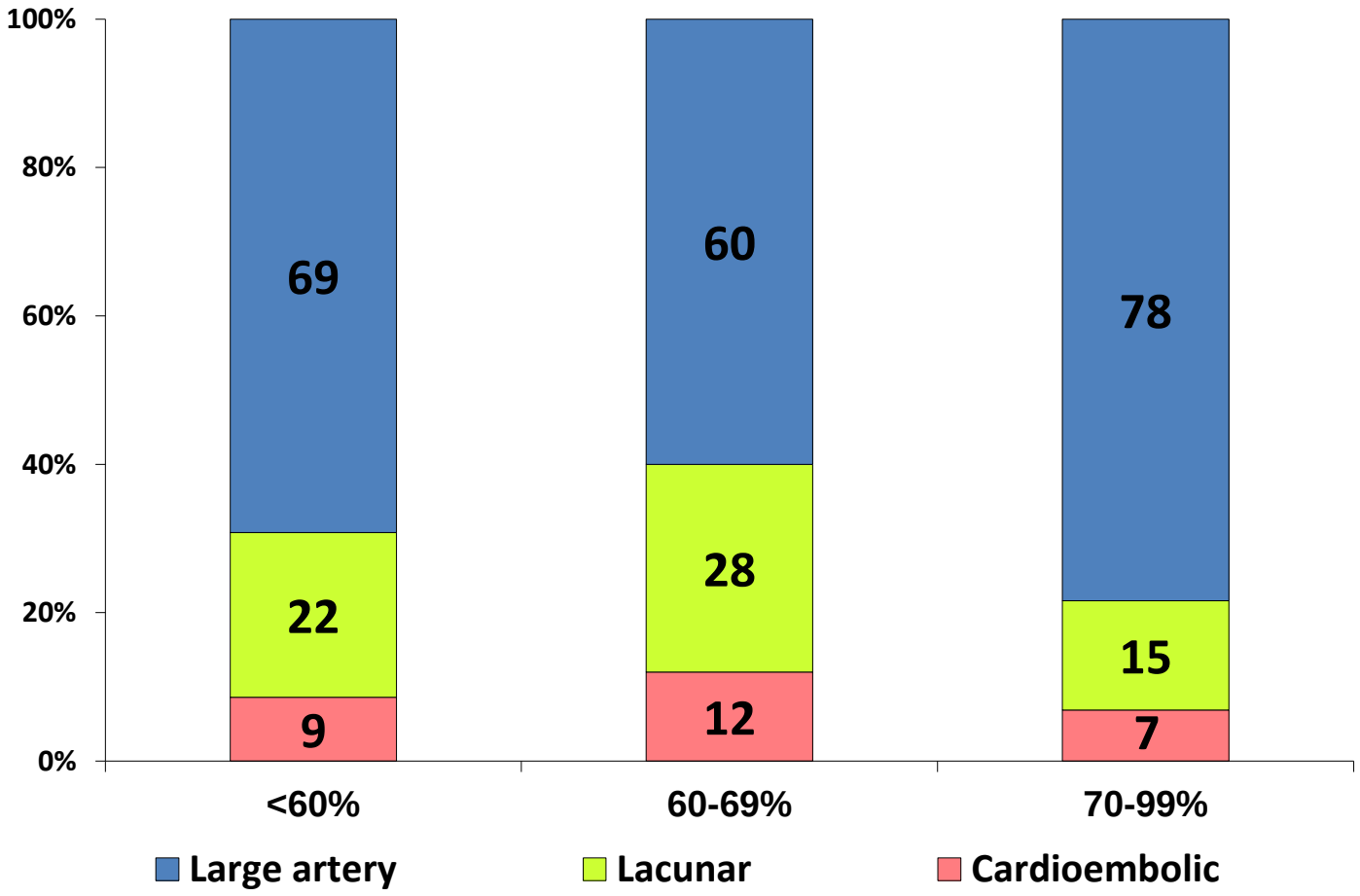
Early risk of recurrent stroke in patients awaiting for carotid surgery

Study	N patients	Follow-up (days)	Recurrent stroke n (%/d)	Recurrent TIA n (%/d)
Blaser 2002, Germany	143	19	8 (0.30)	7 (0.25)
Fairhead 2005, UK	38	69	14 (0.53)	-
Marnane 2011, UK	36	14	3 (0.60)	-

Stroke 2002;33:1057-62 – Neurology 2005;65:371-75 – Neurology 2011;77:738-43.

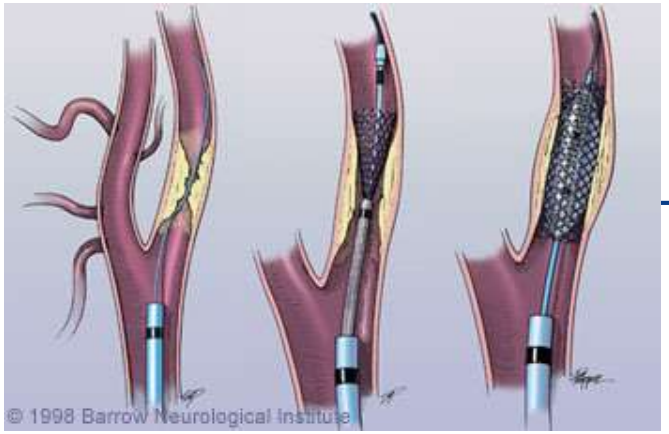
Sténose carotidienne symptomatique

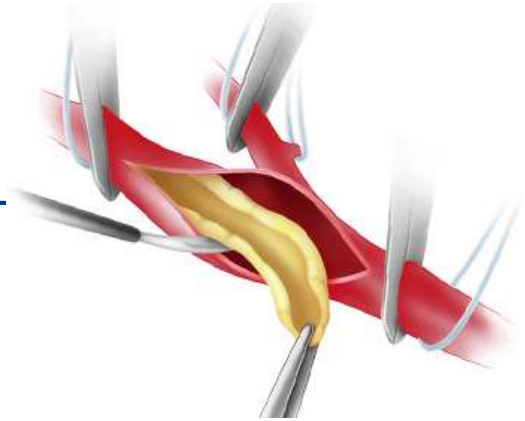
Mécanisme des infarctus cérébraux

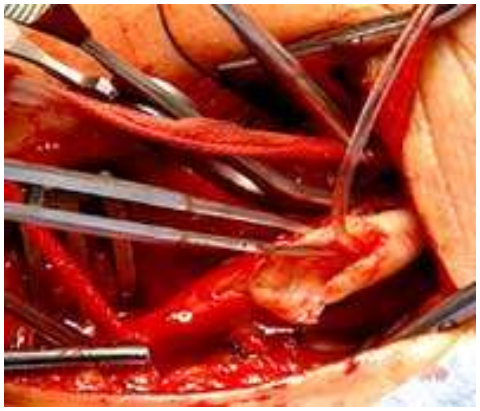


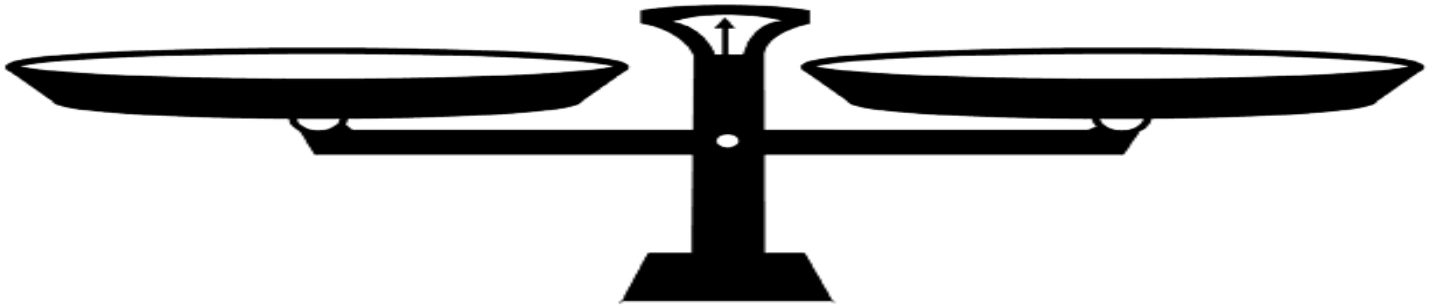
Barnett et al. JAMA 2000;283:1429-36 – Inzitari et al. N Engl J Med 2000;342:1693-700.

Revascularisation Carotidienne





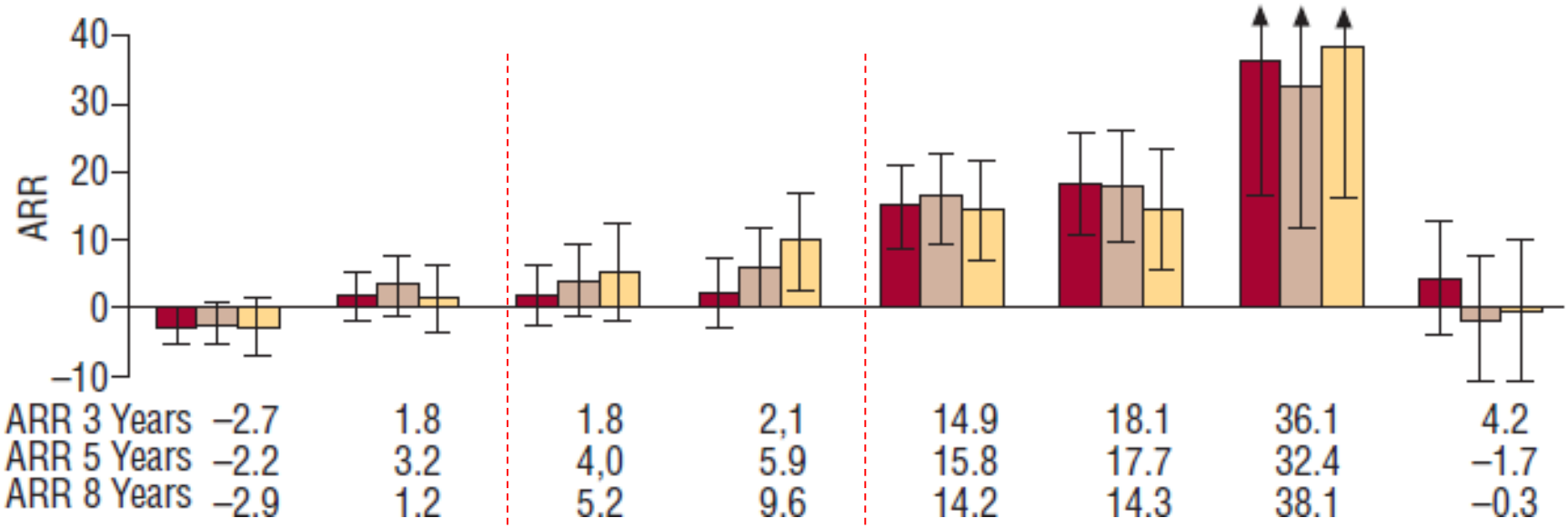




Sténose carotidienne symptomatique

Chirurgie vs. Traitement médical

Ipsilateral ischemic stroke and any operative stroke or death



ARR 3 Years	−2.7	1.8	1.8	2,1	14.9	18.1	36.1	4.2
ARR 5 Years	−2.2	3.2	4,0	5.9	15.8	17.7	32.4	−1.7
ARR 8 Years	−2.9	1.2	5.2	9.6	14.2	14.3	38.1	−0.3

Stenosis* <30% 30-49% 50-59% 60-69% 70-79% 80-89% 90-99% Near Occl.

5 ans

Pas de bénéfice

RRR: 25%
RAR: 5%
NST: 22

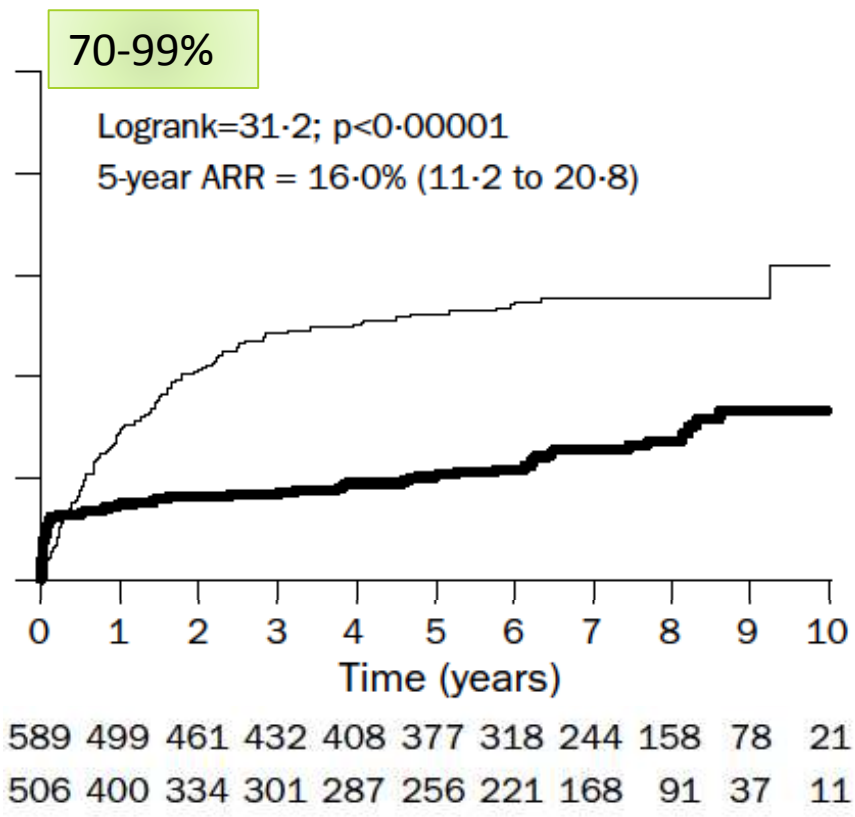
RRR: 61%
RAR: 16%
NST: 6

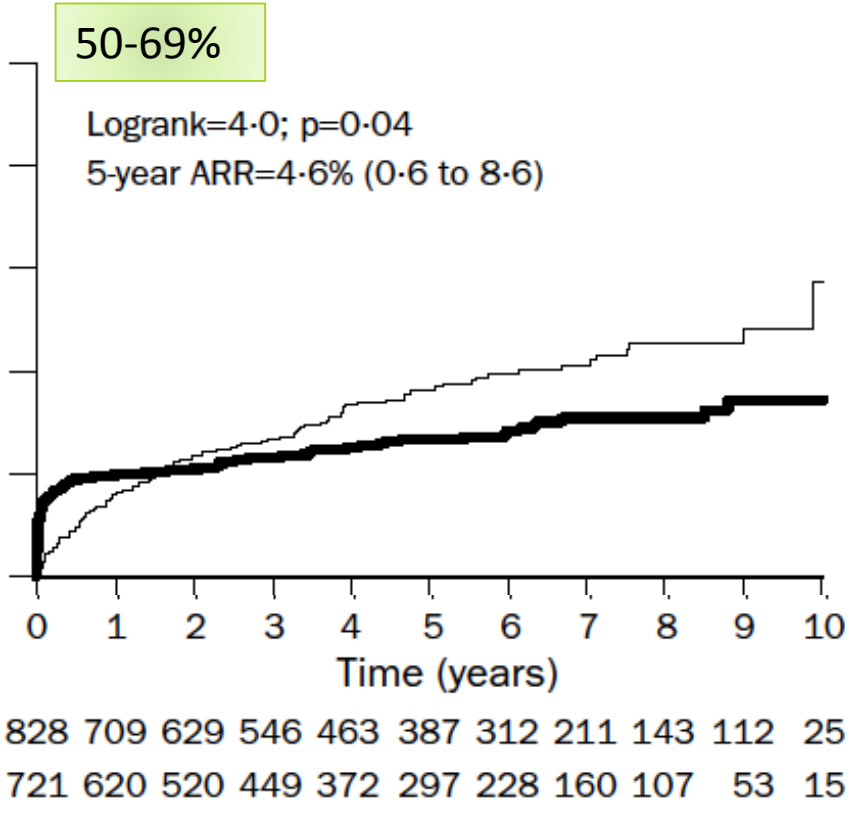
Méta-analyse sur données individuelles ECST, NASCET, et VA309, n = 6092 patients

Sténose carotidienne symptomatique

Chirurgie vs. traitement médical

Ipsilateral ischemic stroke and any operative stroke or death





Operative risks: mortality=1.1% - stroke or death=7.1%

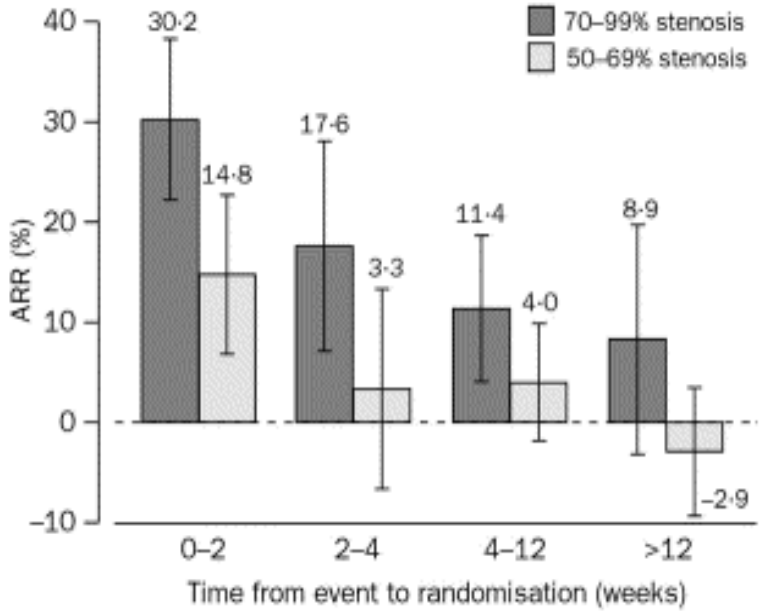
Rothwell PM for the CETC. Lancet 2003;361:107-16.

Sténose carotidienne symptomatique

Chirurgie vs. Traitement médical

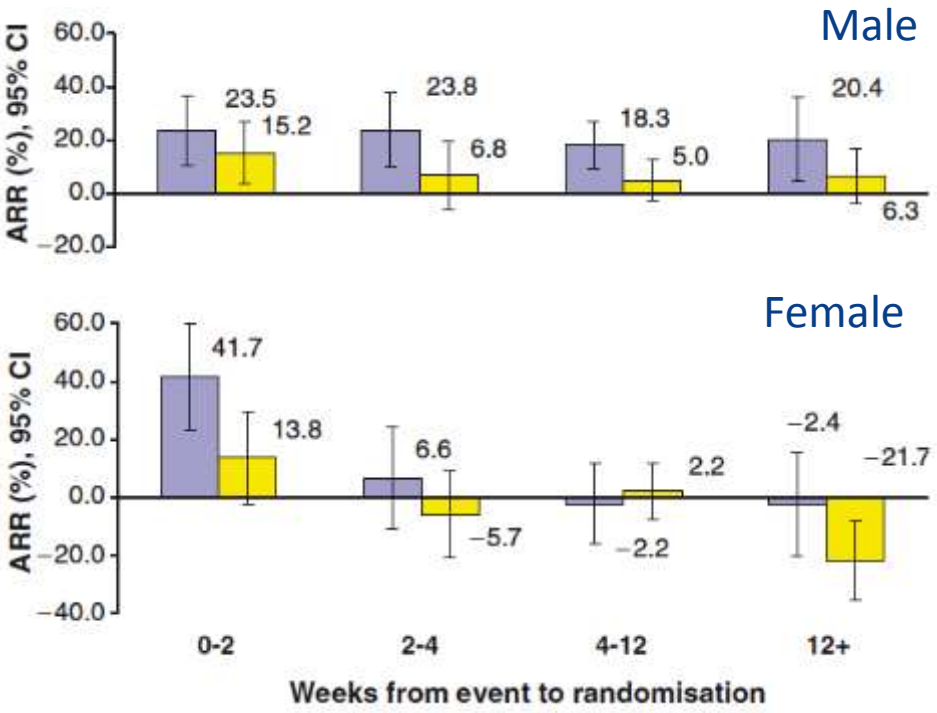
Nombre de patients à traiter pour prévenir 1 événement à 5 ans

Hommes	Femmes	p
9	36	0.003
>75 ans	**<65 ans**	**p**
5	15	0.03
Chir<2 sem	**Chir>12 sem**	**p**
12	125	0.009



Which patients benefit most?

- Benefit of surgery is increased in:
  - **Men**
  - Patients **>75 years**
  - Patients treated **within 2 weeks** after the last event



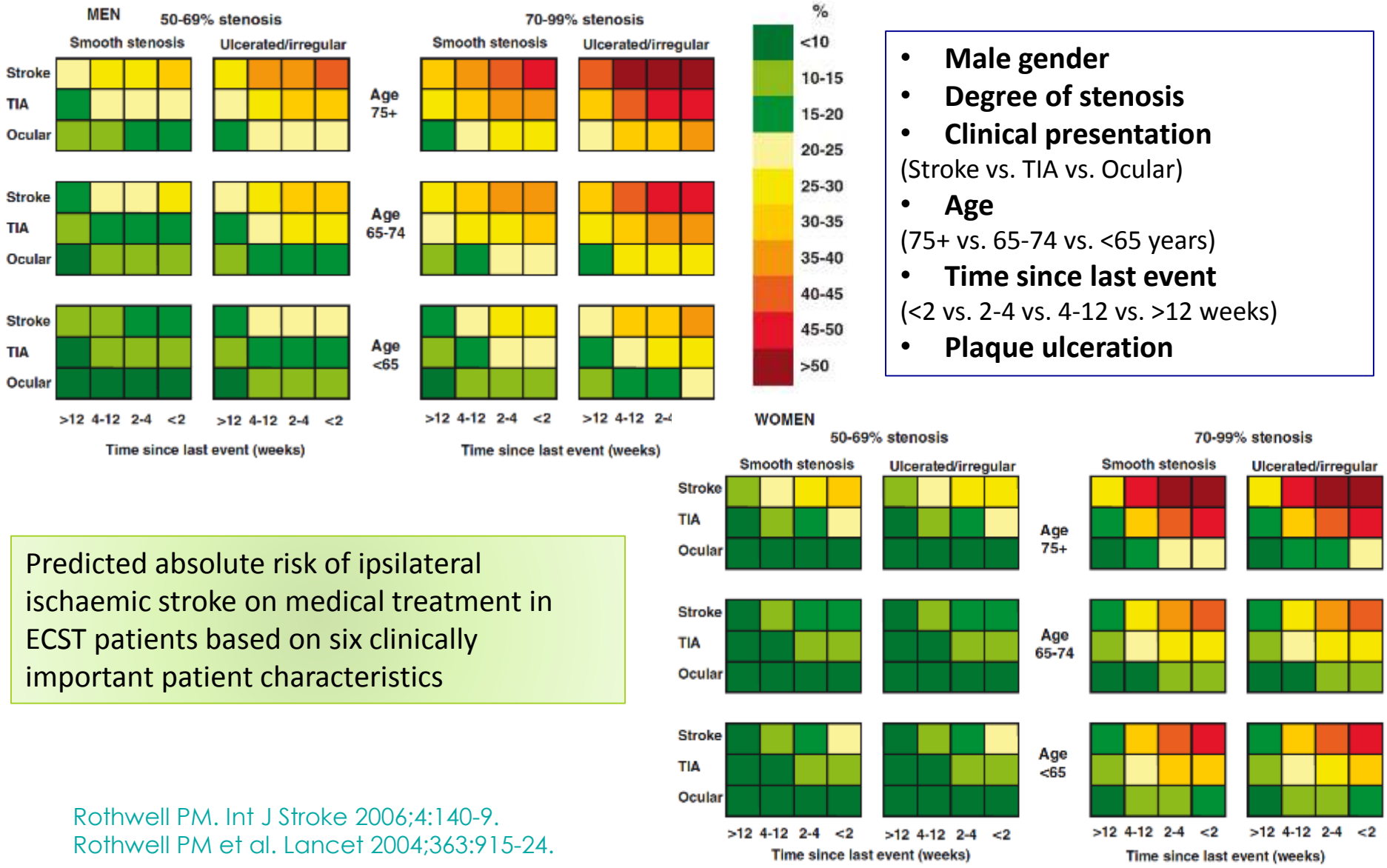
5-year absolute reduction in the risk of ipsilateral ischaemic stroke and any operative stroke or death

50-69%

70-99%

Rothwell PM. Int J Stroke 2006;4:140-9.
Rothwell PM et al. Lancet 2004;363:915-24.

Which patients benefit most?



- **Male gender**
- **Degree of stenosis**
- **Clinical presentation**

(Stroke vs. TIA vs. Ocular)

- **Age**

(75+ vs. 65-74 vs. <65 years)

- **Time since last event**

(<2 vs. 2-4 vs. 4-12 vs. >12 weeks)

- **Plaque ulceration**

Predicted absolute risk of ipsilateral ischaemic stroke on medical treatment in ECST patients based on six clinically important patient characteristics

Rothwell PM. Int J Stroke 2006;4:140-9.
Rothwell PM et al. Lancet 2004;363:915-24.

Symptomatic ICA stenosis

Stenting vs. Endarterectomy

Study	Single vs. Multicentre	N patients	% Stents / Protection	Stopped prematurely
Leicester, 1998	S	23	100 / 0	Yes: harm
Kentucky, 2001	S	104	100 / 0	No
WALLSTENT, 2001	M	219	100 / 0	Yes: harm, futility
CAVATAS, 2001	M	504	26 / 0	No
BACASS, 2006	S	20	100 / 10	No
EVA-3S, 2006	M	527	100 / 86	Yes: harm, futility
SPACE, 2006	M	1196	100 / 25	Yes: shortage of funding
ICSS, 2010	M	1710	100 / 72	No
CREST, 2010	M	1321	100 / 100	No
TOTAL		**5624**		

SAPPHIRE not included because only 29% of patients were symptomatic.

Symptomatic ICA stenosis

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CREST, 2010	M	1321	100 / 100	No
TOTAL		**5624**		

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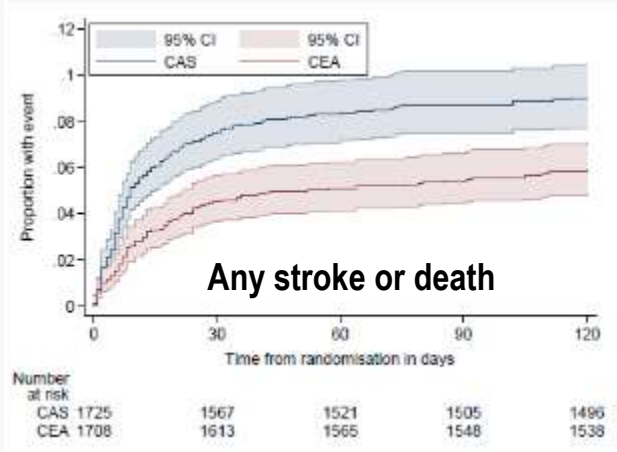
Sténose carotidienne symptomatique

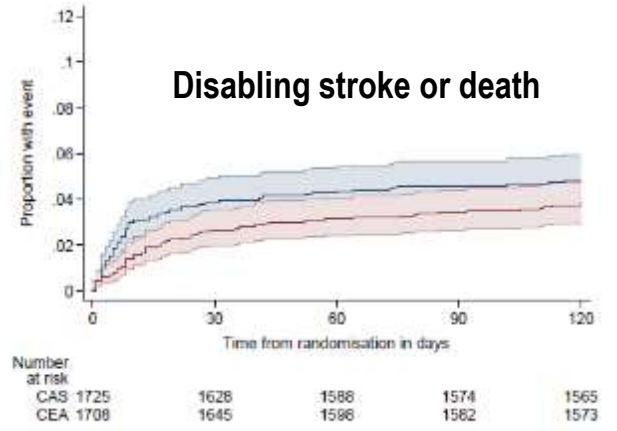
Stenting vs. Chirurgie

Meta-analysis of pooled individual patients data from EVA3S, SPACE, and ICSS (3433 patients)

Per-protocol analysis

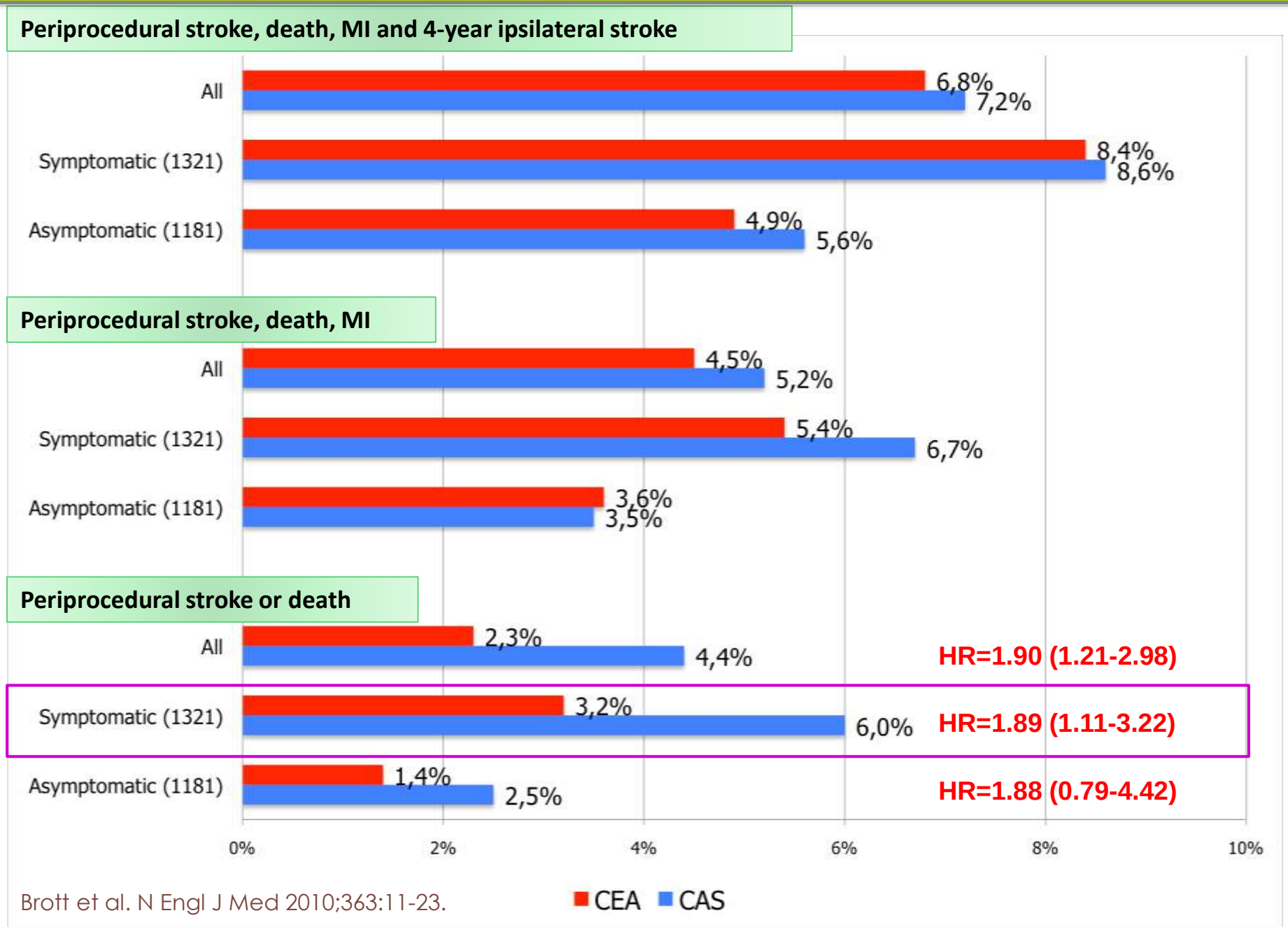
	CAS		CEA		Risk ratio (95% CI)
	Events	Total	Events	Total	
Any stroke or death					
EVA-3S	25 (9·6%)	260	10 (3·9%)	257	2·47 (1·21–5·04)
SPACE	44 (7·4%)	591	35 (6·2%)	567	1·21 (0·79–1·85)
ICSS	61 (7·4%)	828	28 (3·4%)	821	2·16 (1·40–3·34)
Pooled	**130 (7·7%)**	**1679**	**73 (4·4%)**	**1645**	**1·74 (1·32–2·30)**
Heterogeneity: interaction p value=0·10; I^2=57%					
Disabling stroke or death					
EVA-3S	9 (3·5%)	260	5 (1·9%)	257	1·78 (0·60–5·24)
SPACE	30 (5·1%)	591	20 (3·5%)	567	1·44 (0·83–2·50)
ICSS	26 (3·1%)	828	18 (2·2%)	821	1·43 (0·79–2·59)
Pooled	**65 (3·9%)**	**1679**	**43 (2·6%)**	**1645**	**1·48 (1·01–2·15)**
Heterogeneity: interaction p value=0·93; I^2=0					





Carotid Stenting Trialists' Collaboration. Lancet 2010;376:1062-73.

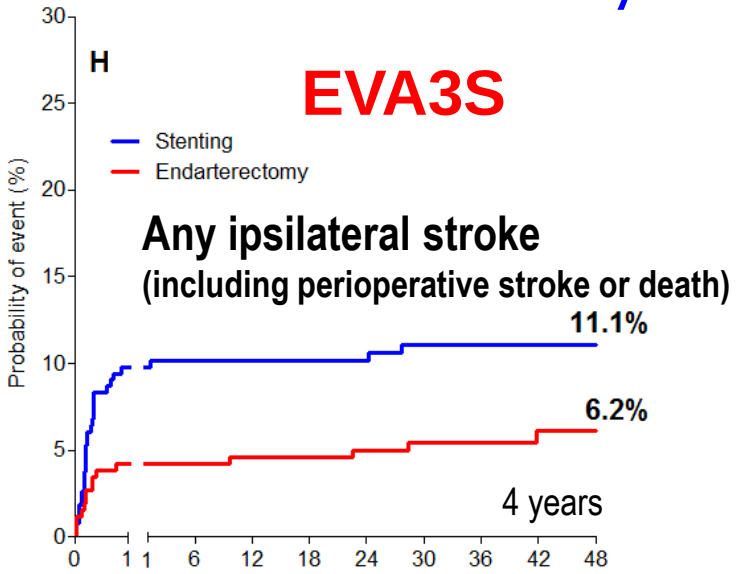
CREST

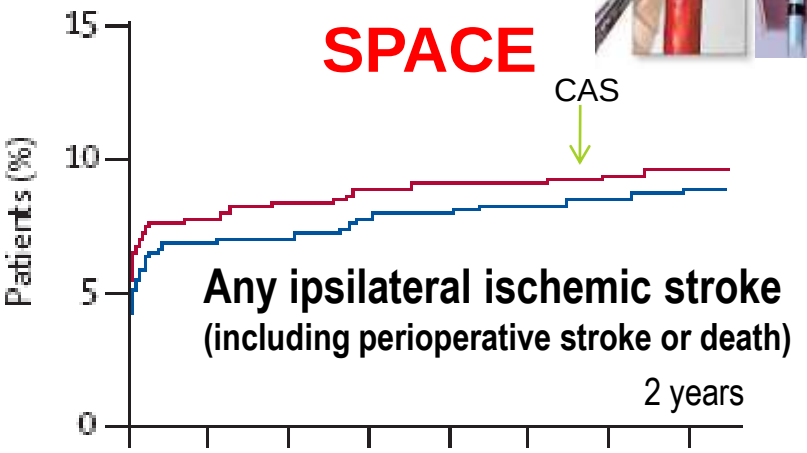


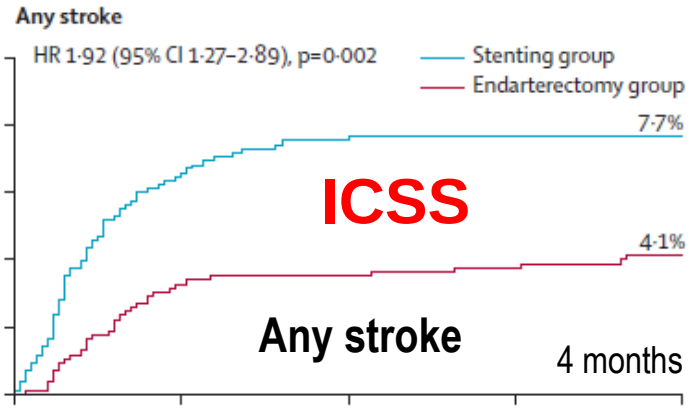
Brott et al. N Engl J Med 2010;363:11-23.

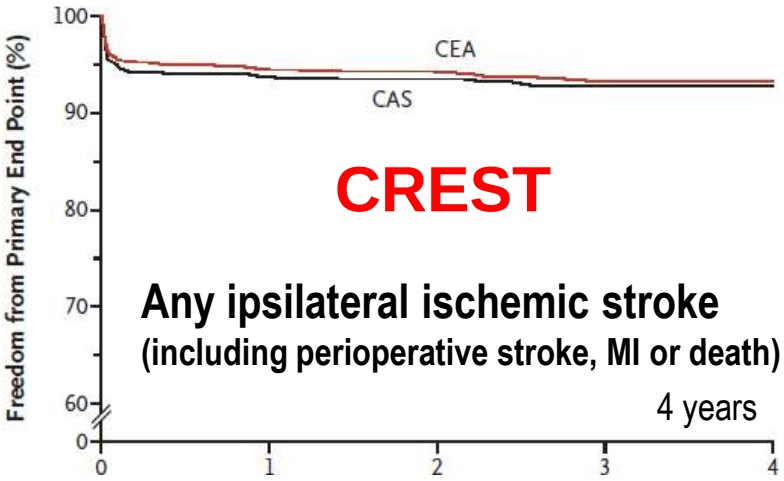
Sténose carotide symptomatique

CAS vs. CEA: effets à moyen terme





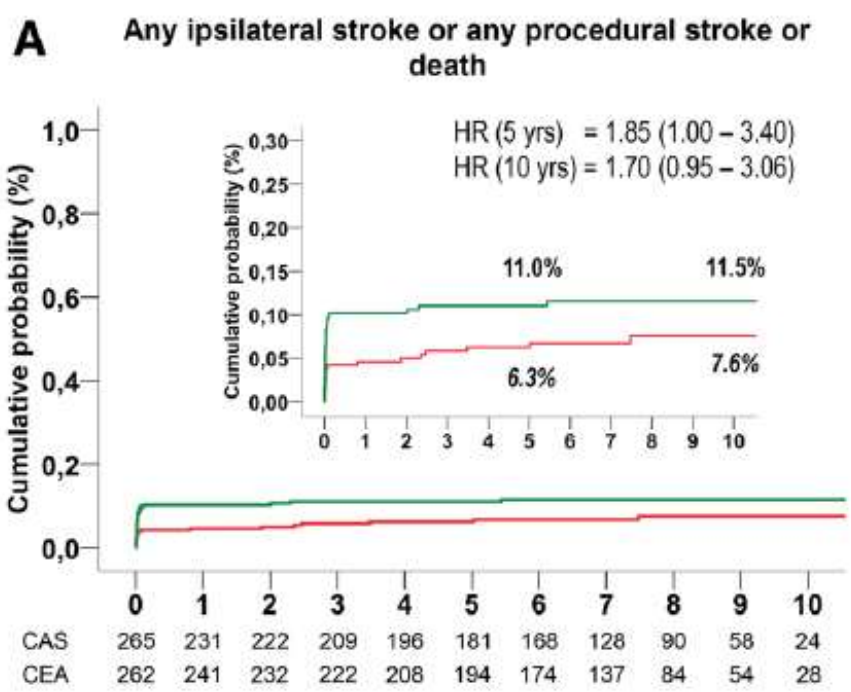


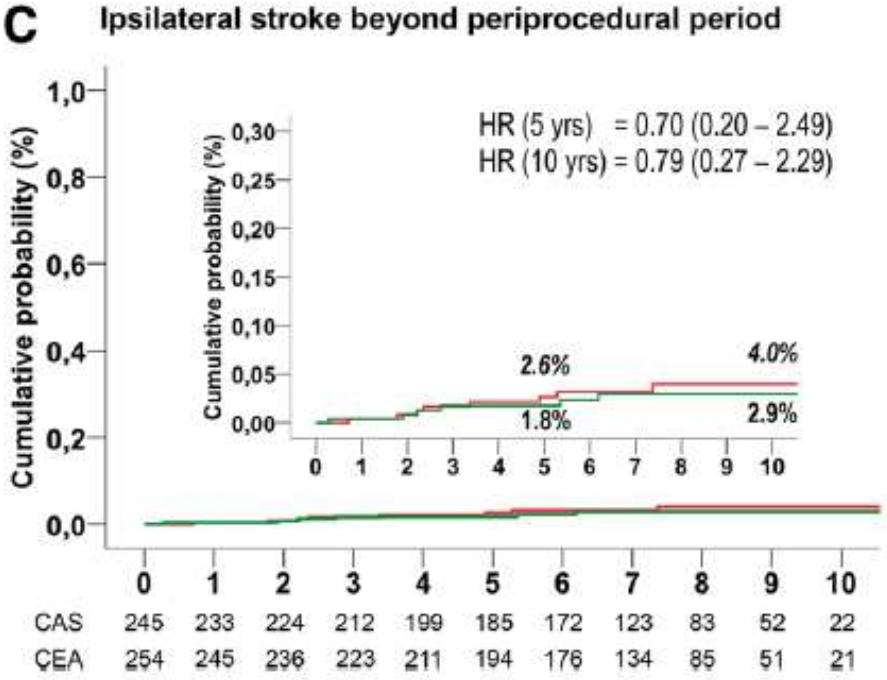


Résultats à long terme

EVA-3S

Maintien de la différence à long terme, expliquée par l'excès de risque initial

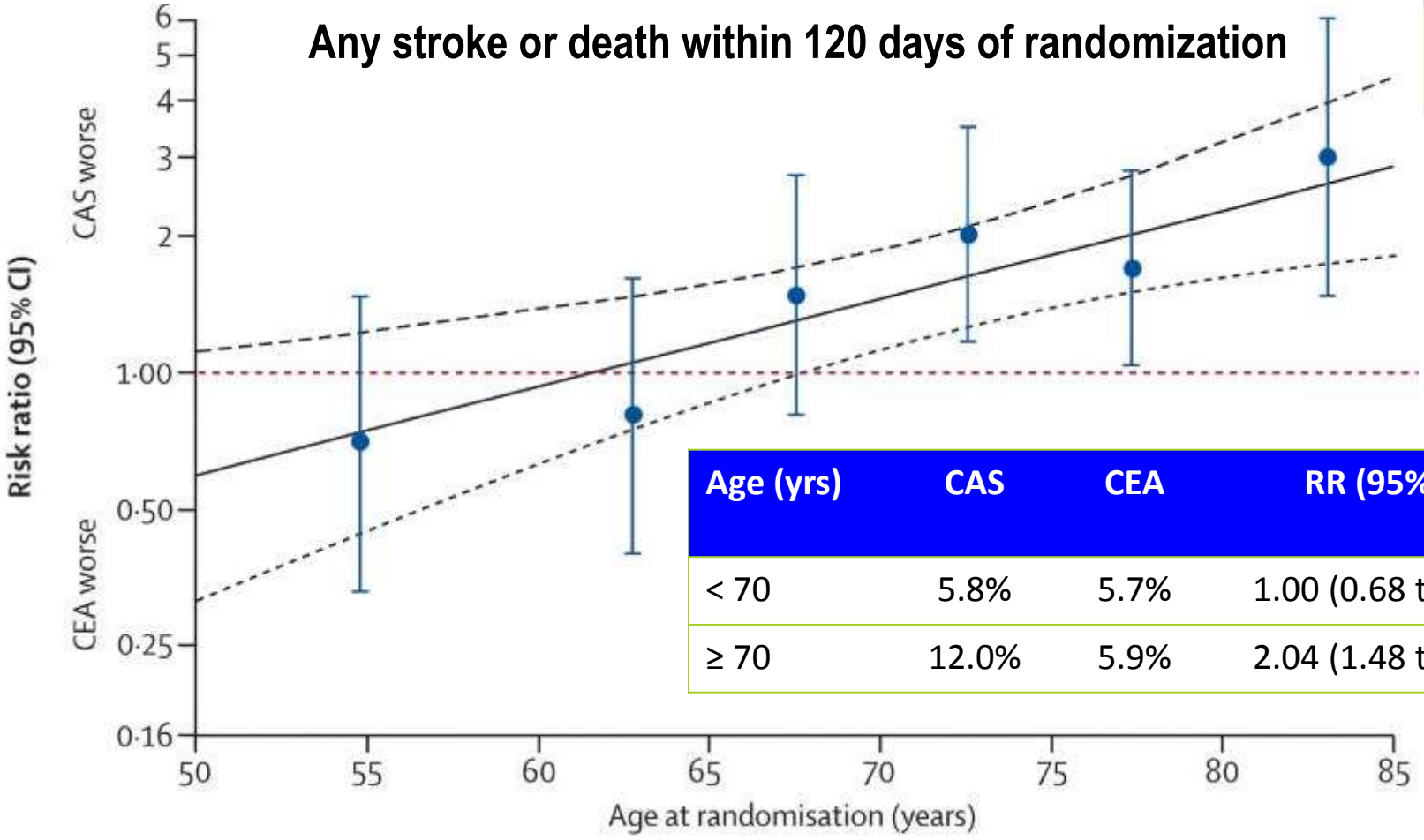




Mas et al. *Stroke*. 2014;45:2750-6.

Sténose carotidienne symptomatique

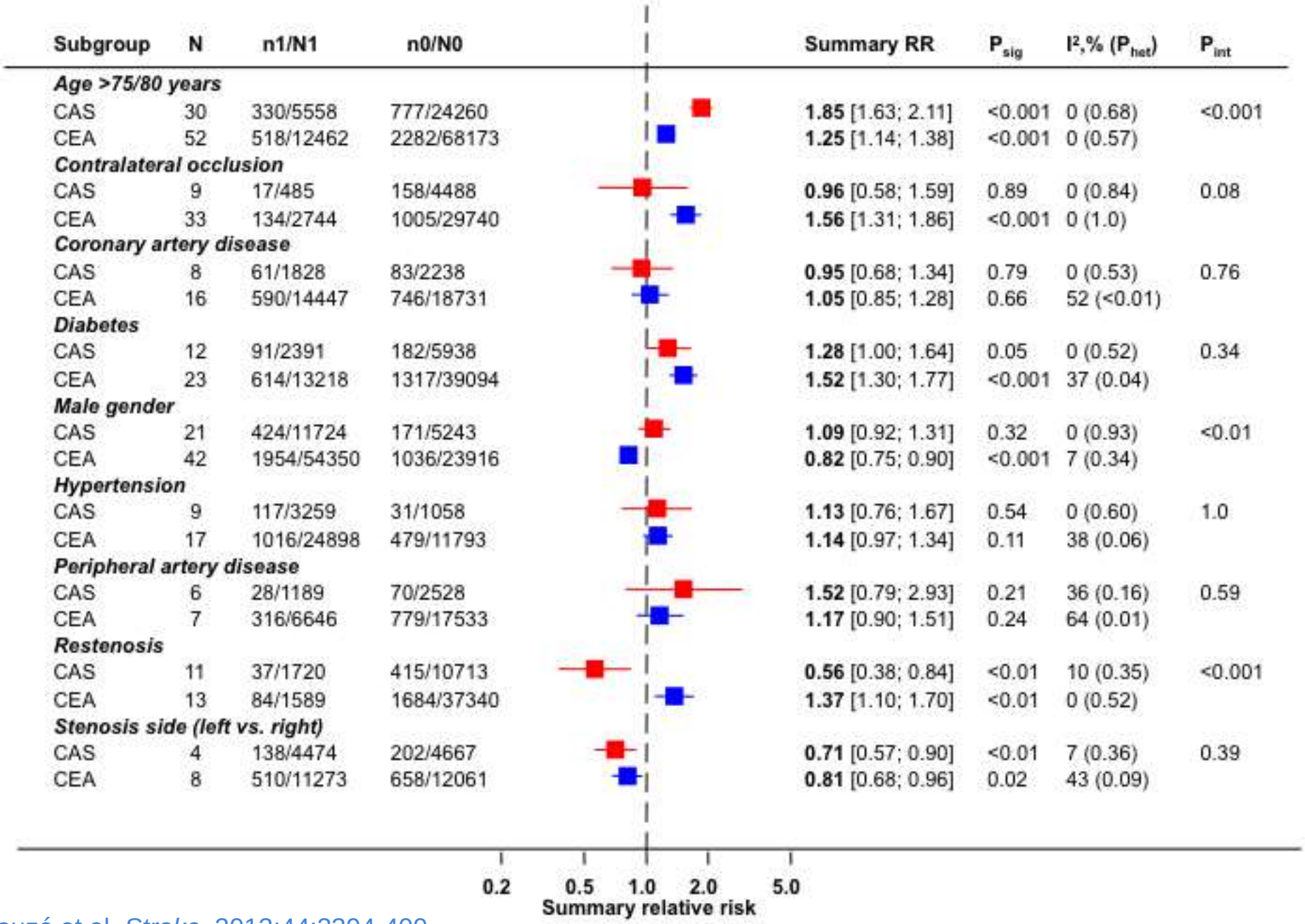
Effet de l'âge



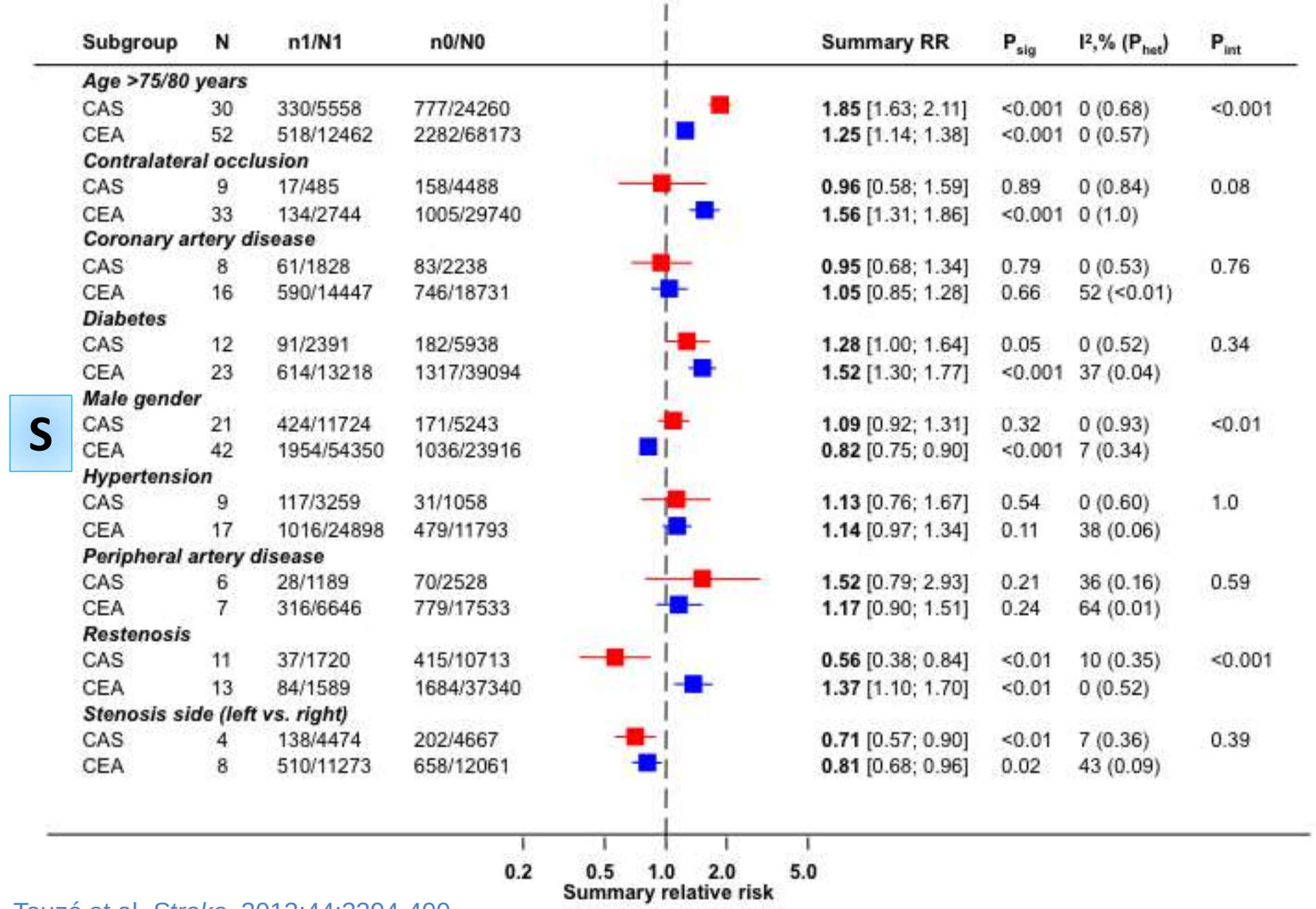
Age (yrs)	CAS	CEA	RR (95% CI)
< 70	5.8%	5.7%	1.00 (0.68 to 1.47)
≥ 70	12.0%	5.9%	2.04 (1.48 to 2.82)

Carotid Stenting Trialists' Collaboration. Lancet 2010;376:1062-73.

Y a t'il d'autres sous-groupes qui pourraient « bénéficier » du traitement endovasculaire ?

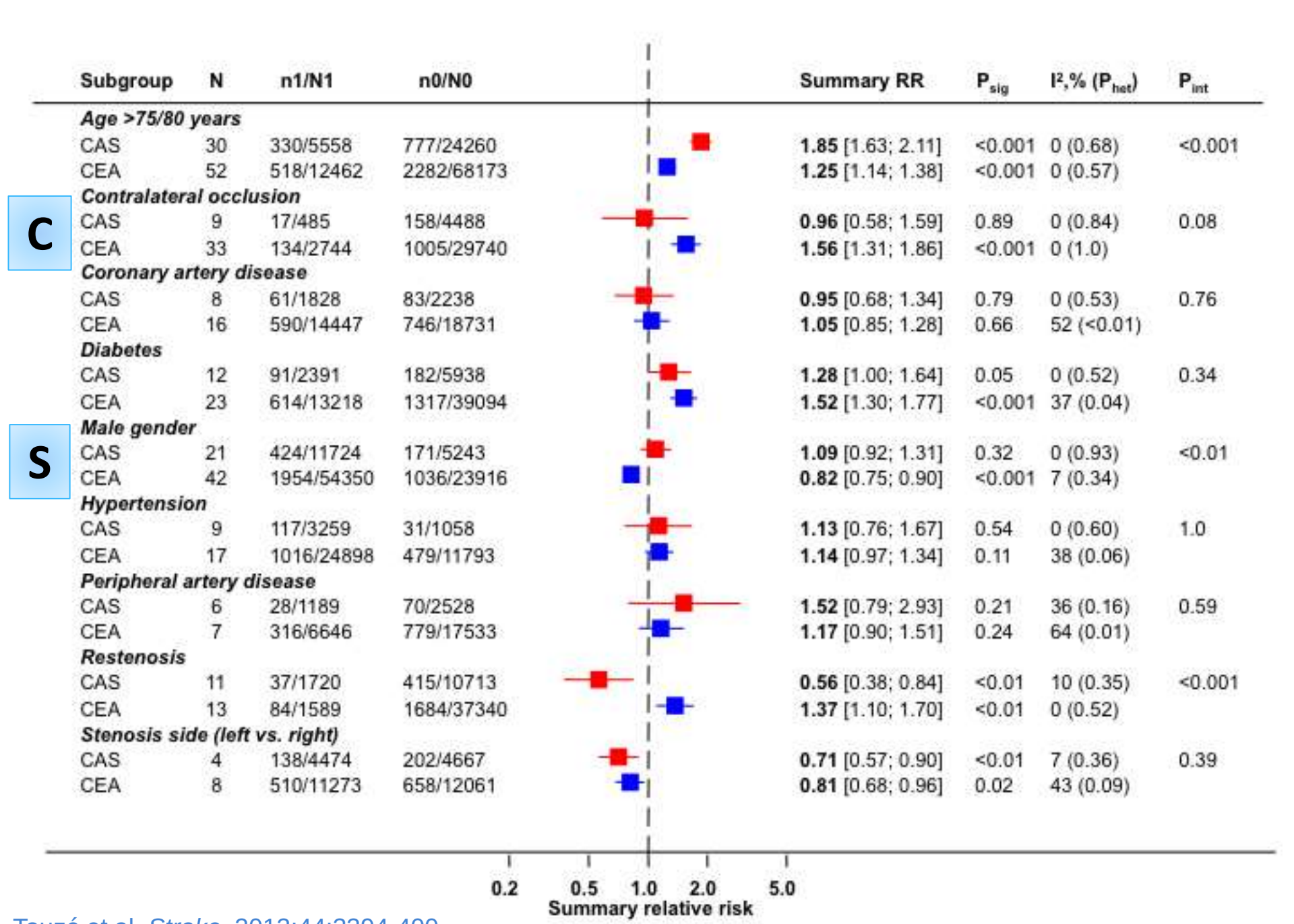


Touzé et al. *Stroke*. 2013;44:3394-400.



S

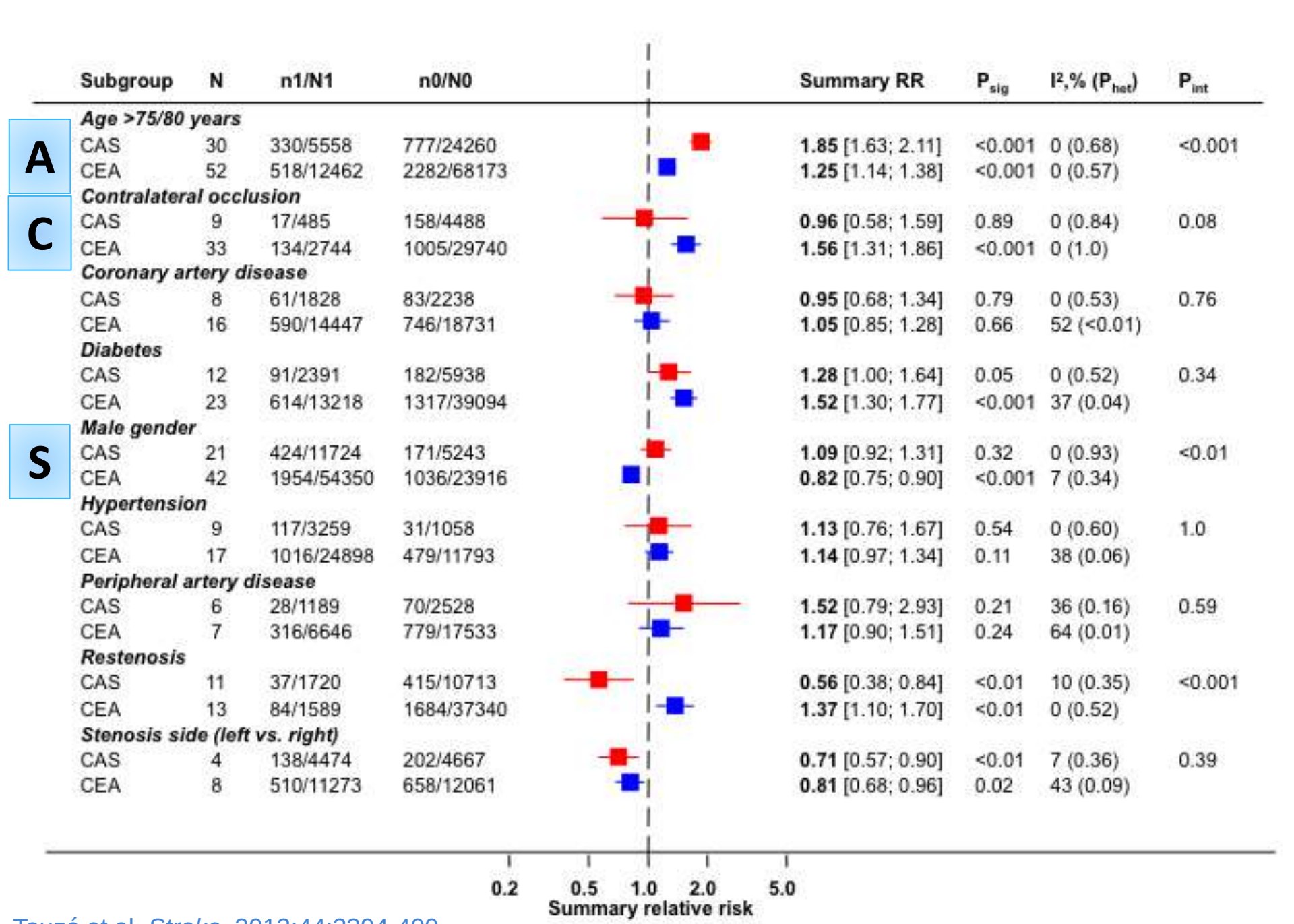
Touzé et al. *Stroke*. 2013;44:3394-400.



C

S

Touzé et al. *Stroke*. 2013;44:3394-400.

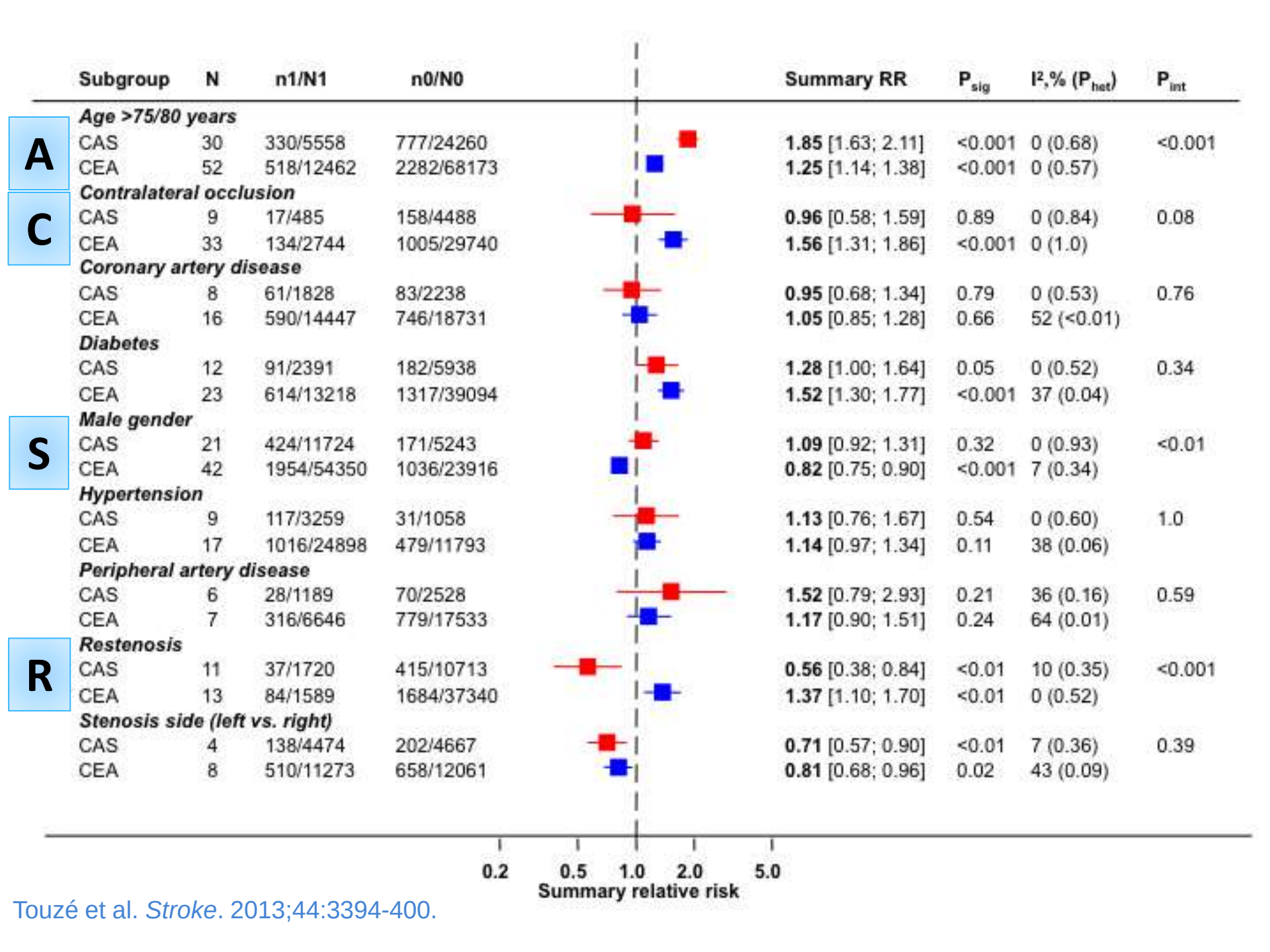


A

C

S

Touzé et al. *Stroke*. 2013;44:3394-400.



Touzé et al. *Stroke*. 2013;44:3394-400.

SCAR Rule

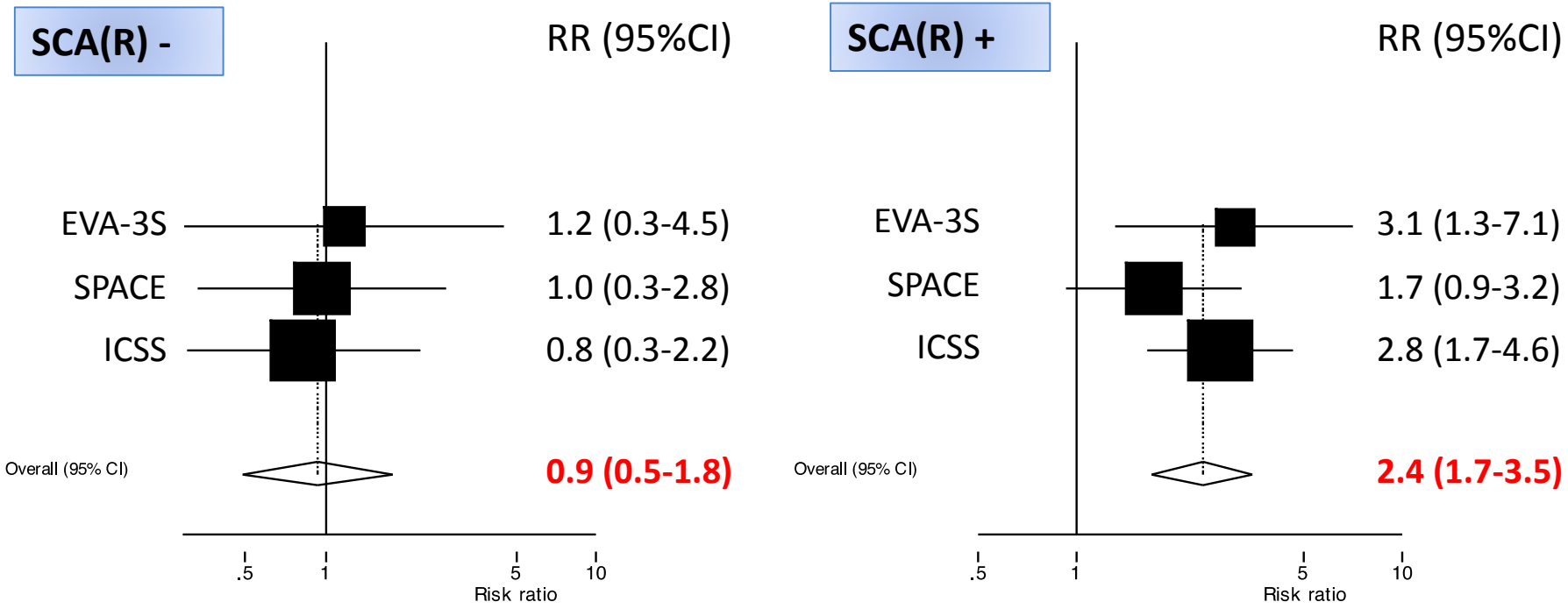
Supplemental table 2 – Categorization of patients according to the 2 potential definitions of the SCAR rule.

	Contralateral occlusion								No contralateral occlusion							
	Restenosis				No restenosis				Restenosis				No restenosis			
	Women		Men		Women		Men		Women		Men		Women		Men	
Age	<75	>75	<75	>75	<75	>75	<75	>75	<75	>75	<75	>75	<75	>75	<75	>75
SCAR primary option	-	-	-	-	-	-	-	-	-	-	-	-	-	+	+	+
SCAR secondary option	-	-	-	-	-	-	-	+	-	-	-	+	-	+	+	+

Touzé et al. *Stroke*. 2013;44:3394-400.

SCAR interaction

- CSTC data (EVA-3S, SPACE, ICSS)
- 3049 patients



P (interaction)=0.05

Touzé et al. *Stroke*. 2013;44:3394-400.

Sténose symptomatique

- Risque de récidive immédiat élevé
- Bénéfice important de la chirurgie carotidienne

- Stenting associé à un sur-risque de complications (AVC/DC) à court terme mais probable équivalence à moyen/long terme
  - Moindre risque d'IDM mais impact faible

- Sous-groupes chez qui le stenting pourraient être équivalent:
  - Age<70 ans
  - Occlusion controlatérale
  - Resténose
  - Femme<75 ans