

# Nouveautés en Neurologie Vasculaire



<i>Company Name</i>	<i>Honoraria/ Expenses</i>	<i>Consulting/ Advisory Board</i>	<i>Funded Research</i>
Astra Zeneca		X	
Boehringer Ingelheim	X		
Bristol Mayer Squibb	X		
Pfizer	X		
Boston Scientific	X		
Servier		X	

# Phase Aiguë

1. Thrombectomie: Hermes-Thrace-Siesta
2. Thrombolyse Enchanted
3. Hématome Patch / Attach 2



## Structured assessment of modified Rankin scale

Has the patient made a complete recovery with **absolutely no** residual signs or symptoms of stroke?

YES

mRS score = 0



NO

Can the patient perform every regular activity that they could undertake prior to the stroke? Regular is defined as more frequently than monthly; includes work, social and leisure activities (eg driving a car, dancing, reading or working)

YES

mRS score = 1



Please briefly document what neurological symptoms/signs are present?

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NO

Can the patient perform all their activities of daily living without assistance?  
ie mobility, dressing, bathing, toileting, feeding, preparing simple meals, travelling locally without supervision.

Can the patient be safely left alone for a period of at least 1 week?

YES

mRS score = 2



What usual activities have ceased?

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A Randomized Trial of Intraarterial  
Treatment for Acute Ischemic Stroke

Endovascular Therapy for Ischemic Stroke  
with Perfusion-Imaging Selection

Randomized Assessment of Rapid  
Endovascular Treatment of Ischemic Stroke

Stent-Retriever Thrombectomy after Intravenous  
t-PA vs. t-PA Alone in Stroke

Thrombectomy within 8 Hours after  
Symptom Onset in Ischemic Stroke

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# Endovascular thrombectomy after large-vessel ischaemic stroke: a meta-analysis of individual patient data from five randomised trials

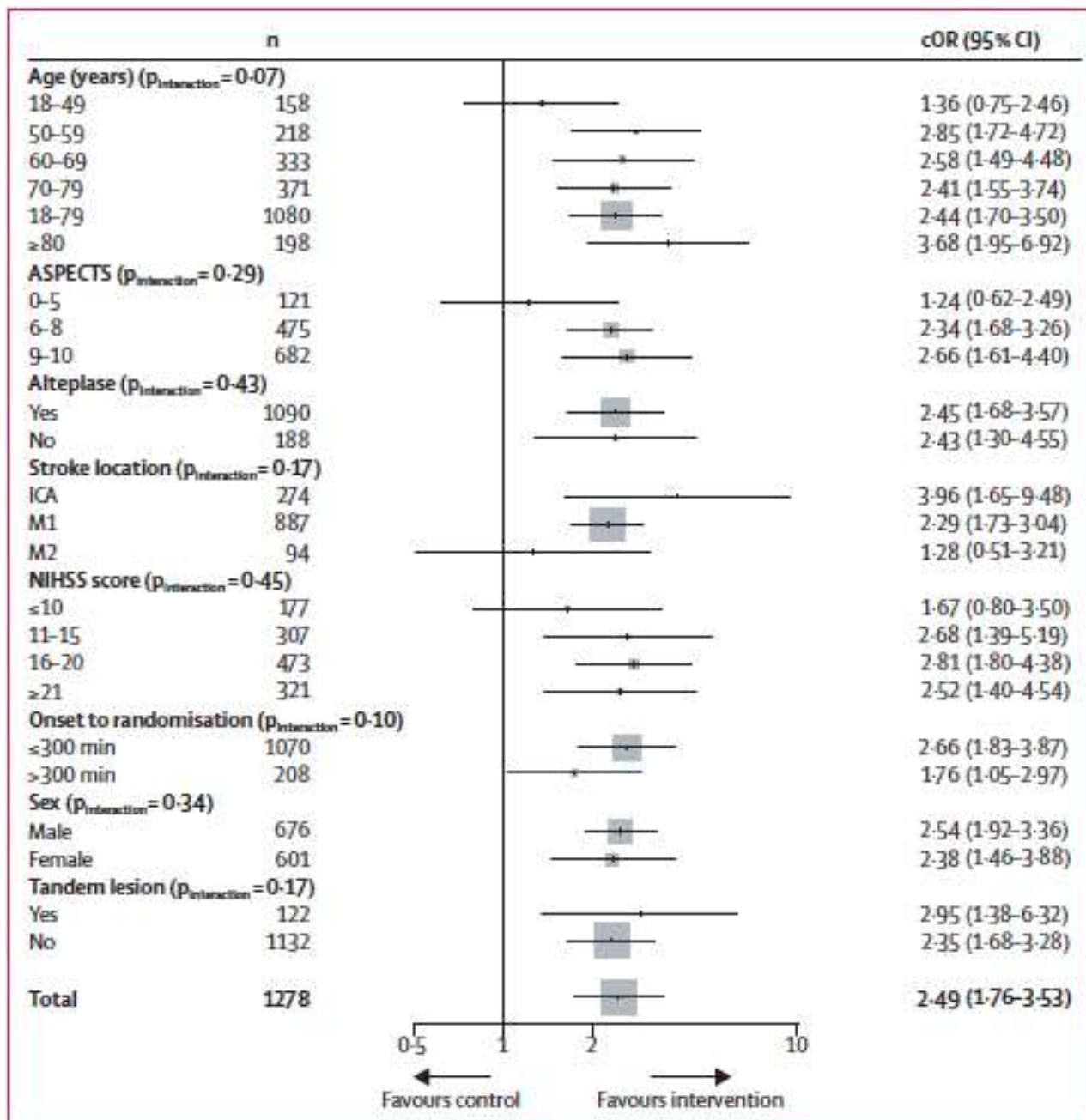
Extraction of Individual Data of 5 Studies

Outcome:

Modified Rankin Scale 0-2

Comparison:

Thrombectomy vs. Best Medical treatment





# Endovascular thrombectomy after large-vessel ischaemic stroke: a meta-analysis of individual patient data from five randomised trials

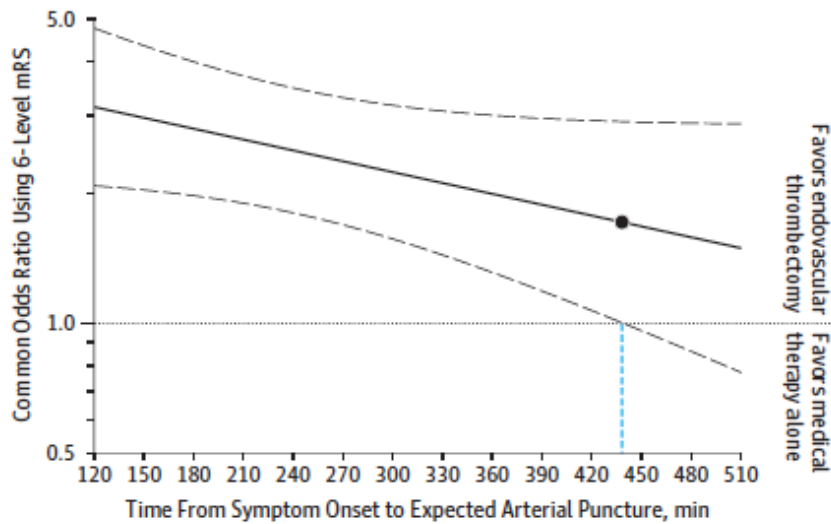
	Intervention population	Control population	Risk difference (%)	
mRS score reduction (shift analysis; primary outcome)*	--	--	--	
mRS score 0-1 at 90 days	26.9% (170/633)	12.9% (83/645)	14.0	→ NNT = 7
mRS score 0-2 at 90 days	46.0% (291/633)	26.5% (171/645)	19.5	→ NNT = 5
NIHSS score 0-2 at 24 h	21.0% (129/615)	8.3% (52/630)	12.7	→ NNT = 7
Early neurological recovery at 24 h	50.2% (309/616)	21.2% (134/633)	29.0	→ NNT = 3

# Time to Treatment With Endovascular Thrombectomy and Outcomes From Ischemic Stroke: A Meta-analysis

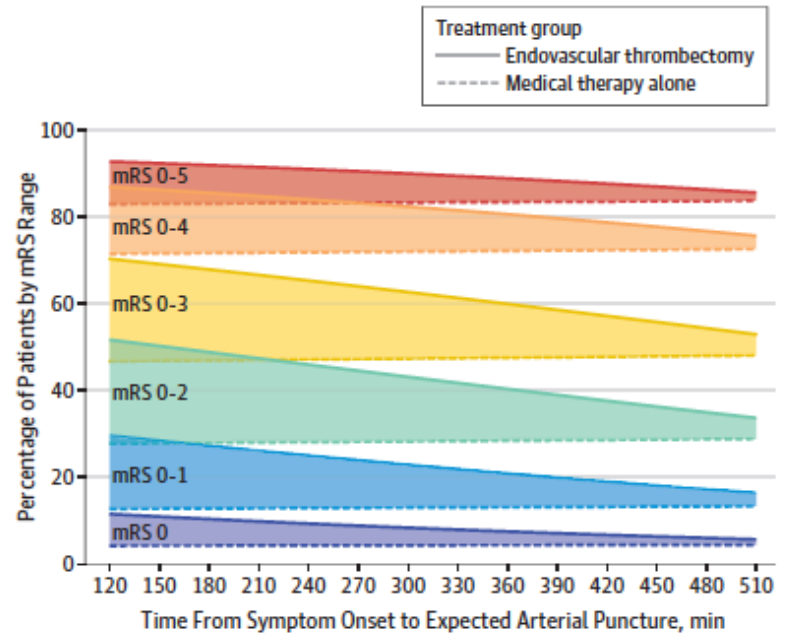
	Endovascular Thrombectomy		Medical Therapy		P Value for Interaction With Treatment Group
	OR (95% CI) per 1-Hour Delay	ARD, % (95% CI) per 1-Hour Delay <sup>a</sup>	OR (95% CI) per 1-Hour Delay	ARD, % (95% CI) per 1-Hour Delay <sup>a</sup>	
<b>ED Arrival-to-Arterial Puncture Time Interval (Expected)<sup>e</sup></b>					
mRS shift <sup>b</sup>	0.56 (0.47 to 0.67)	-16.8	0.98 (0.82 to 1.16)	-1.2	<.001
mRS 0-2	0.55 (0.43 to 0.71)	-14.1 (-19.2 to -8.3)	0.94 (0.74 to 1.19)	-1.2 (-5.4 to 3.5)	.001
Mortality	1.44 (1.11 to 1.87)	5.4 (1.4 to 10.0)	0.98 (0.75 to 1.27)	-0.3 (-4.0 to 3.8)	.03
<b>ED Arrival-to-Reperfusion Time Interval (Expected)<sup>f</sup></b>					
mRS shift <sup>b</sup>	0.57 (0.48 to 0.67)	-16.7	0.95 (0.80 to 1.12)	-2.2	<.001
mRS 0-2	0.56 (0.45 to 0.70)	-13.7 (-18.2 to -8.6)	0.91 (0.73 to 1.13)	-1.8 (-5.7 to 2.4)	.001
Mortality	0.91 (0.88 to 0.93)	-1.2 (-1.6 to -0.9)	1.06 (0.84 to 1.33)	0.9 (-2.5 to 4.8)	.02

**Figure 1. Association of Time From Symptom Onset to Expected Time of Endovascular Thrombectomy Procedure Start (Arterial Puncture) With Disability Levels at 3 Months in Endovascular (n = 633) vs Medical Therapy (n = 645) Groups**

**A** Odds ratio for less disability at 3 mo in endovascular thrombectomy vs medical therapy alone groups by time to treatment



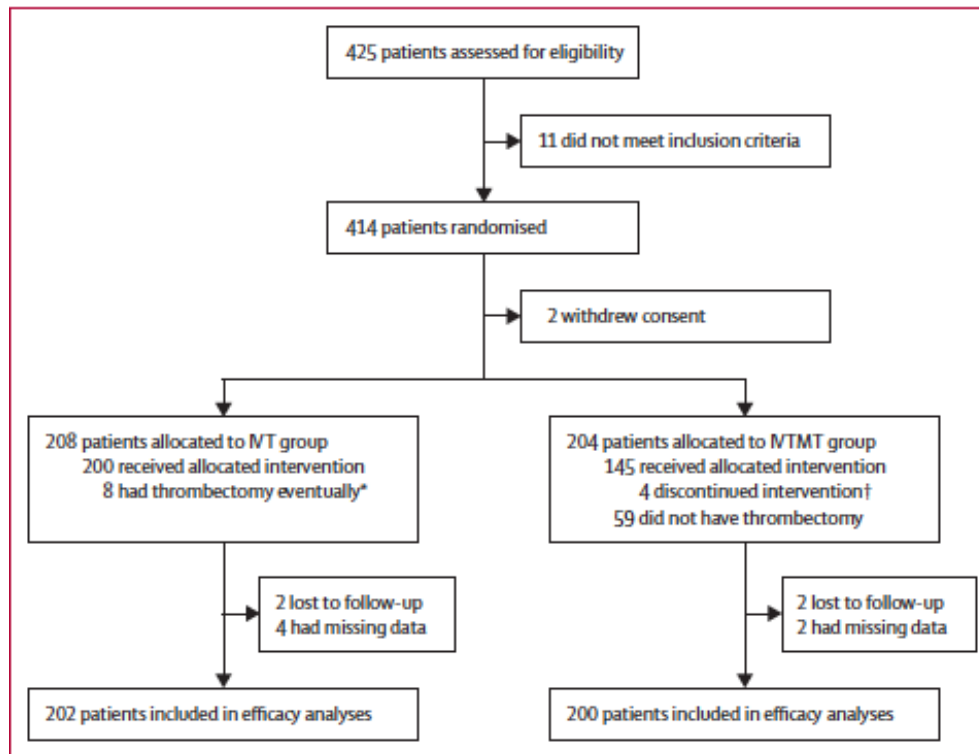
**B** Difference in adjusted 3-mo disability rates between endovascular thrombectomy and medical therapy alone groups by time to treatment





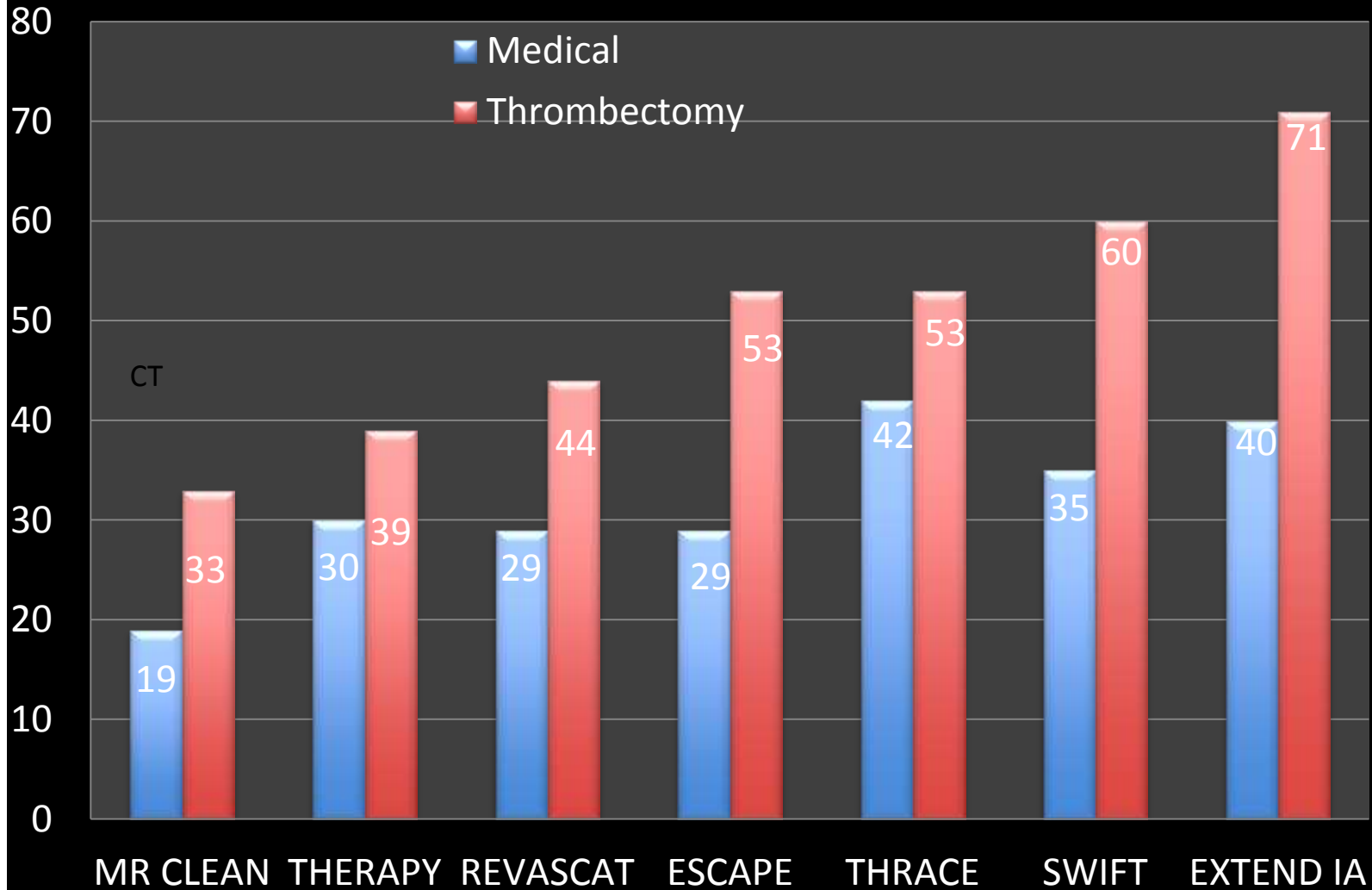
# Mechanical thrombectomy after intravenous alteplase versus alteplase alone after stroke (THRACE): a randomised controlled trial

*Serge Bracad, Xavier Ducrocq, Jean Louis Mas, Marc Soudant, Catherine Oppenheim, Thierry Moulin, Francis Guillemin, on behalf of the THRACE investigators\**



	IVT group	IVTMT group	Odds ratio (95% CI)	p value
Modified Rankin score of 0-2 at 3 months*	85/202 (42%)	106/200 (53%)	1.55 (1.05-2.30)	0.028

## % mRS 0-2 at 3 months



JAMA | Original Investigation

# Effect of Conscious Sedation vs General Anesthesia on Early Neurological Improvement Among Patients With Ischemic Stroke Undergoing Endovascular Thrombectomy A Randomized Clinical Trial

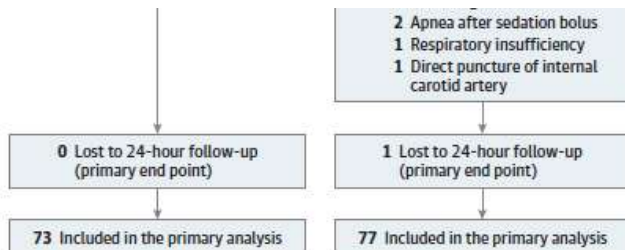
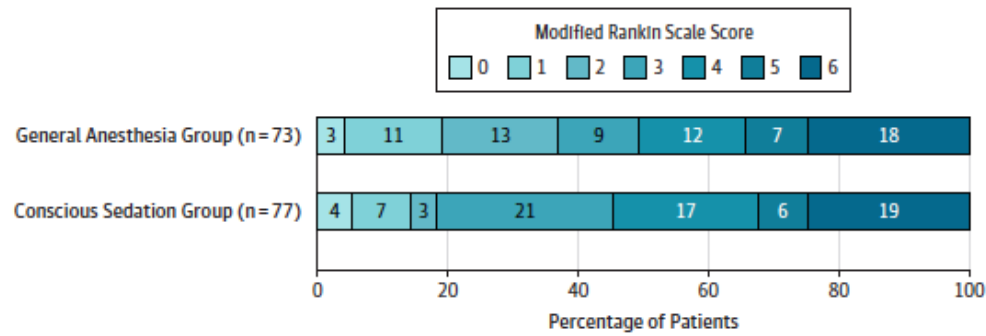
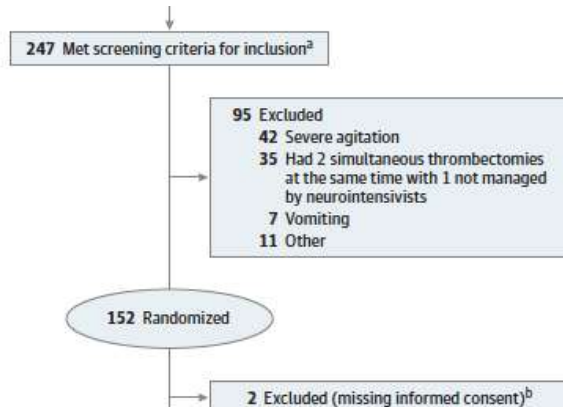
Silvia Schönenberger, MD; Lorenz Uhlmann, MSc; Werner Hacke, MD, PhD; Simon Schieber, MD; Siby Mundiyanapurath, MD; Jan C. Purrucker, MD; Simon Nagel, MD; Christina Klose; Johannes Pfaff, MD; Martin Bandzus, MD; Peter A. Ringleb, MD; Meinhard Kieser, PhD; Markus A. Mohlenbruch, MD; Julian Bosel, MD, FRCGS

Acute Brain Infarction ICA/MCA occlusion, NIHSS > 10

PROBE design: Prospective Open Label, Blinded Outcome Evaluation

Conscious sedation vs. General anesthesia

**DESIGN, SETTING, AND PARTICIPANTS** SIESTA (Sedation vs Intubation for Endovascular Stroke Treatment), a single-center, randomized, parallel-group, open-label treatment trial with blinded outcome evaluation conducted at Heidelberg University Hospital in Germany (April 2014-February 2016) included 150 patients with acute ischemic stroke in the anterior circulation, higher National Institutes of Health Stroke Scale (NIHSS) score (>10), and isolated/combined occlusion at any level of the internal carotid or middle cerebral artery.



# Thrombectomie en attente

1. Comparaison aspiration vs. Stentriever (Etude ASTER)
2. Thrombectomie vs thrombectomie +rtPA
3. Evaluation de la filière de soins
4. Hors délais
  - DAWN Mismatch NIHSS et DWI ou CTP
  - DEFUSE 3 Target Mismatch CTP





# Low-Dose versus Standard-Dose Intravenous Alteplase in Acute Ischemic Stroke

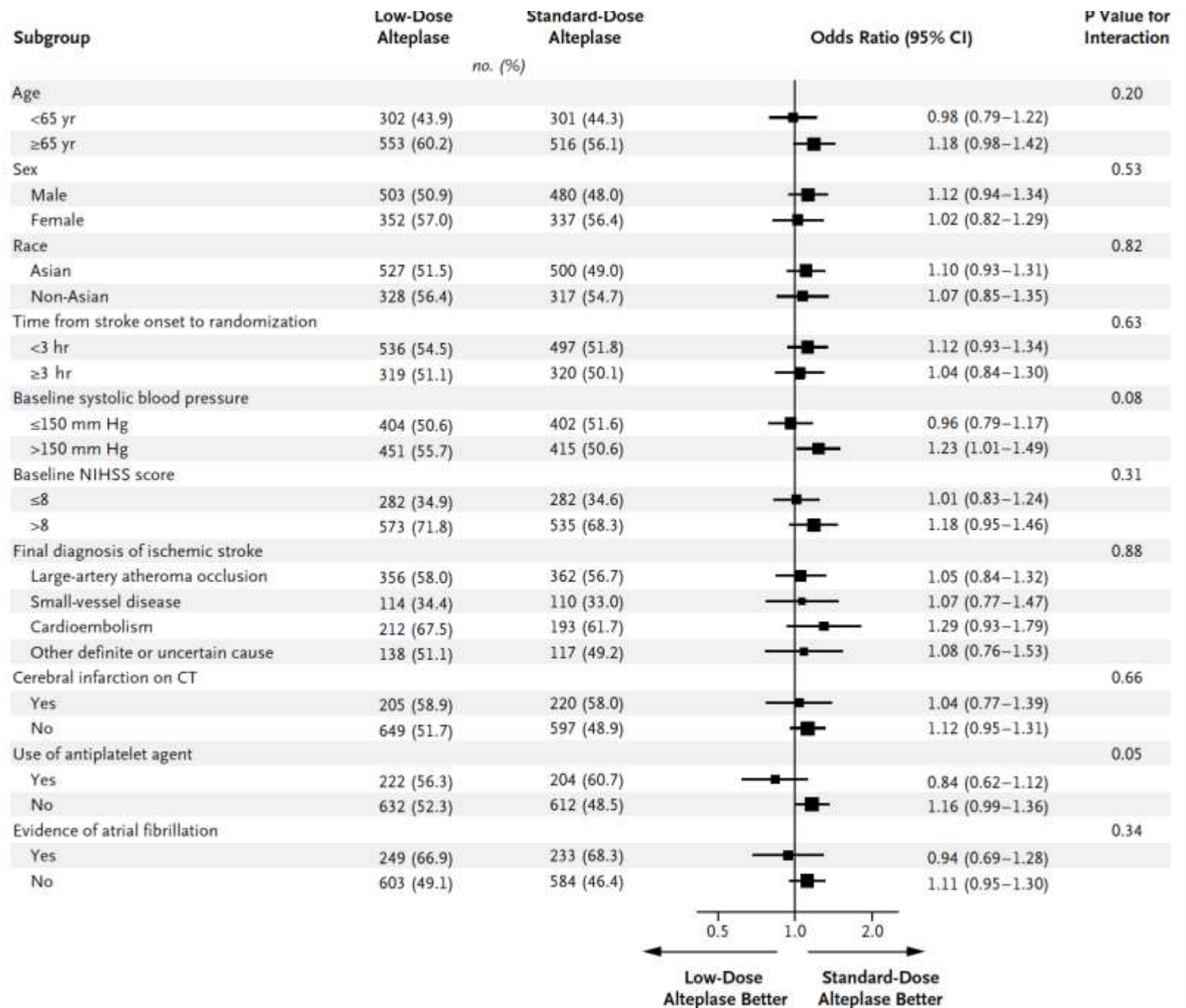
C.S. Anderson, T. Robinson, R.I. Lindley, H. Arima, P.M. Lavados, T.-H. Lee, J.P. Broderick, X. Chen, G. Chen, V.K. Sharma, J.S. Kim, N.H. Thang, Y. Cao, M.W. Parsons, C. Levi, Y. Huang, V.V. Olavarría, A.M. Demchuk, P.M. Bath, G.A. Donnan, S. Martins, O.M. Pontes-Neto, F. Silva, S. Ricci, C. Roffe, J. Pandian, L. Billot, M. Woodward, Q. Li, X. Wang, J. Wang, and J. Chalmers, for the ENCHANTED Investigators and Coordinators\*

Hypothesis: Low dose of tPA 0.6 vs. 0.9 improves recovery along with a lower rate of symptomatic hemorrhage

**Table 2. Primary and Secondary Outcomes at 3 Months.\***

Outcome	Low-Dose Alteplase (N=1654)	Standard-Dose Alteplase (N=1643)	Odds Ratio with Low-Dose Alteplase (95% CI)	P Value†	P Value for Noninferiority‡
Primary outcome: death or disability — no./total no. (%)§	855/1607 (53.2)	817/1599 (51.1)	1.09 (0.95 to 1.25)		0.51
Secondary outcomes					
Symptomatic intracerebral hemorrhage — no. (%)					
By SITS-MOST criteria¶	17 (1.0)	35 (2.1)	0.48 (0.27 to 0.86)	0.01	
By NINDS criteria	98 (5.9)	131 (8.0)	0.73 (0.55 to 0.95)	0.02	

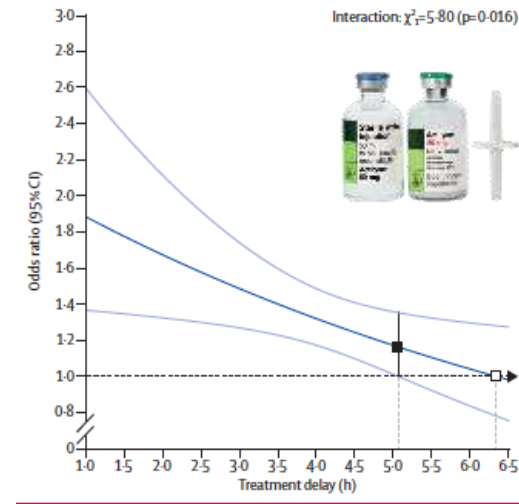
N augmente pas le taux de récupération neurologique  
Mais réduit celui des hémorragies symptomatiques



# Functional outcomes of pre-hospital thrombolysis in a mobile stroke treatment unit compared with conventional care: an observational registry study



Quelle: Berner Feuerwehr



STT

Emberson et al. Lancet Sept 2014

NNT-8

Time from admission to thrombolysis (min)	43.1 (37, 29-51)	NA	NA
Time from onset to thrombolysis (min)††			
Mean (SD)	129.3 (55.5)	96.3 (60.4)	--
Median (IQR)	112 (85-175)	73 (53-120)	<0.0005
Time from onset to thrombolysis ≤60 min	14 (4%)	112 (37%)	<0.0005
Time from onset to thrombolysis ≤90 min	123 (35%)	187 (62%)	<0.0005

	Conventional care (n=353)	STEMO care (n=305)	p value
<b>Primary outcome</b>			
3-month mRS score 0-1	166 (47%)	161 (53%)	0.14
<b>Secondary outcomes</b>			
3-month mRS score 0-3	260 (74%)	253 (83%)	0.004
3-month mortality	37 (10%)	17 (6%)	0.022
3-month mRS score			0.10*
0	106 (30%)	85 (28%)	..
1	60 (17%)	76 (25%)	..
2	55 (16%)	32 (10%)	..
3	39 (11%)	60 (20%)	..
4	37 (10%)	22 (7%)	..
5	19 (5%)	13 (4%)	..
6	37 (10%)	17 (6%)	..

# En attente 2017-18

- Thrombolyse:
  - Hors délai: Target Mismatch CTP: EXTEND-ECASS 4, Wake Up...
  - Boostée: tPA + antithrombine ou anti IIbIIIa...
  - Abandonnée: tPA vs. Placebo ou vs. TNK tPA avant thrombectomie
  - Revisitée: tNK pour minor stroke

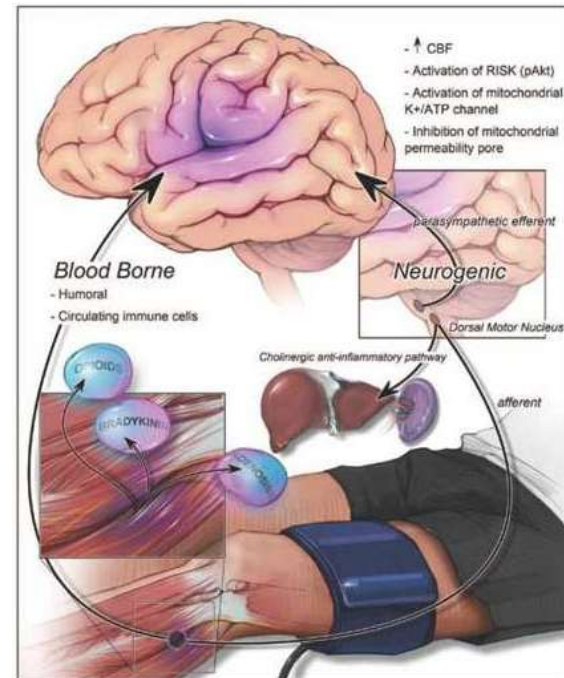
# Neuroprotection=Echec

- Concepts:
  - Randomisation dans l'ambulance: Magnésium, NO
  - Geler la pénombre ischémique: Froid, O2, Anticorps Monoclonaux
  - Traiter Inflammation: Cyclosporine, Natalizumab, Fingolimod
  - ...





- Pré-conditionnement Ischémique



2



t

# Platelet transfusion versus standard care after acute stroke due to spontaneous cerebral haemorrhage associated with antiplatelet therapy (PATCH): a randomised, open-label, phase 3 trial



M Irem Baharoglu\*, Charlotte Cordonnier\*, Rustam Al-Shahi Salman\*, Koen de Gans, Maria M Koopman, Anneke Brand, Charles B Majoie, Ludo F Beenen, Henk A Marquering, Marinus Vermeulen, Paul J Nederkoorn, Rob J de Haan, Yvo B Roos, for the PATCH Investigators†

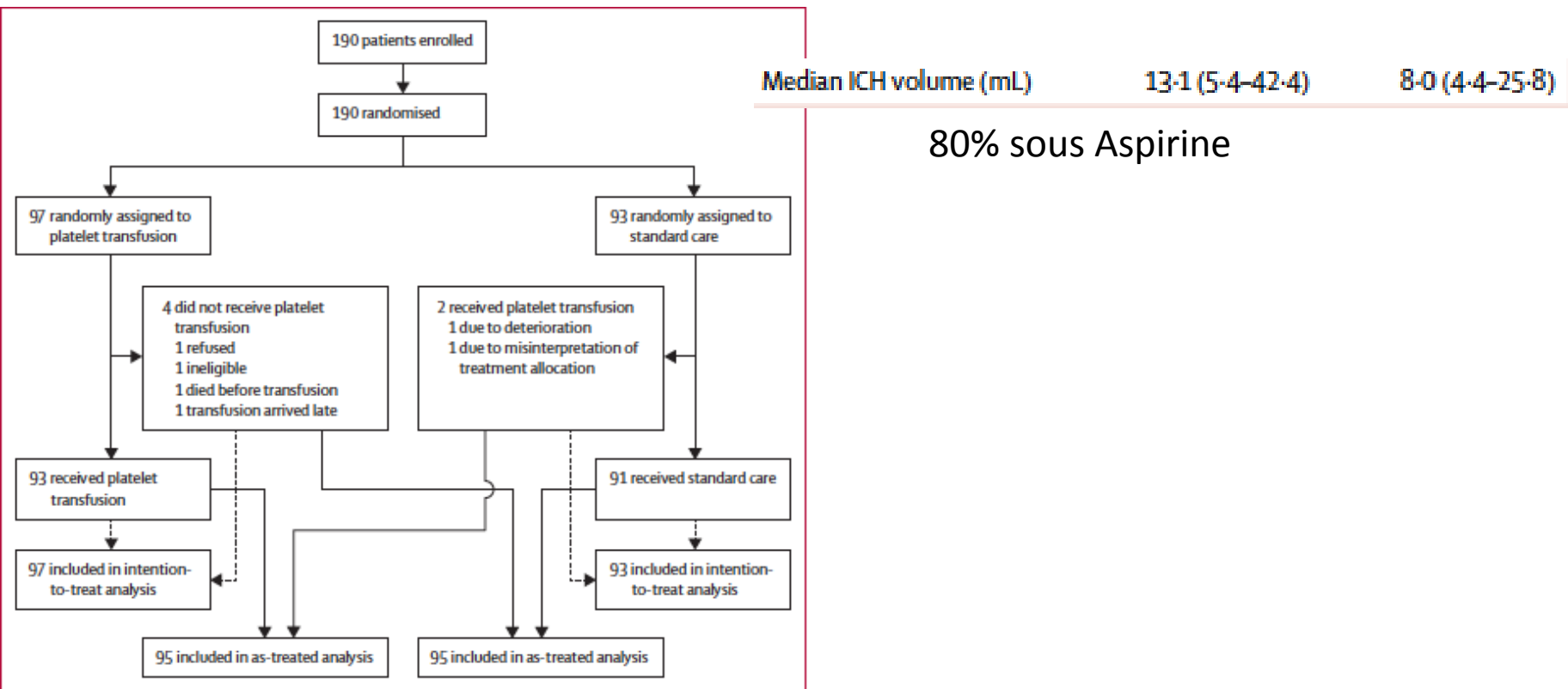
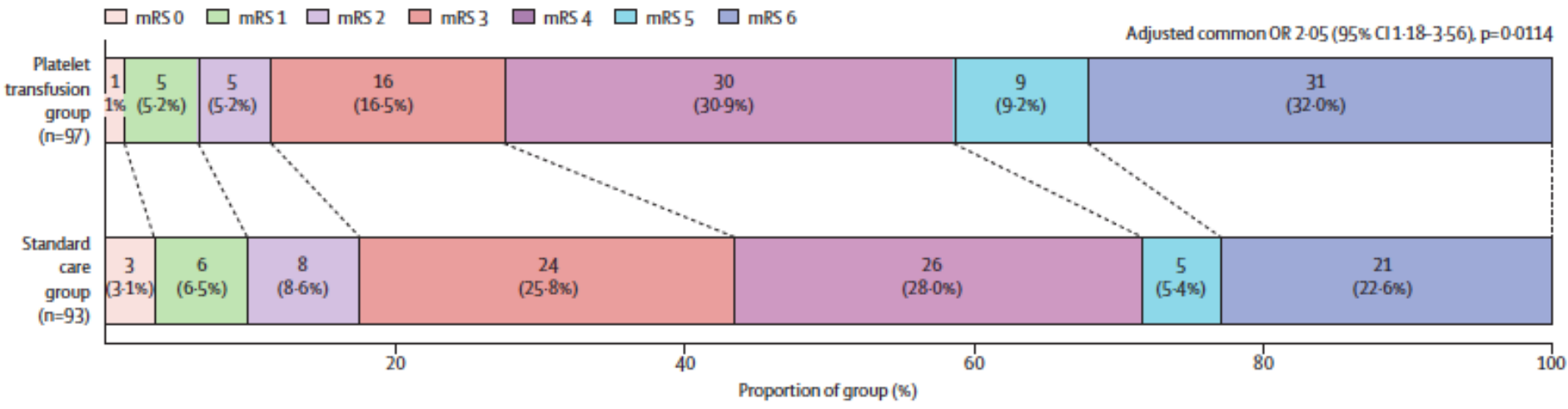
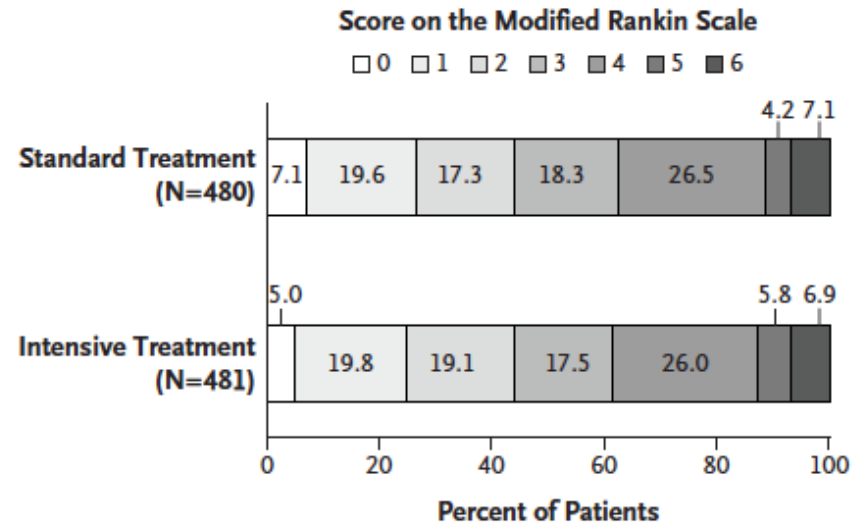
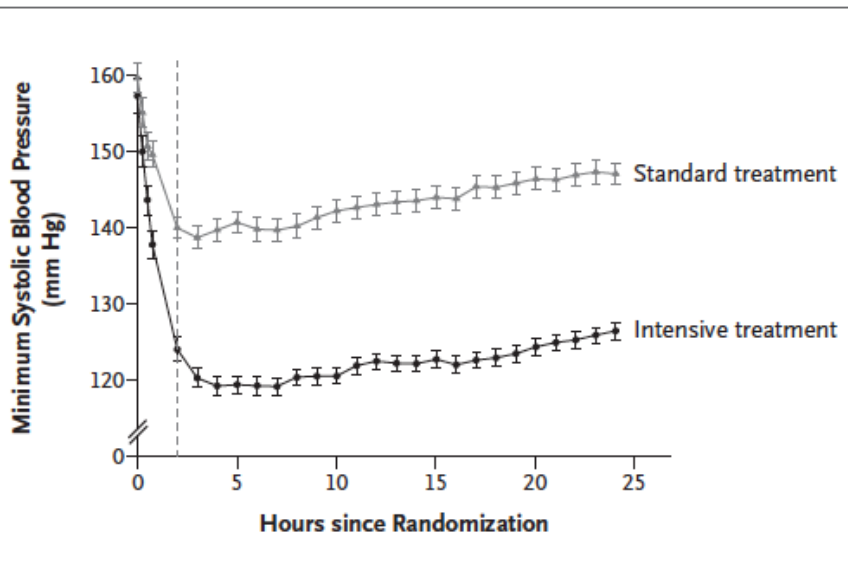


Figure 1: Trial profile



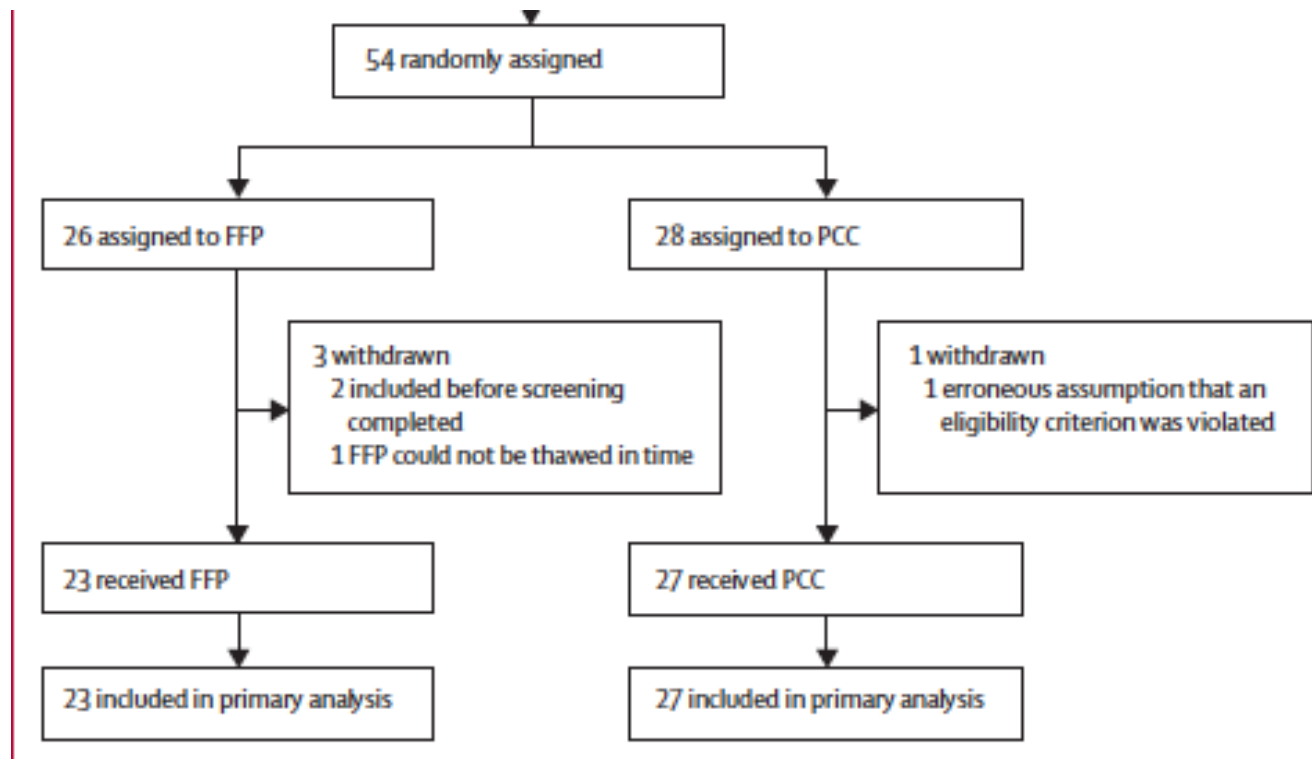
# Intensive Blood-Pressure Lowering in Patients with Acute Cerebral Hemorrhage

Dans les 4.5 h réduction pression artérielle  
Target 110-140 vs. 140-180



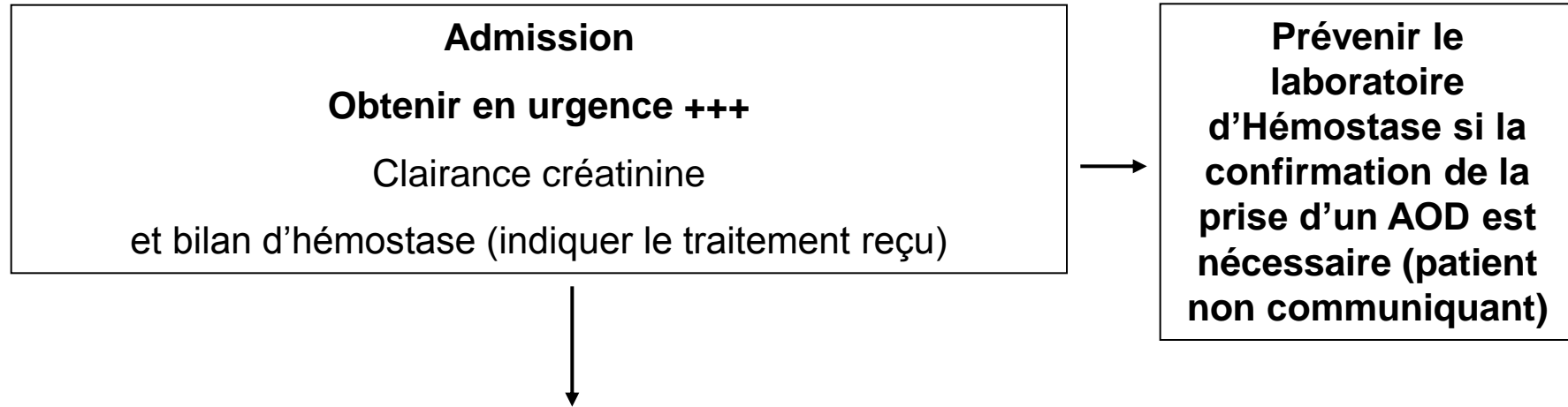


# Fresh frozen plasma versus prothrombin complex concentrate in patients with intracranial haemorrhage related to vitamin K antagonists (INCH): a randomised trial



	Fresh frozen plasma (n=23)	Prothrombin complex concentrate (n=27)	Treatment effect (95% CI)	p value
<b>Primary outcome</b>				
INR $\leq$ 1.2 within 3 h	2 (9%)	18 (67%)	OR 30.6 (4.7 to 197.9)*	0.0003
<b>Imaging data at 3 h¶</b>				
Haematoma expansion (mL)	23.7 (28.4)	9.7 (20.9)	16.9 (2.5 to 31.3)‡	0.023
≥15% growth	16/22 (73%)**	15/26 (58%)**	OR 2.0 (0.6 to 7.3)*	0.29
≥33% growth	13/22 (59%)**	12 (44%)**	OR 3.8 (1.1 to 16.0)*	0.048
<b>Imaging data at 24 h</b>				
Haematoma expansion (mL)	22.1 (27.1)	8.3 (18.3)	16.4 (2.9 to 29.9)‡	0.018
≥15% growth or death	14/20 (70%)††	12/27 (44%)	OR 3.9 (1.0 to 17.6)*	0.044
≥33% growth or death	12/20 (60%) ††	8/27 (30%)	OR 4.8 (1.3 to 20.4)*	0.024

# Protocole d'urgence de réversion de l'effet anticoagulant en cas d'hémorragie intracérébrale sous AOD



**Si l'hémorragie intracérébrale est confirmée par l'imagerie et la prise récente (<48h) d'un AOD est confirmée ou probable**

**Neutraliser l'effet anticoagulant en urgence, sans attendre les résultats des tests biologiques**

Si le patient reçoit le dabigatran, neutraliser le médicament par son antidote spécifique, idarucizumab (Praxbind®) 2 **injections** IV lentes de 2,5 g à 15 minutes **d'intervalle**

Si le patient reçoit un xaban,  
(ou si idarucizumab n'est pas immédiatement disponible pour dabigatran)  
Administrar un concentré de complexe prothrombinique (CCP) non activé (Octaplex®, Kanokad®, Confidex®) 50 UI/kg par voie IV lente ou CCP activé (FEIBA®) 30-50 U/kg par voie IV lente





# Dementia risk after spontaneous intracerebral haemorrhage: a prospective cohort study

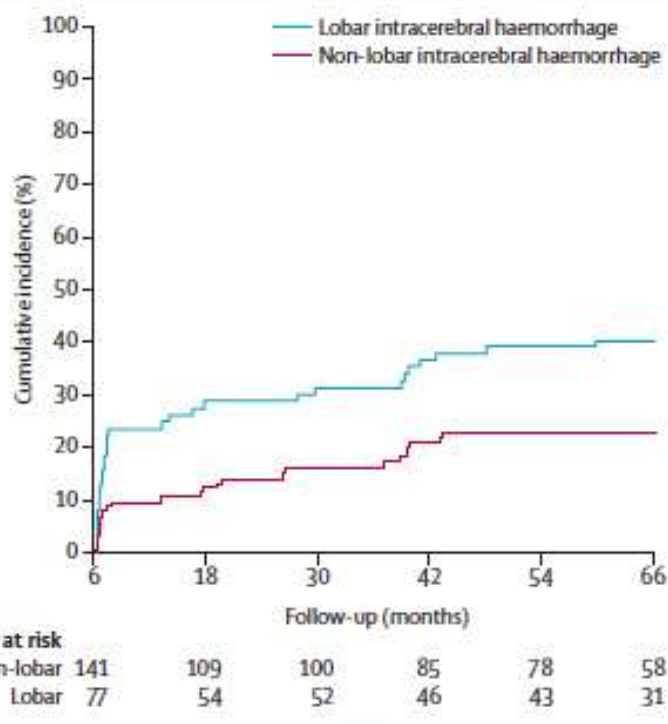


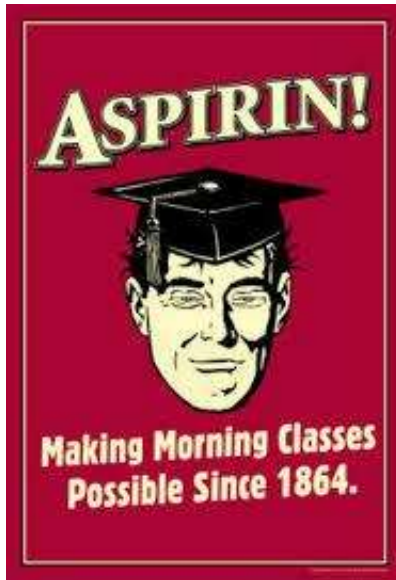
Figure 2: Cumulative rates of new-onset dementia in patients after intracerebral haemorrhage according to lobar location

	1 year post-intracerebral haemorrhage*	4 years post-intracerebral haemorrhage*
<b>History of previous stroke or transient ischaemic attack</b>		
No	14.6% (10.0-20.1)	21.8% (16.1-28.1)
Yes	15.2% (5.4-29.5)	45.5% (27.8-61.6)
<b>Intracerebral haemorrhage location</b>		
Lobar	23.4% (14.6-33.3)	35.1% (24.6-45.7)
Non-lobar	9.2% (5.1-14.7)	20.2% (14.0-27.3)

Data are % (95% CI). Cumulative incidence rates of new-onset dementia were estimated with the Kalbfleisch and Prentice approach. \*31 events at 1 year post-intracerebral haemorrhage and 61 events at 4 years post-intracerebral haemorrhage.

Table 2: Cumulative incidence rates of new-onset dementia according to subgroups of interest

# PREVENTION



# Prevention

1. INTERSTROKE Lancet 2016
2. AIT Nejm Amarenco-Socrates
3. Rothwell Aspirine en prévention Secondaire
4. Pioglitazone IRIS
5. Reco ESC FA

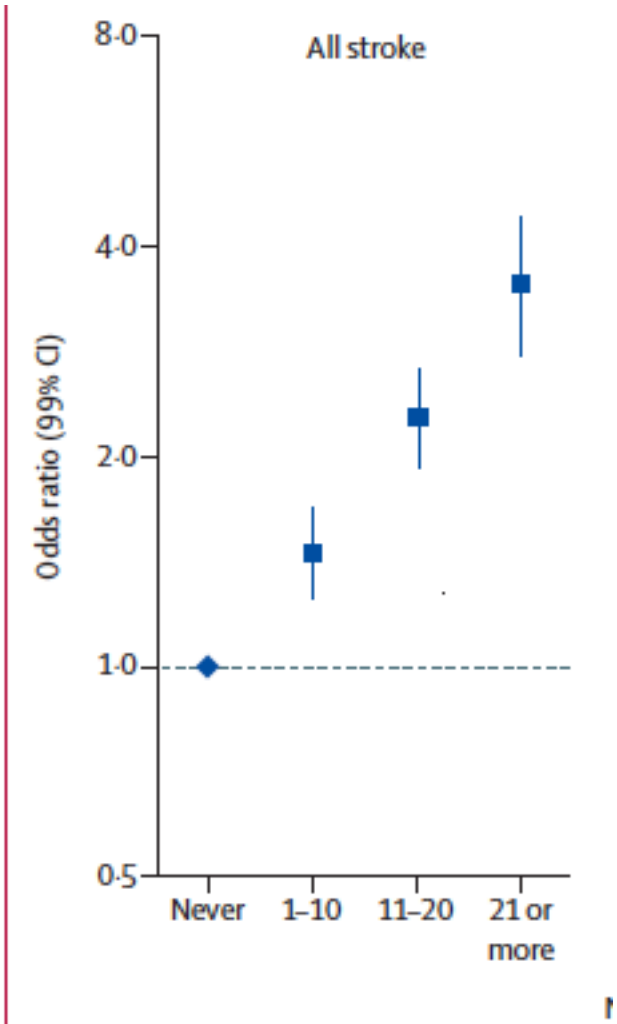
# GLOBAL HEALTH

**Global and regional effects of potentially modifiable risk factors associated with acute stroke in 32 countries (INTERSTROKE): a case-control study**

	Controls		All-stroke cases			
	≤55 years (N=4234)	>55 years (N=9238)	≤55 years (N=4216)		>55 years (N=9231)	
			OR (99% CI)	PAR (99% CI)	OR (99% CI)	PAR (99% CI)
Self-reported history of hypertension or blood pressure ≥140/90 mm Hg	1334/4234 (31.5%)	5045/9238 (54.6%)	4.51 (3.77–5.41)	49.7% (46.0–53.4)	2.55 (2.27–2.85)	46.0% (42.2–49.8)
Current smoking	1242/4231 (29.4%)	1775/9234 (19.2%)	1.66 (1.36–2.02)	16.3% (11.6–22.3)	1.70 (1.47–1.97)	10.9% (8.6–13.7)
Waist-to-hip ratio						
T2 vs T1	1386/4133 (33.5%)	3087/8983 (34.4%)	1.42 (1.15–1.75)	..	1.16 (1.01–1.33)	..
T3 vs T1	1203/4133 (29.1%)	3107/8983 (34.6%)	1.56 (1.23–1.98)	..	1.39 (1.20–1.62)	..
T2+T3 vs T1	..	..	..	23.5% (15.2–34.5)	..	16.0% (9.7–25.2)
Diet, mAHEI score						
T2 vs T1	1460/4234 (34.5%)	3118/9238 (33.8%)	0.78 (0.64–0.95)	..	0.76 (0.67–0.87)	..
T3 vs T1	1313/4234 (31.0%)	3132/9238 (33.9%)	0.68 (0.55–0.86)	..	0.56 (0.48–0.64)	..
T1+T2 vs T3	..	..	..	16.4% (7.9–30.9)	..	26.5% (20.9–33.0)
Regular physical activity	688/4232 (16.3%)	1510/9231 (16.4%)	0.60 (0.45–0.80)	35.3% (21.0–52.8)	0.60 (0.50–0.72)	35.9% (26.4–46.7)
Self-reported history of diabetes or HbA <sub>1c</sub> ≥6.5%	727/4229 (17.2%)	2230/9233 (24.2%)	1.29 (1.04–1.61)	5.6% (2.5–12.1)	1.14 (1.01–1.30)	3.6% (1.4–8.8)
Alcohol intake						
Low or moderate	797/4229 (18.8%)	1349/9230 (14.6%)	1.27 (1.03–1.56)	..	1.09 (0.94–1.27)	..
High or heavy episodic	231/4229 (5.5%)	471/9230 (5.1%)	2.20 (1.49–3.23)	..	2.14 (1.54–2.96)	..
Psychosocial factors	..	..	2.36 (1.60–3.50)	22.8% (14.8–33.3)	2.06 (1.59–2.68)	15.3% (10.5–21.8)
Cardiac causes	73/4234 (1.7%)	595/9238 (6.4%)	4.56 (2.81–7.41)	4.9% (3.8–6.3)	2.94 (2.45–3.53)	10.8% (9.4–12.4)
ApoB/ApoA1 ratio						
T2 vs T1	1219/3702 (32.9%)	2831/8224 (34.4%)	1.30 (1.06–1.60)	..	1.28 (1.13–1.46)	..
T3 vs T1	1275/3702 (34.4%)	2655/8224 (32.3%)	2.01 (1.62–2.49)	..	1.79 (1.56–2.05)	..
T2+T3 vs T1	..	..	..	30.8% (22.6–40.5)	..	25.6% (20.1–31.9)
Composite PAR for all ten risk factors	..	..	..	92.2% (88.8–94.6)	..	90.0% (87.3–92.1)

A Wald test was used to test for interaction between risk factor × age subgroup for all stroke, and  $p_{\text{interaction}}$  was significant ( $p < 0.01$ ) for hypertension, waist-to-hip ratio, diet, and cardiac causes using logistic regression. Apo=apolipoprotein. mAHEI=modified Alternative Healthy Eating Index. OR=odds ratio. PAR=population attributable risk. T=tertile.

**Table 4: Risk factors for all stroke (ischaemic and intracerebral haemorrhage) by age group**

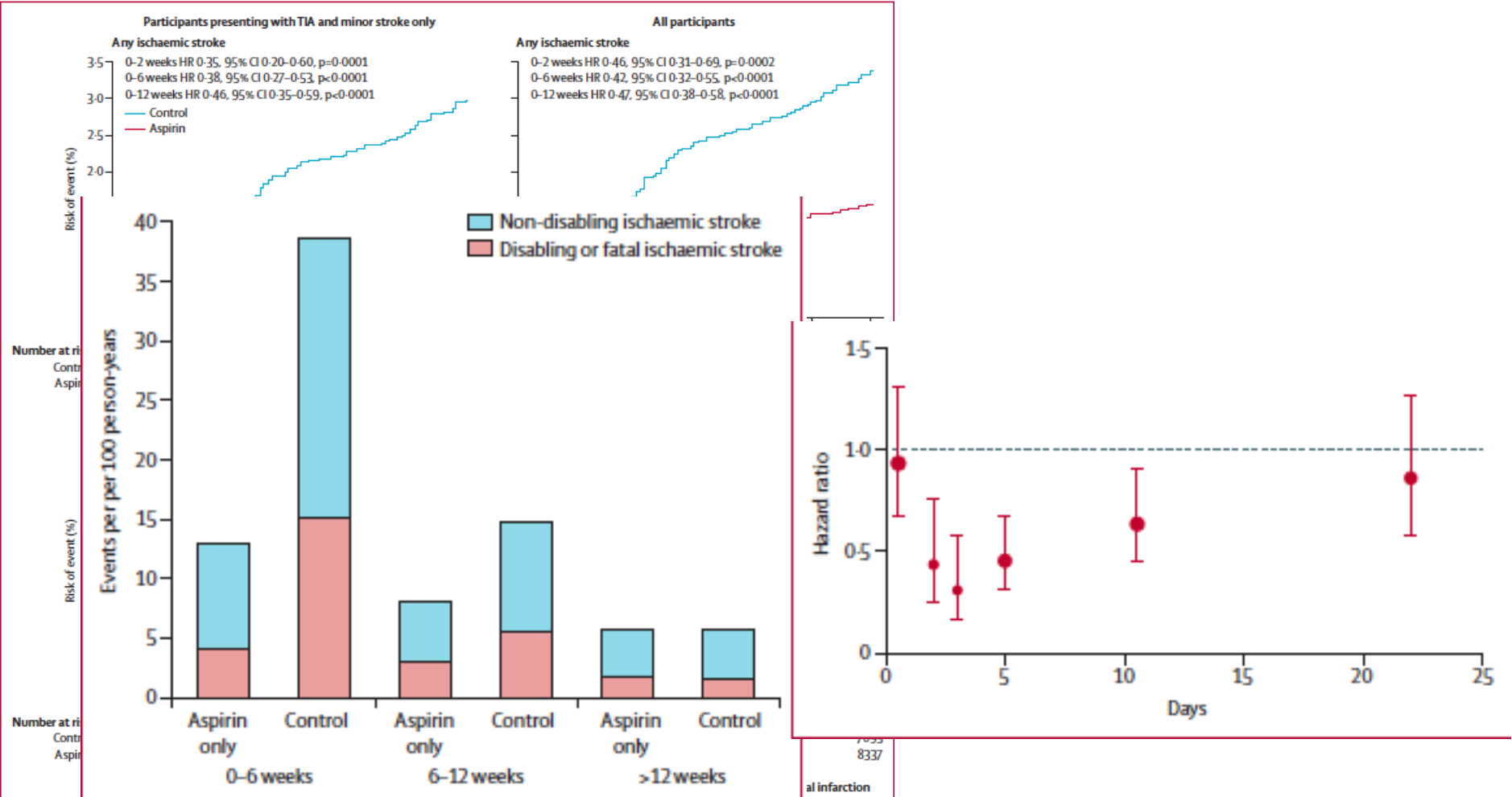


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# Effects of aspirin on risk and severity of early recurrent stroke after transient ischaemic attack and ischaemic stroke: time-course analysis of randomised trials

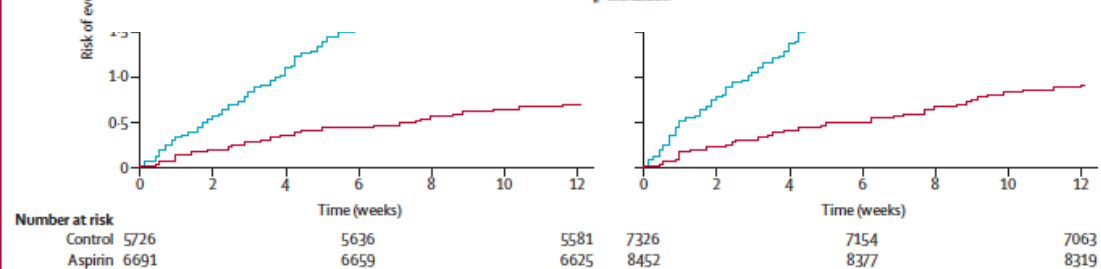


- Réduction de 60% du risque de récurrence: 2.4% vs. 1%.
- Réduction de la sévérité des IC.
- Effet majeur sur les récurrences précoces.



**Figure 2: Pooled analysis of the effect of aspirin only versus control in secondary prevention after transient ischaemic attack and ischaemic stroke on the absolute risk of recurrent ischaemic stroke**

Time course of treatment effect interaction:  $p_{\text{interaction}} < 0.0001$  for both outcomes.



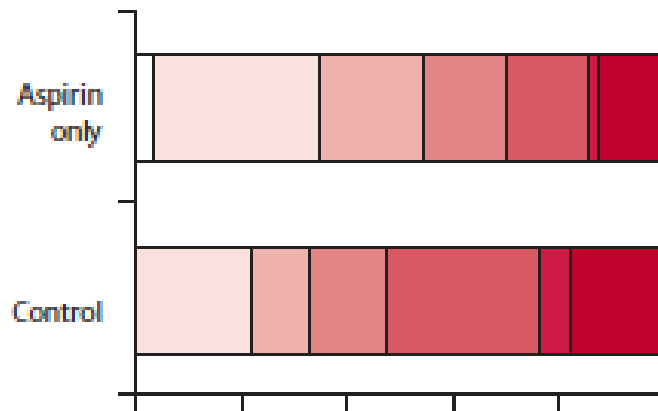


### Aspirin only versus control

6 weeks

mRS<sub>>2</sub>: OR 0.41, 0.22-0.79, p=0.0076

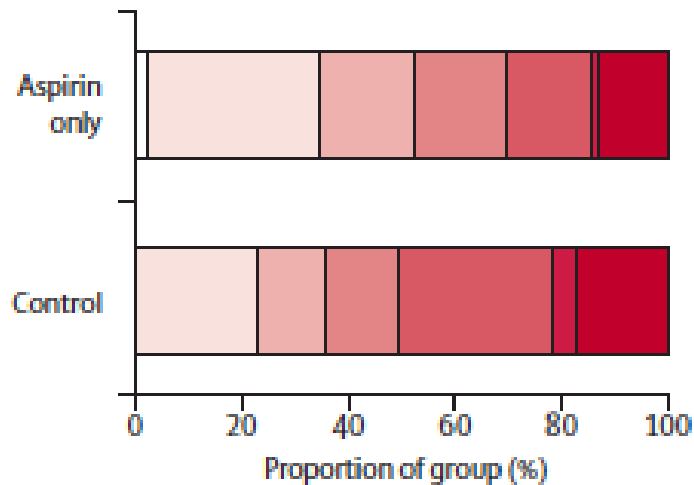
Ordinal regression: OR 0.45, 0.25-0.79,  
p=0.0057



12 weeks

mRS<sub>>2</sub>: OR 0.50, 0.30-0.86, p=0.0118

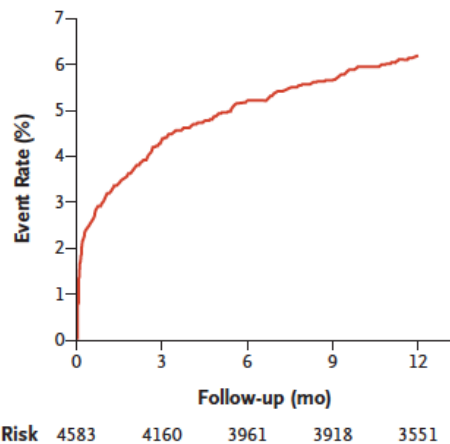
Ordinal regression: OR 0.50, 0.31-0.81,  
p=0.0045





# One-Year Risk of Stroke after Transient Ischemic Attack or Minor Stroke

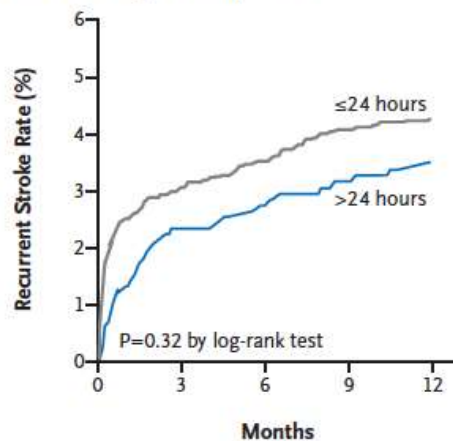
Outcome	Patients (N=4583) no. (%)
<b>Primary outcome</b>	
Major cardiovascular events	274 (6.2)
Death from cardiovascular causes	25 (0.6)
Nonfatal stroke	210 (4.7)
Nonfatal acute coronary syndrome	39 (0.9)
<b>Secondary outcomes</b>	
Death from any cause	80 (1.8)
Stroke or TIA	533 (12.0)
Stroke	224 (5.1)
TIA	326 (7.4)
Intracerebral hemorrhage	16 (0.4)
Acute coronary syndrome	46 (1.1)
Myocardial infarction	16 (0.4)
Bleeding	87 (2.0)
Moderately severe bleeding <sup>†</sup>	16 (0.4)
Major bleeding <sup>‡</sup>	18 (0.4)



**Figure 1.** Cumulative Incidence of the Composite Outcome in the Overall Population.

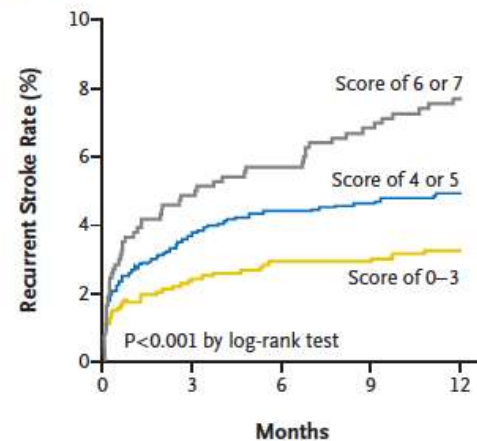
The composite outcome included stroke, an acute coronary syndrome, and death from cardiovascular causes.

**A** Rate of Recurrent Stroke According to Time from Symptom Onset to Evaluation by Stroke Specialist



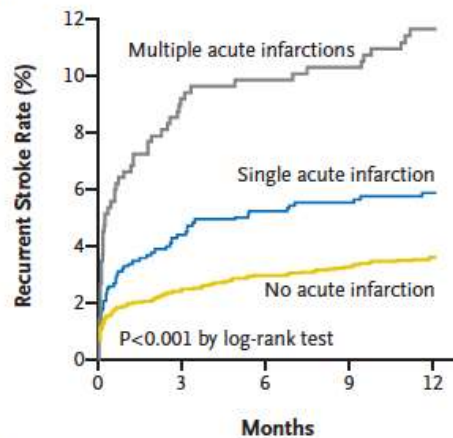
No. at Risk	0	3	6	9	12
$\le 24$ hours	3593	3289	3101	3067	2965
>24 hours	990	926	888	881	850

**B** Rate of Recurrent Stroke According to ABCD<sup>2</sup> Stroke Risk Score



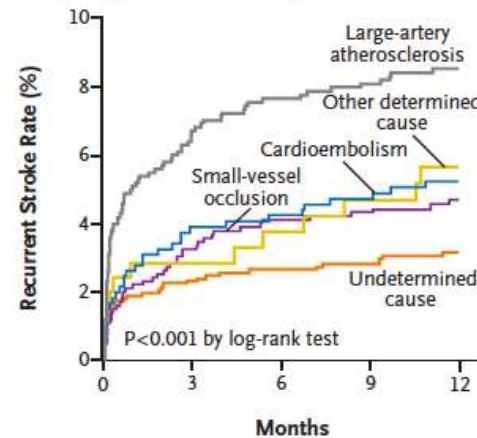
No. at Risk	0	3	6	9	12
Score of 0-3	1294	1221	1175	1166	1063
Score of 4 or 5	1851	1701	1633	1625	1484
Score of 6 or 7	745	684	657	642	596

**C** Rate of Recurrent Stroke According to Finding on Brain Imaging



No. at Risk	0	3	6	9	12
No acute infarction	2946	2699	2570	2542	2289
Single acute infarction	995	926	894	885	821
Multiple acute infarctions	481	414	397	394	357

**D** Rate of Recurrent Stroke According to Cause of TIA or Minor Stroke (TOAST Classification)



No. at Risk	0	3	6	9	12
Large-artery atherosclerosis	987	892	863	853	799
Small-vessel occlusion	983	905	862	857	790
Cardioembolism	641	584	570	561	494
Other determined cause	244	214	205	198	184
Undetermined cause	1354	1263	1206	1199	1085



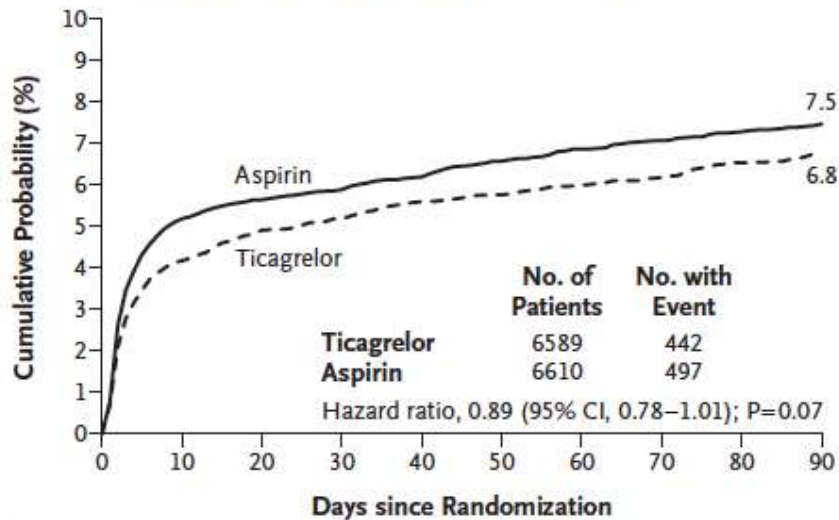
ORIGINAL ARTICLE

# Ticagrelor versus Aspirin in Acute Stroke or Transient Ischemic Attack

Ticagrelor 90 x2 vs. ASA 100 mg

- dans les 24 hrs
- Pendant 3 semaines
- Suivi 3 Mois

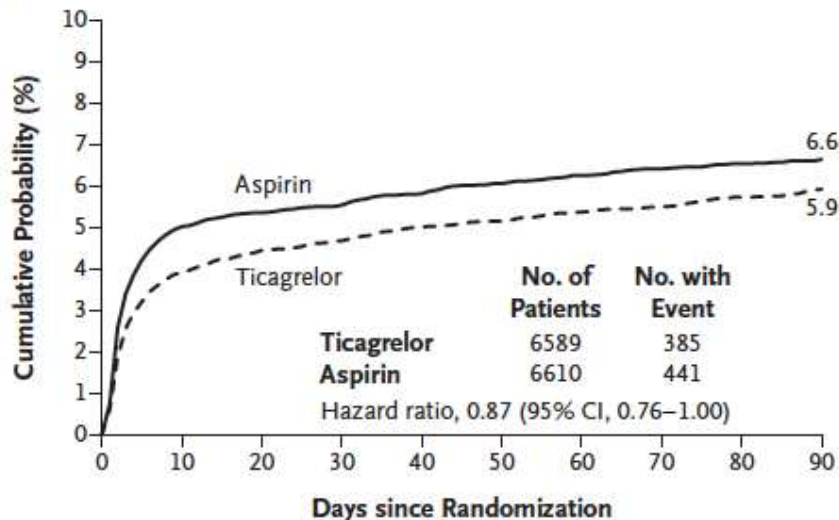
**A Primary End Point: Stroke, Myocardial Infarction, or Death**



**No. at Risk**

Aspirin	6610	6228	6186	6162	6129	6100	6078	6053	6030	4502
Ticagrelor	6589	6265	6216	6186	6153	6141	6118	6094	6058	4574

**B Ischemic Stroke**



**No. at Risk**

Aspirin	6610	6230	6193	6169	6134	6112	6092	6065	6046	4518
Ticagrelor	6589	6272	6230	6204	6169	6157	6133	6102	6073	4587

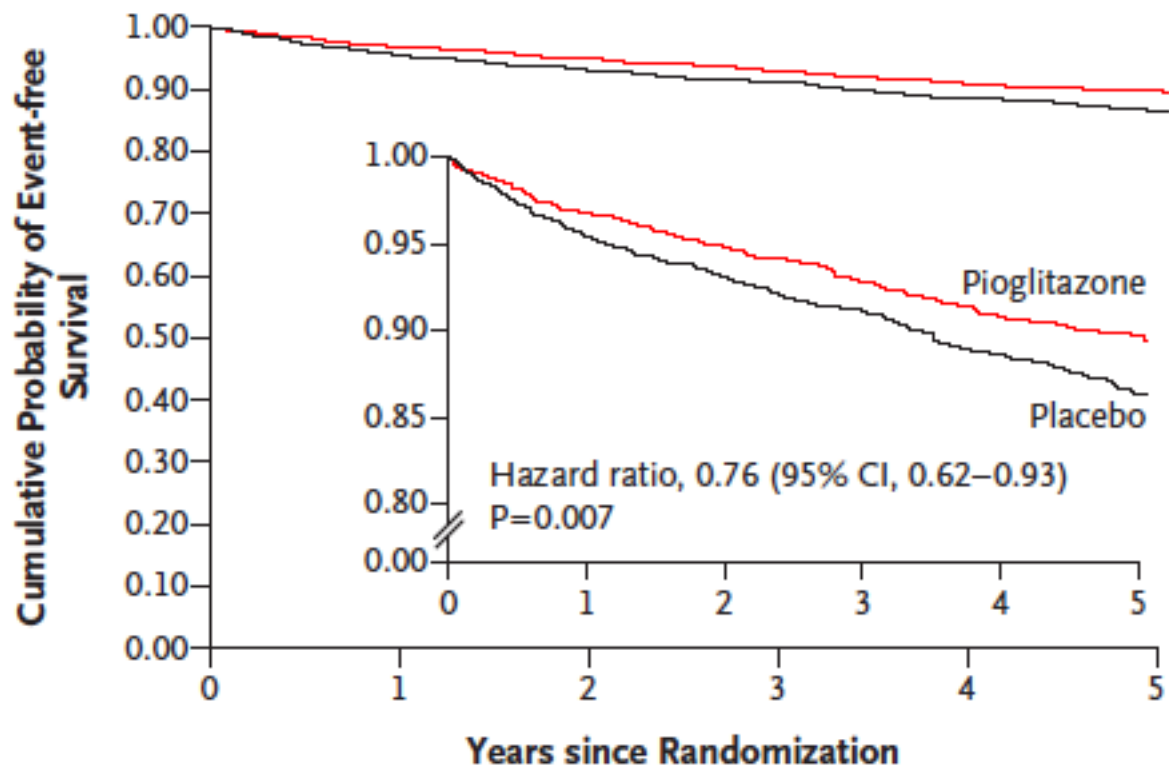
REDUCTION DE 0.7% endpoint Global et IC  
 -NS sur critère primaire  
 - S sur IC p=0.046

# Pioglitazone after Ischemic Stroke or Transient Ischemic Attack

- Résistance à l'Insuline mais pas de diabète-Score HOMA-IR
- Prévention secondaire après AIT ou Infarctus Cérébral
- Endpoint AVC ou IDM

**Table 2. Primary and Secondary Outcomes.**

Outcome	Pioglitazone (N= 1939) <i>no. of patients (%)</i>	Placebo (N= 1937) <i>no. of patients (%)</i>	Hazard Ratio (95% CI)*	Adjusted P Value†
<b>Primary outcome</b>				
Stroke or myocardial infarction‡	175 (9.0)	228 (11.8)	0.76 (0.62– 0.93)	0.007
Stroke	123 (6.3)	150 (7.7)		
Fatal	9 (0.5)	13 (0.7)		
Nonfatal	114 (5.9)	137 (7.1)		
Myocardial infarction	52 (2.7)	78 (4.0)		
Fatal	7 (0.4)	14 (0.7)		
Nonfatal	45 (2.3)	64 (3.3)		
<b>Secondary outcome§</b>				
Stroke	127 (6.5)	154 (8.0)	0.82 (0.61–1.10)	0.19
Acute coronary syndrome: myocardial infarction or unstable angina	96 (5.0)	128 (6.6)	0.75 (0.52–1.07)	0.11
Stroke, myocardial infarction, or serious heart failure¶	206 (10.6)	249 (12.9)	0.82 (0.65–1.05)	0.11
Diabetes mellitus	73 (3.8)	149 (7.7)	0.48 (0.33–0.69)	<0.001
Death from any cause	136 (7.0)	146 (7.5)	0.93 (0.73–1.17)	0.52



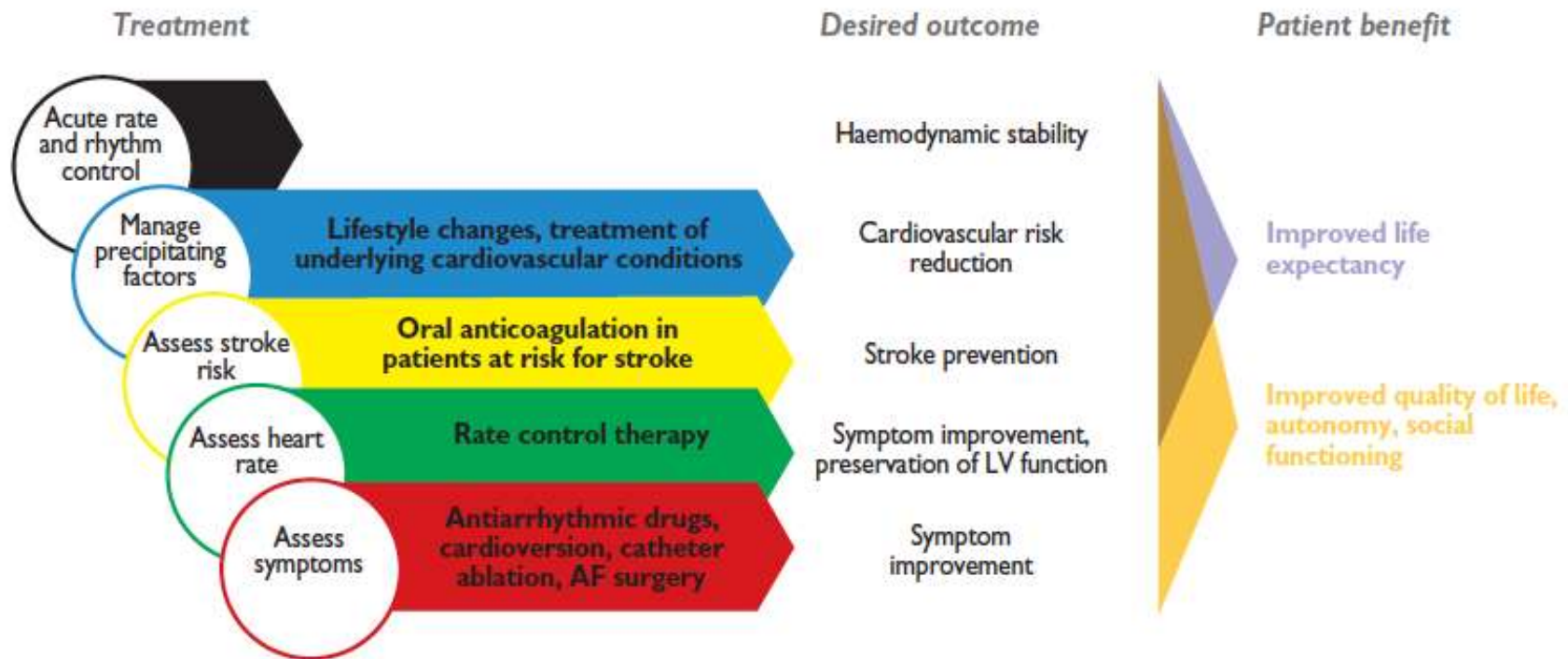
**No. at Risk**

Pioglitazone	1939	1793	1701	1491	1196	481
Placebo	1937	1778	1690	1476	1182	459



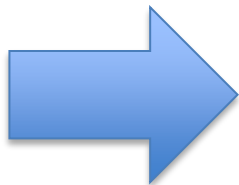
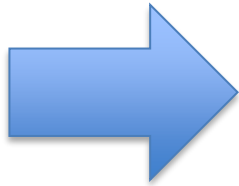
# Fibrillation Auriculaire et AVC

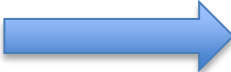
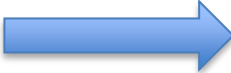


## Recommandations Européennes-ESC



AF = atrial fibrillation; LV = left ventricular.

Recommendations	Class <sup>a</sup>	Level <sup>b</sup>
Opportunistic screening for AF is recommended by pulse taking or ECG rhythm strip in patients >65 years of age.	I	B
In patients with TIA or ischaemic stroke, screening for AF is recommended by short-term ECG recording followed by continuous ECG monitoring for at least 72 hours.	I	B
It is recommended to interrogate pacemakers and ICDs on a regular basis for atrial high rate episodes (AHRE). Patients with AHRE should undergo further ECG monitoring to document AF before initiating AF therapy.	I	B
In stroke patients, additional ECG monitoring by long-term non-invasive ECG monitors or implanted loop recorders should be considered to document silent atrial fibrillation.	IIa	B
Systematic ECG screening may be considered to detect AF in patients aged >75 years, or those at high stroke risk.	IIb	B



	Anticoagulation with heparin or LMWH immediately after an ischaemic stroke is not recommended in AF patients.	<b>III (harm)</b>	<b>A</b>
	In patients who suffer a TIA or stroke while on anticoagulation, adherence to therapy should be assessed and optimized.	<b>IIa</b>	<b>C</b>
	In patients who suffer a moderate-to-severe ischaemic stroke while on anticoagulation, anticoagulation should be interrupted for 3–12 days based on a multidisciplinary assessment of acute stroke and bleeding risk.	<b>IIa</b>	<b>C</b>
	In AF patients who suffer a stroke, aspirin should be considered for prevention of secondary stroke until the initiation or resumption of oral anticoagulation.	<b>IIa</b>	<b>B</b>
	Systemic thrombolysis with rtPA is not recommended if the INR is above 1.7 (or, for patients on dabigatran, if aPTT is outside normal range).	<b>III (harm)</b>	<b>C</b>
	NOACs are recommended in preference to VKAs or aspirin in AF patients with a previous stroke.	<b>I</b>	<b>B</b>
	After TIA or stroke, combination therapy of OAC and an antiplatelet is not recommended.	<b>III (harm)</b>	<b>B</b>
	After intracranial haemorrhage, oral anticoagulation in patients with AF may be reinitiated after 4–8 weeks provided the cause of bleeding or the relevant risk factor has been treated or controlled.	<b>IIb</b>	<b>B</b>

**Patient with AF suffering from an intracranial bleed on OAC**  
If acute event: establish intensity of anticoagulation (see bleeding flow chart)

**Contra-indication  
for OAC**

**Consider further information to allow informed judgement**

**Factors supporting withholding of OAC:**

- Bleeding occurred on adequately dosed NOAC or in setting of treatment interruption or underdosing
- Older age
- Uncontrolled hypertension
- Cortical bleed
- Severe intracranial bleed
- Multiple microbleeds (e.g. >10)
- Cause of bleed cannot be removed or treated
- Chronic alcohol abuse
- Need for dual antiplatelet therapy after PCI

**Factors supporting reinitiation of OAC:**

- Bleeding occurred on VKA or in setting of overdose
- Traumatic or treatable cause
- Younger age
- Well controlled hypertension
- Basal ganglia bleed
- No or mild white matter lesions
- Surgical removal of subdural haematoma
- Subarachnoid bleed: aneurysm clipped or coiled
- High-risk of ischaemic stroke

**Patient or next of kin choice informed  
by multidisciplinary team advice**

**No stroke  
protection  
(no evidence)**

**LAA  
occlusion  
(IIbC)**

**Initiate or resume OAC, choosing  
an agent with low intracranial bleeding risk,  
after 4–8 weeks (IIbB)**

## Sensitivity analysis: OAC-treated standard care patients

ICH patients with AF treated either by standard medical care or LAAO.  
All standard care patients started oral anticoagulant within 180 days after ICH

Clinical outcome	LAAO vs. Standard care Hazard ratio (95%CI)	Relative risk reduction (%)
Ischemic stroke/major bleeding/mortality	0.26 (0.09-0.80)	74%
Ischemic stroke	0.32 (0.06-1.56)	68%
Major bleeding	0.66 (0.11-3.94)	34%
ICH	0.51 (0.05-5.65)	49%
Mortality	0.28 (0.06-1.36)	72%

## Conclusion

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- These study data suggests transcatheter LAAO to be a beneficial stroke prevention strategy in patients with atrial fibrillation and prior intracerebral hemorrhage
- The results should be confirmed in a randomized clinical trial
- STROKECLOSE – a randomized clinical trial – will start in the Nordic countries in 2016



# **CLOSE: Closure of patent foramen ovale, oral anticoagulants or antiplatelet therapy to prevent stroke recurrence: Study design**

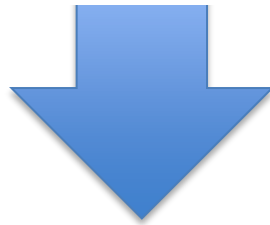
## Inclusion criteria

- Males or females,  $16 \leq \text{age} \leq 60$  years.
- Recent ( $\leq 6$  months) ischaemic stroke (or retinal ischaemia), initial or recurrent, confirmed by cerebral imaging (presence of signs of recent infarction corresponding to the clinical signs) regardless of the duration of symptoms (less than or greater than 24 h).
- Modified Rankin score  $\leq 3$ .
- Absence of another identifiable cause of stroke (or retinal ischaemia) on a thorough aetiological work.
- Presence of a PFO with at least one of the following characteristics:
  - PFO with large shunt  $> 30$  microbubbles on TTE or TEE detected either spontaneously or exclusively during provocation manoeuvres.
  - PFO associated with atrial septal aneurysm on TEE: base of aneurysm  $\geq 15$  mm and excursion  $> 10$  mm.

FERMETURE + antiagrégant vs ANTIAGREGANT vs. ANTICOAGULANT ORAL AVK ou AOD



SUIVI 5 ANS



RECIDIVE AVC  
Présentation à l'ESOC



# FUTUR/PREVENTION

- 1- Antiagrégant
  - Analyse sous groupe SOCRATES-Atherosclerosis+++
  - POINT ASA+CDG vs. ASA
  - Autres: PARFAIT: études inh liaison plaquettes/thrombine...
- 2- AOD pour les Infarctus Cérébraux de cause indéterminée
- 3- Hypocholestérolémiant: TST, PSK-9

# CONCLUSIONS

- AVC ISCHEMIQUE
  - PHASE AIGUE:
    - Pas de critère de sélection supplémentaire pour la thrombectomie
    - Time is brain mais pas de bénéfice/mobile stroke unit
    - Aspirine réduit rsq récurrence précoce et sévérité
  - PREVENTION
    - AIT et Risque d'AVC
    - Echech Ticagrelor mais à suivre/atherome + autres molécules
    - Cet année CLOSE

- AVC hémorragique:
  - Echech contrôle +++ TA<140 et transfusion plaquettes / patient/ antiagrégants
  - Codification des traitement hémostatiques
    - Complexe prothrombinique et Praxbind