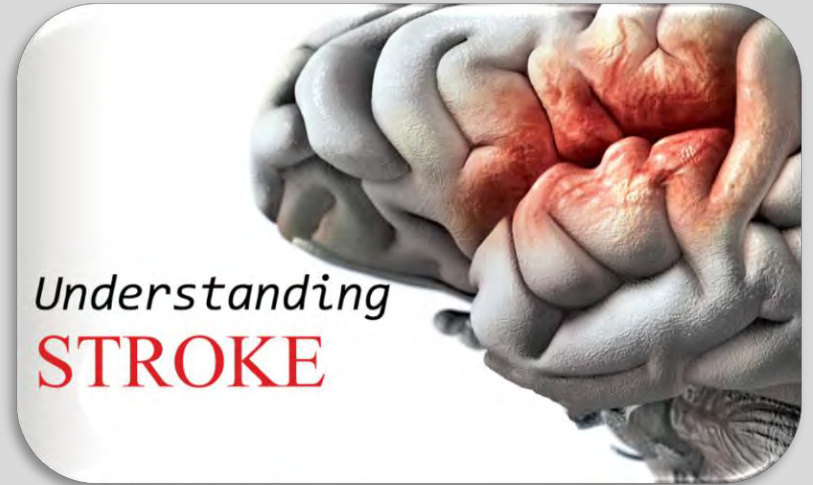


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AVC

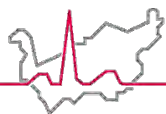
nouveautés 2019

Dr Christophe Bonvin

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Médecin adjoint – Service de neurologie – Hôpital du Valais

christophe.bonvin@hopitalvs.ch



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Chiffres en Suisse et Valais



L'ACCIDENT VASCULAIRE CÉRÉBRAL (AVC) EN SUISSE



victimes par année

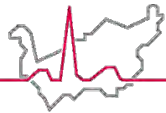


600 à 700
victimes d'un AVC en Valais

40% SE REMETTENT
COMPLETEMENT

35% RESTENT
HANDICAPÉS

25% DÉCÈDENT



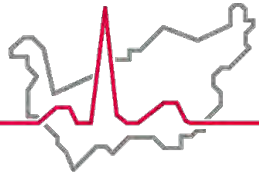
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Séquelles après AVC : **la face cachée**



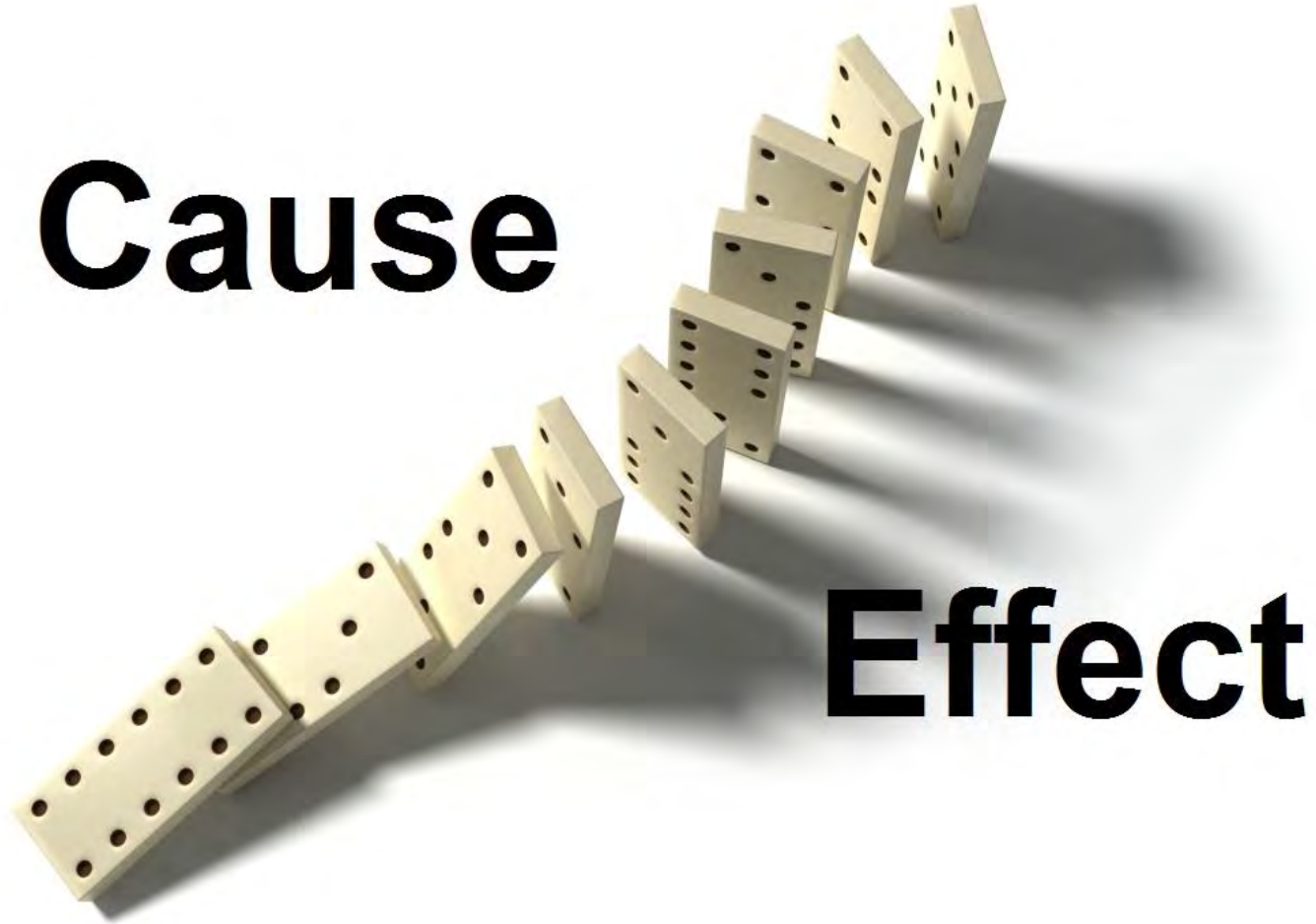
Paralysie et troubles des mouvements
Troubles sensitifs
Douleurs
Trouble du langage
Troubles visuels

Fatigue
Vertiges
Maux de tête (céphalées)
Impulsivité et agressivité
Changement de personnalité
Troubles de la concentration
Problèmes de planification
Troubles émotionnels
Troubles du sommeil
Dépression
Démence
Epilepsie

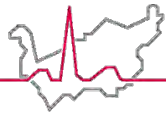


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Cause



Effect



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Les facteurs de risques cardiovasculaires

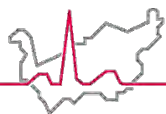
Global and regional effects of potentially modifiable risk factors associated with acute stroke in 32 countries (INTERSTROKE): a case-control study



90%
facteurs de risques

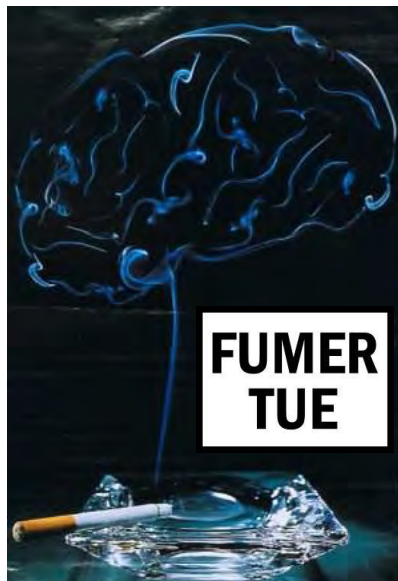
90% des AVC dépendent de **10 principaux facteurs de risques à connaître !** La prévention des AVC est une réalité. Agissez dès aujourd'hui !

1. Hypertension artérielle
2. Tabagisme actif ou passif
3. Cholestérol et excès de lipides
4. Régime alimentaire déséquilibré
5. Surpoids et obésité
6. Diabète
7. Manque d'activité physique
8. Excès d'alcool
9. Fibrillation auriculaire
10. Pauvreté et manque d'instruction



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Prévention ... style de vie !



STOP !!!



Attention !



Encore et encore

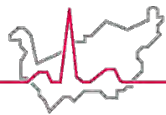


Sans excès :

♂ 2 verres/j ♀ 1 verre/j



Question de choix !



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Chocolate ♥ NOIR ! Bon pour le cœur et le cerveau

DARK CHOCOLATE 

GOOD FOR YOUR ♥ & BRAIN **HELPS CONTROL BLOOD SUGAR**

HIGH IN VITAMINS & MINERALS **REDUCE STRESS**

FULL OF ANTIOXIDANTS

22 DAYS  **COUGH RELIEF**

22DAYSNUTRITION.COM

Facteurs de risque et AVC

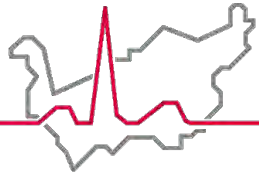
Agir !!!

Non modifiables

- Antécédents familiaux
- Antécédents personnels (AIT ou AVC)
- Sexe masculin (sténoses carotidiennes)
- Âge (surtout si > 60)
- Génétique (CADASIL, Fabry, troubles de la coagulations, ...)
- Migraine avec aura ♀

Modifiables

- HTA ♀
 - Associé à 60% des AVC
 - Plus la TA augmente, plus le risque augmente
- Diabète ♀
- Hyperlipidémie (LDL)
- Surcharge pondérale ♀
- Sédentarité
- Tabagisme (y.c. cannabis)
- OH
- Apnée du sommeil
- Fibrillation auriculaire ♀



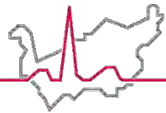
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TA < 130/80
TA < 140/80

Normaliser la pression artérielle

Anti-hypertenseurs



ESC/ESH 2018 Guidelines



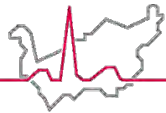
Table 23 Office blood pressure treatment target range

Age group	Office SBP treatment target ranges (mmHg)					Office DBP treatment target range (mmHg)
	Hypertension	+ Diabetes	+ CKD	+ CAD	+ Stroke ^a /TIA	
18 - 65 years	Target to 130 <i>or lower if tolerated</i> Not <120	Target to 130 <i>or lower if tolerated</i> Not <120	Target to <140 to 130 <i>if tolerated</i>	Target to 130 <i>or lower if tolerated</i> Not <120	Target to 130 <i>or lower if tolerated</i> Not <120	70–79
65 - 79 years ^b	Target to 130-139 <i>if tolerated</i>	Target to 130-139 <i>if tolerated</i>	Target to 130-139 <i>if tolerated</i>	Target to 130-139 <i>if tolerated</i>	Target to 130-139 <i>if tolerated</i>	70–79
≥80 years ^b	Target to 130-139 <i>if tolerated</i>	Target to 130-139 <i>if tolerated</i>	Target to 130-139 <i>if tolerated</i>	Target to 130-139 <i>if tolerated</i>	Target to 130-139 <i>if tolerated</i>	70–79
Office DBP treatment target range (mmHg)	70–79	70–79	70–79	70–79	70–79	

CAD = coronary artery disease; CKD = chronic kidney disease (includes diabetic and non-diabetic CKD); DBP = diastolic blood pressure; SBP = systolic blood pressure; TIA = transient ischaemic attack.

^aRefers to patients with previous stroke and does not refer to blood pressure targets immediately after acute stroke.

^bTreatment decisions and blood pressure targets may need to be modified in older patients who are frail and independent.



Anti-hypertenseurs

**Cause d'AVC
inutile**

- **BUT:**
 - **TA < 130/80 (< 60 ans)**
 - **TA 130-140/80 (> 60 ans)**

- **Préférer ... les médicaments qui baissent la TA:**
 - **Combinaison** plus efficace !
 - **IEC** (perindopril notamment)
 - **Sartans**

- **Adaptation des cibles selon ...**
 - Effets secondaires
 - Atteinte carotidienne bilatérale sévère
 - Démence vasculaire

HTA non compliquée

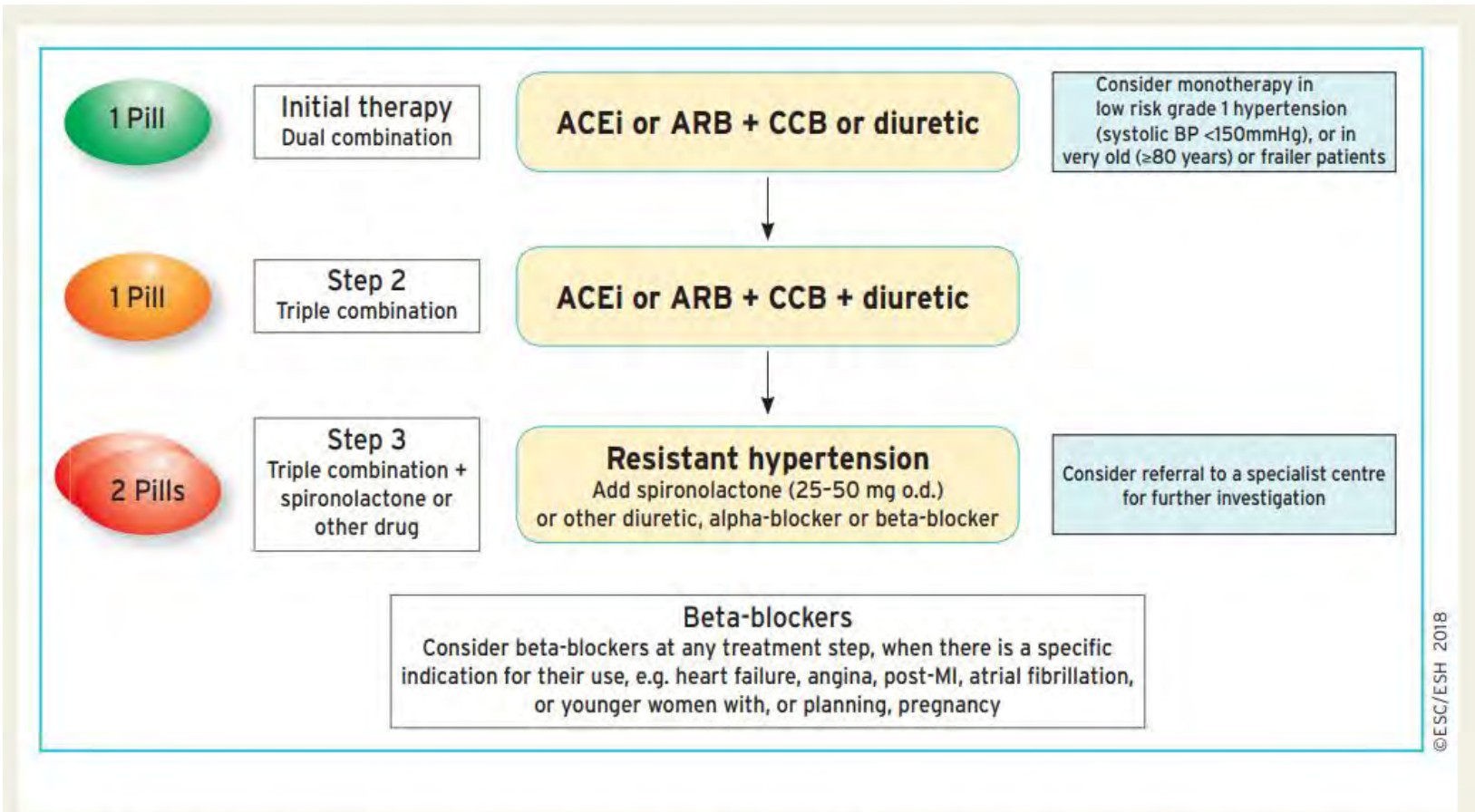
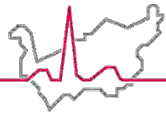
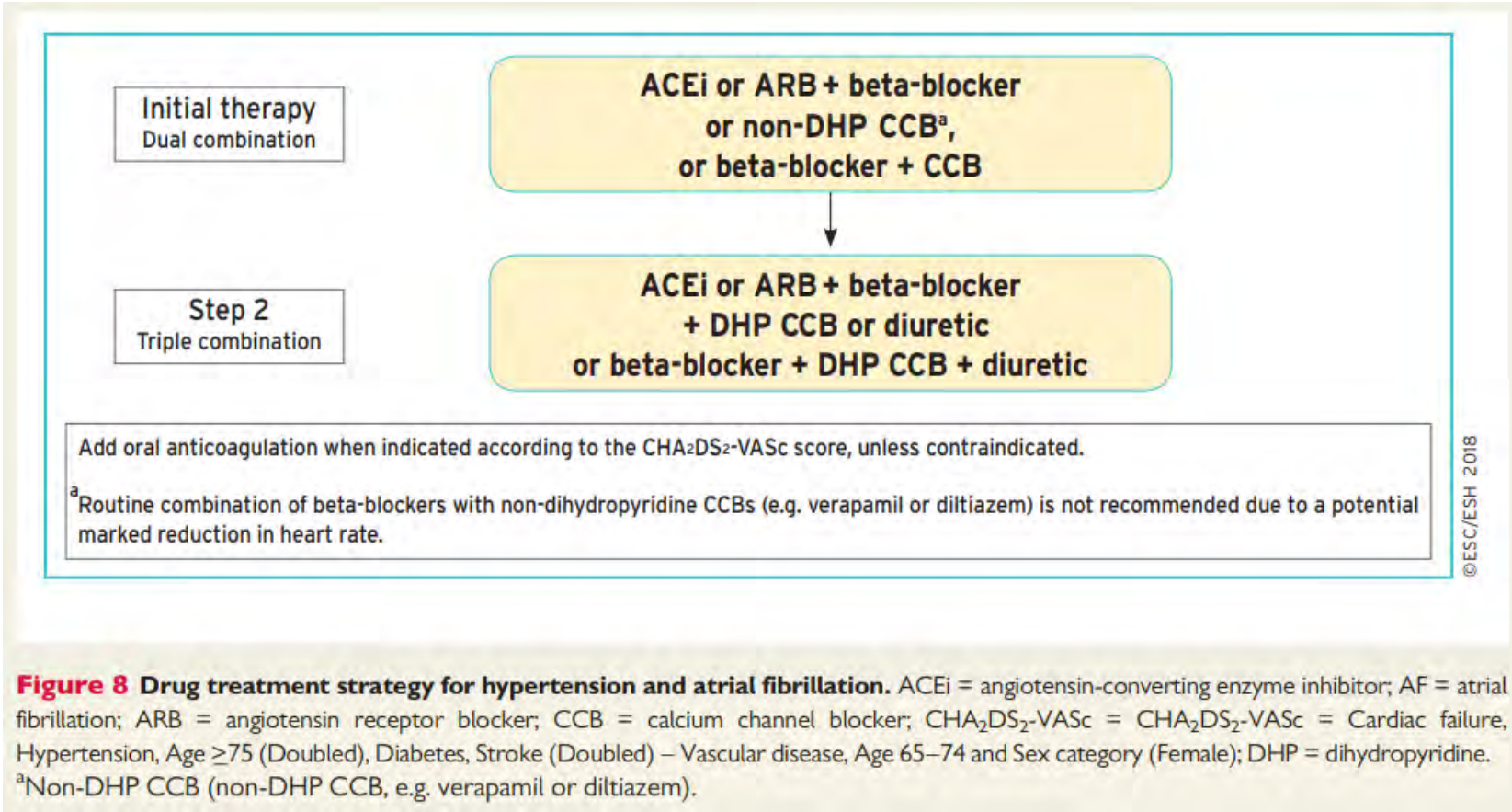
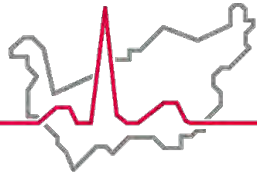


Figure 4 Core drug treatment strategy for uncomplicated hypertension. The core algorithm is also appropriate for most patients with HMOD, cerebrovascular disease, diabetes, or PAD. ACEi = angiotensin-converting enzyme inhibitor; ARB = angiotensin receptor blocker; CCB = calcium channel blocker; HMOD = hypertension-mediated organ damage; MI = myocardial infarction; o.d. = omni die (every day); PAD = peripheral artery disease.



HTA et FA





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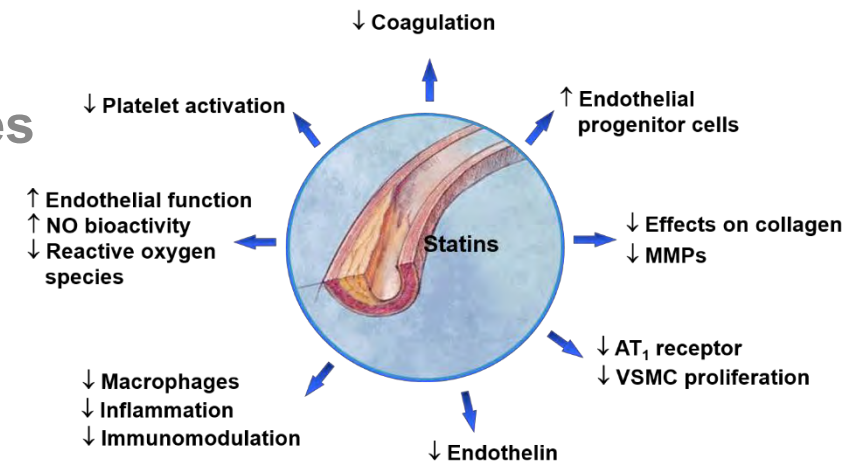


Cholestérol total < 5
LDL < 1.8 (2.5 si Ø FRCV)

Diminuer le cholestérol
Eviter la formation de plaques

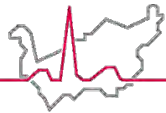
Statines

Polémique stupide !



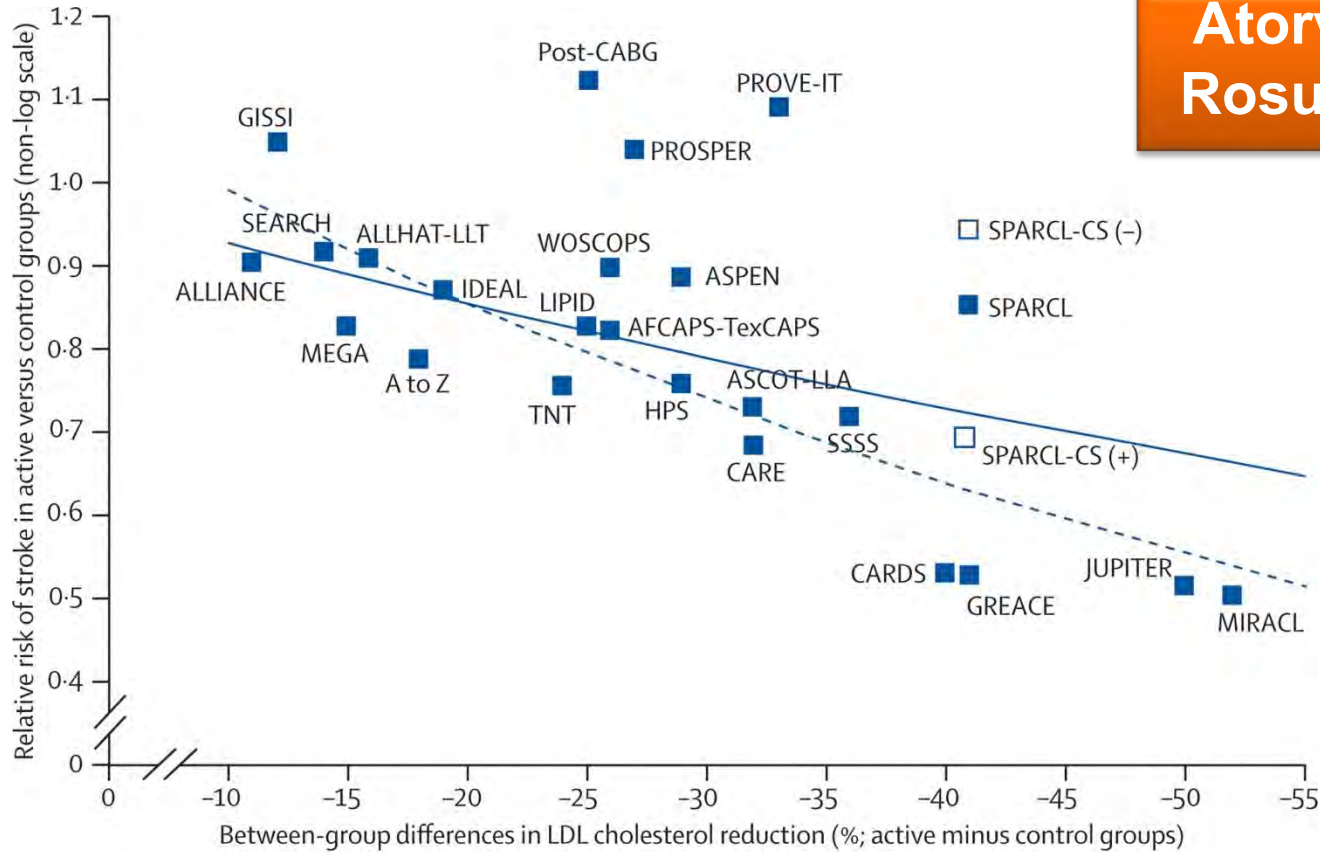
MMPs = matrix metalloproteinases

Liao JK, Am J Cardiol 2005;96(suppl 1):24F



Réduction du LDL-c et incidence d'AVC

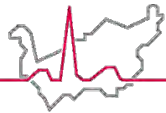
**Atorvastatine
Rosuvastatine**



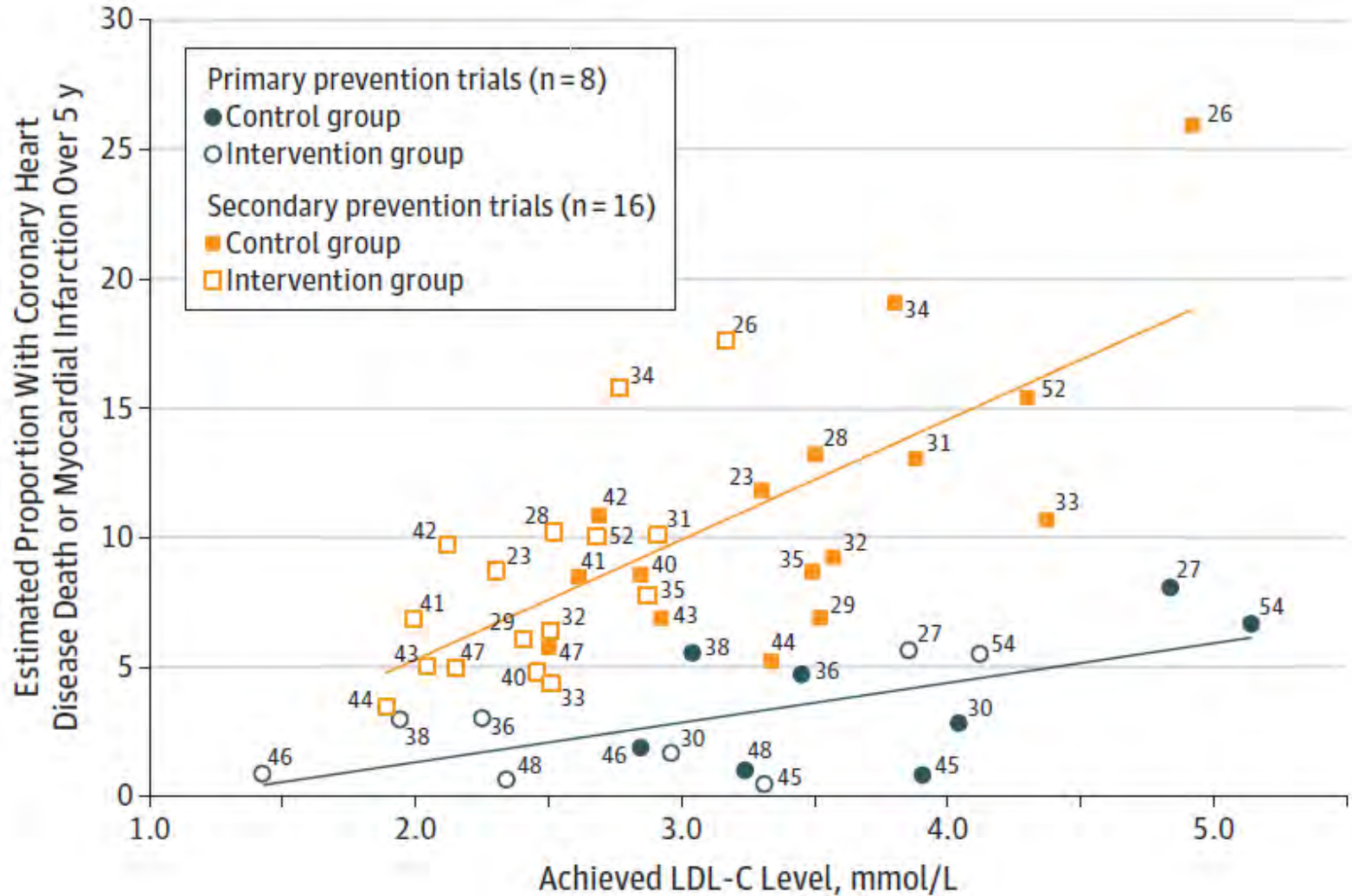
Estimates of relative risk reduction

- 10% LDL reduction: relative risk reduction 7.5% (2.3–12.5) overall
relative risk reduction 13.5% (7.7–18.8) for primary prevention of stroke
- 1 mmol/L (39 mg/dL) LDL reduction: relative risk reduction 21.1% (6.3–33.5) overall
relative risk reduction 35.9% (21.7–47.6) for primary prevention of stroke

Bénéfices coronariens à 5 ans de baisser le LDL-cholestérol



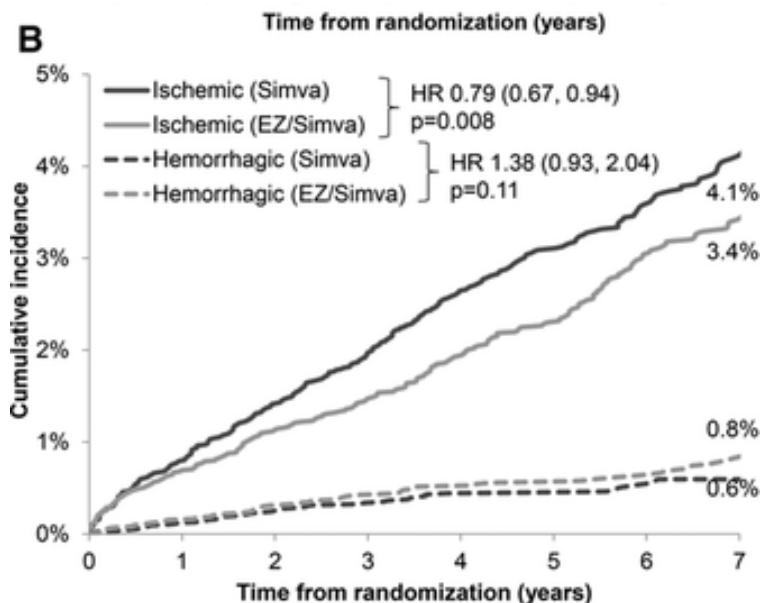
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JAMA. 2016;316(12):1289-1297. doi:10.1001/jama.2016.13985

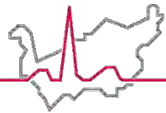
Place de l'EZETIMIBE

Prevention of Stroke with the Addition of Ezetimibe to Statin Therapy in Patients With Acute Coronary Syndrome in **IMPROVE-IT**



L'ajout de l'Ezetimibe à une statine chez un coronarien stable réduit le risque d'AVC

Atozet, Inegy, ...



Dyslipidémies induites

Elévation du LDL	Hypertriglycéridémie	Diminution du HDL
<ul style="list-style-type: none">• Hypothyroïdie• Hépatopathies choléstatiques• Syndrome néphrotique• Anorexie nerveuse• Grossesse	<ul style="list-style-type: none">• Diabète sucré de type 2• Insuffisance rénale chronique• Obésité• Médicaments : œstrogènes, thiazidiques, bêtabloquants, inhibiteurs de la protéase, corticostéroïdes, rétinoïdes, cyclosporine• Alcool• Consommation excessive de sucres	<ul style="list-style-type: none">• Diabète sucré de type 2• Tabagisme• Obésité• Sédentarité

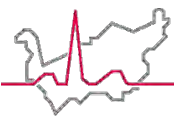
www.gsla.ch

Prévalence 1/200-300

- hypercholestérolémie familiale
- hyperlipidémie familiale combinée
- hypertriglycéridémie familiale

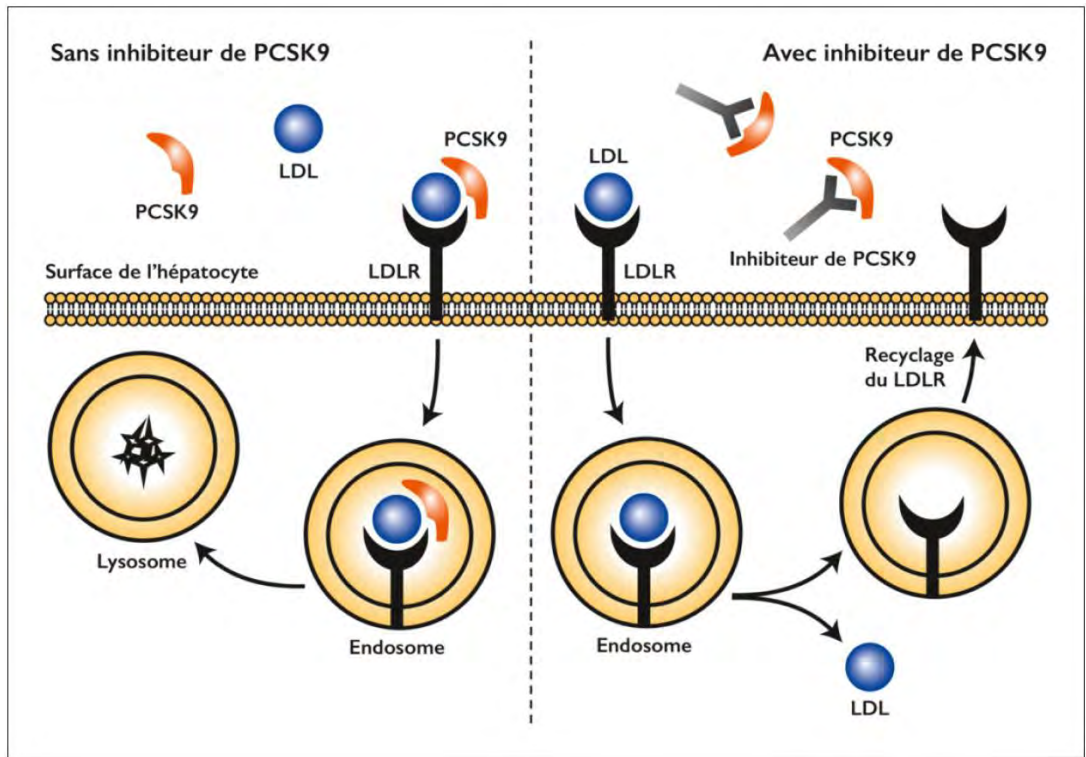


Inhibiteurs de la PCSK9



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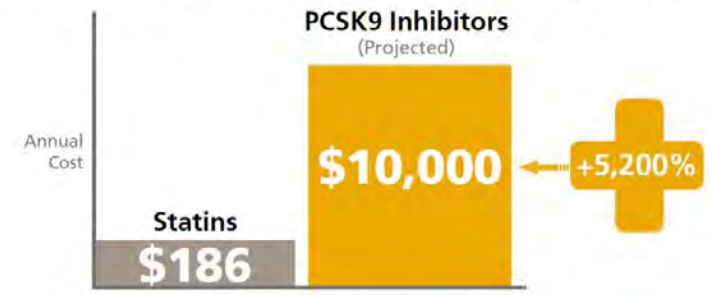
PCSK9 inhibitors shown to lower LDL cholesterol 2 ways:



Source: McKenney JM. Understanding PCSK9 and anti-PCSK9 therapies. J Clin Lipidol. 2015;9:170-86.

Average Annual Cost of Therapy

Costs could soar with widespread use of PCSK9 Inhibitors



Statin cost: WAC drug cost for atorvastatin. OptumRx Q2-2015 utilization data. Medical Marketing & Media. Analyst gives PCSK9 preview. March 25, 2014.

SMF 2017;17(45):979-986 + [SITE](#)

Inhibiteurs de la PCSK9

FOURIER (evolovumab)

Stable ATS disease

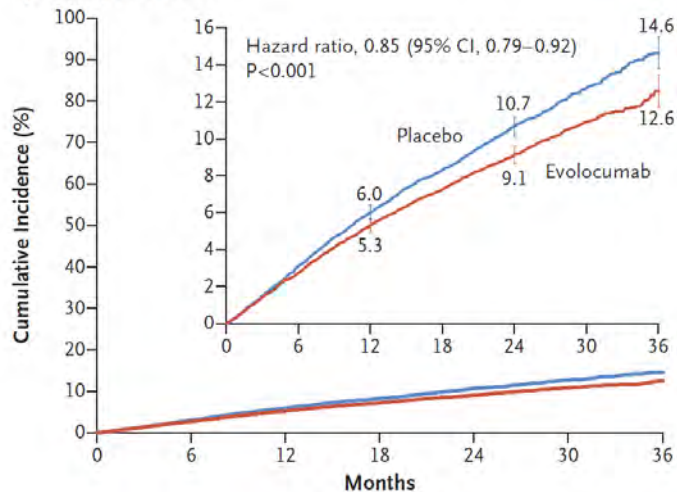
Primary outcome of MCE

- ↓ nonfatal MI, stroke, coronary revascularization by 20%
- NNT=75 over 2 yrs
- Mean LDL: 0.78*

Secondary Outcomes

- No ↓ overall or CV mortality
- CV death low (< 2%) in both grps
- **SE:** injection-site reactions (2%)

Primary Efficacy End Point



ODYSSEY OUTCOME (alirocumab)

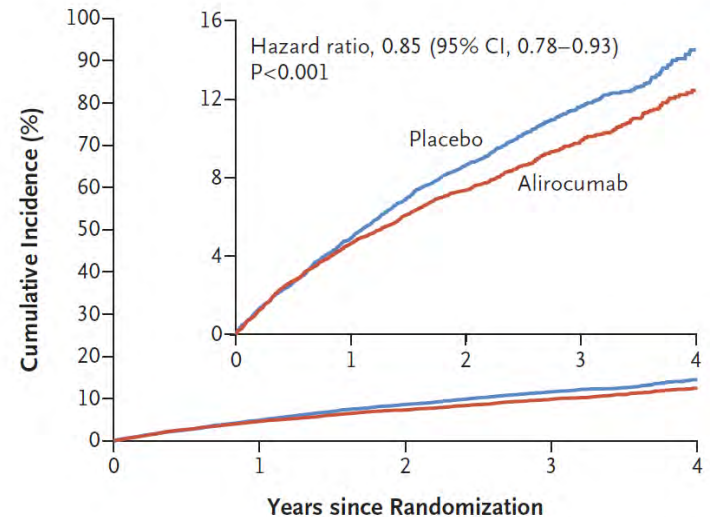
Post-ACS

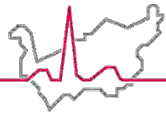
Primary outcome of MCE

- ♥ death, MI, ischemic stroke, unstable angina requiring H
- NNT=63 over 4 yrs
- Mean LDL: 0.78*

Secondary Outcomes

- ↓ all-cause and CV mortality, major and any coronary event
- CV death (2.5 vs 2.9%)
- **SE:** injection-site reactions (3.8%)





Prescription des inhibiteurs PCSK9 limitée

- **Prescription limitée** : angiologie, diabétologie, endocrinologie, cardiologie, néphrologie, neurologie, + lipidologue
- www.medforms.ch

Anamnèse du patient

- Cardiopathie coronarienne connue/Athérosclérose
- Syndrome coronaire aigu
 - Infarctus du myocarde
 - Accident vasculaire / AIT
 - Revascularisation coronaire
 - Athéropathie oblitérante des membres inférieurs (AOMI)
- La pression artérielle est contrôlée
- Le diabète sucré est absent ou contrôlé (HbA1c inférieur à 7,5%) HbA1c:
- Une abstinence à la nicotine est recherchée
- Un régime alimentaire existe en accompagnement

1er événement	2nd événement	3ème événement

LDL-C actuel: mmol/l sans thérapie PCSK9i avec thérapie PCSK9i

Hypollémiant	mg (dose max. tolérée)	+Ézétimibe (optionnel)	Durée [mois] (au moins 3 mois)	LDL-C obtenue [mmol/l]	Indications en cas d'intolérance aux statines		
					Myalgies	Hépatopathie	CK valeur *
Atorvastatine		<input type="checkbox"/>			<input type="checkbox"/>	<input type="checkbox"/>	
Rosuvastatine		<input type="checkbox"/>			<input type="checkbox"/>	<input type="checkbox"/>	
Fluvastatine		<input type="checkbox"/>			<input type="checkbox"/>	<input type="checkbox"/>	

Adressez-nous les patients à risque pour une prescription d'i-PCSK9

70% sont expliqués par 3 mécanismes

▪ **Microangiopathie**

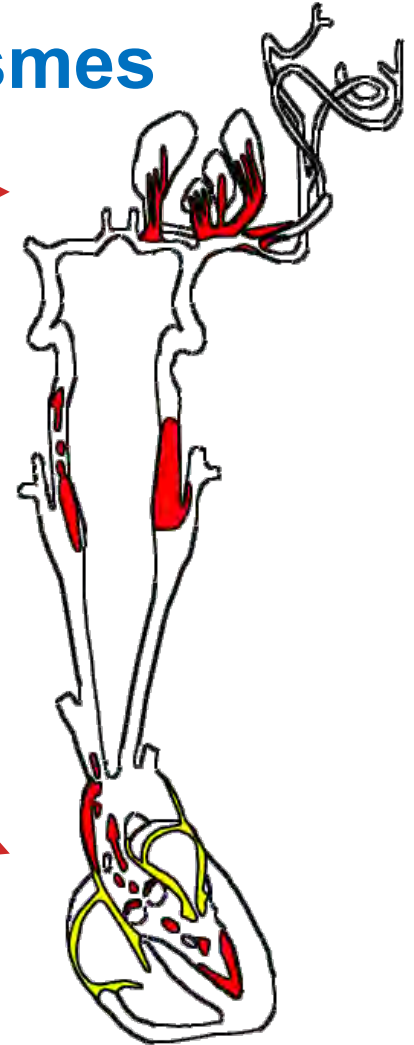
- Infarctus lacunaires

▪ **Macroangiopathie**

- Athéromatose/sténose carotidienne
et des artères majeures

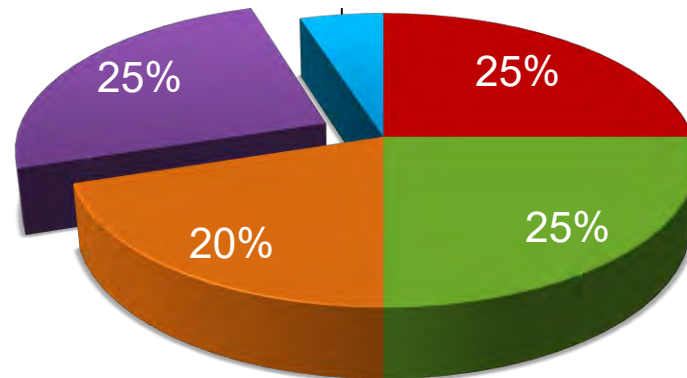
▪ **Cardioembolique**

- FA et flutter auriculaire
- FOP
- Infarctus (↓FE, dyskinésie, thrombus cardiaque)
- Valvulopathies (végétations, tumeurs, ...)
- Athéromatose aortique



Classification des causes d'AVC

- **Cardioembolique (FA, ...)**
- **Microangiopathie (HTA, diabète, ...)**
- **Athéromatose (cholestérol, Tabac, HTA, ...)**
- ***Indéterminée***
- **Autres (dissection, vasculite, état procoagulant, génétique, iatrogène etc.)**

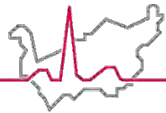


KEY CLINICAL POINTS

CRYPTOGENIC STROKE

- One quarter of patients with ischemic stroke have no probable cause found after standard workup, including echocardiography, inpatient cardiac telemetry or 24-hour Holter monitoring, magnetic resonance imaging or computed tomographic (CT) imaging of topographic features of the infarct in the brain, and magnetic resonance or CT angiographic assessment of neck and brain arteries. Additional investigation identifies a likely mechanism in more than half these patients.
- Most cryptogenic ischemic strokes are embolic in origin, arising from proximal arterial sources, the heart, or venous sources (with right-to-left shunts).
- Investigation in patients with cryptogenic stroke typically includes evaluation for atherosclerotic and nonatherosclerotic arteriopathies, cardiac sources of embolism (structural and rhythm abnormalities), and disturbances of coagulation.
- Patent foramen ovale is found in up to half of young adults with cryptogenic stroke but is also found in one quarter of healthy persons.
- Occult, low-burden, paroxysmal atrial fibrillation is increasingly recognized as a source of cryptogenic stroke, especially in older patients.

ESUS : embolic stroke of undetermined source



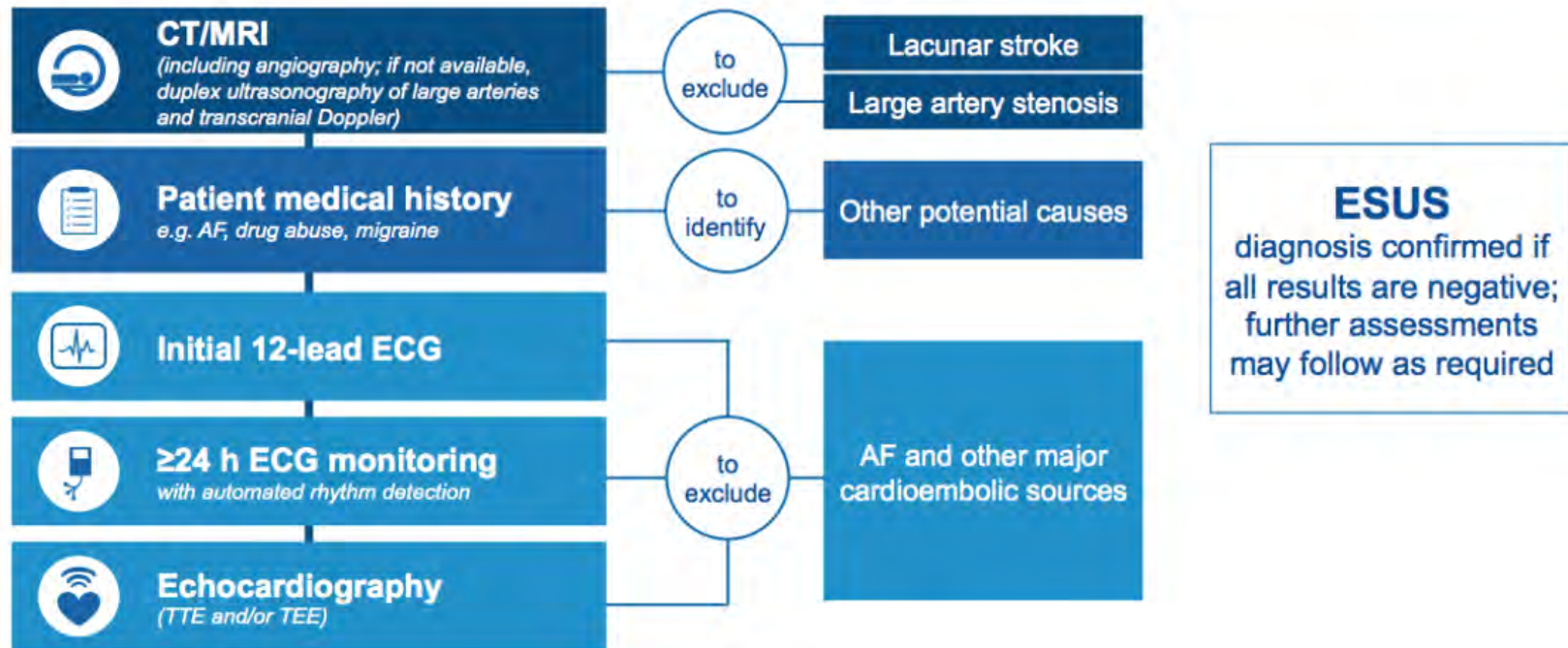
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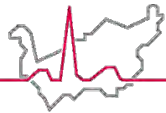
EMBOLIC STROKE OF UNDETERMINED SOURCE

Cryptogenic ischemic strokes that are superficial, or deep but large, are almost always due to emboli arriving in the brain from an arterial, cardiac, or transcerebral source. Intrinsic large artery diseases, such as in situ thrombosis or vasospasm, are uncommon causes. Recently, this long-standing clinical insight was formalized as the clinical construct “embolic stroke of undetermined source.” Embolic strokes of undetermined source are operationally defined as nonlacunar brain infarcts without substantial proximal arterial stenosis or major cardioembolic sources,⁷ and they represent 80 to 90% of all cryptogenic ischemic strokes.

Quels examens pour **confirmer ESUS**

ESUS can be confirmed after few diagnostic steps





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AVC cryptogéniques ... en partie cardioemboliques

- **FA présente chez 15 à 25% des AVC cryptogéniques si monitoring cardiaque prolongé.**

→ Rechercher activement la FA

EDITORIAL

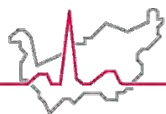
Ashis H. Tayal, MD
David J. Callans, MD

Occult atrial fibrillation in ischemic stroke
Seek and you shall find

Stollberger C, Eur J Neurol. 2009;16:160; Elijevich L, J Stroke Cerebrovasc Dis. 2009;18:185; Amarenco P, Cerebrovasc Dis. 2009;27(suppl 1):97
Tayal AH, Neurology 2010;74:1662; <http://www.boehringer-ingenelheim.com>

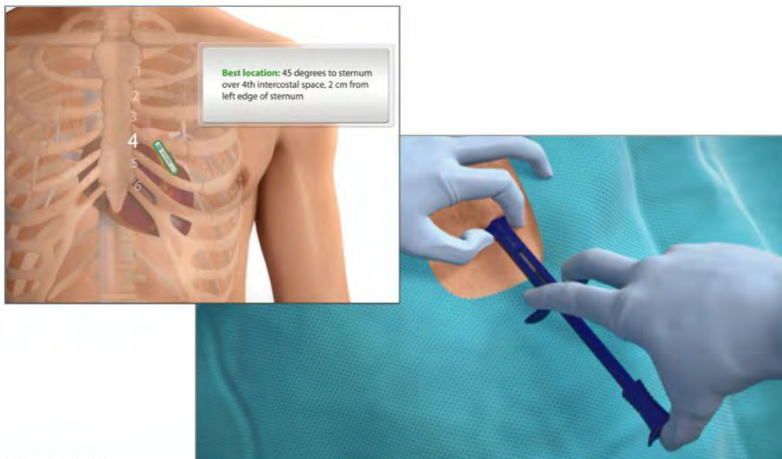
ECG → Holter → R-test

→ Monitoring prolongé implanté



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REVEAL LINQ™ INSERTION



Source: Medtronic Inc.

26

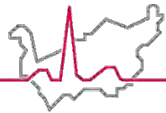
Medtronic

Evolution 2009 → 2014



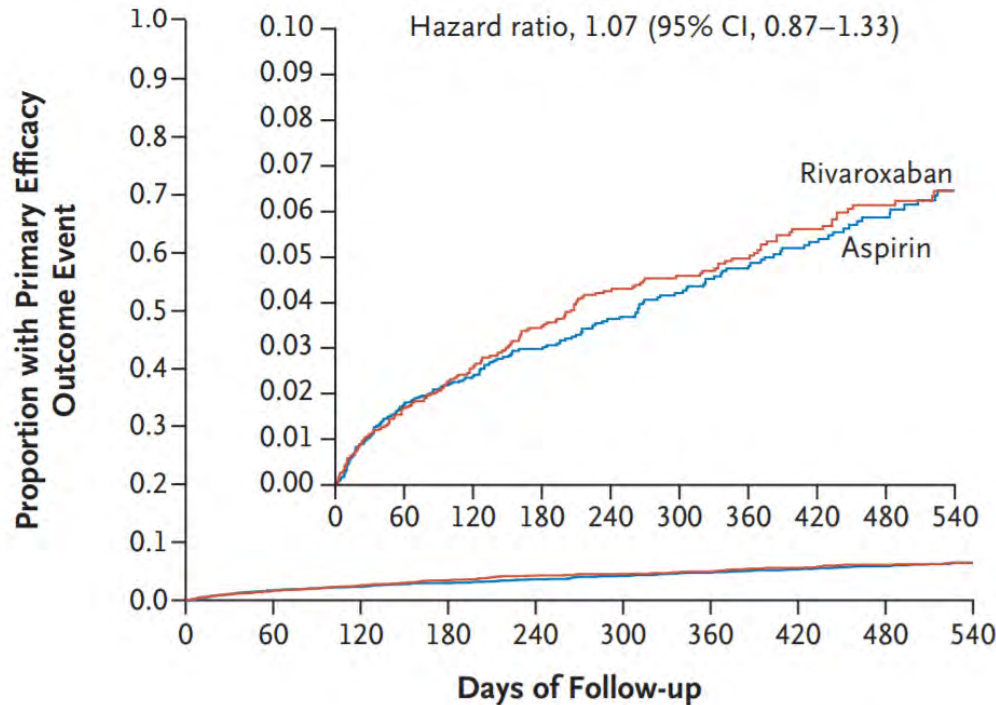
Infos Medtronic

AVC cryptogénique : Antiagrégant ou Anticoaguation ?

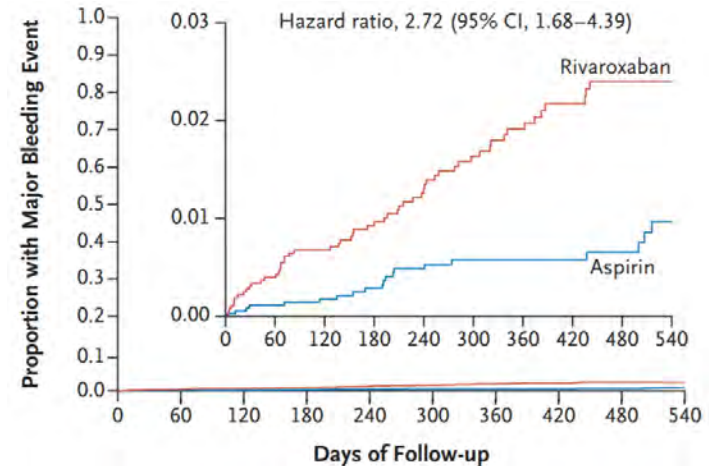


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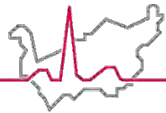
- **NAVIGATE-ESUS** (rivaroxaban 15mg vs Aspirine 100mg)
- **7213 p**
- **HR 1.07, (P=0.52), pas de différence, risque hémorragique**



Négatif !



AVC cryptogénique : Antiagrégant ou Anticoaguation ?



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- **RE-SPECT ESUS (Dabigatran 150/110mg vs Aspirine 100mg)**
- **5390 p**
- **HR 0.85 (0.69-1.03, P=0.1) en faveur du Dabigatran**
- **Séparation des courbes**
- **Publication à venir**

Presque positif !

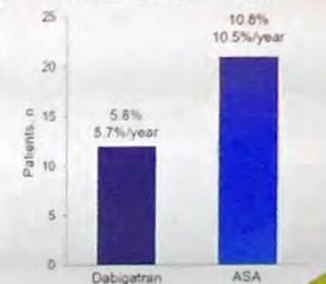
Conclusions

- In patients with ESUS, who had at least 20 hours of baseline monitoring, dabigatran was not superior to ASA for prevention of recurrent stroke, and did not significantly increase the risk of major bleeding compared with ASA
- There is no significant heterogeneity of treatment effect according to duration of baseline monitoring for AF
- AF was detected (by cardiac monitoring, adverse event reporting, etc.) in around 7.5% (430/5390) of patients over the average 19 months of study follow-up
- Among patients with detection of AF, in an exploratory analysis, there were numerically fewer recurrent strokes with dabigatran

Recurrent strokes according to AF confirmed during the trial

Characteristic	Dabigatran (N = 2695)	ASA (N = 2695)
Patients with AF, n (%)	208 (7.7)	195 (7.2)
Time of first AF onset since randomization, days		
Mean (SD)	308 (276)	284 (285)
Median (range)	232 (0-1117)	196 (0-1088)
Patients with AF and recurrent stroke, n (%)	20 (9.6)	30 (15.4)

Recurrent strokes in patients with AF, after first confirmed AF*



*Recurrent strokes after first AF confirmed could also be second or third stroke. Covariates in Cox proportional hazards model: age (< or ≥ 75 years), creatinine clearance (< or ≥ 50 mL/min), prior stroke or transient ischemic attack (yes or no).

DOAC dans les AVC cryptogéniques

RE-SPECT ESUS

enrolment completed in
December 2017 after
randomization of 5,390 patients

1:1 randomization, double-blinded

dabigatran 150 mg twice daily

aspirin 100 mg once daily

primary endpoint: time to first recurrent stroke
(ischemic, hemorrhagic, or unspecified)

NAVIGATE ESUS

terminated in
October 2017 due to
futility for the primary endpoint
after enrolment of 7,214 patients

1:1 randomization, double-blinded

rivaroxaban 15 mg once daily

aspirin 100 mg once daily

primary endpoint: time to first recurrent stroke
(ischemic, hemorrhagic, or unspecified),
magnetic resonance imaging-positive transient
ischemic attack, or systemic embolism

ATTICUS

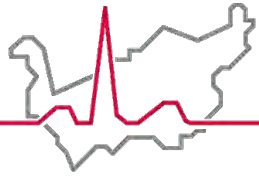
active, up to 600 patients with
embolic stroke of undetermined
source and additional risk factors
for subclinical atrial fibrillation;
continuous or daily ECG monitoring

1:1 randomization, open-label

apixaban 5 mg twice daily

aspirin 100 mg once daily

primary endpoint: new ischemic lesions on
magnetic resonance imaging after 12 months

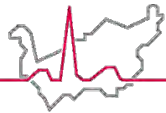


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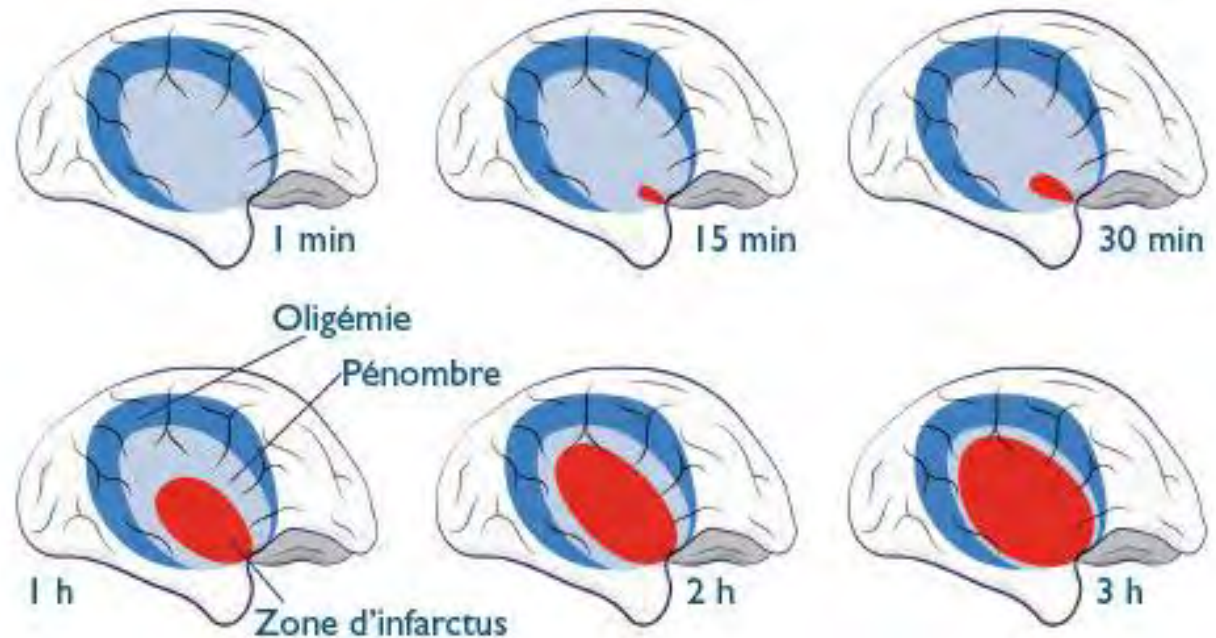
Progrès incroyables de l'imagerie cérébrale

La pénombre: un phénomène dynamique dans le temps et l'espace

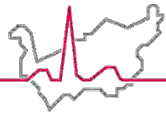


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- Lorsqu'un AVC survient, chaque **minute**, le cerveau perd environ **2 millions de neurones !**

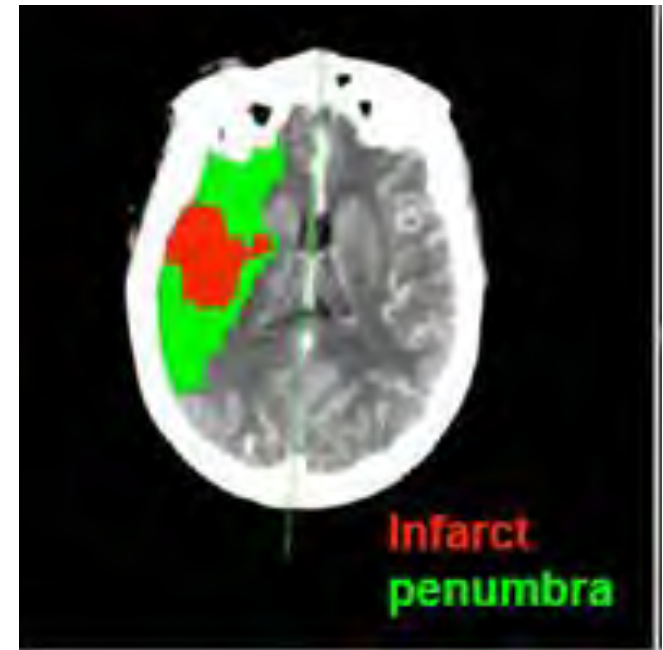
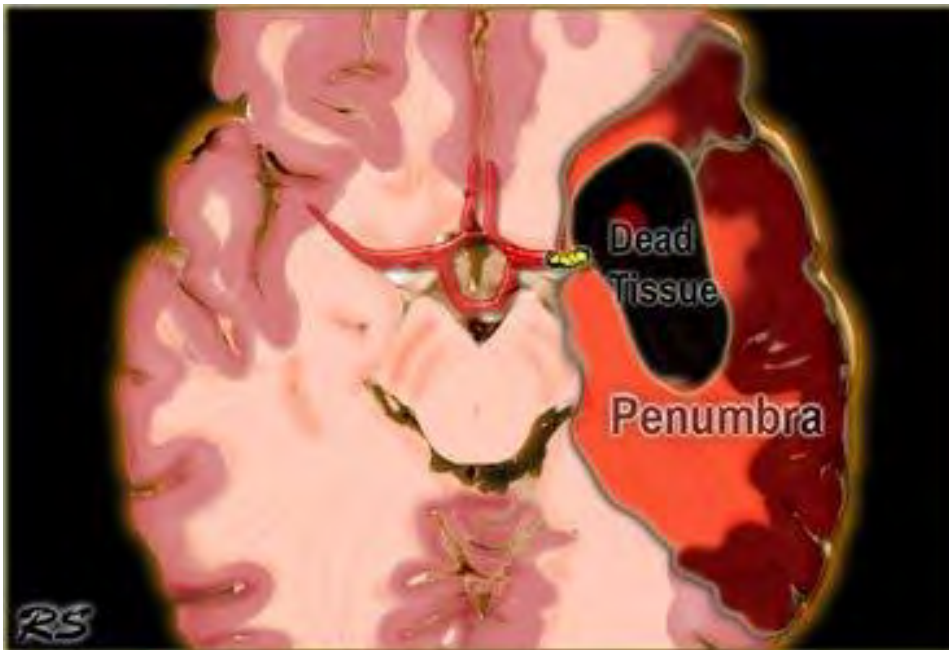


Rev Med Suisse 2015; volume 11.1476 – Jones, J Neurosurg 1981;54:773 – Baron, Cerebrovasc Dis 1999;9:193

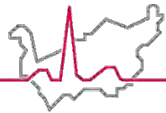


La pénombre ischémique

- La **pénombre** est remplacée par l'**infarctus** en cas de non-recanalisation de l'artère



Softwares automatiques pour la sélection des patients (détermination du core et de la pénombre)



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Spital Wallis

iSchemaView **RAPID**

 Brainomix®



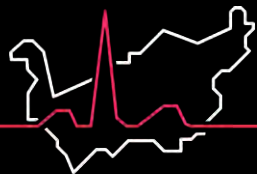
e-STROKE SUITE



RAPID automated neurovascular imaging platform
at your fingertips



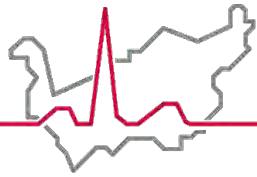
www.i-rapid.com <https://brainomix.com/e-stroke-suite>



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Spital Wallis



**Traitements : 20 ans de
progrès significatifs**

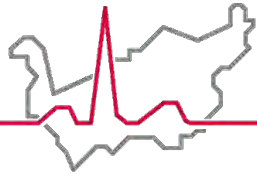


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1. Hospitalisation en **Stroke Unit**
2. **Revascularisation** (thrombolyse IV et traitement endovasculaire)

**Interventions bénéfiques
AVC aigus**



Hôpital du Valais
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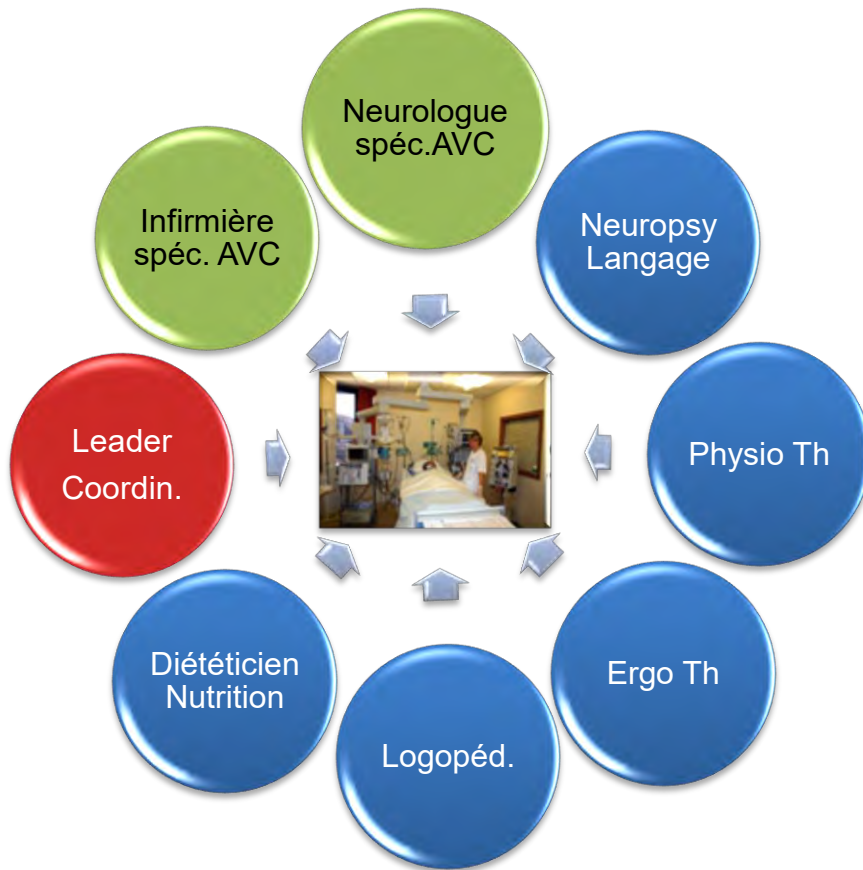
Stroke Unit

Stroke Unit / Stroke Center

Prise en charge spécialisée et centralisée pour tous les AVC !

Bénéfice d'une Stroke Unit (unité cérébrovasculaire)

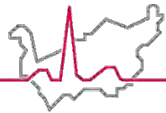
- Approche **coordonnée et multidisciplinaire**
- Equipe **spécialisée**
- **Monitoring** continu



↓ Mortalité
 ↓ Déficit / Handicap
 ↓ Institutionnalisation
 ↓ Coûts de santé

- ← Urgences
- ← Radiologie
- ← Soins intensifs
- ← Cardiologie
- ← Chirurgie vasculaire
- ← Neurochirurgie
- ← Rehabilitation / Gériatrie
- ← Médecine interne

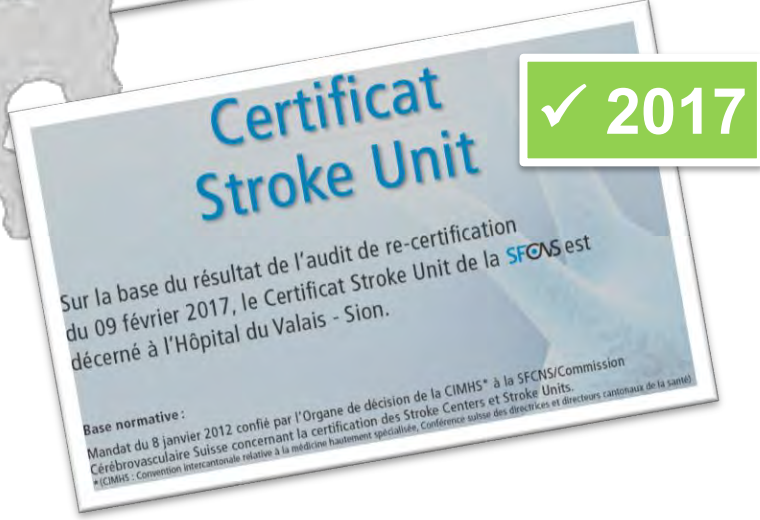
14 Stroke Units et 10 Stroke Centers suisses un *réseau intégré* d'unités *certifiées*



Hôpital du Valais
Spital Wallis



Unité cérébrovasculaire du Valais



Evolution des AVC hospitalisés

Engagement du Dr C. Bonvin
spéc. maladies cérébrovasculaires

1^{er} certification Stroke Unit

	2006	2007	2008	2009	2010	2011	2012	2013	2014	2015	2016	2017	2018
AVC	39	146	238	328	388	410	440	450	475	510	532	550	579
TIV / TEV	0	14	14	36	51	83	61	85	80	103	112	141	164
% recan.	0%	10%	6%	11%	13%	20%	14%	19%	17%	20%	23%	25%	28%



Première thrombolyse à Sion
Prof. J. Ghika



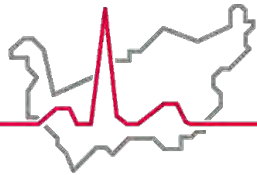
Mise en place de la Stroke Unit



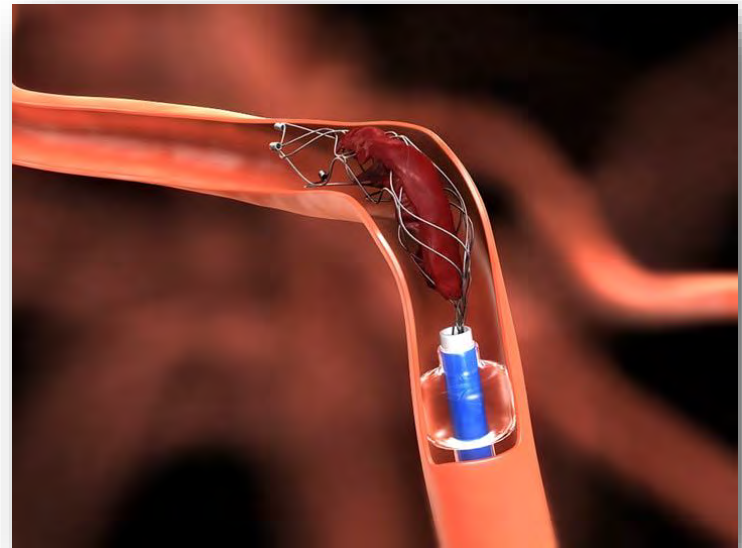
Activation de la filière AVC avec OCVS/Urg
Information des services préhospitaliers



Etudes d'évidence
ttt endovasculaire



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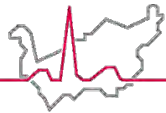


Evidence depuis 1995

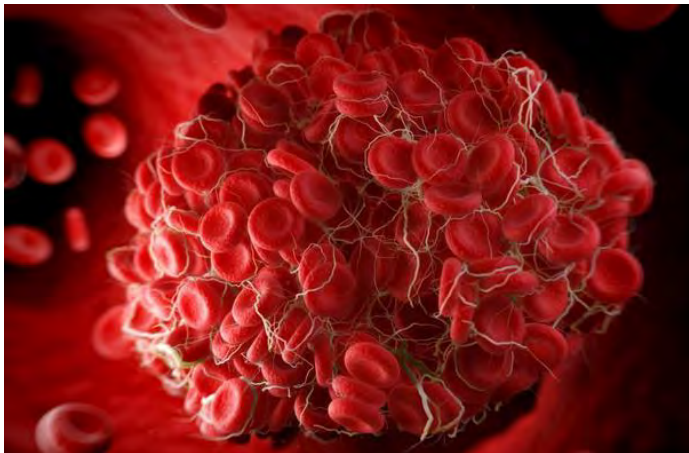
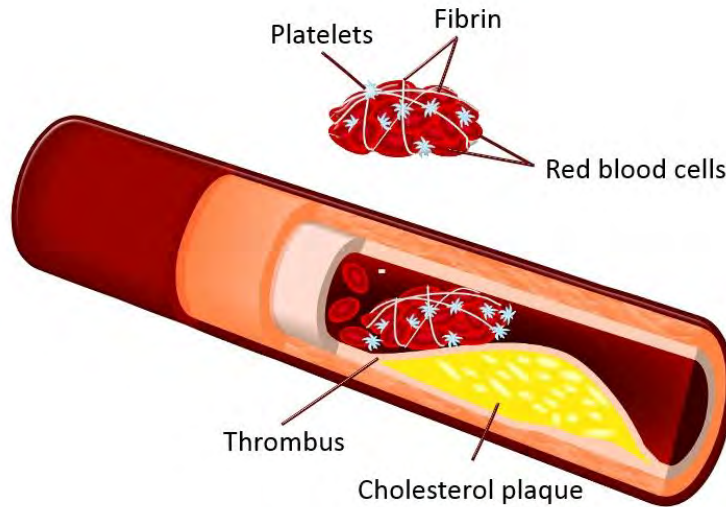
Revascularisation

Thrombolyse (TIV) : «dissoudre» le caillot

Evidence depuis 1995



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- streptokinase
- urokinase
- **altéplase**
- retéplase
- ténecteplase
(2017-2018)



Tenecteplase versus Alteplase before Thrombectomy for Ischemic Stroke

B.C.V. Campbell, P.J. Mitchell, L. Churilov, N. Yassi, T.J. Kleinig, R.J. Dowling, B. Yan, S.J. Bush, H.M. Dewey, V. Thijs, R. Scroop, M. Simpson, M. Brooks, H. Asadi, T.Y. Wu, D.G. Shah, T. Wijeratne, T. Ang, F. Miteff, C.R. Levi, E. Rodrigues, H. Zhao, P. Salvaris, C. Garcia-Esperon, P. Bailey, H. Rice, L. de Villiers, H. Brown, K. Redmond, D. Leggett, J.N. Fink, W. Collecutt, A.A. Wong, C. Muller, A. Coulthard, K. Mitchell, J. Clouston, K. Mahady, D. Field, H. Ma, T.G. Phan, W. Chong, R.V. Chandra, L.-A. Slater, M. Krause, T.J. Harrington, K.C. Faulder, B.S. Steinfors, C.F. Bladin, G. Sharma, P.M. Desmond, M.W. Parsons, G.A. Donnan, and S.M. Davis,
for the EXTEND-IA TNK Investigators*

THE NEW ENGLAND JOURNAL OF MEDICINE

ORIGINAL ARTICLE

Tenecteplase versus alteplase for management of acute ischaemic stroke (NOR-TEST): a phase 3, randomised, open-label, blinded endpoint trial

Nicola Logallo, Vojtech Novotny, Jörg Assmus, Christopher EKvistad, Lars Altheheld, Ole Morten Renning, Bente Thommessen, Karl-Friedrich Amthor, Hege Ihle-Hansen, Martin Kurz, Håkon Tobro, Kamaljit Kaur, Magdalena Stankiewicz, Maria Carlsson, Åse Marsund, Titto Idicula, Anne Hege Aamodt, Christian Lund, Halvor Næss, Ulrike Waje-Andreassen, Lars Thomassen

Summary

Background Tenecteplase is a newer thrombolytic agent with some pharmacological advantages over alteplase. Previous phase 2 trials of tenecteplase in acute ischaemic stroke have shown promising results. We aimed to investigate the safety and efficacy of tenecteplase versus alteplase in patients with acute stroke who were eligible for intravenous thrombolysis.

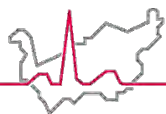


Lancet Neurol 2017
Published Online
August 2, 2017
[http://dx.doi.org/10.1016/S1474-4422\(17\)30253-3](http://dx.doi.org/10.1016/S1474-4422(17)30253-3)

A Randomized Trial of Tenecteplase versus Alteplase for Acute Ischemic Stroke

Mark Parsons, M.D., Neil Spratt, M.D., Andrew Bivard, B.Sc., Bruce Campbell, M.D., Kong Chung, M.D., Ferdinand Miteff, M.D., Bill O'Brien, M.D., Christopher Bladin, M.D., Patrick McElduff, Ph.D., Chris Allen, M.D., Grant Bateman, M.D., Geoffrey Donnan, M.D., Stephen Davis, M.D., and Christopher Levi, M.D.

N Engl J Med 2012;366:1099-107



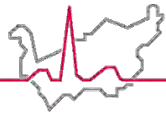
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Meilleure méthode ...



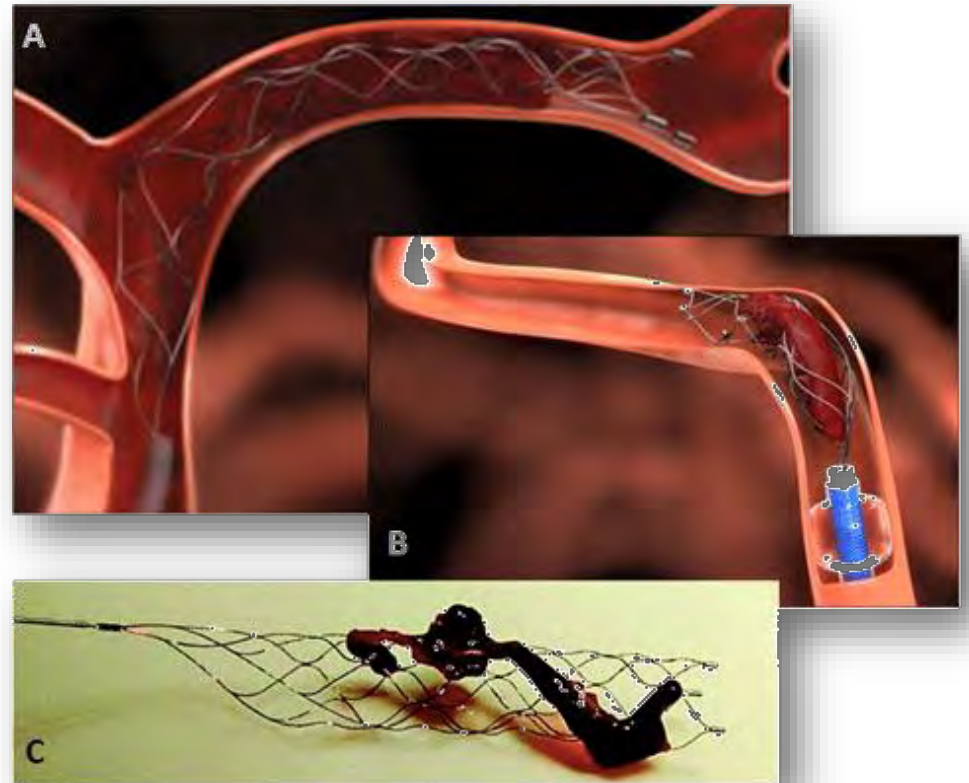
Traitement endovasculaire (TEV)

Evidence depuis 2015



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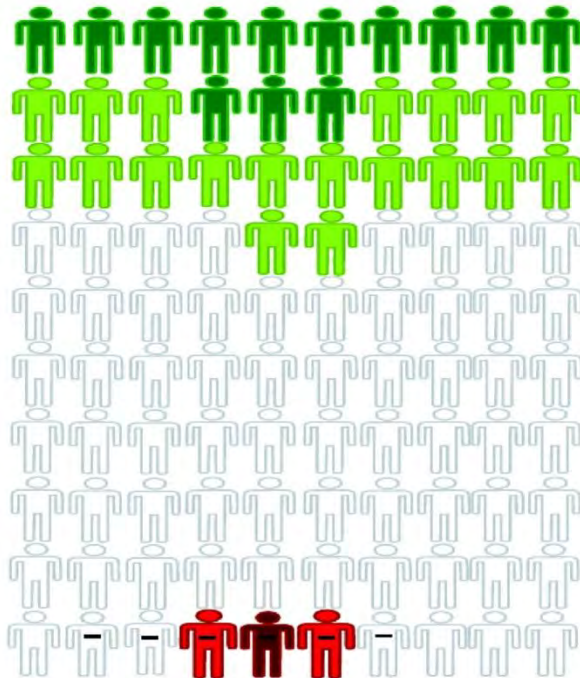
- Cas bien **sélectionnés, vaisseaux accessible**
PAS POUR TOUT LE MONDE !!!
- En bonne santé
- **Geste ultra-spécialisé**
- **Neuroradiologie interventionnelle**
- **MHS → Stroke Center**



Bénéfice et risque de la TIV et TEV

Thrombolyse (TIV)

TPA for Cerebral Ischemia within 3 Hours of Onset-Changes in Outcome Due to Treatment



Changes in final outcome as a result of treatment:

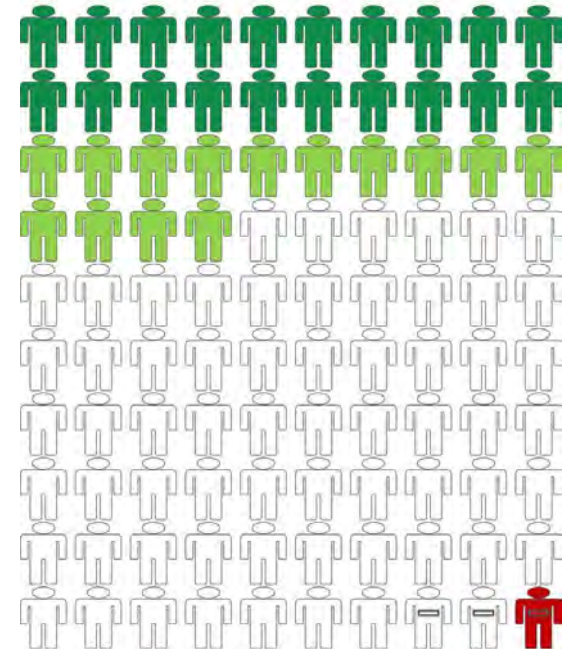
- Normal or nearly normal
- Better
- No major change
- Worse
- Severely disabled or dead

Early course:

- No early worsening with brain bleeding
- Early worsening with brain bleeding

Thrombectomie (TEV)

Thrombectomy Plus tPA vs tPA Alone
(tPA-Eligible Patients)



Changes in final outcome as a result of treatment:

- Able to live independently
- Other improvement
- No major change
- Other worsening
- Severely disabled or dead

Early course:

- New territory infarct
- Early worsening with brain bleeding (SICH)*

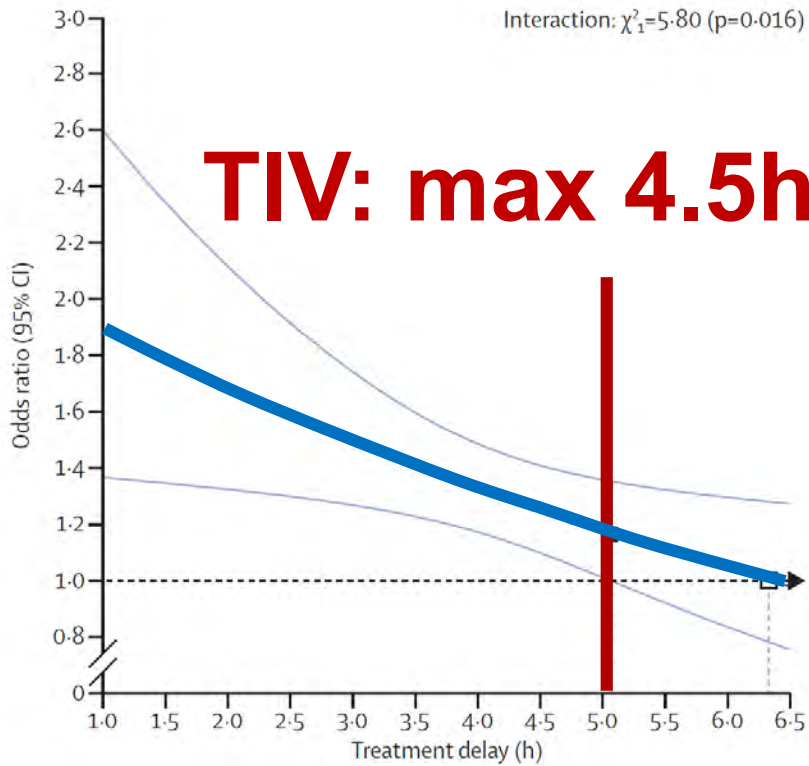
(*No differences observed in the rate of SICH due to thrombectomy)

<https://doi.org/10.1161/STROKEAHA.109.566935> - Stroke. 2010;41:300-306

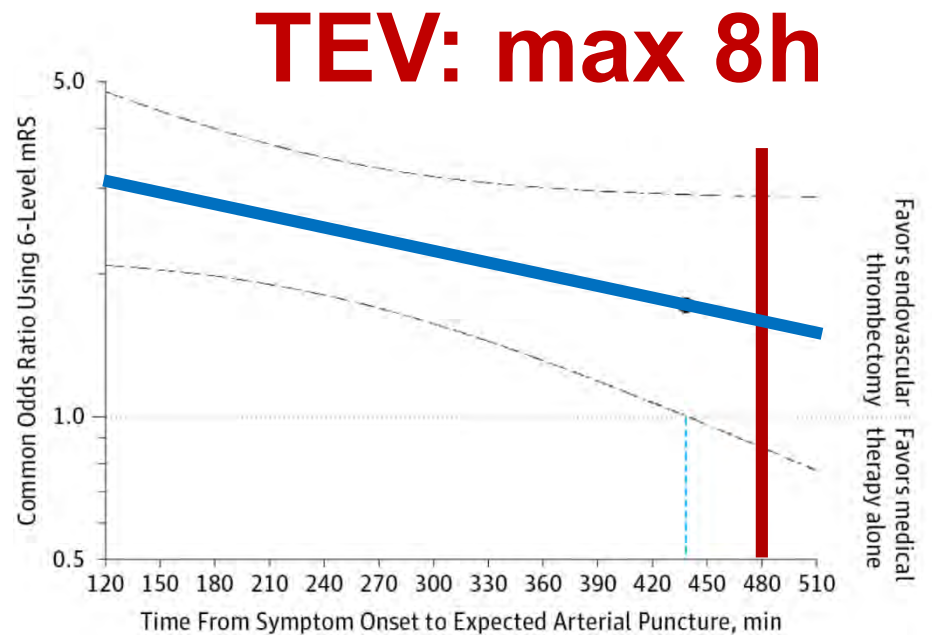
<https://doi.org/10.1161/STROKEAHA.117.018715> - Stroke. 2018;49:90-97

L'AVC est une urgence !

Le pronostic dépend de la rapidité de traitement

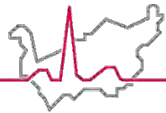


A Odds ratio for less disability at 3 mo in endovascular thrombectomy vs medical therapy alone groups by time to treatment



Emberson, Lees, Lyden et al, The Lancet 2014 – JL Saver, JAMA. 2016;316(12):1279

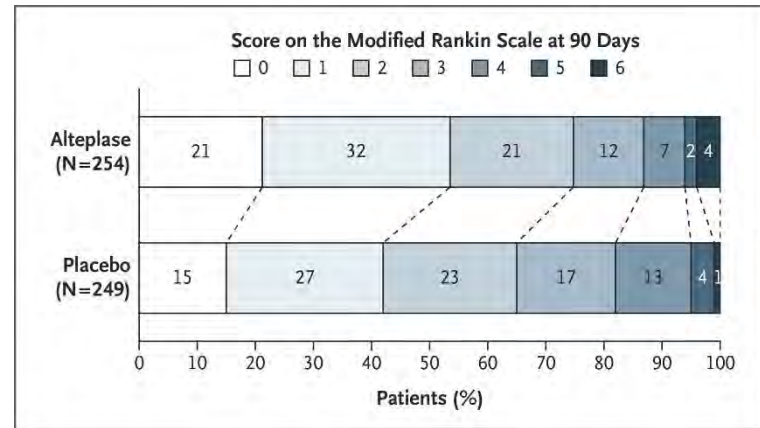
La prise en charge urgente (P1) des AVC doit être étendue à 24h depuis le début des symptômes



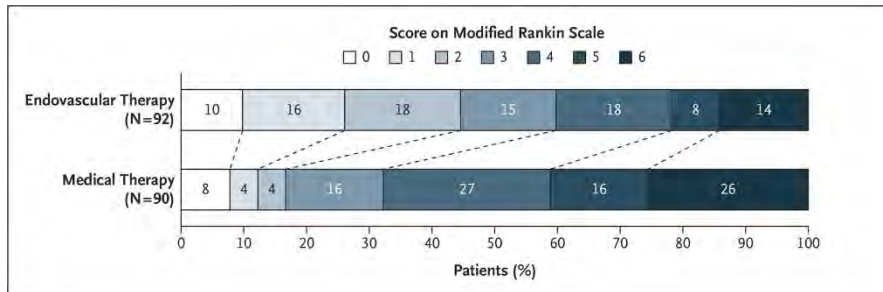
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TIV et TEV possible → 24h (cas sélectionnés)
Nouvelles études 2018: DAWN, DEFUSE 3, WAKE-UP

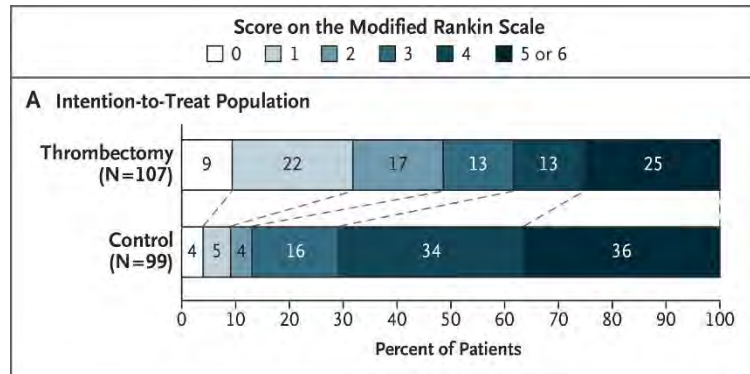
WAKE-UP (TIV)



DEFUSE 3 (TEV)



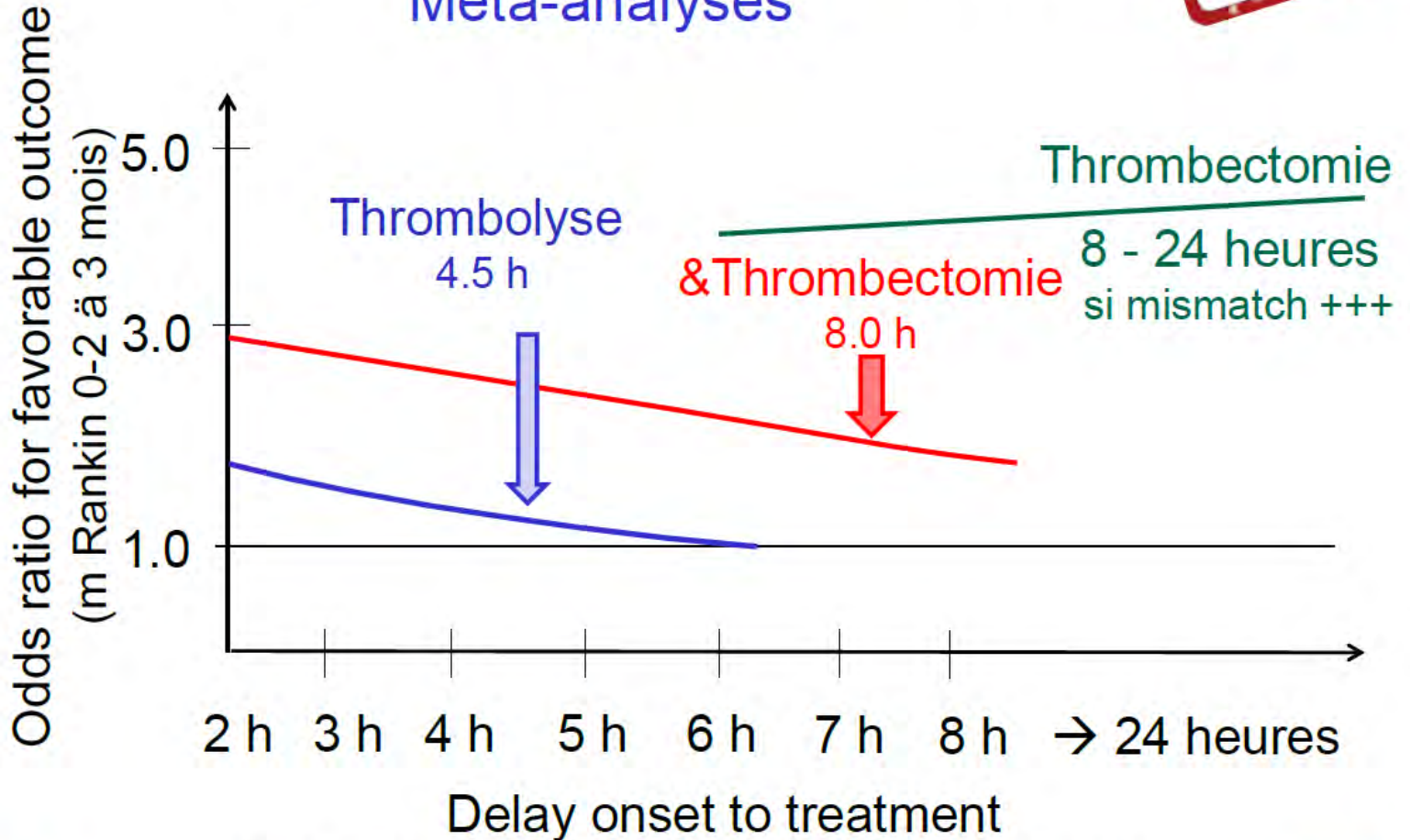
DAWN (TEV)



DAWN: <https://www.nejm.org/doi/full/10.1056/NEJMoa1706442>, DEFUSE 3: <https://www.nejm.org/doi/full/10.1056/NEJMoa1713973>, WAKE-UP: <https://www.nejm.org/doi/full/10.1056/NEJMoa1804355>

Efficacy of acute recanalisation

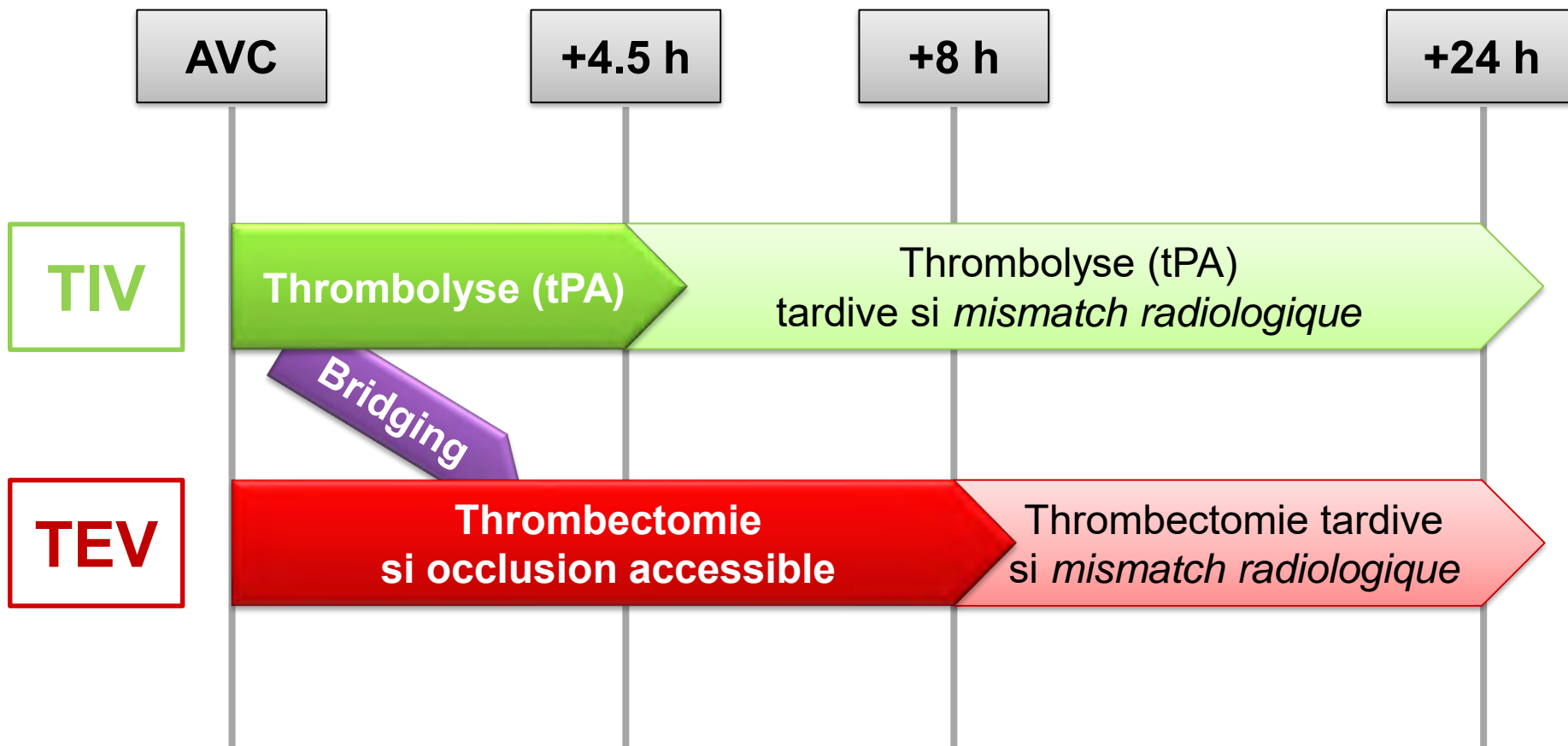
Meta-analyses



Emberson/STTC Lancet 2004; Saver/HERMES JAMA 2016
Jobin/AURORA ESOC 2018; Thomalla/WAKEUP NEJM 2018



Revascularisation des AVC : résumé nouveautés 2018



TIV = Thrombolysse intraveineuse, TEV = Traitement endovasculaire (Stroke Center), Bridging = TIV puis TEV, mismatch radiologique = imagerie spécialisée

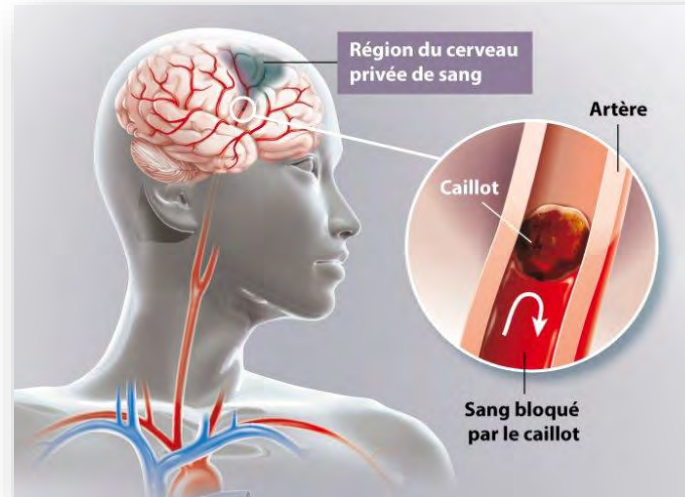
Thrombolyse intraveineuse (TIV)

Thrombectomie endovasculaire (TEV)



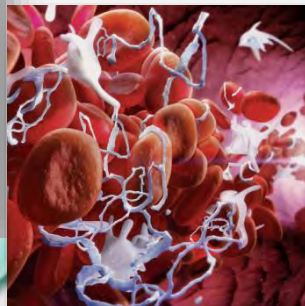
**Stroke
Unit ou
Center**

1995 (TIV)



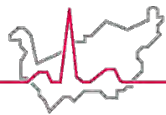
**MHS :
Stroke
Center**

2015 (TEV)



Evolution des traitements CHVR 2012 – 2018

Doublement en 4 ans !



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TYPE DE TRAITEMENT

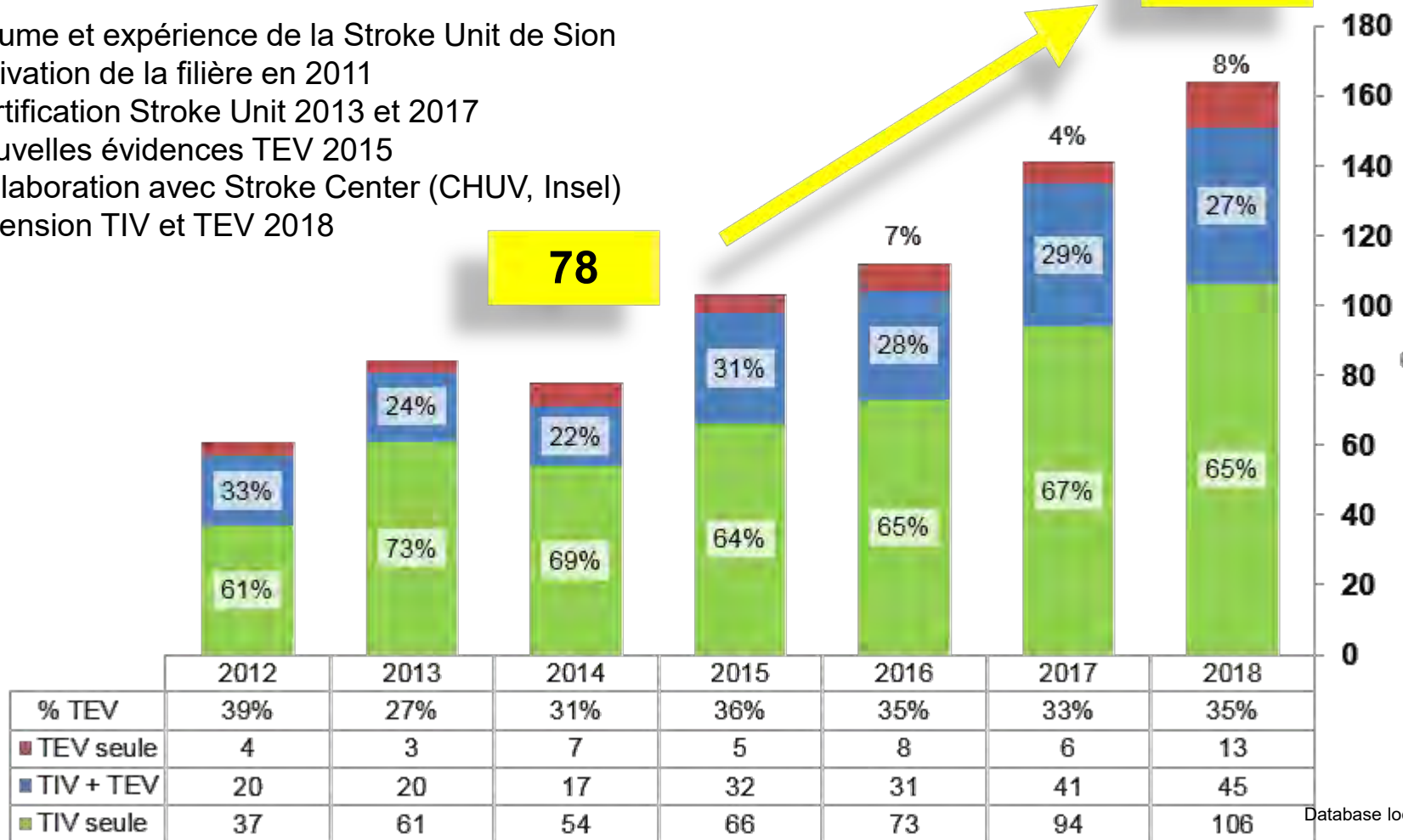
■ TIV seule ■ TIV + TEV ■ TEV seule

**TEV
(1/3)**

164

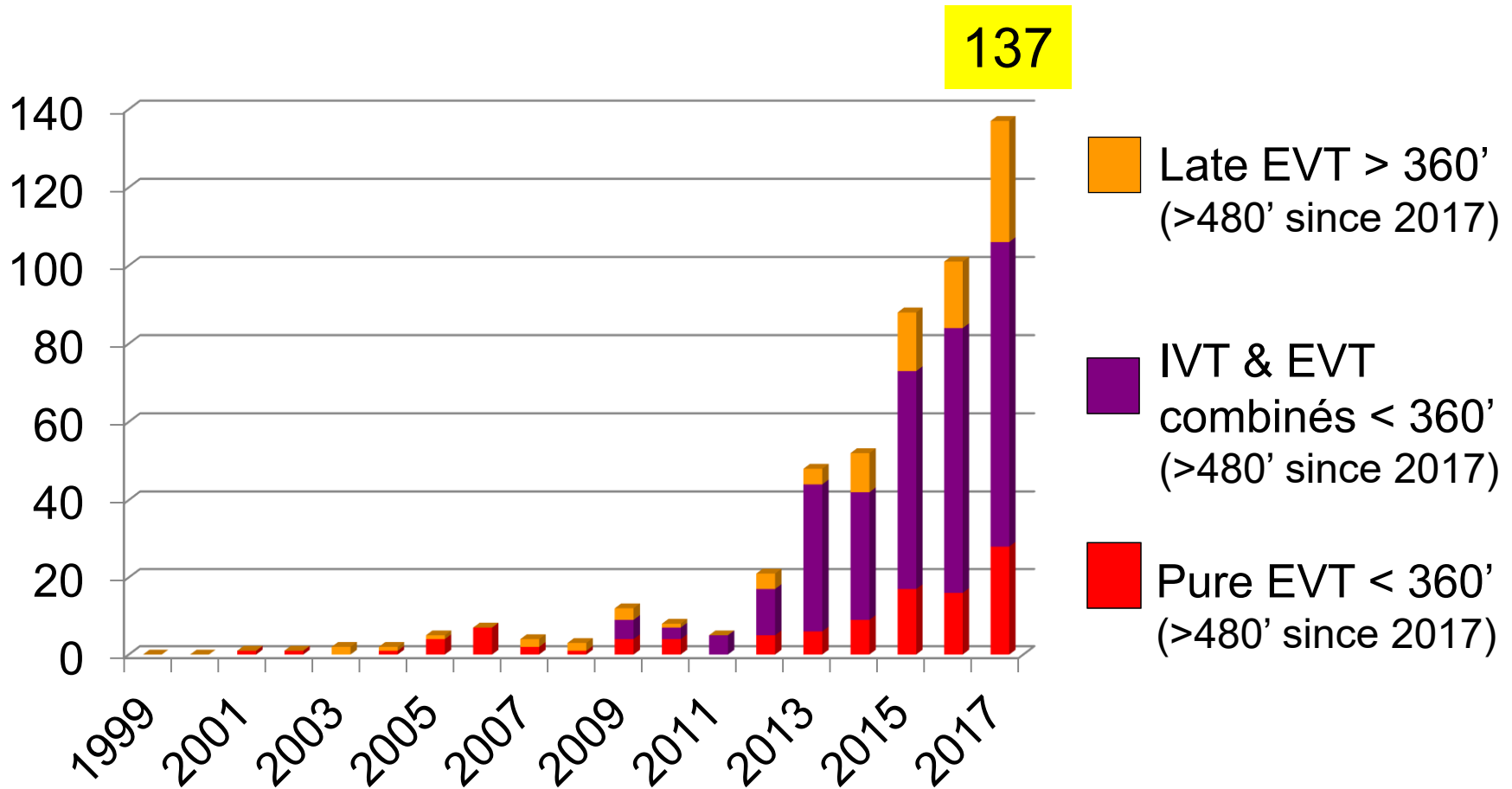
78

- Volume et expérience de la Stroke Unit de Sion
- Activation de la filière en 2011
- Certification Stroke Unit 2013 et 2017
- Nouvelles évidences TEV 2015
- Collaboration avec Stroke Center (CHUV, Insel)
- Extension TIV et TEV 2018



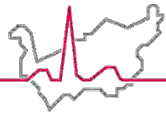
Database locale 2018

Number of endovascular treatments for acute ischemic stroke at CHUV (N=360)



Only endovascular treatments effectively performed

Source:  P. Michel / A. Eskandari



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Spital Wallis

Nouvelles filières pour les cas particuliers ?

Mobile
stroke unit



«drip & drive»



AVC
en
Valais

«drip & ship»



Stroke Unit
Sion

«mothership»

Stroke Center
CHUV, Insel,
HUG

«reverse»

1/3 patients
thrombolysés

Filière AVC 2019 (ne pas diffuser)



PLAN PROVISOIRE

**Suspicion d'AVC
Annonce au 144**

**Nouveau déficit
neurologique**

Etat préalable du patient
à relativiser !

Bonne qualité de vie
(mRS ≤ 3)

relatif !

Qualité de vie limitée
(mRS ≥ 4)

OU

Délai depuis le début de l'AVC



≤ 24h ou
au réveil

24 – 72h

> 72h

G-FAST *

P1



P2

P2

P3

Annonce (checklist)
Acheminement

027 603 1888
Neuro + Urg

027 603 8568
Urg

décision

Pas filière

1 99 88
Filière interne

Destination



Hôpital de Sion
Stroke Unit



repêchage !

S1

Hôpital
de proximité

027 603 1888
Neuro + Urg

Annonce du cas
au neuro
dans les 24h

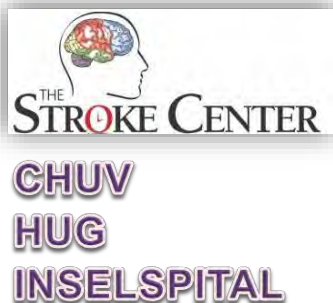
* par l'ambulancier

Neuro garde 24h/24
027 603 44 55

Transfert
Stroke Center



Nouvelle filière valaisanne des AVC 2019



coopération

Sion

Unité cérébrovasculaire du Valais



Sierre
CRR - SUVA
Berner Klinik



Reha Brig



Médias
Campagnes d'information
Médecin
Famille

Médecin traitant
Médecins spécialistes
Patient

OCVS
Urgences H
Services infirmiers

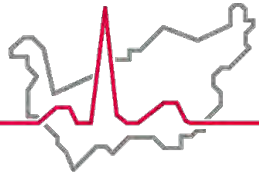
Urgences H
Stroke Unit Sion
(Service de neuro)
Soins intensifs
Stroke Center

Hôpitaux et cliniques de soins
CRR
CTR
Hôpitaux de gériatrie

Domicile
CMS
EMS
CTR
Soins palliatifs

www.attaquerebrale.ch

Adapté des recommandations canadiennes pour la pratique optimale de soins de l'AVC



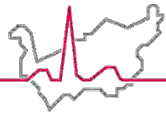
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1. Antithrombotiques
2. Statines
3. Anti-hypertenseurs



Les 3 lignes thérapeutiques principales



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Aspirine... le traitement des 100 dernières années



Traiter 100 patients
pour en améliorer 1 !

Antiplaquettaire ou anticoagulation ?

■ Antiplaquettaires

- AVC sur athéromatose
- AVC lacunaires (microangiopathie)
- AVC d'origine indéterminée (y.c ESUS)



■ Anticoagulation

- AVC avec source cardiaque définie
- AVC
 - à haut risque (FA, valves mécaniques, ...)
 - à bas risque mais AVC récidivant (évidence limitée)
 - sténose ou dissection subocclusive aiguë (évidence limitée)

Choix des antithrombotiques après AVC

- **La plupart du temps y.c ESUS → antiagrégants**
 - Clopidogrel (Plavix)
 - Aspirine (si pas de FRCV)
 - Combinaison ASA+Clopi
 - **3 mois** si athéromatose complexe vulnérable
 - **21 jours** si AVC mineur ou AIT à haut risque (Etude POINT et CHANCE)
 - Autres dans de très rares cas

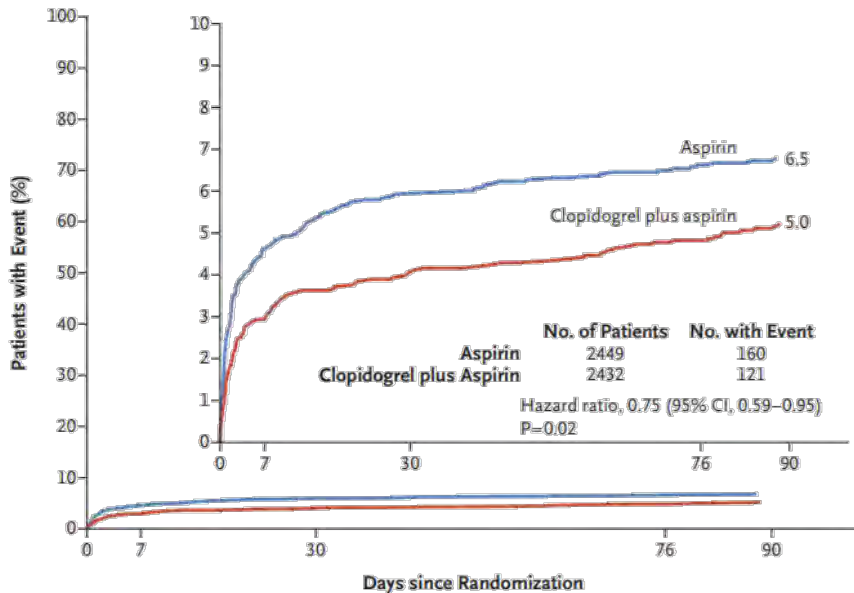
- **Certains AVC spéciaux (d'origine cardiaque, états hypercoagulables, ...) → anticoagulants**
 - Sintrom / Marcoumar
 - **Nouveaux anticoagulants oraux (DOAC)**



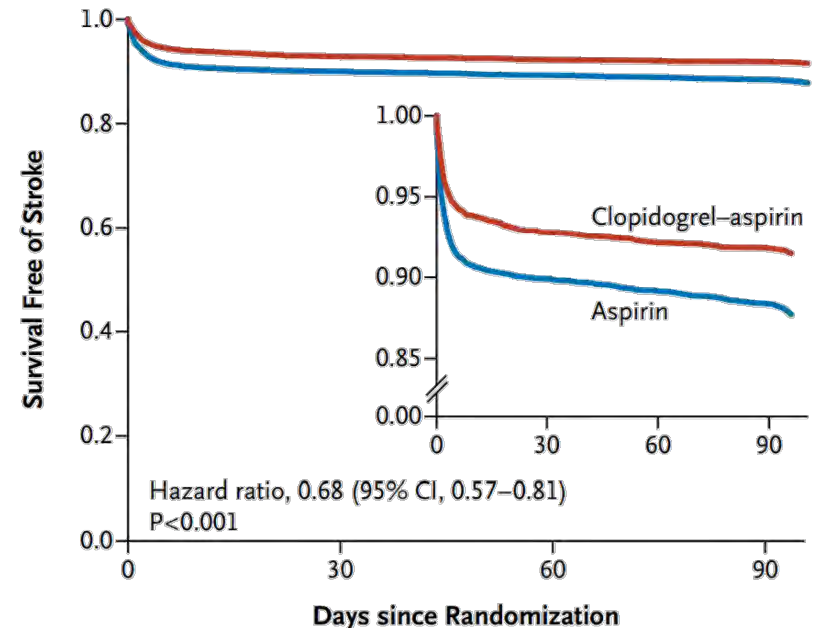
■ 21 JOURS (3 semaines)

**Combinaison
ASA 100 + Clopi 75 meilleure !!!**

Etude POINT 2018



Etude CHANCE 2013

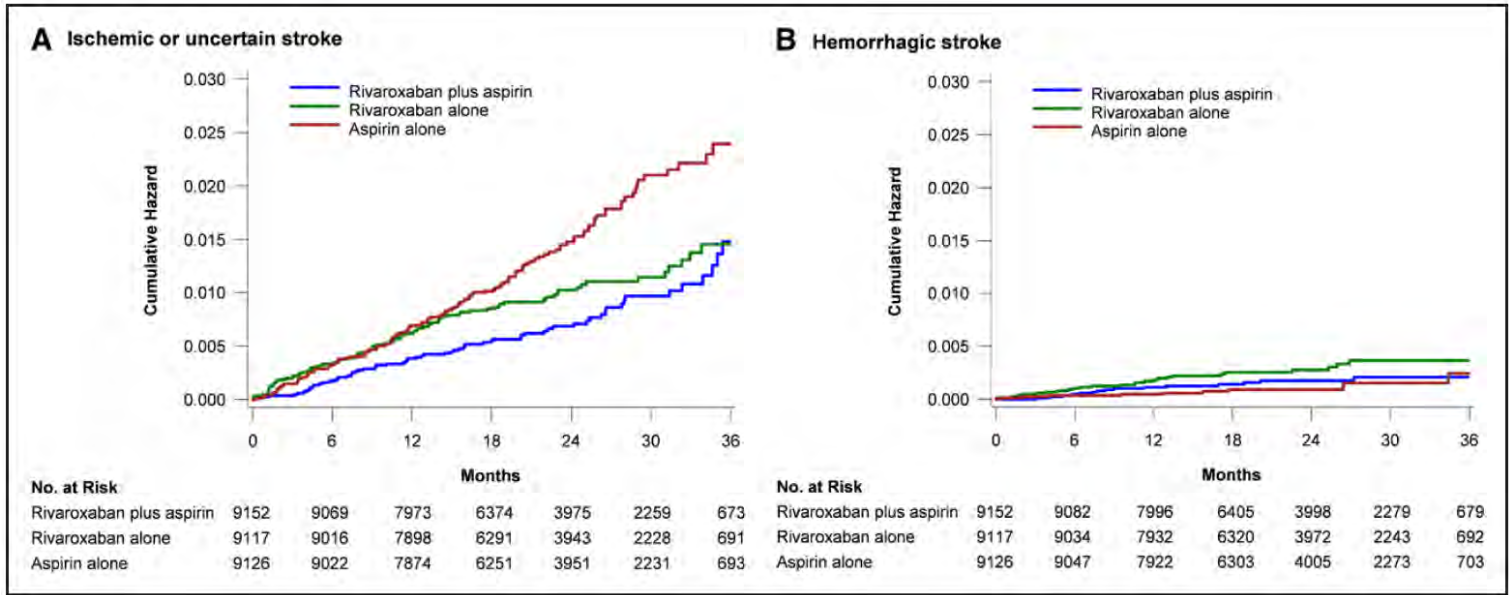
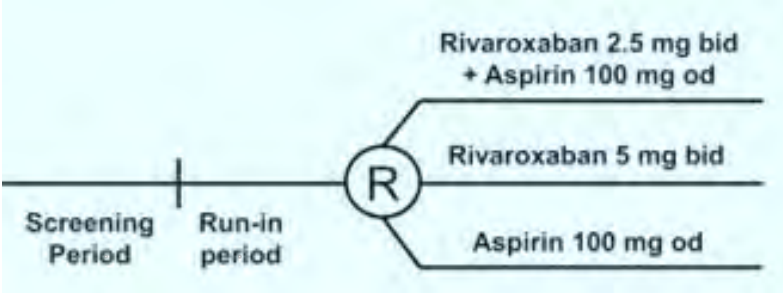


Quelle protection optimale chez patient athéromateux ou vasculopathe stable?

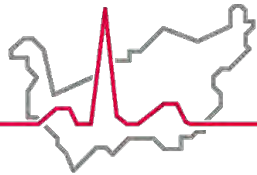


- **COMPASS trial, 27'000 patients**
- **Pas de FA mais athéromatose vasculaire stable (CAD, PAD, ATS carotidienne)**

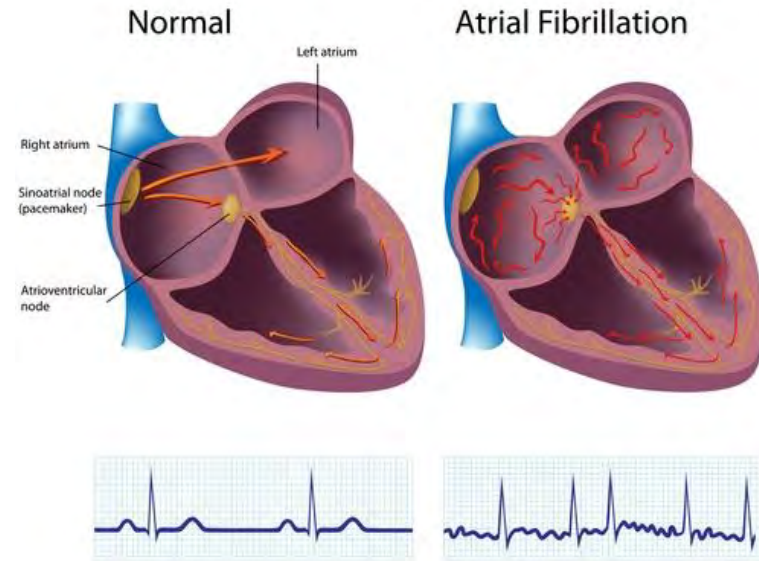
Combinaison
 ASA 100 + Rivaro 2x2.5 meilleure !!!



Circulation. 2019;139:1134–1145. DOI: 10.1161/CIRCULATIONAHA.118.035864

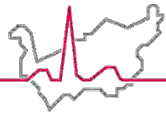


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AVC cryptogénique

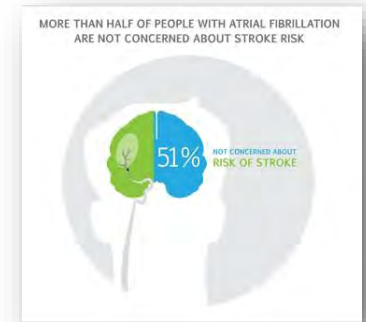
Fibrillation auriculaire



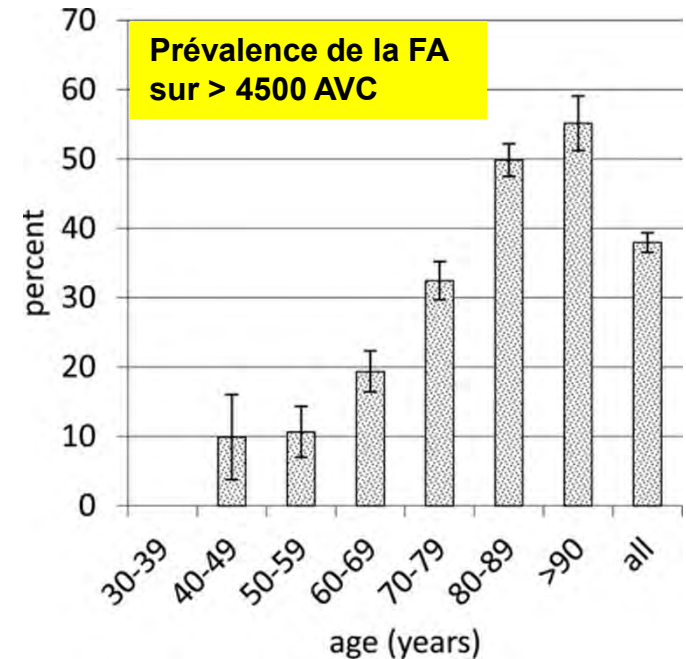
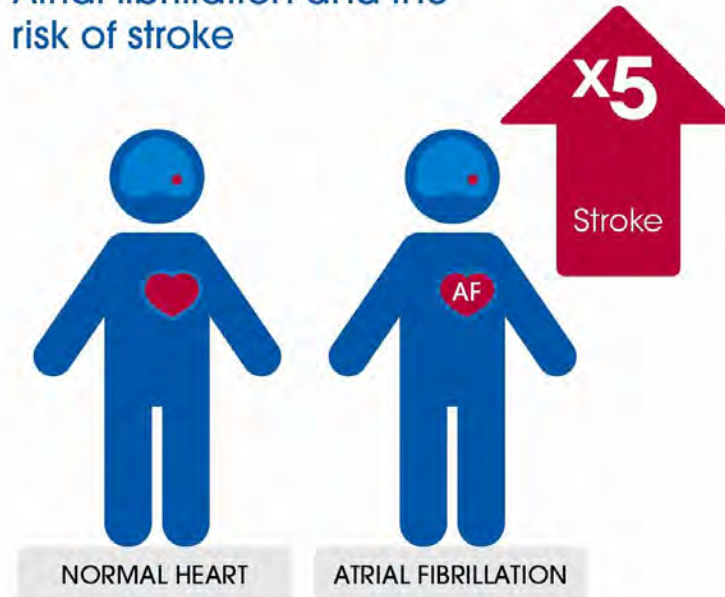
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Accident vasculaire cérébral et FA

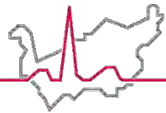
- **Parfois transitoire**
- **9x sur 10 : asymptomatique !!!**
- **Mortalité double à 10ans**
- **Responsable de 25-30% de tous les AVC**



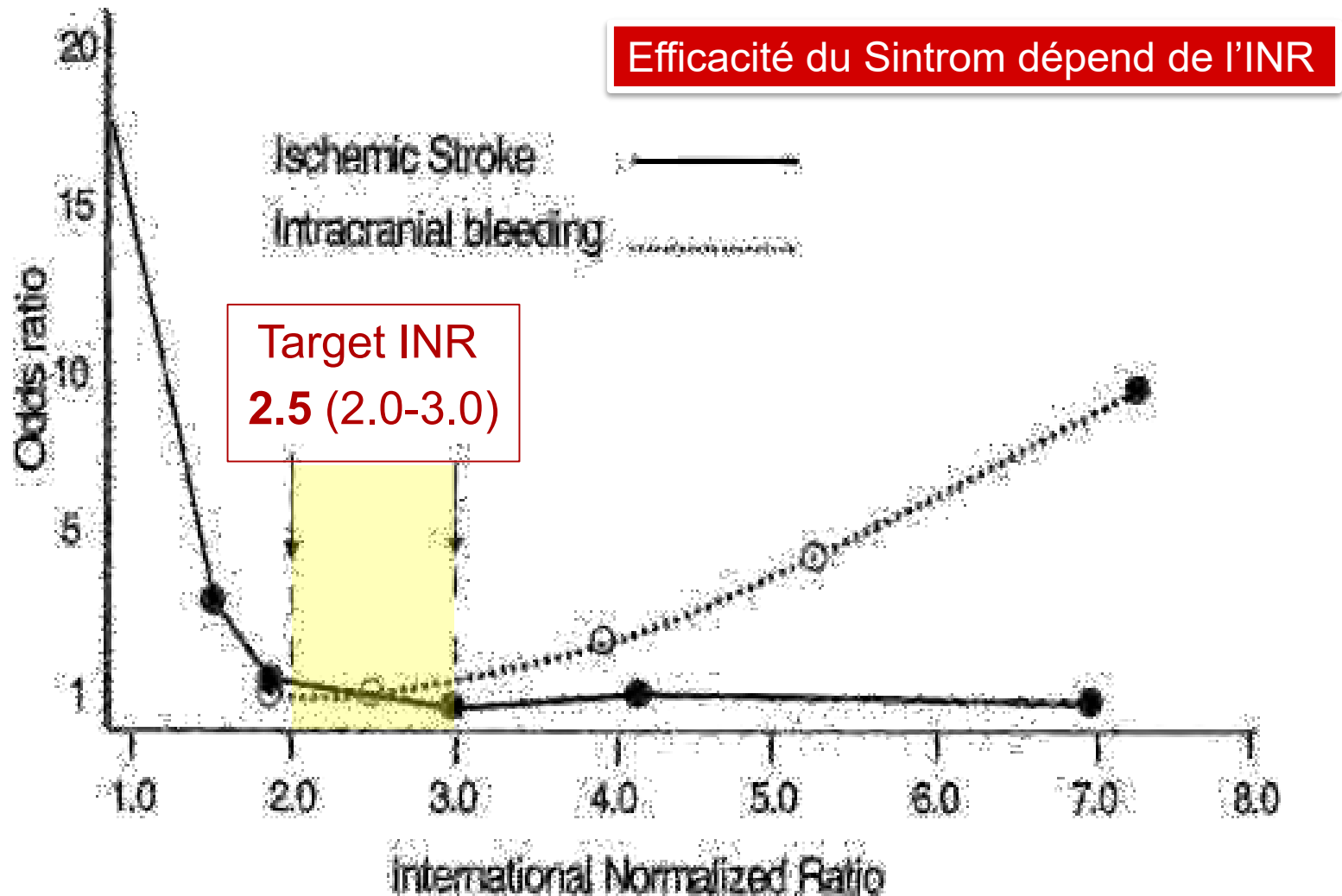
Atrial fibrillation and the risk of stroke

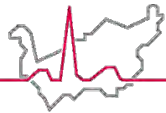


<https://doi.org/10.1161/STROKEAHA.113.002329> Stroke. 2013;44:3103-3108 - Boehringer Ingelheim



Du Sintrom aux Anticoagulants directs (DOAC)





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Bénéfices des DOAC vs Sintrom

DOACs:

↓15% **récidive** d'AVC

↓15% **mortalité**

↓10-15% **hémorragies** majeures

↓55% **hémorragies** intracérébrales



Cause d'AVC inutile !

Eliquis[®]
Pradaxa[®]
Xarelto[®]
Lixiana[®]



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Tous les DOAC ne sont pas égaux !!!

Protection contre les AVC

Risque hémorragique digestif en particulier

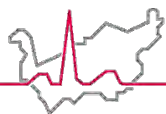
Interactions

Gestion des 3 points clés : **WAR !**

W=Weight, A=Age, R=Renal function

DOAC et risque d'hémorragie digestive

Meilleur profil = Apixaban (Eliquis®)



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In nonvalvular AF, DOAC-related risk for GI bleeding was lower with apixaban than dabigatran or rivaroxaban

Relative association of different direct oral anticoagulant drugs with gastrointestinal bleeding*

Comparisons (median follow-up)	N	Events/100 patient-y	HR (95% CI)†
Rivaroxaban (113 d) vs dabigatran (120 d)	31 574	2.74 vs 2.02	1.20 (1.00 to 1.45)
Apixaban (89 d) vs rivaroxaban (106 d)	13 130	1.34 vs 3.54	0.33 (0.22 to 0.49)
Apixaban (89 d) vs dabigatran (120 d)	13 084	1.38 to 2.73	0.39 (0.27 to 0.58)

*HR = hazard ratio; CI defined in Glossary. Groups were matched using propensity scores based on sociodemographic variables, comorbid conditions, and previous warfarin use.

†Treatment x age interaction: rivaroxaban vs dabigatran, P = 0.10; apixaban vs rivaroxaban, P = 0.36; apixaban vs dabigatran, P = 0.54.

SYSTEMATIC REVIEWS AND META-ANALYSES

Siddharth Singh, Section Editor

Risk of Gastrointestinal Bleeding in Patients Taking Non-Vitamin K Antagonist Oral Anticoagulants: A Systematic Review and Meta-analysis

Corey S. Miller,^{*,a} Alastair Dorreen,^{†,a} Myriam Martel,[§] Thao Huynh,^{||} and Alan N. Barkun^{§,¶}

	Studies, n	ITT patients	OR (95% CI)
Primary outcome			
Major GI bleeding	28	129,357	0.98 (0.80–1.21)
Secondary outcomes			
Total GI bleeding	3	3390	1.47 (0.97–2.22)
CRNM GI bleeding	8	16,969	0.93 (0.64–1.36)
Minor GI bleeding	1	222	3.32 (0.25–44.34)
Upper GI bleeding	4	23,224	0.96 (0.77–1.20)
Lower GI bleeding	4	23,211	0.88 (0.67–1.15)
Subgroup analyses			
Individual NOAC			
Apixaban	9	43,647	0.81 (0.64–1.02)
Dabigatran	5	27,485	1.27 (1.04–1.55)
Edoxaban	6	31,050	0.93 (0.78–1.11)
Rivaroxaban	8	27,175	1.40 (1.15–1.70)
Comparator			
Warfarin	14	95,311	0.96 (0.75–1.21)
Enoxaparin	9	23,167	0.99 (0.47–2.05)
Aspirin	1	5599	0.85 (0.39–1.84)
Placebo	4	5280	2.50 (0.61–10.16)

<http://dx.doi.org/10.7326/ACPJC-2017-167-4-021>

Clinical Gastroenterology and Hepatology 2017;15:1674–1683 <http://dx.doi.org/10.1016/j.cgh.2017.04.031>

Effectiveness and Safety of Apixaban, Dabigatran, and Rivaroxaban Versus Warfarin in Frail Patients With Nonvalvular Atrial Fibrillation

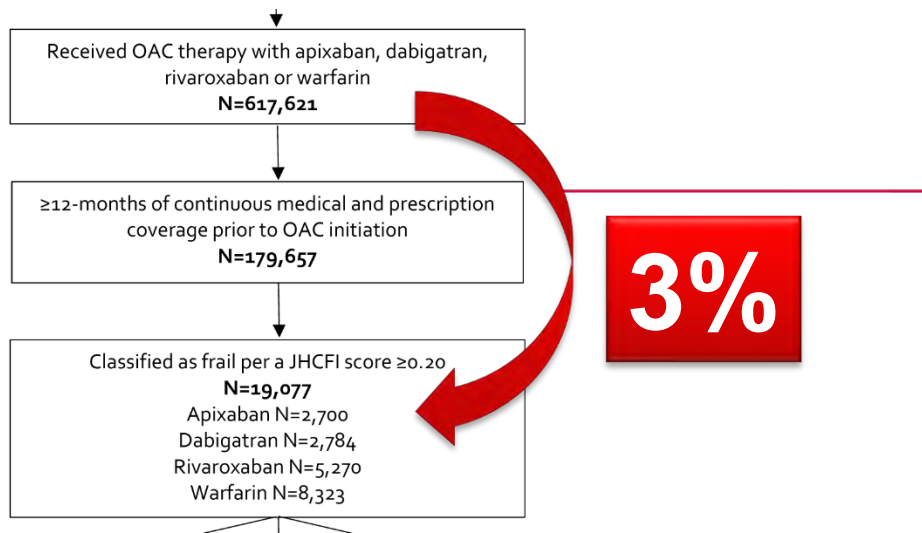
Brandon K. Martinez, PharmD; Nitesh A. Sood, MD; Thomas J. Bunz, PharmD, PhD; Craig I. Coleman, PharmD

Conclusions—Our study found rivaroxaban but not apixaban or dabigatran to be associated with reduced SSE versus warfarin in frail nonvalvular atrial fibrillation patients. No direct-acting oral anticoagulants demonstrated a significant difference in major bleeding versus warfarin. (*J Am Heart Assoc.* 2018;7:e008643. DOI: 10.1161/JAHA.118.008643.)

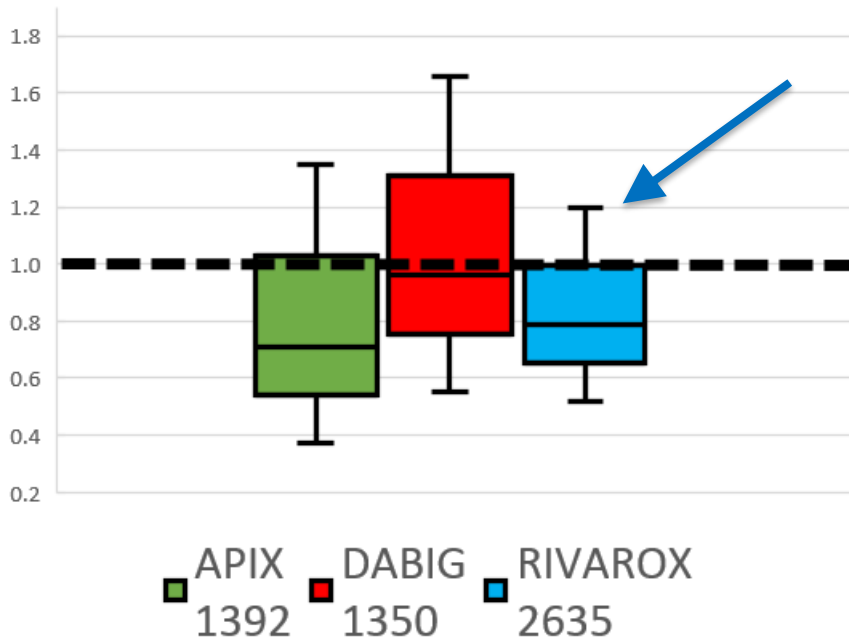
Table 2. Baseline Characteristics of Propensity Score–Matched Frail Direct-Acting Oral Anticoagulant and Warfarin Patients With Nonvalvular Atrial Fibrillation

Variable	Apixaban (n=1392)	Warfarin (n=1392)	Absolute Standardized Difference (%)	Dabigatran (n=1350)	Warfarin (n=1350)	Absolute Standardized Difference (%)	Rivaroxaban (n=2635)	Warfarin (n=2635)	Absolute Standardized Difference (%)
Age, y, median (IQR)*	86 (83, 89)	86 (83, 89)	0.00	85 (82, 88)	86 (82, 89)	0.01	85 (82, 89)	86 (82, 89)	0.01
65 to 74 y, %	1.4	1.7	0.01	2.5	2.1	0.03	2.1	2.4	0.02
≥75 y, %	98.4	98.3	0.01	97.5	97.9	0.02	97.8	97.5	0.02
Male sex, %	63.7	62.8	0.01	64.7	62.7	0.02	65.2	64.4	0.02
JHCFI score, median (IQR)	0.30 (0.24, 0.40)	0.30 (0.24, 0.39)	0.00	0.28 (0.23, 0.35)	0.28 (0.24, 0.37)	0.00	0.28 (0.24, 0.38)	0.29 (0.24, 0.38)	0.00
Receiving reduced dose, %	56.1	NA	NA	41.3	NA	NA	56.5	NA	NA

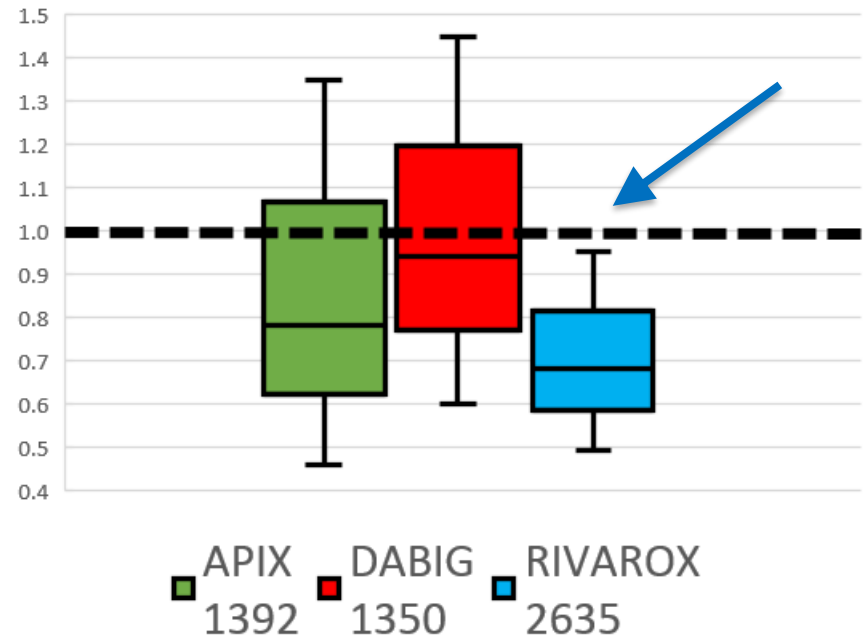
Hypersélection !

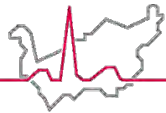


SSE at 1y (HR), DOAC vs VKA



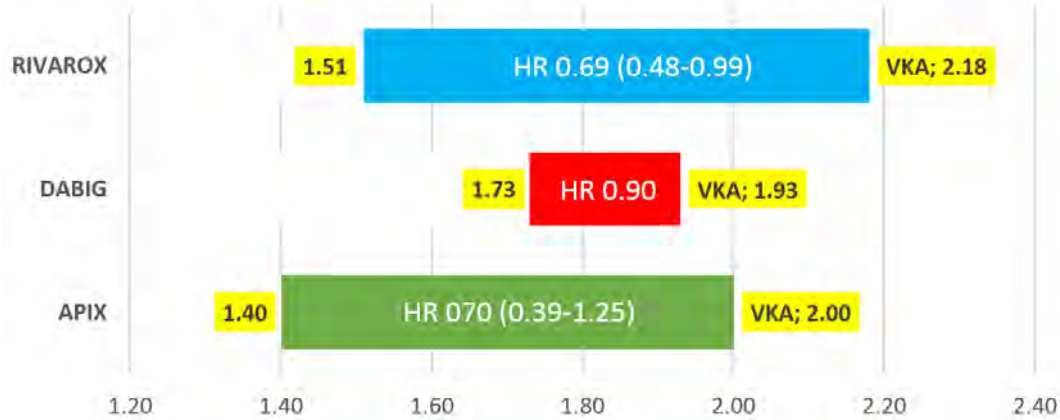
SSE at 2y (HR), DOAC vs VKA





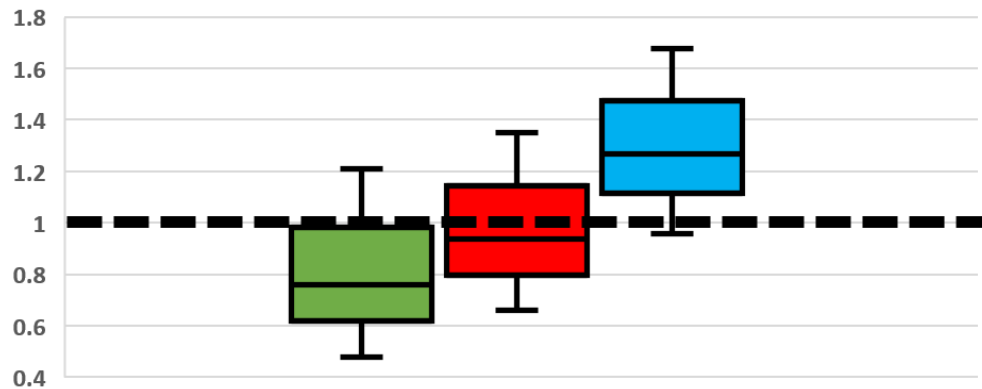
Stroke and GI bleedings

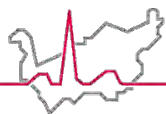
ISCHEMIC STROKE events / 100-P-Y



GI bleedings at 2y

■ APIX ■ DABIG ■ RIVAROX





Poster session ACC.18 ... pas les mêmes résultats !

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ACC.18

290
JACC March 20, 2018
Volume 71, Issue 11

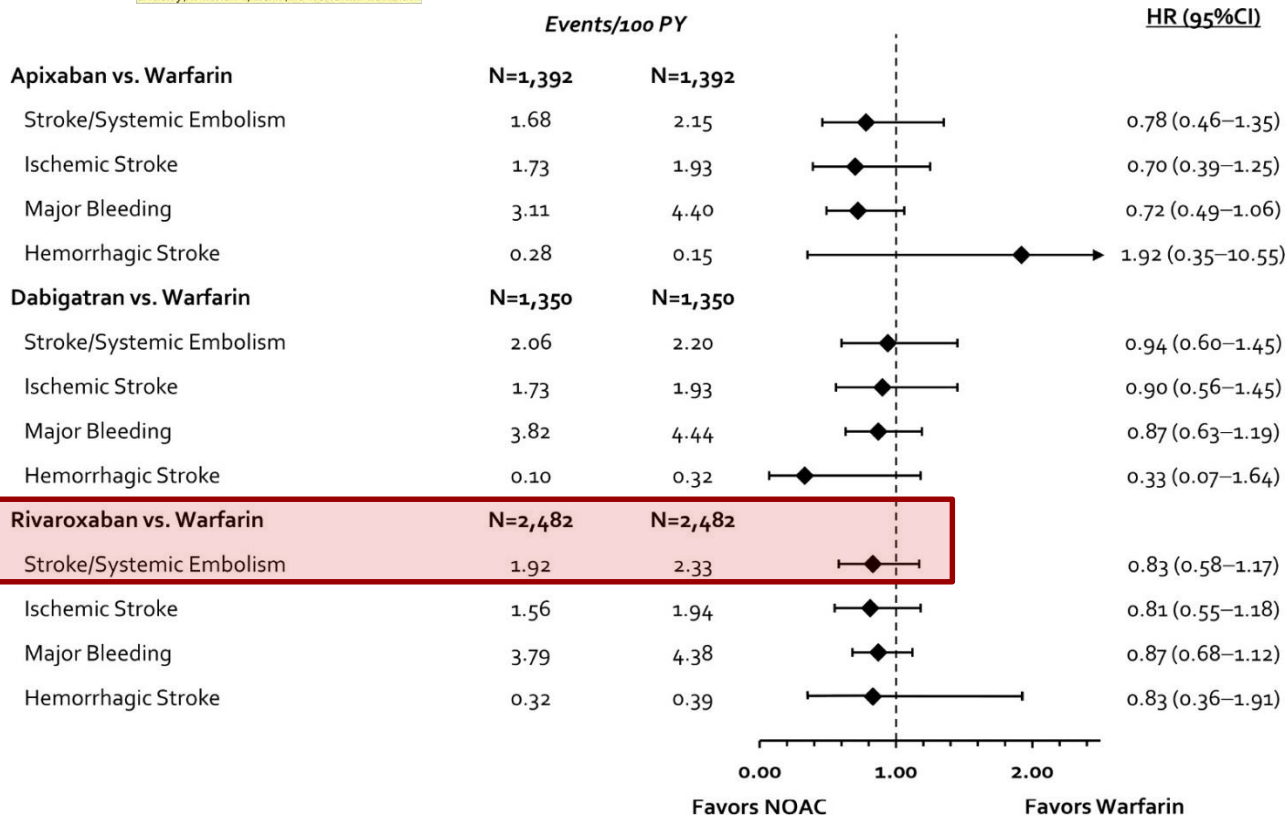
Sources of Funding

This study was supported by Bayer AG, Berlin, Germany. The sponsor had no role in study design; in the collection, analysis and interpretation of data; in the writing of the report; or in the decision to submit the article for publication.

Arrhythmias and Clinical EP

EFFECTIVENESS AND SAFETY OF APIXABAN, DABIGATRAN AND RIVAROXABAN VERSUS WARFARIN IN FRAIL PATIENTS WITH NONVALVULAR ATRIAL FIBRILLATION

Moderated Poster Contributions
Arrhythmias and Clinical EP Moderated Poster Theater, Poster Hall, Hall A/B
Sunday, March 11, 2018, 10:00 a.m.-10:10 a.m.



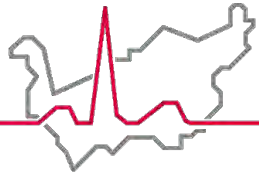
[https://doi.org/10.1016/S0735-1097\(18\)30831-3](https://doi.org/10.1016/S0735-1097(18)30831-3)

Vous devriez savoir

→ informez vos patients



- **Eliquis®**
 - **Pas de restriction** particulière pour la prise
- **Xarelto®**
 - Toujours **durant les repas**
 - sinon absorption du médicament diminue !!!
 - risque de sous-anticoagulation !!!
- **Dabigatran®**
 - **Ne jamais ouvrir les capsules**
 - sinon biodisponibilité augmente de 80%
 - risque de sur-anticoagulation !!!



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Traitement ?
Faut-il intervenir ?

**"La vérité d'aujourd'hui
n'est pas forcément
celle de demain"**

Foramen Ovale Perméable

FOP un facteur de risque pour les AVC ?

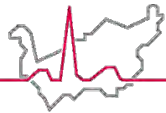
- Prévalence du FOP dans la **population générale = 25%**

→ **le FOP n'est pas une maladie !**



- Risque d'AVC chez les personnes en BSH avec FOP : HR 1.5
- Prévalence du FOP chez les **AVC cryptogénique = 40%**
- Sur l'ensemble des AVC, l'implication du FOP est mineure
- **Causalité ?** (embolie paradoxale, thrombus local, ...)
- **Facteurs favorisant controversés** (taille RLS, ASIA, TVP...)
- **Récidive faible ~1 % par an**, (idem AVC cryptogéniques)
- **Autre étiologie retrouvée chez 40% des récurrences**

→ **PRUDENCE DANS L'ATTITUDE, *primum non nocere***

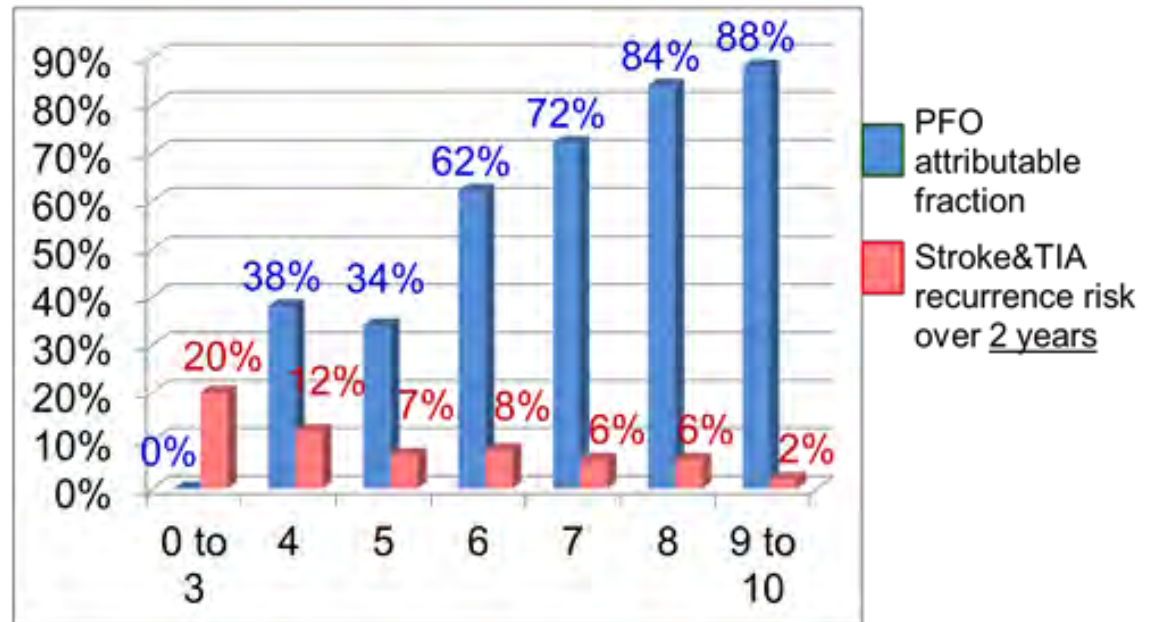


RoPE score

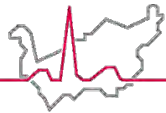
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RoPE score		
No history of hypertension		1
No history of diabetes		1
No history of stroke or TIA		1
Non - smoker		1
Cortical infarct on imaging		1
Age	18 - 29 years	5
	30 - 39 years	4
	40 - 49 years	3
	50 - 59 years	2
	60 - 69 years	1
	≥ 70 years	0
Score 0-10 (10 = maximal risk)		

Increasing RoPE score
→ Increasing « PFO attributable fraction »
→ Decreasing TIA/Stroke recurrence risk

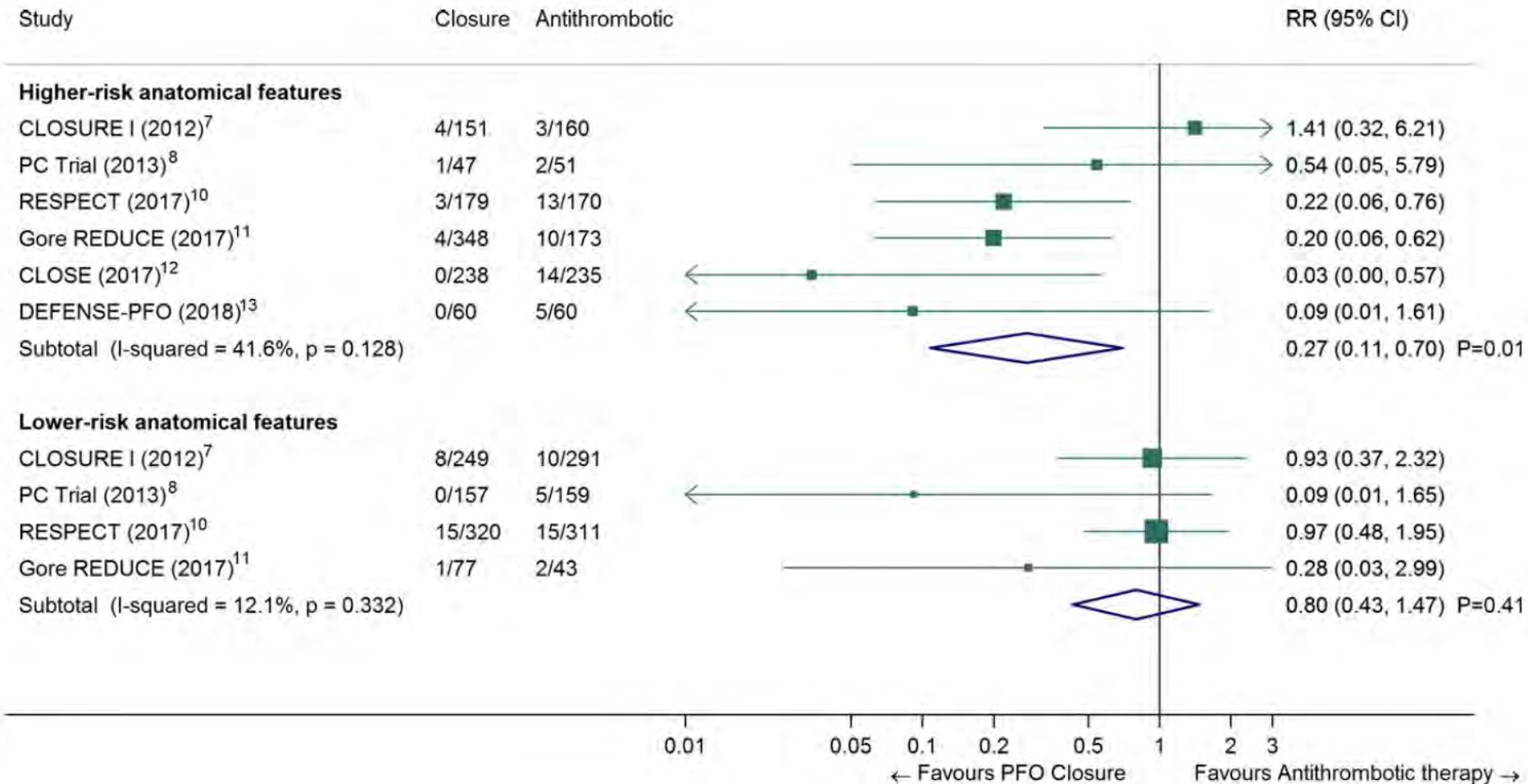


Méta-analyse : Fermeture de FOP supérieure au traitement antithrombotique



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- Pour les FOP à risque (modérés/larges et/ou ASIA)

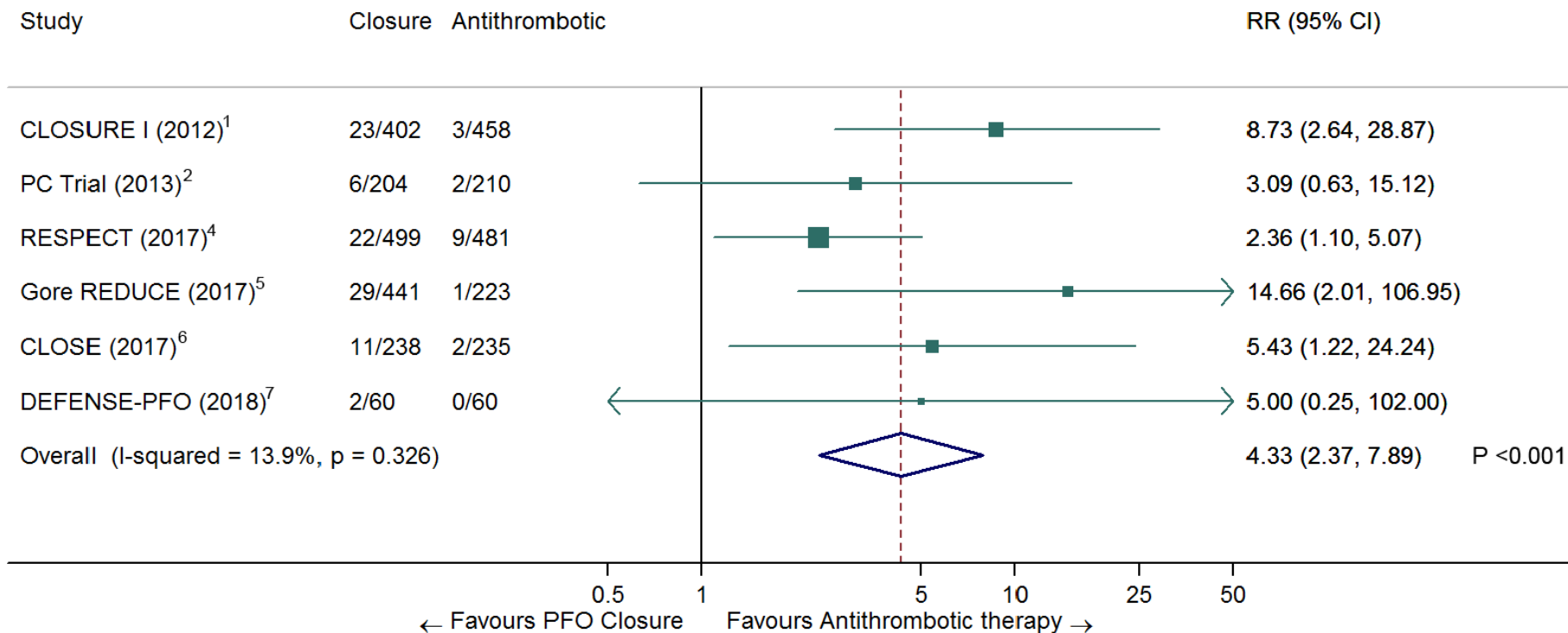


<https://doi.org/10.1161/JAHA.117.008356>

Méta-analyse : Fermeture de FOP augmente de 4.3x le risque de FA nouvelle



- certains devices font mieux (Amplatzer)



Risques liés à la fermeture du FOP :

- **7% dans cette analyse rétrospective de 1887 patients (10.9% > 60 ans vs 4.9% ≤ 60 ans)**
- **2.6% dans la méta-analyse des études**

Table 2. Risk of Adverse Outcomes During Hospitalization for Patent Foramen Ovale Closure

Characteristic*	Rate of Adverse Outcomes (95% CI)
Total adverse outcomes	7.0% (5.9%–8.2%)
Individual adverse outcomes†	
Atrial fibrillation/flutter	3.7% (2.9%–4.6%)
Vascular complication	3.0% (2.3%–3.9%)
Hematoma/hemorrhage only	2.7% (2.0%–3.5%)
Cardiac tamponade/perforation	0.5% (0.2%–0.9%)
Death	0.3% (0.1%–0.6%)
Pneumothorax/hemothorax	0.1% (0%–0.3%)

CI indicates confidence interval.

*Data are presented as % (95% CI), unless otherwise specified.

†Numbers do not sum to group totals because some patients had multiple outcomes.

Fermeture de FOP : *mes recommandations 2018*

- Les études ne permettent pas de conclure si dans certains cas, l'anticoagulation pourrait être supérieure à la fermeture

In conclusion, there is now enough evidence to reasonably conclude that PFO closure is superior to antithrombotic therapy with regard to the risk of stroke recurrence in patients with cryptogenic stroke. Patients with an associated atrial septal aneurysm or a large shunt may benefit more from PFO closure. This is a step forward that will benefit many patients.

Clinique	FOP	Traitement
Asymptomatique	FOP ± ASIA	aucun
AVC cryptogénique	FOP léger et/ou absence d'ASIA	Aspirine 100mg
	FOP modéré/sévère et/ou ASIA	Proposer fermeture FOP → colloque multidisciplinaire

At the systems level, the management of patients with PFO and cryptogenic stroke requires close coordination between neurologists and cardiologists expert in the evaluation and treatment of neurocardiovascular disease.⁴⁰ An emerging model is a jointly

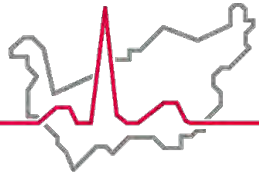
▪ Colloque neurovasculaire multidisciplinaire

- Neurologues
- Cardiologues
- (Hématologues)
- *Vous*

Email: neurovasc@hopitalvs.ch

Secrétariat: **027 603 18 40**

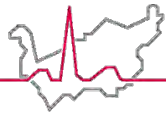
FAX: **027 603 40 93**



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Endartériectomie ? Stenting? Traitement conservateur ?

Sténose carotidienne



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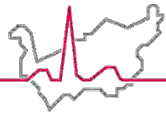
Endartériectomie et stenting carotidien

The NEW ENGLAND JOURNAL *of* MEDICINE

ORIGINAL ARTICLE

Long-Term Results of Stenting versus Endarterectomy for Carotid-Artery Stenosis

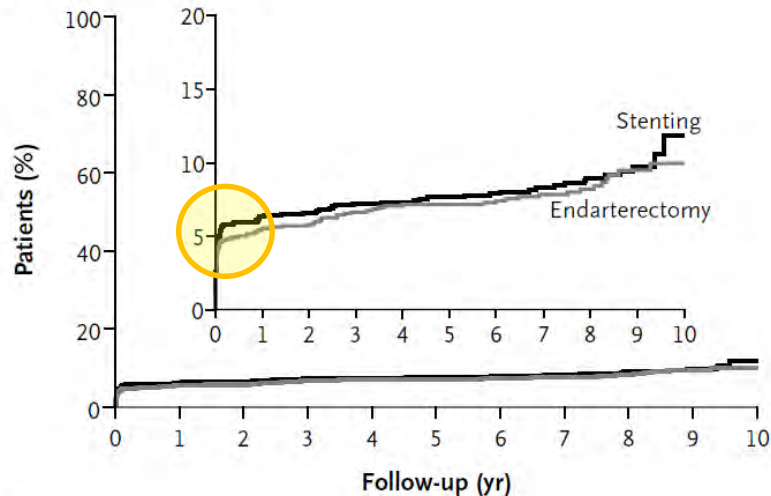
Thomas G. Brott, M.D., George Howard, Dr.P.H., Gary S. Roubin, M.D., Ph.D.,



Pas de différence majeure à 10 ans, **mais**

- Les courbes se suivent étroitement jusqu'à 10 ans, mais il y a une **divergence initiale** qui perdure, liée à la **surmortalité et un risque augmenté d'AVC x3 périprocédural (30 jours)**

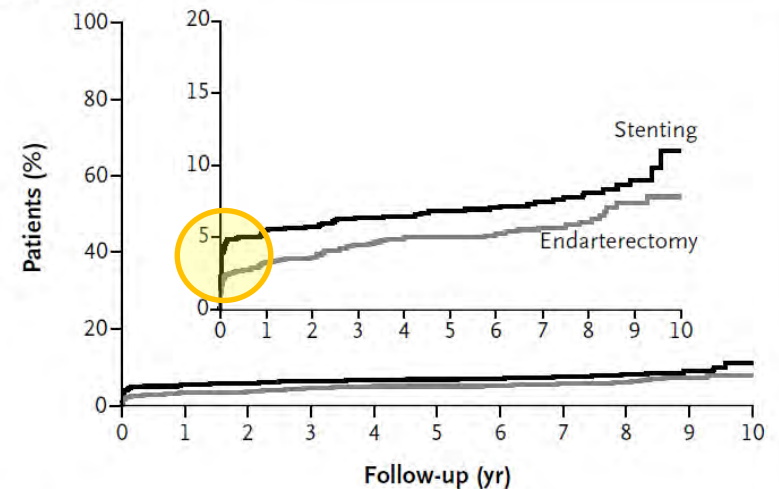
A Primary Composite End Point



No. at Risk

Endarterectomy	1240	1104	1036	949	833	736	695	620	438	243	66
Stenting	1262	1103	1041	972	884	774	738	676	477	264	68

B Stroke or Death

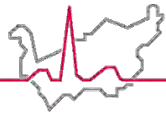


No. at Risk

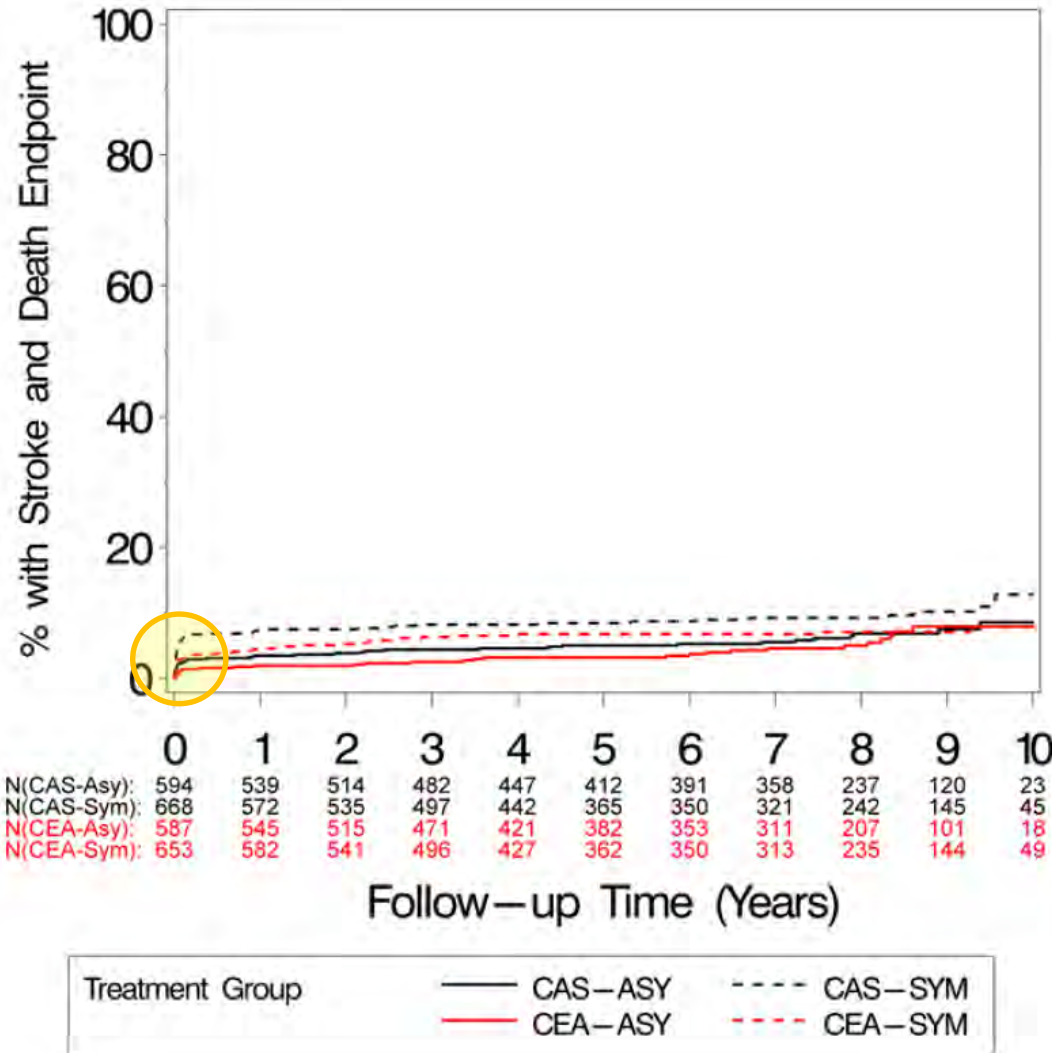
Endarterectomy	1240	1127	1056	967	848	744	703	624	442	245	67
Stenting	1262	1111	1049	979	889	777	741	679	479	265	68

In the case of stenting, more than half the ipsilateral-vessel strokes over a 10-year period occurred within the first month

Idem pour sympto vs asymptomatique. La divergence est surtout initiale !

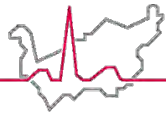


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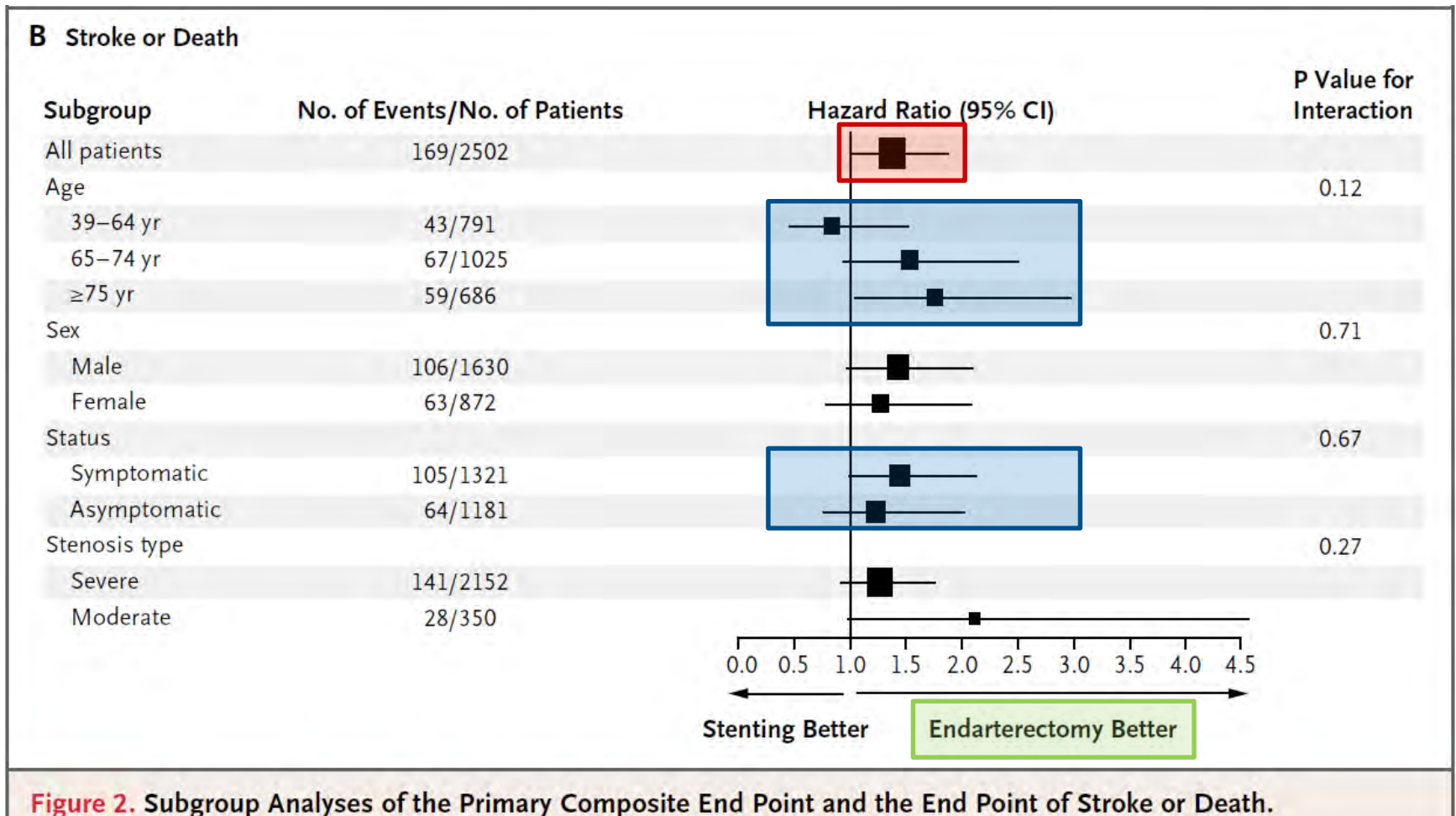


The Stroke and Death endpoint included any stroke or death from any cause during the periprocedural period or ipsilateral stroke within 10 years after randomization. The Kaplan–Meier curves are for asymptomatic (ASY) and symptomatic (SYM) patients undergoing carotidartery stenting (CAS) and those undergoing carotid endarterectomy (CEA) in whom the stroke and death endpoint occurred, according to year of follow-up

Les patients âgés avec sténose symptomatique et les hommes bénéficient plus de l'endartériectomie



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Colloque multidisciplinaire des sténoses

- Neurologues, chirurgiens vasculaires, neuroradiologues
- Colloque hebdo: **LUNDI 17:00** salle de radiologie étage B
- neurovasc@hopitalvs.ch
- Recommandations générales (à individualiser !):

Sexe	Âge	Sympto		Asympto
		50-69%	70-99%	70-99%
Homme	< 70	CEA (CAS)	CEA (CAS)	NON (CEA)
	≥ 70	CEA	CEA	NON (CEA)
Femme	< 70	CEA (NON)	CEA (CAS)	NON (CEA)
	≥ 70	CEA (NON)	CEA	NON

CEA : endartériectomie, CAS : stenting, NON : traitement conservateur, () : 2^e choix

Questions?

Merci
pour
votre
attention

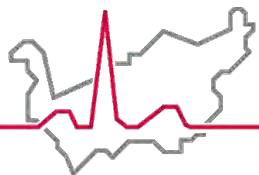


**WITH A STROKE,
TIME LOST IS BRAIN LOST.**

Learn more at StrokeAssociation.org or 1-888-4-STROKE.

Ad
Council

American Stroke
Association.
A Division of American
Heart Association



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Mon téléphone : 027 603 85 63

Neuro garde : 027 603 44 55