

# Découvertes fortuites de lésions neurovasculaires

QUALITÉ

INTÉGRITÉ

INNOVATION

COLLABORATION

PERFORMANCE

QUALITÉ

INTÉGRITÉ

INNOVATION

COLLABORATION

PERFORMANCE

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# Conflits d'intérêts

- Aucun

# PLAN

Épidémiologie, signification clinique et prise en charge générale des lésions neurovasculaires de découverte fortuite

- Lésions ischémiques
  - Microvasculaires
  - Infarctus subclinique
- Lésions hémorragiques
  - Microhémorragies (microbleeds)
  - Sidérose superficielle
- Anomalies vasculaires structurales
  - Anévrismes
  - Malformations artérioveineuses
  - Angiomes caverneux



PHOTOS: ADRIEN WILLIAMS, CHRISTOPHER BARRETT, PAISY MCEIROW

# Lésions fortuites: Études populationnelles

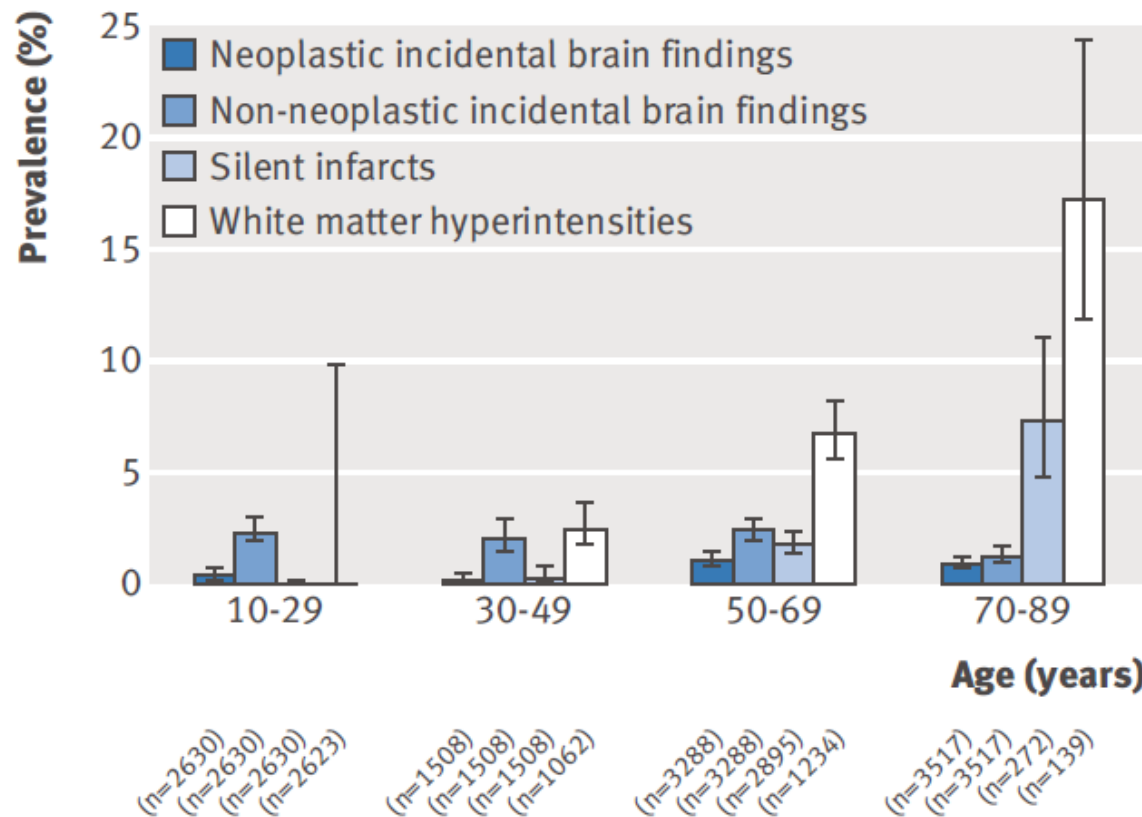
BMJ

n=19,559

Incidental findings on brain magnetic resonance imaging: systematic review and meta-analysis *BMJ* 2009;339:b3016

| Study                        | Country     | Total sample size | Mean (range) age (years) | % male |
|------------------------------|-------------|-------------------|--------------------------|--------|
| Wahlund 1989 <sup>w2</sup>   | Sweden      | 101               | NS (NS)                  | NS     |
| Yue 1997 <sup>w3</sup>       | USA         | 3672              | NS (≥65)                 | NS     |
| Katzman 1999 <sup>w4</sup>   | USA         | 1000              | 29 (3-83)                | 55     |
| Onizuka 2001 <sup>w5</sup>   | Japan       | 4000              | 56 (24-85)               | 50     |
| Lubman 2002 <sup>w6</sup>    | Australia   | 98                | 27 (NS)                  | 63     |
| Kim 2002 <sup>w7</sup>       | USA         | 225               | 11 (0-18)                | 44     |
| Illes 2004 <sup>w8</sup>     | USA         | 151               | 47 (18-90)               | 54     |
| Goehde 2005 <sup>w9</sup>    | Germany     | 298               | 50 (31-73)               | 83     |
| Tsushima 2005 <sup>w10</sup> | Japan       | 1113              | 53 (22-84)               | 68     |
| Weber 2006 <sup>w11</sup>    | Germany     | 2536              | 21 (17-35)               | 100    |
| Alphs 2006 <sup>w12</sup>    | USA         | 656               | 61 (35-82)               | 100    |
| Kumra 2006 <sup>w13</sup>    | USA         | 60                | NS (10-21)               | NS     |
| Baumgart 2007 <sup>w14</sup> | Germany     | 1007              | 55 (40-67)               | 71     |
| Vernooij 2007 <sup>w1</sup>  | Netherlands | 2000              | 63 (46-97)               | 48     |
| Lee 2008 <sup>w15</sup>      | Taiwan      | 2164              | 52 (17-89)               | 57     |
| Kumar 2008 <sup>w16</sup>    | Australia   | 478               | NS (60-64)               | 53     |

# Études populationnelles: lésions ischémiques



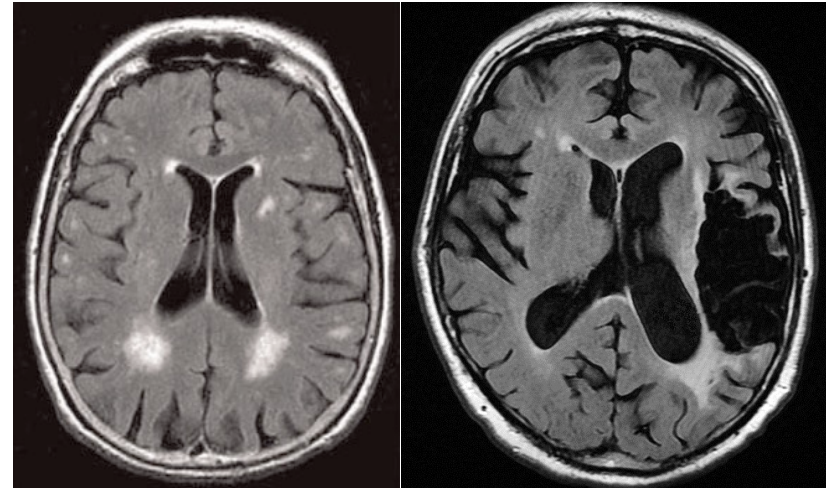
BMJ 2009;339:b3016

# Brain Vascular Malformations

BMJ

Incidental findings on brain magnetic resonance imaging:  
systematic review and meta-analysis *BMJ* 2009;339:b3016

|                                                     | Number<br>with<br>abnormality | Number<br>needed<br>to scan | Prevalence (%)<br>(95% CI)                                                            | Prevalence (%)<br>(95% CI) |
|-----------------------------------------------------|-------------------------------|-----------------------------|---------------------------------------------------------------------------------------|----------------------------|
| <b>Structural vascular abnormalities (n=15 559)</b> |                               |                             |                                                                                       |                            |
| Aneurysm                                            | 67                            | 286                         |    | 0.35 (0.13 to 0.67)        |
| Cavernous malformation                              | 23                            | 625                         |  | 0.16 (0.10 to 0.23)        |
| Arteriovenous malformation                          | 7                             | 2000                        |  | 0.05 (0.01 to 0.10)        |

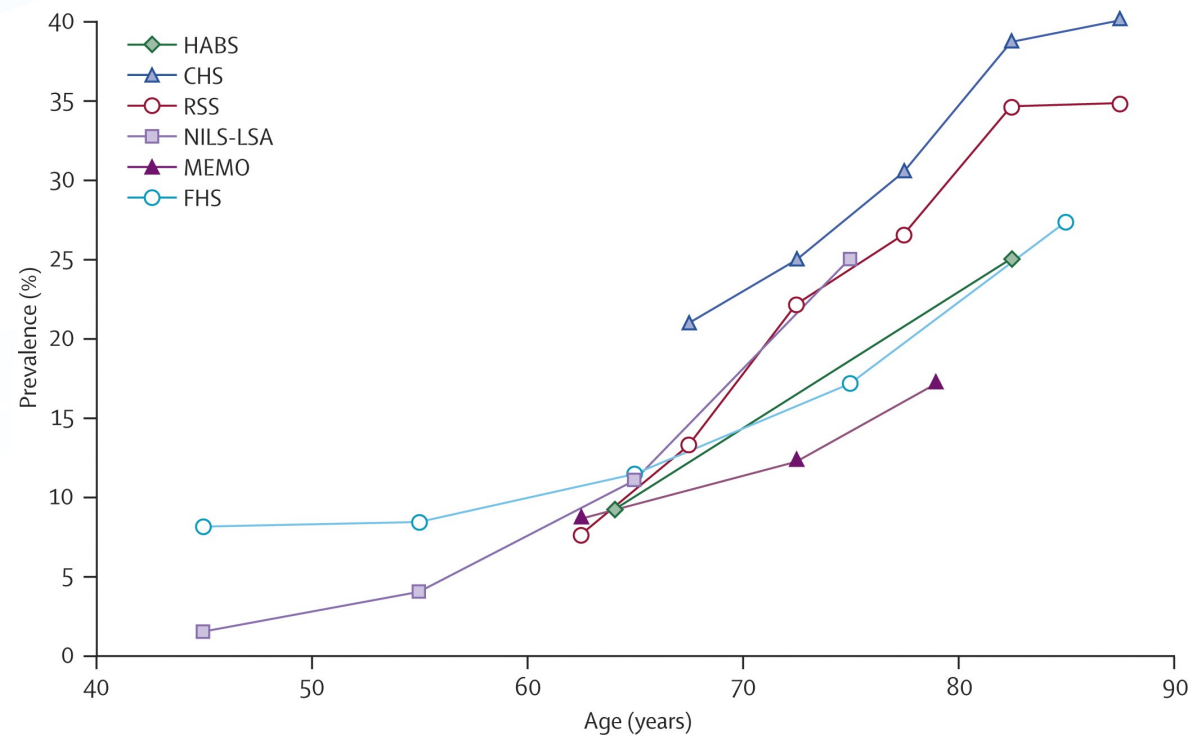


# Anomalies ischémiques

Microvasculaires (anomalies de la matière blanche)

Infarctus subclinique

# Anomalies de la matière blanche

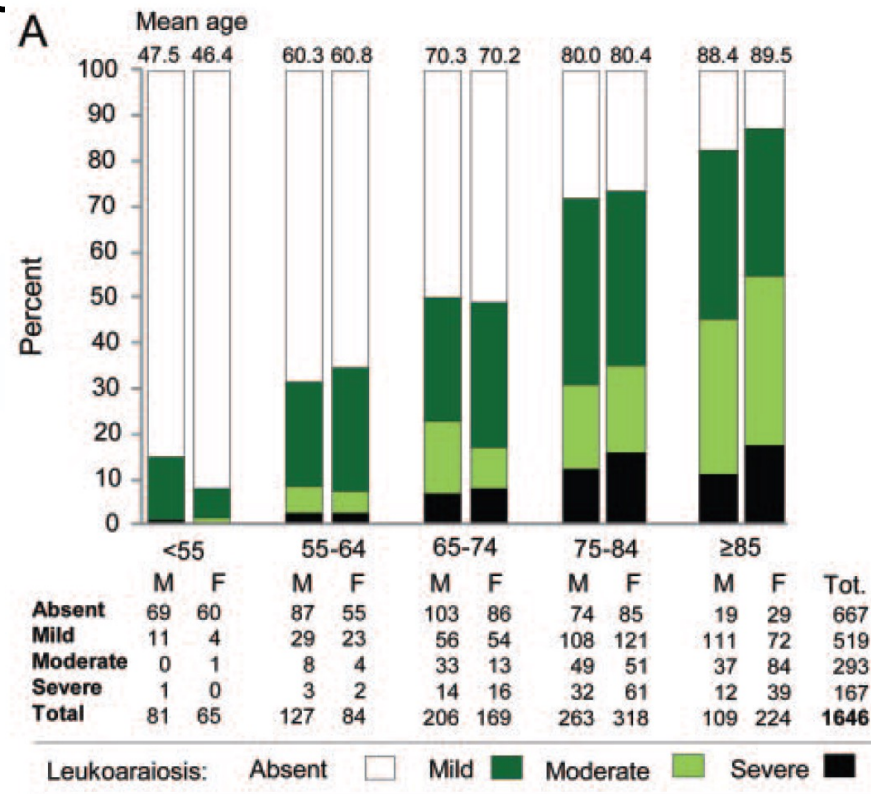


Lancet. 2007 Jul;6(7):611-9

# Anomalies de la matière blanche

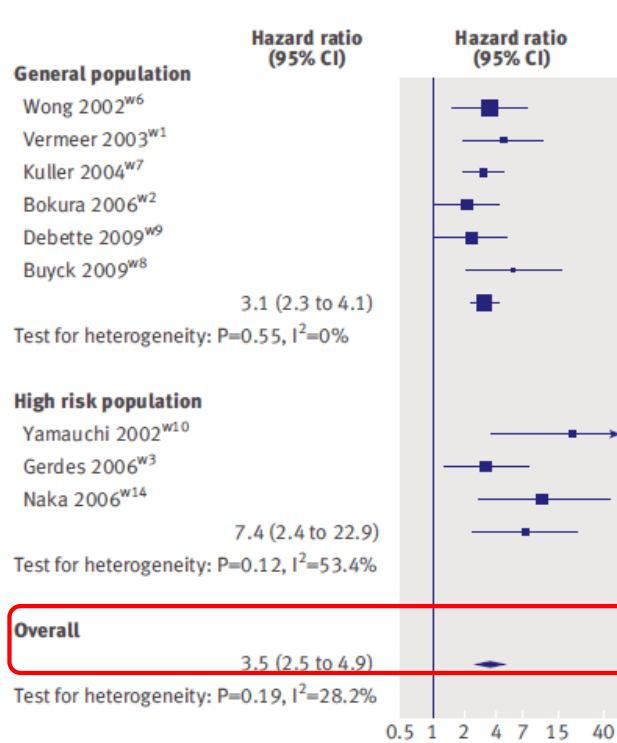
- Significative

Age- and sex-specific distribution of leukoaraiosis on CT and MRI scans

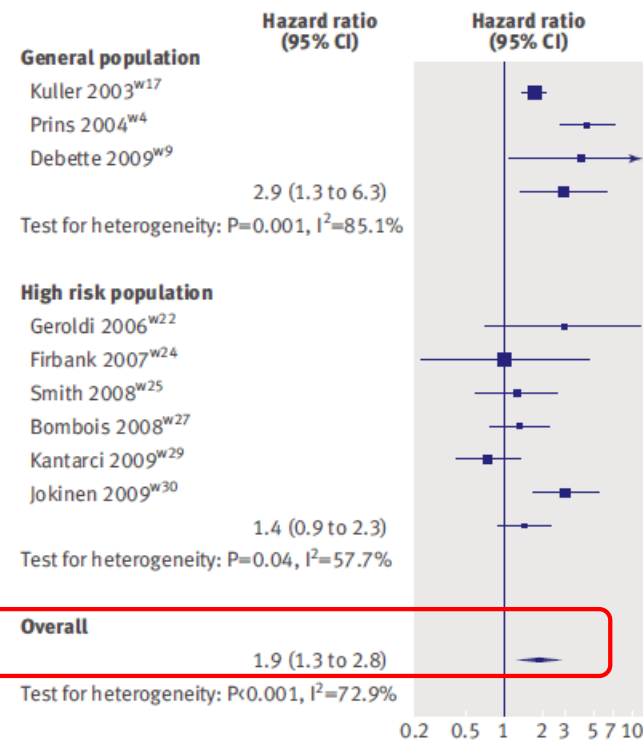


Neurology 2012;79:1215–1222

# Leucoaraïose: signification clinique

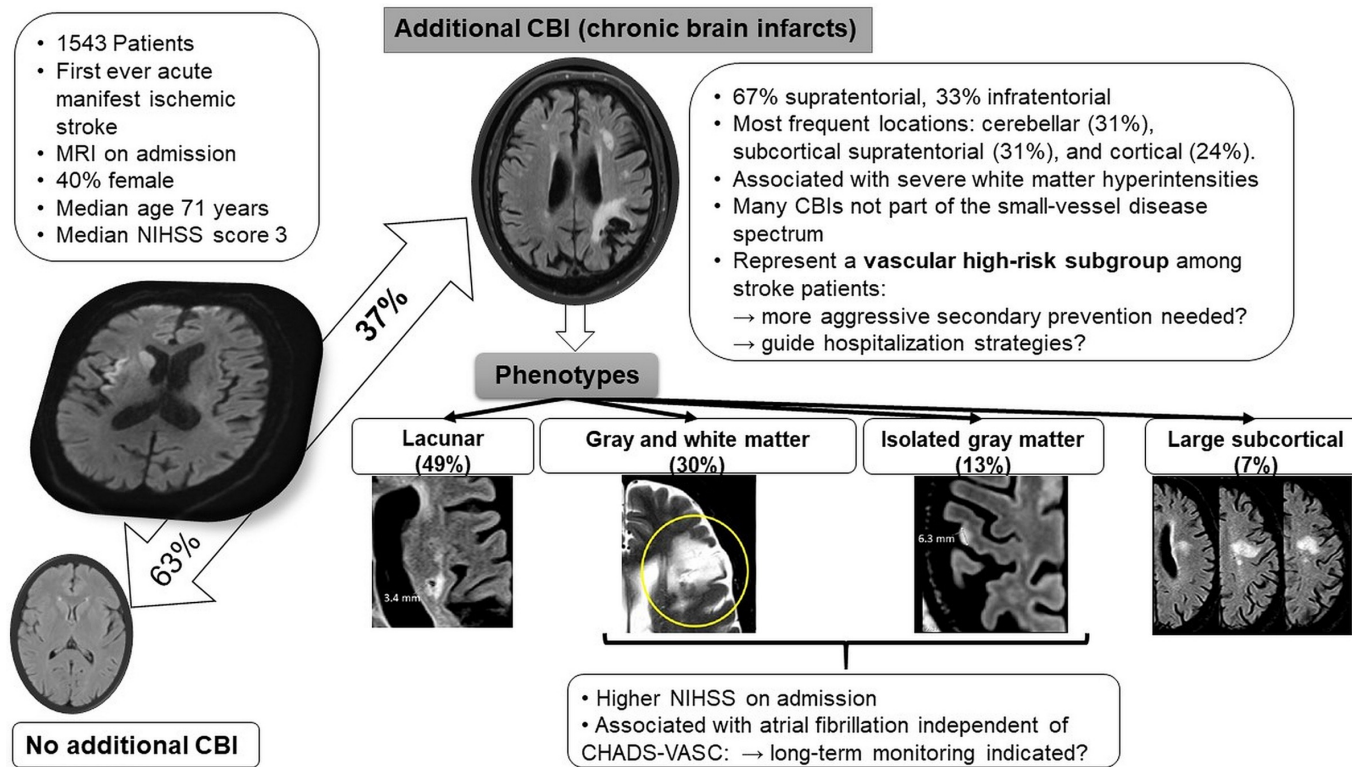


**Fig 2** | Inverse variance meta-analysis of studies testing association of white matter hyperintensities with incident stroke



**Fig 3** | Inverse variance meta-analysis of studies testing association of white matter hyperintensities with incident dementia

# AVC aigu: prévalence des lésions subcliniques



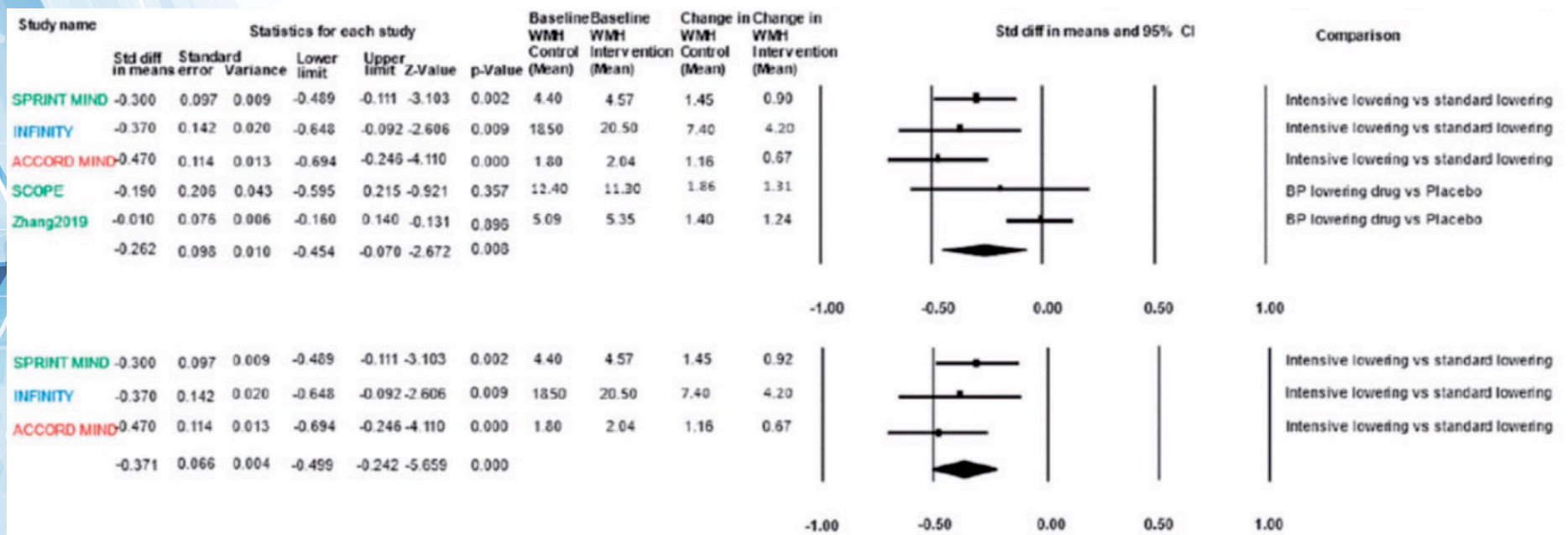
# Diagnostic radiologiques des lésions ischémiques: recommandations AHA

| Diagnosis by neuroimaging                                                                                                                            |
|------------------------------------------------------------------------------------------------------------------------------------------------------|
| MRI has greater sensitivity than CT for diagnosis of silent cerebrovascular disease.                                                                 |
| Minimum MRI acquisition standards are provided in Table 2.                                                                                           |
| Radiology reports should describe silent cerebrovascular disease according to STRIVE. <sup>16</sup>                                                  |
| WMHs of presumed vascular origin should be reported with the use of a validated visual rating scale such as the Fazekas scale for MRI. <sup>19</sup> |

| Sequence                | Purpose                                                                                                                      |
|-------------------------|------------------------------------------------------------------------------------------------------------------------------|
| T1-weighted             | Important for discriminating lacunes from dilated PVS, discriminating gray from white matter, and studying brain atrophy     |
| DWI                     | Most sensitive sequences for acute ischemic lesions; positive up to several weeks after event                                |
| T2-weighted             | Brain structure; differentiate lacunes from WMH and PVS; identify old infarcts                                               |
| FLAIR                   | Identify WMHs and established cortical or large subcortical infarcts; differentiate white matter lesion from PVS and lacunes |
| T2*-weighted SWI or GRE | Detect hemorrhage, cerebral microbleeds, and siderosis                                                                       |

*Stroke*. 2017;48:e44-e71.

# Lésions microvasculaires: anti-HTA



# SPRINT-MIND: impact sur la cognition

## POPULATION

6029 Men  
3332 Women



Adults aged  $\geq 50$  years  
with hypertension and  
without diabetes or stroke

Mean age: 68 years

## LOCATIONS

102  
US sites  
(including Puerto Rico)



## INTERVENTIONS

9361 Patients randomized  
8563 Patients analyzed  
( $\geq 1$  cognitive assessment)

4278

**Intensive control**  
(Target SBP  $< 120$  mm Hg)

4285

**Standard control**  
(Target SBP  $< 140$  mm Hg)

Median treatment period, 3.3 years



## PRIMARY OUTCOME

Occurrence of adjudicated probable dementia

## SECONDARY OUTCOMES

Adjudicated mild cognitive impairment (MCI)  
Composite outcome of MCI or probable dementia

## FINDINGS

### PRIMARY OUTCOME: Adjudicated probable dementia

**Intensive control**

149 patients  
(7.2 cases/1000 person-years)

**Standard control**

176 patients  
(8.6 cases/1000 person-years)

Hazard ratio: **0.83** (95% CI, 0.67-1.04)

### SECONDARY OUTCOME: Adjudicated MCI

**Intensive control**

287 patients  
(14.6 cases/1000 person-years)

**Standard control**

353 patients  
(18.3 cases/1000 person-years)

Hazard ratio: **0.81** (95% CI, 0.69-0.95)

### SECONDARY OUTCOME: Composite outcome

**Intensive control**

402 patients  
(20.2 cases/1000 person-years)

**Standard control**

469 patients  
(24.1 cases/1000 person-years)

Hazard ratio: **0.85** (95% CI, 0.74-0.97)

JAMA. 2019;321(6):553-561

# COMPASS: impact sur la cognition

- RCT, double aveugle, effet additif du rivaroxaban faible dose aux antiplaquettaires, population avec vasculopathie stable
- 27000 patients, suivi 2 ans

**Table 2. Cognitive and Functional Scores by Treatment**

|                                            | Overall |              | Rivaroxaban 2.5 mg bid +Aspirin |              | Rivaroxaban 5 mg bid |              | Aspirin 100 mg od |              | Rivaroxaban 2.5 mg +Aspirin vs. Aspirin |         | Rivaroxaban 5 mg vs. Aspirin |         |
|--------------------------------------------|---------|--------------|---------------------------------|--------------|----------------------|--------------|-------------------|--------------|-----------------------------------------|---------|------------------------------|---------|
|                                            | N       | Mean (SD)    | N                               | Mean (SD)    | N                    | Mean (SD)    | N                 | Mean (SD)    | Estimate (95% CI)                       | P Value | Estimate (95% CI)            | P Value |
| <b>MoCA</b>                                |         |              |                                 |              |                      |              |                   |              |                                         |         |                              |         |
| Interval between baseline and follow-up, y | 1654    | 2.01 (0.68)  | 549                             | 2.02 (0.69)  | 556                  | 2.01 (0.65)  | 549               | 1.99 (0.69)  |                                         |         |                              |         |
| Baseline                                   | 1874    | 24.77 (3.87) | 631                             | 24.81 (3.81) | 621                  | 24.74 (3.91) | 622               | 24.76 (3.89) |                                         |         |                              |         |
| Final                                      | 1666    | 24.86 (3.74) | 552                             | 25.02 (3.59) | 563                  | 24.77 (3.74) | 551               | 24.77 (3.89) |                                         |         |                              |         |
| Change                                     | 1654    | 0.02 (3.02)  | 549                             | 0.12 (2.95)  | 556                  | -0.04 (3.13) | 549               | -0.01 (2.97) | 0.12 (-0.23 to 0.48)                    | 0.497   | -0.03 (-0.39 to 0.32)        | 0.851   |
| Decrease or no change                      | 946     | -1.95 (2.05) | 313                             | -1.82 (1.90) | 323                  | -2.01 (2.24) | 310               | -2.01 (1.97) | 0.98 (0.77 to 1.24)                     | 0.855   | 0.94 (0.74 to 1.19)          | 0.585   |
| Increase                                   | 708     | 2.65 (1.91)  | 236                             | 2.69 (1.98)  | 233                  | 2.68 (1.91)  | 239               | 2.59 (1.84)  |                                         |         |                              |         |

# COMPASS: impact sur lésions subcliniques

**Table 1. Incident MRI Findings by Treatment Group**

|                                           |                |                            |                  |                   | Rivaroxaban 2.5 mg+Aspirin vs Aspirin |         | Rivaroxaban 5 mg vs Aspirin |         |
|-------------------------------------------|----------------|----------------------------|------------------|-------------------|---------------------------------------|---------|-----------------------------|---------|
|                                           | Overall        | Rivaroxaban 2.5 mg+Aspirin | Rivaroxaban 5 mg | Aspirin 100 mg od | OR (95% CI)                           | P Value | OR (95% CI)                 | P Value |
| <u>Incident covert infarct*</u>           |                |                            |                  |                   |                                       |         |                             |         |
| All N (%)                                 | 47 (3.3%)      | 13 (2.7%)                  | 17 (3.6%)        | 17 (3.5%)         | 0.77 (0.37–1.60)                      | 0.480   | 1.02 (0.52–2.03)            | 0.951   |
| Nonlacunar                                | 28 (1.9%)      | 9 (1.9%)                   | 6 (1.3%)         | 13 (2.7%)         | 0.70 (0.29–1.64)                      | 0.407   | 0.46 (0.18–1.23)            | 0.123   |
| Total no. of incident covert infarcts     | 64             | 24                         | 18               | 22                |                                       |         |                             |         |
| <u>White matter hyperintensity volume</u> |                |                            |                  |                   |                                       |         |                             |         |
| Baseline median (IQR)                     | 4.7 (2.5–10.0) | 4.7 (2.5–9.6)              | 4.8 (2.5–10.6)   | 4.5 (2.4–9.7)     |                                       |         |                             |         |
| Follow-up median (IQR)                    | 6.2 (3.1–12.5) | 6 (3.1–12.6)               | 6.35 (3.1–13.0)  | 6 (3–12.0)        |                                       |         |                             |         |
| Increase in volume from baseline          | 950 (65.7%)    | 312 (64.9%)                | 318 (66.7%)      | 320 (65.7%)       | 0.96 (0.74–1.26)                      | 0.783   | 1.04 (0.80–1.36)            | 0.753   |
| <u>Other clinical outcomes†</u>           |                |                            |                  |                   |                                       |         |                             |         |
| Ischemic stroke                           | 11 (0.8%)      | 2 (0.4%)                   | 0 (0%)           | 9 (1.8%)          | 0.23 (0.05–1.05)                      | 0.04    | ...                         | ...     |

# Infarctus subclinique: ASA

## The SILENCE Study

- RCT, ASA vs placebo (double aveugle)
- Suivi 4 ans

TABLE 2: Primary endpoint occurrences.

|                     | ASA n=36   controls n=47 |           | p-value (Fisher Exact) |
|---------------------|--------------------------|-----------|------------------------|
|                     | n (%)                    | n (%)     |                        |
| <i>New SBIs</i>     | 1 (2.8)                  | 6 (12.8)  | 0.103                  |
| <i>Stroke</i>       | 1 (2.8)                  | 2 (4.3)   |                        |
| <i>TIA</i>          | -                        | 1 (2.1)   |                        |
| <i>No CV events</i> | 34 (94.4)                | 38 (80.9) |                        |

### Evidence-based Recommendation

We suggest against antiplatelet treatment in patients with ccSVD as a means to reduce the clinical outcome events of ischaemic or haemorrhagic strokes, cognitive decline or dementia, dependency, death, MACE, mobility, or mood disorders.

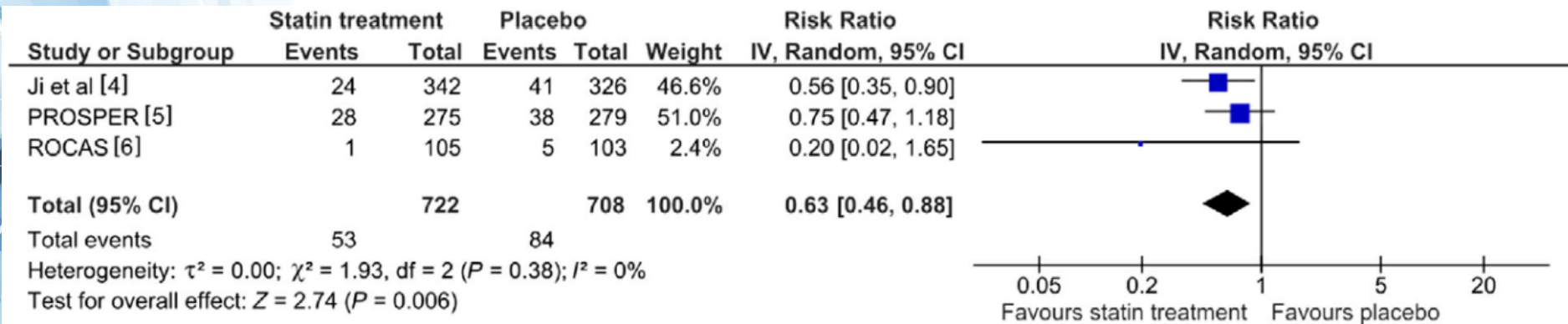
Quality of evidence: **Very low**⊕

Strength of recommendation: **Weak against intervention** ↓?

Stroke Res Treat. 2018; 2018: 7532403

European Stroke Journal. 2021, Vol. 6(2) CXI–CLXII

# Lésions ischémiques subcliniques: statine



# Anomalies ischémiques: recommandation AHA/ASA

## Prevention of stroke in patients with WMHs of presumed vascular origin

Implement preventive care recommended by AHA/ASA guidelines for primary prevention of ischemic stroke.

It is not clear whether WMH alone, in the absence of other risk factors, is a sufficient reason for aspirin therapy.

The clinician should be aware that there is an increased risk for future stroke, and it is reasonable to consider this information when making decisions about anticoagulation for atrial fibrillation, revascularization for carotid stenosis, treatment of hypertension, and initiation of statin therapy. However, the clinician should also be aware that the role of WMH burden in these decisions has not been studied in RCTs.

## Prevention of stroke in patients with silent brain infarcts

Take a careful history to determine whether the infarction was symptomatic.

Implement preventive care recommended by AHA/ASA guidelines for primary prevention of ischemic stroke.

The effectiveness of aspirin to prevent stroke has not been studied in this setting.

The clinician should be aware that there is an increased risk for future stroke, and it is reasonable to consider this information when making decisions about anticoagulation for atrial fibrillation, revascularization for carotid stenosis, treatment of hypertension, and initiation of statin therapy. However, the clinician should also be aware that the role of silent brain infarcts in these decisions has not been studied in RCTs.

# Anomalies ischémiques: conduite à tenir

| Investigations for patients with silent cerebrovascular disease                              |
|----------------------------------------------------------------------------------------------|
| Assess common vascular risk factors and assess pulse for atrial fibrillation.                |
| Consider carotid imaging when there is silent brain infarction in the carotid territory.     |
| Consider echocardiography when there is an embolic-appearing pattern of silent infarction.   |
| Consider noninvasive CT or MR angiography when there are large (>1.0 cm) silent hemorrhages. |

# Lésions ischémiques: approche clinique

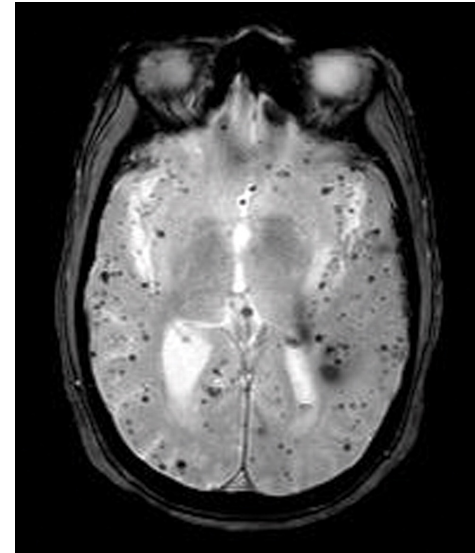
- Revoir l'imagerie
  - Type de lésion
    - Hyperintensités de la matière blanche, lacunes, infarctus cortical, lésion cavitaire
  - Distribution
    - multifocal, périventriculaire, confluent, patron spécifique
  - Sévérité (fonction de l'âge, facteurs de risque vasculaires)
- Recherche d'un événement explicatif
  - Déficit neurologique aigu compatible
  - Chirurgie vasculaire ou cardiaque

# Lésions ischémiques: approche clinique

- Examen clinique
  - Signes vitaux
  - Examen neurologique (perte de champs visuels, atteinte sensitivomotrice subtile)
  - Dépistage de troubles cognitifs
  - Troubles de l'humeur
  - Bilan sanguin

# Lésions ischémiques: investigation

- Recherche de facteurs de risque vasculaire
  - HTA, diabète, tabagisme, fibrillation auriculaire
  - Autres facteurs de risque (maladie coronarienne, syndrome métabolique, insuffisance cardiaque, apnée du sommeil, insuffisance rénale chronique)
- En fonction du type de lésion et de l'examen clinique
  - Examen du rythme cardiaque
  - Échocardiographie
  - Imagerie carotidienne



# Anomalies hémorragiques

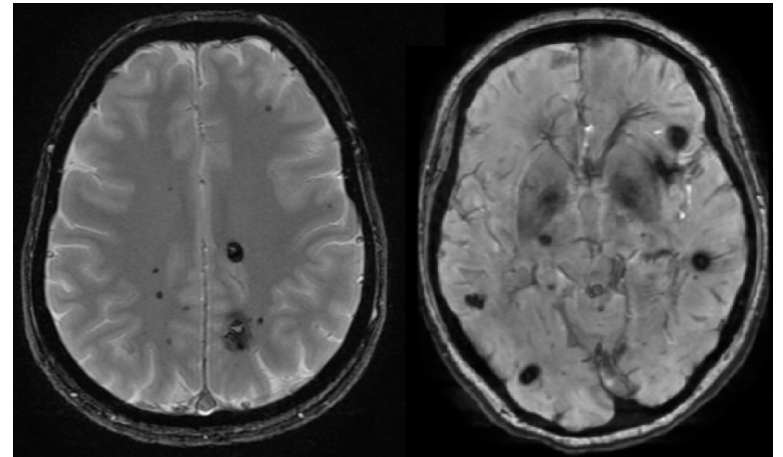
Microhémorragies (microbleeds)

Sidérose superficielle

# Lésions avec artéfact de susceptibilité

- Différentiel

- CAA
- Microangiopathie hypertensive
- Calcifications
- Cavernomatose
- Radiothérapie
- Trauma (dommage axonal diffus)
- Sepsis/endocardite
- Métastases hémorragiques (mélanome, carcinome rénal)
- (...)



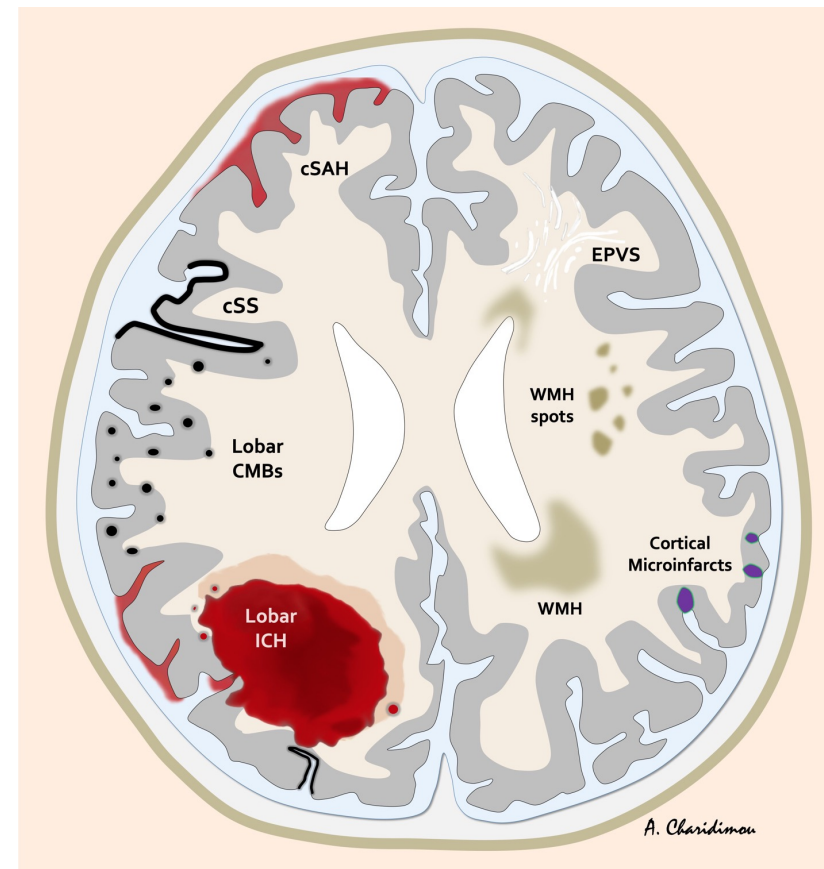
# CAA: signes suggestifs

|                                                      | OR (95% CI)         | p value |
|------------------------------------------------------|---------------------|---------|
| At least two strictly lobar cerebral microbleeds     | 2.42 (1.33–4.39)    | 0.0040  |
| At least one focus of cortical superficial siderosis | 36.53 (8.70–153.90) | <0.0001 |
| Perivascular spaces in the centrum semiovale         | 3.17 (1.66–6.08)    | 0.0010  |
| White matter hyperintensities in a multispot pattern | 2.04 (1.06–3.91)    | 0.032   |

OR=odds ratio.

**Table 3:** Multivariable logistic regression of MRI markers' association with neuropathologically defined CAA in the whole cohort

*Lancet Neurol* 2022; 21: 714–25

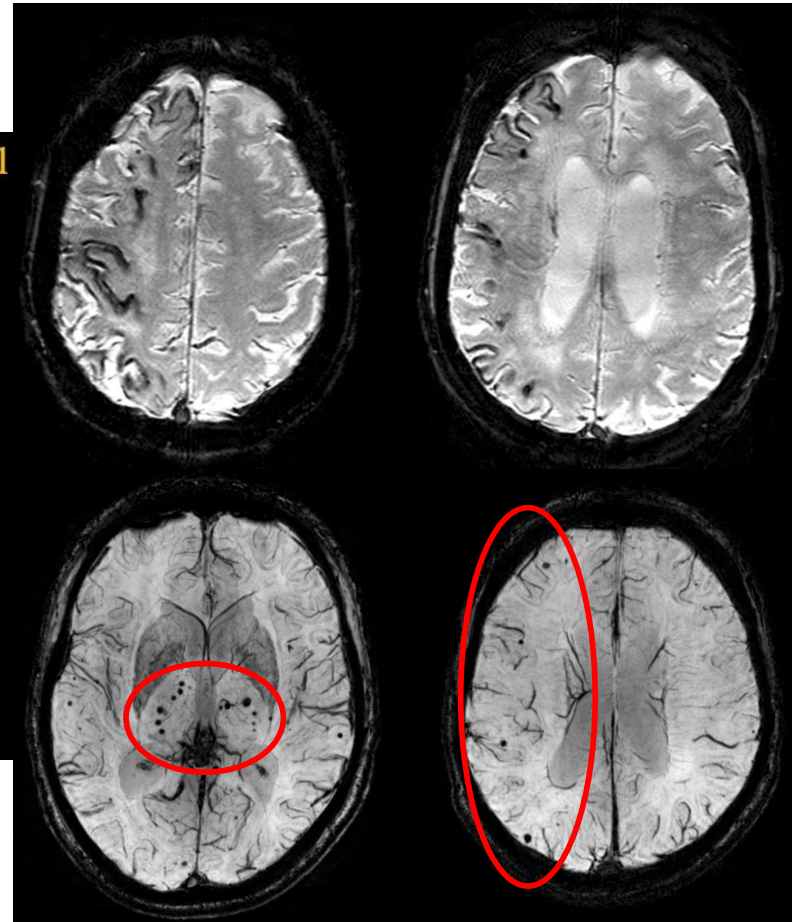
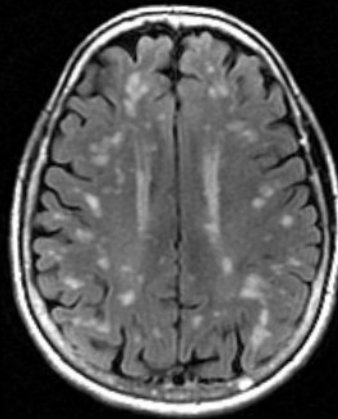


# CAA: signes suggestifs

Abundant (>20/hemisphere)  
Perivascular spaces in  
centrum semiovale



Multiple (>10) subcortical  
spot WMH pattern



# Risque hémorragique sous anticoagulation

- CROMIS-2
  - Étude observationnelle
  - 1490 patients, FA sous anticoagulation, suivi 2.3 ans

|                                                    | Absolute event rate* | Rate per 1000 patient-years (95% CI) | Absolute rate increase per 1000 patient-years (95% CI) | Univariable hazard ratio (95% CI) | Adjusted hazard ratio (95% CI)† |
|----------------------------------------------------|----------------------|--------------------------------------|--------------------------------------------------------|-----------------------------------|---------------------------------|
| <b><u>Symptomatic intracranial haemorrhage</u></b> |                      |                                      |                                                        |                                   |                                 |
| No cerebral microbleeds                            | 7/2654               | 2.6 (1.1 to 5.4)                     | 1 (ref)                                                | 1 (ref)                           | 1 (ref)                         |
| Cerebral microbleeds present                       | 7/712                | 9.8 (4.0 to 20.3)                    | 7.2 (2.9 to 14.9)                                      | 3.73 (1.31 to 10.64)              | 3.67 (1.27 to 10.60)            |
| 1 cerebral microbleed                              | 2/367                | 5.4 (0.7 to 19.7)                    | 2.8 (-0.4 to 14.3)                                     | 2.04 (0.42 to 9.84)               | 2.03 (0.42 to 9.83)             |
| ≥2 cerebral microbleeds                            | 5/345                | 14.4 (4.7 to 33.8)                   | 11.8 (3.6 to 28.4)                                     | 5.58 (1.77 to 17.58)              | 5.46 (1.70 to 17.51)            |
| <b><u>Recurrent ischaemic stroke</u></b>           |                      |                                      |                                                        |                                   |                                 |
| No cerebral microbleeds                            | 39/2608              | 15.0 (10.6 to 20.4)                  | 1 (ref)                                                | 1 (ref)                           | 1 (ref)                         |
| Cerebral microbleeds present                       | 17/704               | 24.1 (14.1 to 38.7)                  | 9.1 (3.5 to 18.3)                                      | 1.62 (0.92 to 2.87)               | 1.53 (0.85 to 2.76)             |
| 1 cerebral microbleed                              | 9/362                | 24.9 (11.4 to 47.2)                  | 9.9 (0.8 to 32.2)                                      | 1.68 (0.82 to 3.47)               | 1.75 (0.84 to 3.65)             |
| ≥2 cerebral microbleeds                            | 8/341                | 23.4 (10.1 to 46.2)                  | 8.4 (-0.5 to 25.8)                                     | 1.56 (0.73 to 3.35)               | 1.32 (0.60 to 2.93)             |

*Lancet Neurol* 2018; 17: 539–47

# NAVIGATE-ESUS: impact des microhémorragies

- RCT
- AVC ESUS
- Rivaroxaban vs ASA (double aveugle)
- 3699/7213 patients

**eTable 8.** Efficacy in CMB Subgroups–Intracerebral Hemorrhage

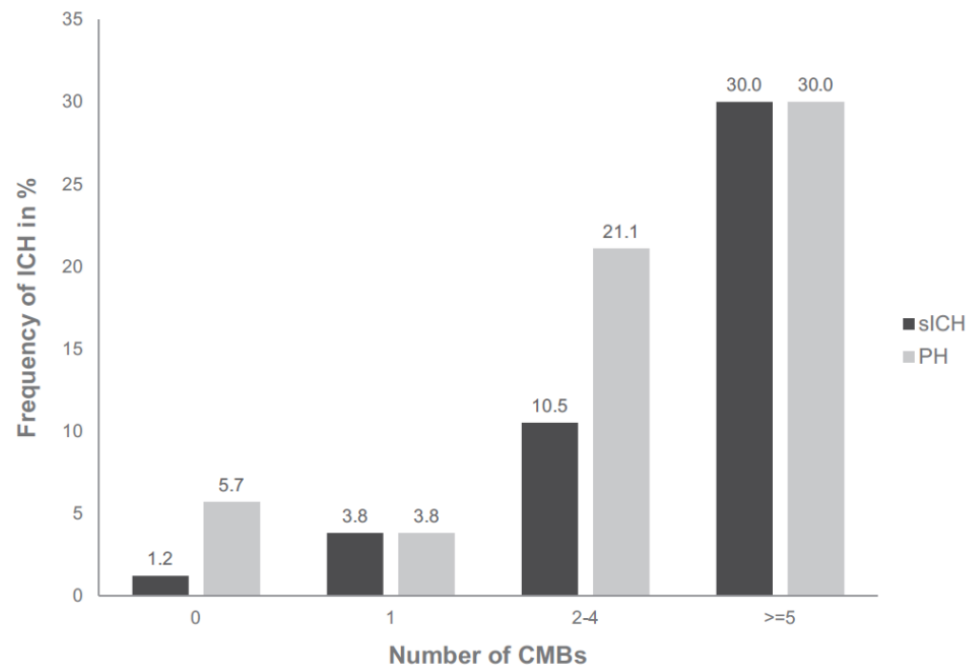
| Subgroup            | Rivaroxaban assigned (N = 1872) |                                       | Aspirin-assigned (N = 1827) |                                       | Hazard ratio (95% CI) | P value for interaction |
|---------------------|---------------------------------|---------------------------------------|-----------------------------|---------------------------------------|-----------------------|-------------------------|
|                     | No. Rand                        | No. events (events rate) <sup>a</sup> | No. Rand                    | No. events (events rate) <sup>a</sup> |                       |                         |
| CMB presence        |                                 |                                       |                             |                                       |                       |                         |
| None                | 1672                            | 6 (0.4)                               | 1632                        | 2 (0.1)                               | 2.96 (0.60-14.66)     | NA                      |
| CMB                 | 200                             | 3 (1.6)                               | 195                         | 1 (0.5)                               | 3.12 (0.32-30.01)     | .97                     |
| CMB burden          |                                 |                                       |                             |                                       |                       |                         |
| None                | 1672                            | 6 (0.4)                               | 1632                        | 2 (0.1)                               | 2.96 (0.60-14.66)     | NA                      |
| 1-2                 | 104                             | 1 (1.0)                               | 114                         | 0 (0.0)                               |                       | NA                      |
| 3 or more           | 59                              | 2 (3.5)                               | 43                          | 1 (2.4)                               | 1.43 (0.13-15.82)     | .89                     |
| CMB topography      |                                 |                                       |                             |                                       |                       |                         |
| None                | 1672                            | 6 (0.4)                               | 1632                        | 2 (0.1)                               | 2.96 (0.60-14.66)     | NA                      |
| Strictly deep/mixed | 152                             | 2 (1.4)                               | 134                         | 1 (0.7)                               | 1.98 (0.18-21.92)     | NA                      |
| Strictly lobar      | 45                              | 1 (2.2)                               | 57                          | 0 (0.0)                               |                       | .96                     |

Abbreviations: CMB, cerebral microbleed; NA, not applicable.

<sup>a</sup>Event rates reported in 100-person years.

*JAMA Neurol.* 2021;78(1):11-20

# Thrombolyse en présence de microhémorragies



*Stroke. 2014;45:2900-2905*

# Anomalies hémorragiques: recommandation AHA/ASA

| Anticoagulation and other therapies in patients with silent microbleeds                                                |
|------------------------------------------------------------------------------------------------------------------------|
| It is reasonable to provide anticoagulation therapy to patients with microbleeds when there is an indication (eg, AF). |
| When anticoagulation is needed, a novel oral anticoagulant is preferred over warfarin.                                 |
| Percutaneous closure of the left atrial appendage could be considered as an alternative to anticoagulation.            |
| It is reasonable to provide antiplatelet therapy to patients with microbleeds when there is an indication.             |
| MRI screening for microbleeds is not needed before the initiation of antithrombotic therapies.                         |
| Individuals with silent microbleeds are at increased future risk of both ischemic stroke and ICH.                      |
| Implement preventive care recommended by AHA/ASA guidelines for primary prevention of ischemic stroke.                 |
| It is reasonable to provide preventive care recommended by AHA/ASA guidelines for prevention of ICH.                   |

| Safety of acute ischemic stroke therapy in patients with silent microbleeds                                                                                           |
|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| It is reasonable to administer intravenous alteplase to patients with acute ischemic stroke and evidence of microbleeds if it is otherwise indicated.                 |
| It is reasonable to perform endovascular thrombectomy in patients with acute ischemic stroke and evidence of microbleeds.                                             |
| In acute ischemic stroke patients with microbleeds, bypassing intravenous alteplase therapy to proceed directly to endovascular thrombectomy is an unproven strategy. |

*Stroke*. 2017;48:e44-e71.

# Lésions microhémorragiques: récapitulatif

## Revoir l'imagerie

- Type de lésion (microhémorragies, sidérose, atteinte matière blanche, autre lésion)
- Distribution (corticale, profonde)
- Sévérité

## Prise en charge clinique

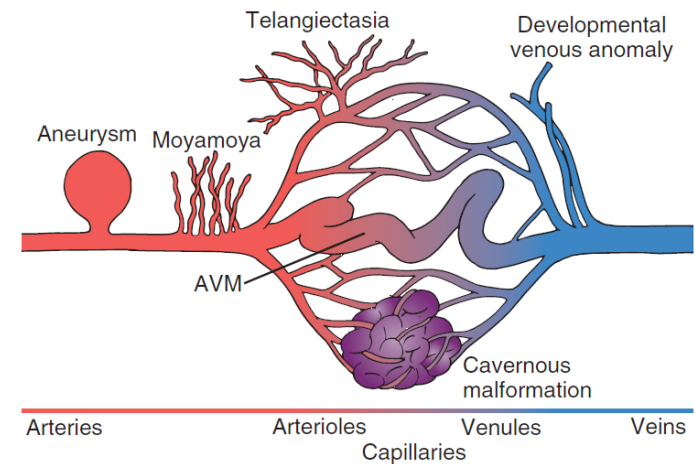
- Risque d'AVC ischémique et hémorragique accru
- Recherche des facteurs de risque vasculaires
- Révision des antécédents (AVC, sepsis/endocardite, chirurgie majeure, radiation, cavernomatose familiale...)
- Questionnaire, examen neurologique, dépistage cognitif

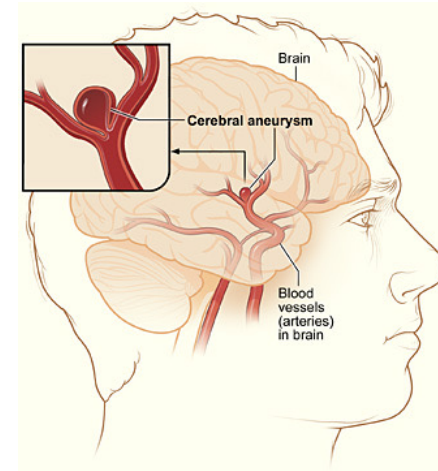
## Traitement

- Prévention primaire vasculaire
- Semblable à microangiopathie ischémique
- Traitement agressif HTA
- Antithrombotique/thrombolyse iv demeurent indiqués en présence d'une condition le justifiant

# Anomalies vasculaires structurales

- Anévrisme
- Malformation artérioveineuse
- Angiome caverneux





# Anévrisme artériel intracrânien

# Anévrisme: risque de rupture annuel

|                                                                                                                                                                                                                                                              | <7 mm    |          | 7-12 mm | 13-24 mm | ≥25 mm |
|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|----------|----------|---------|----------|--------|
|                                                                                                                                                                                                                                                              | Group 1* | Group 2† |         |          |        |
| Cavernous carotid artery (n=210)                                                                                                                                                                                                                             | 0%       | 0%       | 0%      | 3.0%     | 6.4%   |
| Anterior cerebral artery, anterior communicating artery, middle cerebral artery, or internal carotid artery (excluding cavernous segment) (n=1037)                                                                                                           | 0%       | 1.5%     | 2.6%    | 14.5%    | 40%    |
| Posterior circulation‡ or posterior communicating artery (n=445)                                                                                                                                                                                             | 2.5%     | 3.4%     | 14.5%   | 18.4%    | 50%    |
| *No history of subarachnoid haemorrhage. †History of subarachnoid haemorrhage from a separate aneurysm. ‡Any vertebrobasilar or posterior cerebral artery segment aneurysm. Reproduced from Wiebers and colleagues, <sup>36</sup> by permission of Elsevier. |          |          |         |          |        |
| <b>Table 2: 5-year cumulative aneurysm rupture rates according to size and location of unruptured aneurysm</b>                                                                                                                                               |          |          |         |          |        |

# HSA: facteurs de risque modifiables

**Table 2**

Results from multivariate model<sup>a</sup> on significant modifiable risk factors of subarachnoid haemorrhage.

|                         | Adjusted odds ratio | P value | Population attributable risk (95%CI) |
|-------------------------|---------------------|---------|--------------------------------------|
| History of hypertension | 1.79 (1.28–2.50)    | 0.0007  | 21% (10–30%)                         |
| Current smoking         | 3.69 (2.53–5.38)    | <0.0001 | 30% (23–37%)                         |

# HSA et habitudes de vie

**TABLE 2. Risk of Subarachnoid Hemorrhage Associated With Cigarette Smoking and Use of Alcohol**

| Exposure                          | Cases<br>(%)<br>(n=149) | Controls<br>(%)<br>(n=298) | Age- and<br>gender-adjusted risk* |          |
|-----------------------------------|-------------------------|----------------------------|-----------------------------------|----------|
|                                   |                         |                            | OR                                | 95% CI   |
| Cigarette smoking (149 sets)†     |                         |                            |                                   |          |
| Never smoker                      | 26.8                    | 52.4                       | 1.0                               | ...      |
| Former smoker                     | 22.8                    | 28.9                       | 1.8                               | 1.0–3.2  |
| Light smoker (≤1 pack/day)        | 26.8                    | 13.3                       | 4.1                               | 2.3–7.3  |
| Heavy smoker (>1 pack/day)        | 23.5                    | 5.4                        | 11.1                              | 5.0–24.9 |
| Missing                           | 0.0                     | 1.3                        | ...                               | ...      |
| Alcohol Use (147 sets)†           |                         |                            |                                   |          |
| Nondrinker                        | 25.0                    | 23.3                       | 1.0                               | ...      |
| Light drinker (<1 drink/day)      | 40.5                    | 59.2                       | 0.7                               | 0.4–1.1  |
| Moderate drinker (1–2 drinks/day) | 14.2                    | 11.1                       | 1.5                               | 0.7–3.0  |
| Heavy drinker (>2 drinks/day)     | 20.3                    | 6.3                        | 3.8                               | 1.7–8.4  |
| Missing                           | 0.7                     | 3.7                        | ...                               | ...      |

\*Odds ratio (OR) and 95% confidence intervals (95% CI) were derived from conditional logistic regression, taking into account matching on age, gender, and respondent type.

†For trend,  $p < 0.001$ .

# Anévrimes: recommandations

## AHA

### Risk Factors for Aneurysm Development, Growth, and Rupture: Recommendations

1. Given that smoking appears to increase the risk of UIA formation, patients with UIA should be counseled regarding the importance of smoking cessation (*Class I; Level of Evidence B*).
2. Given that hypertension may play a role in growth and rupture of IAs, patients with UIA should monitor blood pressure and undergo treatment for hypertension (*Class I; Level of Evidence B*).

*Stroke*. 2015;46:2368-2400

European Stroke Journal 2022, Vol. 7(3) LXXXI–CVI

## ESO

### Evidence-based recommendation

In adult patients with UIA who smoke, we recommend smoking cessation.

Quality of evidence: **Very low** ⊕

Strength of recommendation: **Strong for intervention** ↑↑

In adult patients with UIA and hypertension, we recommend treatment of increased blood pressure.

Quality of evidence: **Very low** ⊕

Strength of recommendation: **Strong for intervention** ↑↑

In adult patients with UIA, we suggest to not start treatment with acetylsalicylic acid to decrease the risk of aneurysm growth or rupture.

Quality of evidence: **Very low** ⊕

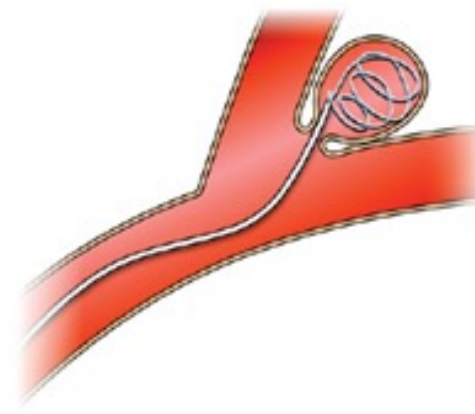
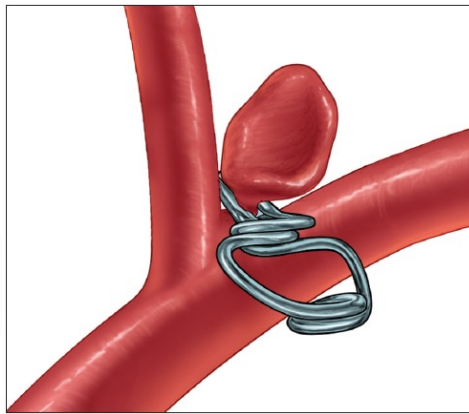
Strength of recommendation: —

In adult patients with UIA, we suggest to not start treatment with statins to decrease the risk of aneurysm growth or rupture.

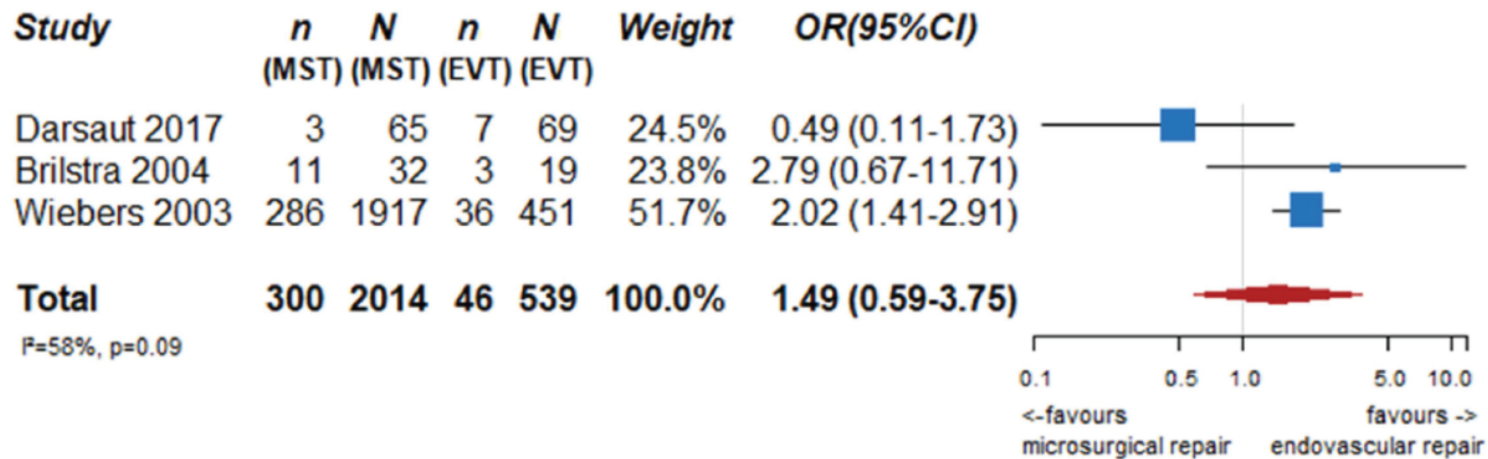
Quality of evidence: **Very low** ⊕

Strength of recommendation: —

# Options interventionnelles: clip - coil



# Options interventionnelles: clip - coil



**Figure 2.** PICO 2 – association between microsurgical aneurysm repair, compared to endovascular aneurysm repair and risk of periprocedural stroke.

*n*: number of events; *N*: number of patients; MST: microsurgical treatment; EVT: endovascular treatment; CI: confidence interval; OR: odds ratio.

# Anévrismes: recommandations

## AHA

### Comparative Efficacy of Clipping Versus Coiling: Recommendations

1. Surgical clipping is an effective treatment for UIAs that are considered for treatment (*Class I; Level of Evidence B*).
2. Endovascular coiling is an effective treatment for select UIAs that are considered for treatment (*Class IIa; Level of Evidence B*).
3. Patients with UIAs who are considered for treatment should be fully informed about the risks and benefits of both endovascular and microsurgical aneurysm clipping (*Class I; Level of Evidence B*).
4. Endovascular coiling is associated with a reduction in procedural morbidity and mortality over surgical clipping in selected cases but has an overall higher risk of recurrence (*Class IIb; Level of Evidence B*).

*Stroke*. 2015;46:2368-2400

## ESO

### Evidence-based recommendation

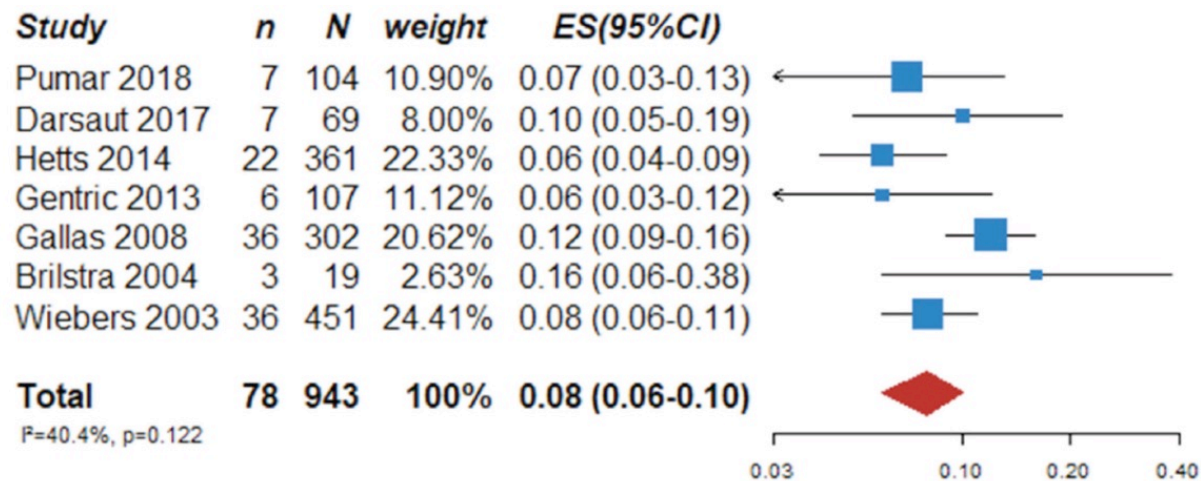
In adult patients with UIA, we cannot make an overall recommendation that states which UIA treatment modality (either endovascular or microsurgical) is preferred based on the current data.

Quality of evidence: **Very low** ⊕

Strength of recommendation: –

European Stroke Journal 2022, Vol. 7(3) LXXXI–CVI

# Traitement endovasculaire: risque périprocédural



**Figure 6.** Periprocedural stroke events rates in studies assessing endovascular treatment in patients with unruptured intracranial aneurysm.

*n*: number of events; *N*: number of patients; CI: confidence interval; ES: estimated rate of periprocedural stroke events.

# Anévrismes: recommandations

## AHA

2. Patients with aneurysms with documented enlargement during follow-up should be offered treatment in the absence of prohibitive comorbidities (*Class I; Level of Evidence B*).
3. Treatment of UIAs in patients with a family history of IA is reasonable even in aneurysms at smaller sizes than spontaneously occurring IAs (*Class IIa; Level of Evidence B*).

*Stroke*. 2015;46:2368-2400

## ESO

### Evidence-based recommendation

In adult patients in whom the estimated 5-year risk of aneurysm rupture is higher than the risk of the preventive treatment modality, we suggest preventive aneurysm repair with the treatment modality that is most effective and safe for that particular aneurysm.

Quality of evidence: **Very low** ⊕

Strength of recommendation: **Weak for intervention** ↑?

In adult patients with growth of a UIA detected at follow up imaging, we suggest preventive aneurysm repair. However, despite an increased risk of rupture in such patients, this risk remains to be weighed against the risk of treatment complications.

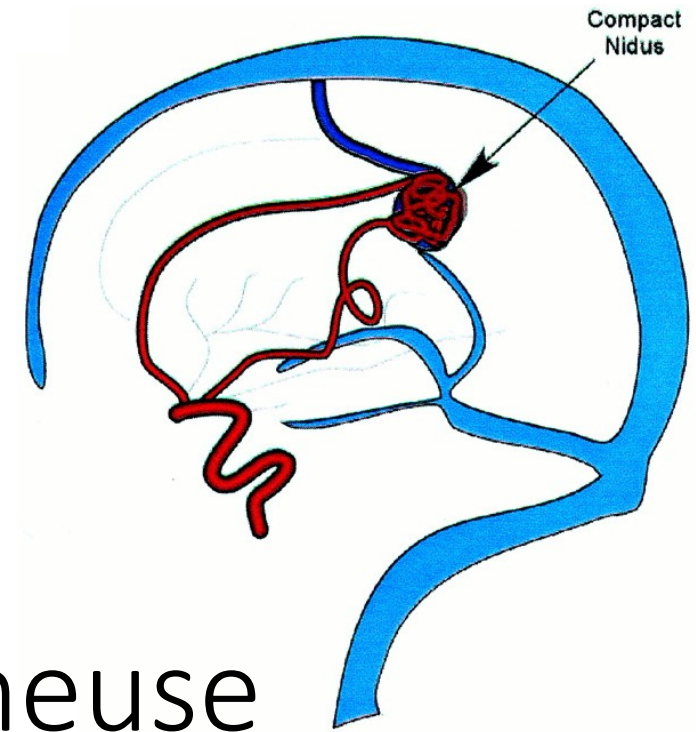
Quality of evidence: **Very low** ⊕

Strength of recommendation: **Weak for intervention** ↑?

European Stroke Journal 2022, Vol. 7(3) LXXXI–CVI

# Anévrismes: récapitulatif

- Risque de rupture spontanée globalement faible
- Suivi clinique
  - Recherche et traitement des facteurs de risque vasculaires
  - Traitement HTA, cessation tabagique
  - Pas d'indication de statine/ASA mais études randomisées en cours
- Suivi radiologique
  - Probablement indiqué, mais intervalles non spécifiés
  - Imagerie de choix: MRA (TOF)
- Suivi et prise en charge peut être référé à un centre de haut volume

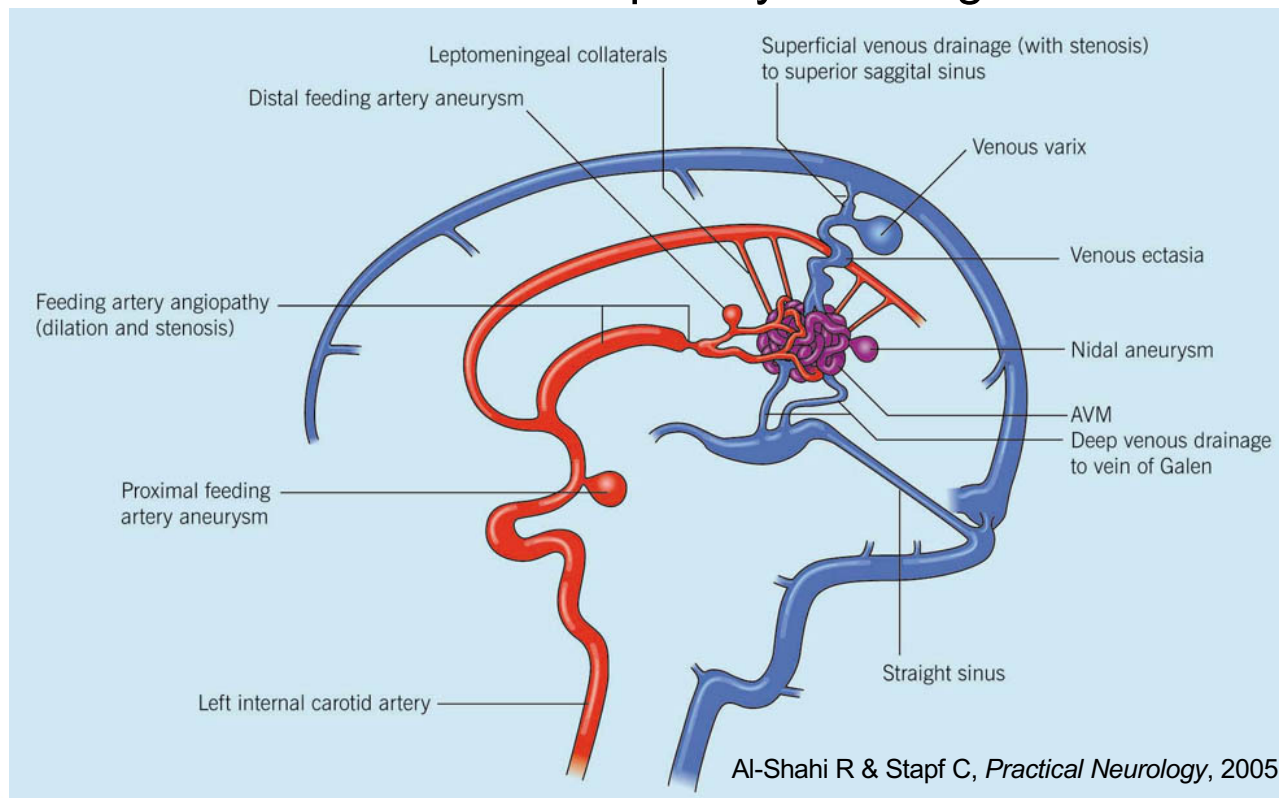


# Malformation artérioveineuse

MAV

# Brain Arteriovenous Malformations

## A multidisciplinary challenge



# MAV: caractéristiques cliniques

- Prévalence: 1/2000
- Asymptomatique à la présentation dans 30-40%

**TABLE 1. Age Distribution in 999 Brain AVM Patients**

| Age, y             | Berlin   | Paris    | Middle and Far East | New York | Toronto | All |
|--------------------|----------|----------|---------------------|----------|---------|-----|
| 0 to 9.9           | 4 (3%)   | 65 (17%) | 18 (12%)            | 11 (3%)  | ...     | 10% |
| Adjusted residuals | -2.5     | 5.7*     | 1.0                 | -5.0*    |         |     |
| 10 to 19.9         | 16 (14%) | 72 (19%) | 23 (16%)            | 47 (14%) | ...     | 16% |
| Adjusted residuals | -0.7     | 1.7      | -0.2                | -1.2     |         |     |
| 20 to 29.9         | 22 (19%) | 91 (24%) | 31 (21%)            | 82 (25%) | ...     | 23% |
| Adjusted residuals | -1.1     | 0.3      | -0.6                | 0.9      |         |     |
| 30 to 39.9         | 28 (24%) | 70 (18%) | 32 (22%)            | 83 (25%) | ...     | 22% |
| Adjusted residuals | 0.7      | -2.3     | 0.0                 | 1.8      |         |     |
| 40 to 49.9         | 15 (13%) | 43 (11%) | 27 (18%)            | 58 (18%) | ...     | 15% |
| Adjusted residuals | -0.5     | -2.5     | 1.4                 | 1.9      |         |     |
| 50 to 59.9         | 14 (12%) | 33 (9%)  | 9 (6%)              | 31 (9%)  | ...     | 9%  |
| Adjusted residuals | 1.3      | -0.3     | -1.3                | 0.4      |         |     |
| ≥60                | 16 (14%) | 12 (3%)  | 6 (4%)              | 17 (5%)  | ...     | 5%  |
| Adjusted residuals | 4.5*     | -2.4     | -0.7                | -0.1     |         |     |

**TABLE 2. Morphological Characteristics in 1289 Brain AVM Patients**

| Characteristic        | Berlin   | Paris     | Middle and Far East | New York  | Toronto   | All |
|-----------------------|----------|-----------|---------------------|-----------|-----------|-----|
| Eloquence of location | 82 (71%) | 259 (69%) | 101 (66%)           | 197 (70%) | 220 (78%) | 71% |
| Adjusted residuals    | -0.1     | -1.3      | -1.3                | -0.5      | 3.1*      |     |
| Deep drainage         | 66 (57%) | 211 (56%) | 91 (60%)            | 146 (52%) | ...       | 55% |
| Adjusted residuals    | 0.36     | 0.25      | 1.23                | -1.52     |           |     |
| AVM <3 cm             | 26 (23%) | 101 (31%) | 43 (32%)            | 76 (27%)  | 185 (68%) | 38% |
| Adjusted residuals    | -3.6†    | -3.1*     | -1.6                | -4.5†     | 11.6†     |     |
| AVM 3-6 cm            | 73 (63%) | 196 (60%) | 84 (62%)            | 192 (68%) | 78 (28%)  | 55% |
| Adjusted residuals    | 2.0      | 2.2       | 1.7                 | 5.0†      | -10.1†    |     |
| AVM >6 cm             | 16 (14%) | 30 (9%)   | 9 (7%)              | 16 (6%)   | 11 (4%)   | 7%  |
| Adjusted residuals    | 2.9*     | 1.6       | -0.3                | -1.2      | -2.4      |     |

Stroke. 2000;31:1307-1310

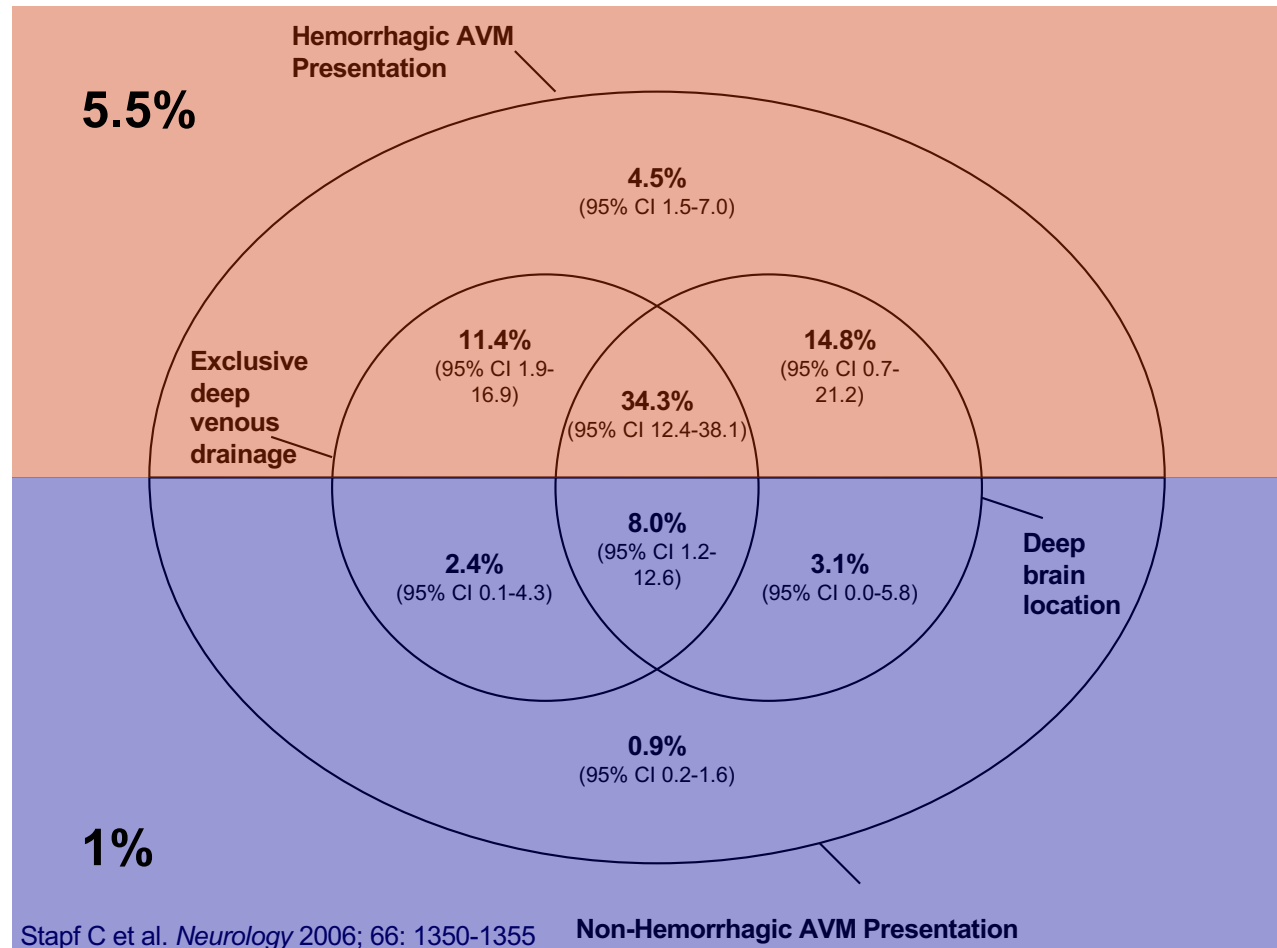
# MAV: caractéristiques cliniques

**TABLE 3. Clinical Characteristics in 1289 Brain AVM Patients**

| Type of Presentation             | Berlin   | Paris     | Middle and Far East | New York  | Toronto   | All |
|----------------------------------|----------|-----------|---------------------|-----------|-----------|-----|
| Hemorrhage                       | 49 (42%) | 212 (54%) | 87 (57%)            | 148 (49%) | 173 (60%) | 53% |
| Adjusted residuals               | −2.50    | 0.3       | 1.0                 | −1.9      | 2.6       |     |
| Persistent neurological deficit  | 9 (8%)   | 14 (4%)   | 9 (6%)              | 35 (13%)  | ...       | 7%  |
| Adjusted residuals               | 0.2      | −3.6*     | −0.5                | 4.1*      |           |     |
| Progressive neurological deficit | 5 (4%)   | 19 (5%)   | 11 (8%)             | 10 (4%)   | ...       | 5%  |
| Adjusted residuals               | −0.3     | 0.0       | 1.7                 | −1.2      |           |     |
| Reversible neurological deficit  | 13 (12%) | 20 (5%)   | 10 (7%)             | 32 (12%)  | ...       | 8%  |
| Adjusted residuals               | 1.3      | −2.8      | −0.6                | 2.5       |           |     |
| Chronic headache                 | 21 (19%) | 57 (16%)  | 18 (13%)            | 28 (10%)  | ...       | 14% |
| Adjusted residuals               | 1.6      | 1.2       | −0.3                | −2.2      |           |     |
| Focal seizure                    | 12 (11%) | 35 (9%)   | 11 (8%)             | 29 (11%)  | ...       | 10% |
| Adjusted residuals               | 0.4      | −0.3      | −0.8                | 0.7       |           |     |
| Generalized seizure              | 39 (35%) | 110 (29%) | 39 (27%)            | 81 (29%)  | ...       | 30% |
| Adjusted residuals               | 1.2      | −0.3      | −0.6                | −0.1      |           |     |

Stroke. 2000;31:1307-1310

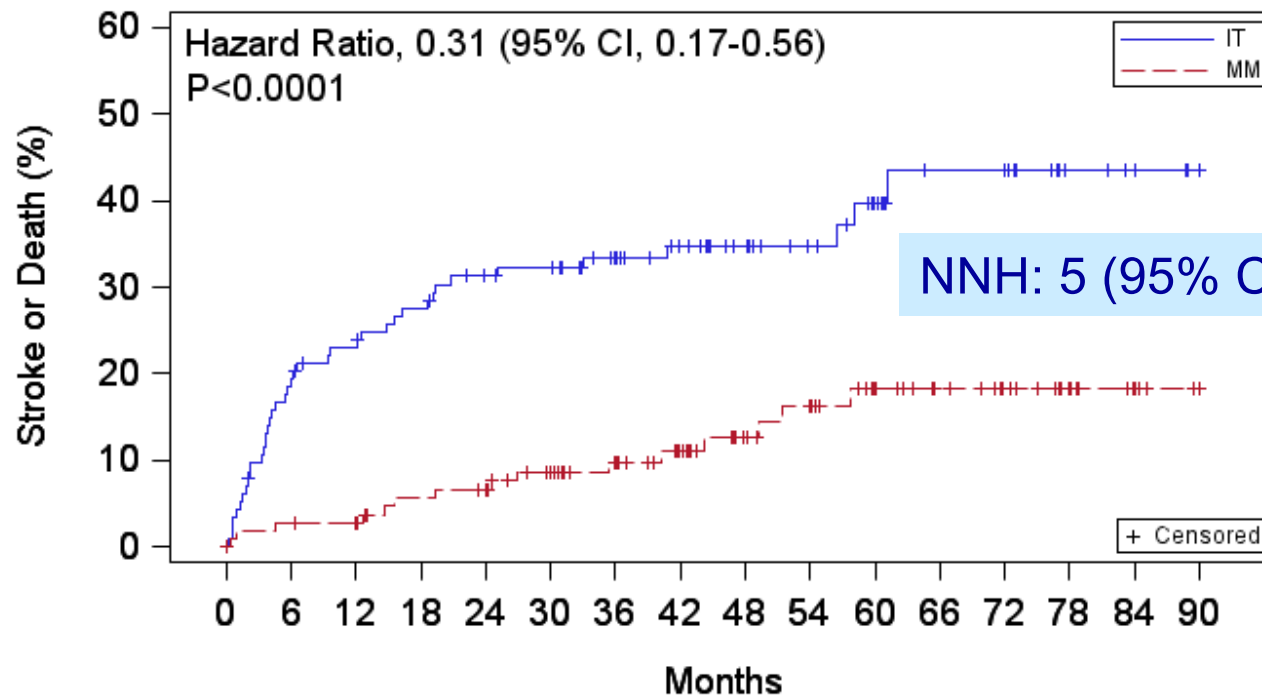
# The Columbia AVM Hemorrhage Risk Model



# ARUBA

Primary outcome, n=226

“As Randomized” (time to 1<sup>st</sup> stroke or death)



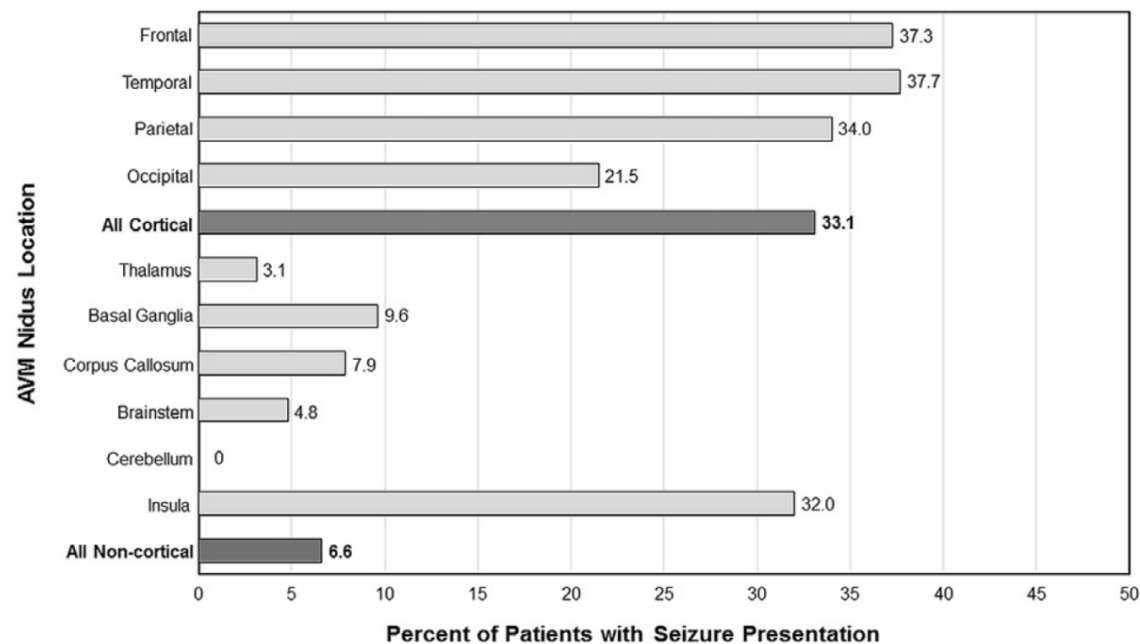
|    |     |     |     |    |    |    |    |    |    |    |    |    |    |    |   |   |
|----|-----|-----|-----|----|----|----|----|----|----|----|----|----|----|----|---|---|
| IT | 116 | 91  | 85  | 79 | 72 | 69 | 56 | 43 | 35 | 28 | 20 | 14 | 14 | 6  | 4 | 1 |
| MM | 110 | 105 | 103 | 97 | 95 | 86 | 77 | 65 | 51 | 46 | 36 | 28 | 21 | 14 | 8 | 4 |

# MAV: convulsions

**Table 2.** Comparison of AVM Angioarchitectural Features in Patients with and without Seizure Presentation

| Factor                            | AVMs in Patients with Seizure Presentation (n = 229)                       | AVMs in Patients without Seizure Presentation (n = 778)                 | P value   |
|-----------------------------------|----------------------------------------------------------------------------|-------------------------------------------------------------------------|-----------|
| Diameter (mean $\pm$ SD cm)       | 2.7 $\pm$ 0.9                                                              | 2.2 $\pm$ 0.9                                                           | < 0.0001* |
| Volume (mean $\pm$ SD mL)         | 4.8 $\pm$ 3.8                                                              | 3.1 $\pm$ 3.1                                                           | < 0.0001* |
| <u>Cortical location</u>          | 203 (88.7%)                                                                | 411 (52.8%)                                                             | < 0.0001* |
| Eloquent location                 | 146 (63.8%)                                                                | 529 (68.0%)                                                             | 0.230     |
| Associated aneurysms <sup>†</sup> | 10 (4.4%)                                                                  | 42 (5.4%)                                                               | 0.541     |
| Single draining vein              | 102 (44.5%)                                                                | 472 (60.7%)                                                             | < 0.0001* |
| <u>Deep venous drainage</u>       | 84 (36.7%)                                                                 | 471 (60.5%)                                                             | < 0.0001* |
| Spetzler-Martin grade             | I: 36 (15.7%), II: 90 (39.3%), III: 80 (34.9%), IV: 22 (9.6%), V: 1 (0.4%) | I: 111 (14.3%), II: 264 (33.9%), III: 318 (40.9%), IV: 85 (10.9%), V: 0 | 0.156     |
| RBAS (mean $\pm$ SD)              | 1.22 $\pm$ 0.46                                                            | 1.15 $\pm$ 0.46                                                         | 0.034*    |
| VRAS                              | 0-1: 64 (27.9%), 2: 81 (35.4%), 3: 78 (34.1%), 4: 6 (2.6%)                 | 0-1: 175 (22.5%), 2: 309 (39.7%), 3: 198 (25.5%), 4: 96 (12.3%)         | < 0.0001* |

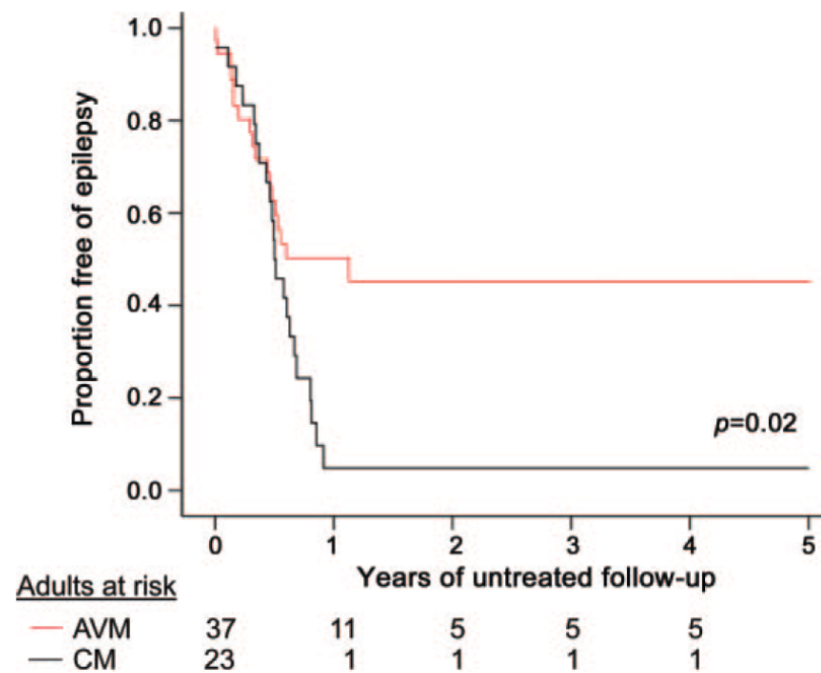
# MAV: convulsions



**Figure 1.** Bar plot showing the frequency of AVM patients with seizure presentation, stratified by nidus location.

# MAV: risque d'épilepsie

**Figure 2** Five-year risk of developing epilepsy after a first-ever unprovoked seizure



Neurology. 2011;76:1548–1554

# MAV: déficit neurologique focal

Clinical signs of focal neurological deficits in 53 patients presenting with unruptured BAVM.

|                                   | Stable<br>(n=11) | Progressive<br>(n=19) | Fluctuating or Reversible<br>(n=23) | Total<br>(N=53) |
|-----------------------------------|------------------|-----------------------|-------------------------------------|-----------------|
| <b>Motor</b>                      |                  |                       |                                     |                 |
| Monoparesis                       | 2                | 1                     | 2                                   | 5               |
| Hemiparesis                       | 2                | 5                     | 4                                   | 11              |
| <b>Sensory</b>                    |                  |                       |                                     |                 |
| Hypesthesia                       | 1                | 6                     | 7                                   | 14              |
| Paresthesia                       | 1                | 0                     | 2                                   | 3               |
| Hemi-/quadrantanopia              | 4                | 2                     | 2                                   | 8               |
| <b>Brainstem/Cerebellar signs</b> |                  |                       |                                     |                 |
| Limb ataxia                       | 0                | 2                     | 1                                   | 3               |
| Dysarthria                        | 1                | 1                     | 1                                   | 3               |
| Cognitive deficits                | 2                | 4                     | 4                                   | 10              |

| <b>Model 1</b>                |                   |                                            |
|-------------------------------|-------------------|--------------------------------------------|
|                               | <b>Odds ratio</b> | <b>95% confidence interval<sup>*</sup></b> |
| <b>Age (year)</b>             | 1.03              | 1.00 – 1.05                                |
| <b>Women</b>                  | 2.14              | 1.15 – 3.97                                |
| <b>Lobar location</b>         | Not included      | Not included                               |
| <b>Deep location</b>          | 2.46              | 1.24 – 4.88                                |
| <b>Brainstem location</b>     | 5.62              | 1.65 – 19.23                               |
| <b>Venous ectasia</b>         | 1.91              | 1.01 – 3.64                                |
| <b>Mean AVM diameter (cm)</b> | Not included      | Not included                               |

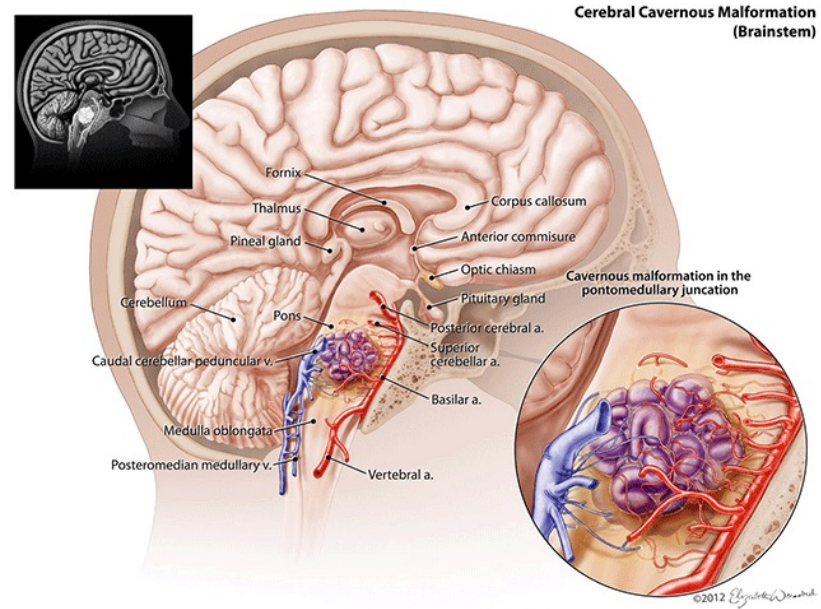
*J Neurol Sci.* 2009 December 15; 287(1-2): 126–130

# MAV: recommandations

- Lignes directrices
  - AHA: non prescriptives
  - ESO: inexistantes

# Malformation artérioveineuse non rompue

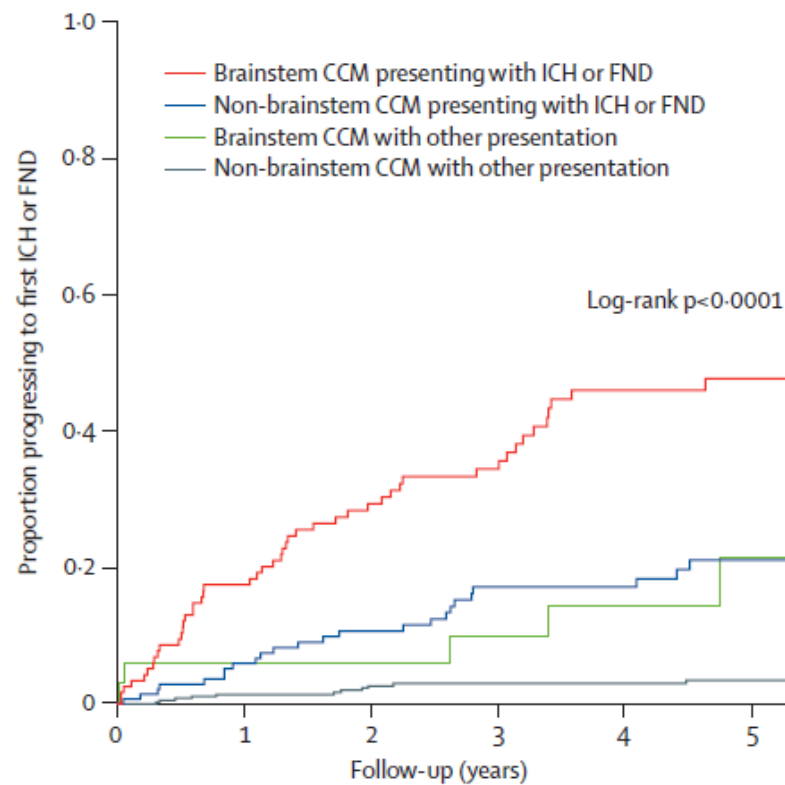
- Condition principalement non chirurgicale
- Présentation clinique variée
  - Céphalées
  - Déficit neurologique focal
  - Convulsions
- Référence en centre de haut volume pour prise en charge



# Angiome caverneux

Cavernome

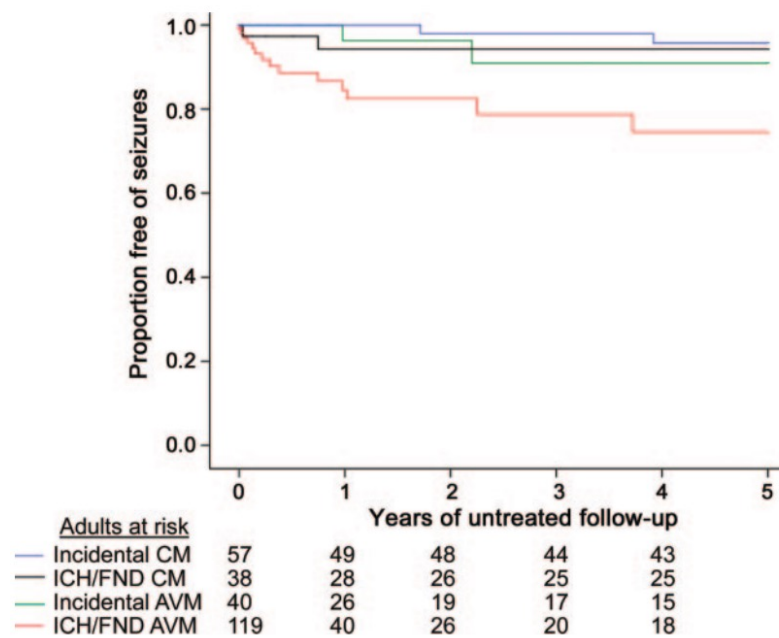
# Cavernome: histoire naturelle



Lancet Neurol. 2016;15(2):166-173

# Cavernome: risque de convulsion

Figure 1 Five-year risk of a first-ever unprovoked seizure



Neurology. 2011;76:1548–1554

# Cavernome: histoire naturelle

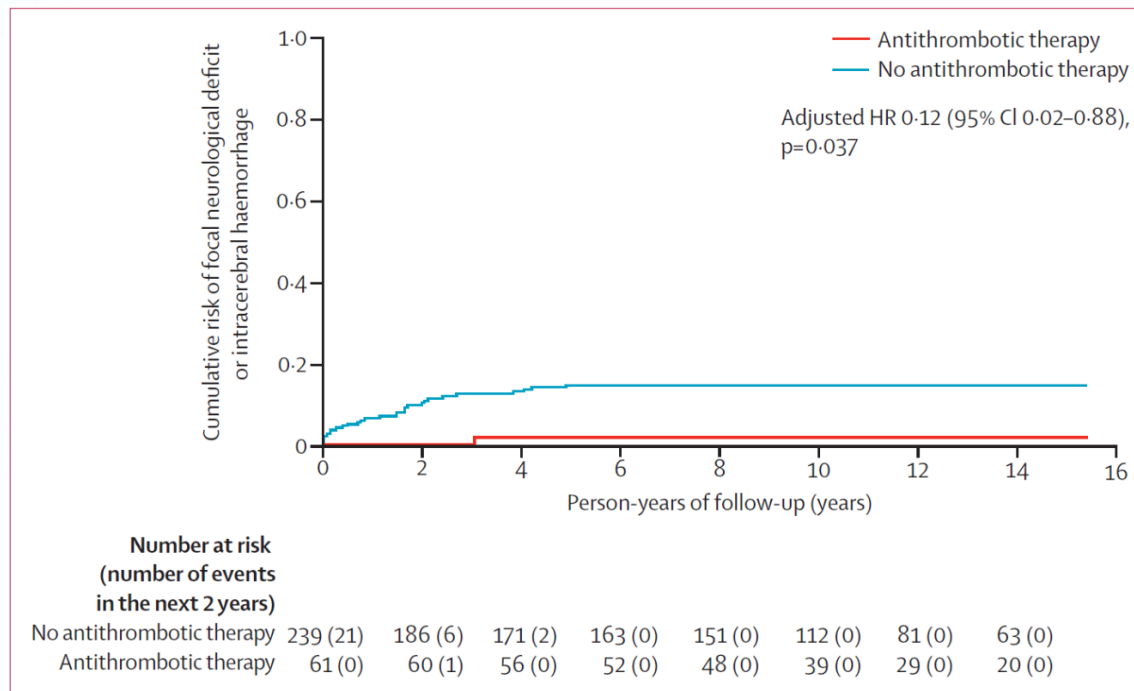
|                                                 | Number of people (%) | Number of outcome events during 5-year follow-up | Hazard ratio (95% CI)* | Estimated 5-year risk (95% CI) |
|-------------------------------------------------|----------------------|--------------------------------------------------|------------------------|--------------------------------|
| <b>Primary outcome: ICH (n=1620)</b>            |                      |                                                  |                        |                                |
| ICH or FND presentation, brainstem CCM location | 495 (31%)            | 135                                              | 10.2 (5.0-23.9)        | 30.8% (26.3-35.2)              |
| ICH or FND presentation, other CCM location     | 327 (20%)            | 45                                               | 5.6 (3.7-9.4)          | 18.4% (13.3-23.5)              |
| Other presentation, brainstem CCM location      | 80 (5%)              | 4                                                | 1.8 (1.3-2.6)          | 8.0% (0.1-15.9)                |
| Other presentation, other CCM location          | 718 (44%)            | 20                                               | Reference              | 3.8% (2.1-5.5)                 |

CCM=cerebral cavernous malformation. FND=non-haemorrhagic focal neurological deficit. ICH=intracranial haemorrhage. \*Bootstrapped 95% CIs: 10 000 samples with replacement.

**Table 2: Hazard ratios and estimated 5-year risks of outcome events for core predictors in prognostic models**

Lancet Neurol. 2016;15(2):166-173

# Cavernome: antithrombotiques



**Figure 1: Kaplan-Meier plot**

Risk of first intracranial haemorrhage or persistent or progressive focal neurological deficit due to cerebral cavernous malformations according to antithrombotic therapy use during 15 years of follow-up in the Scottish Audit of Intracranial Vascular Malformations.

*Lancet Neurol* 2019; 18: 935–41

# Cavernome: antithrombotiques

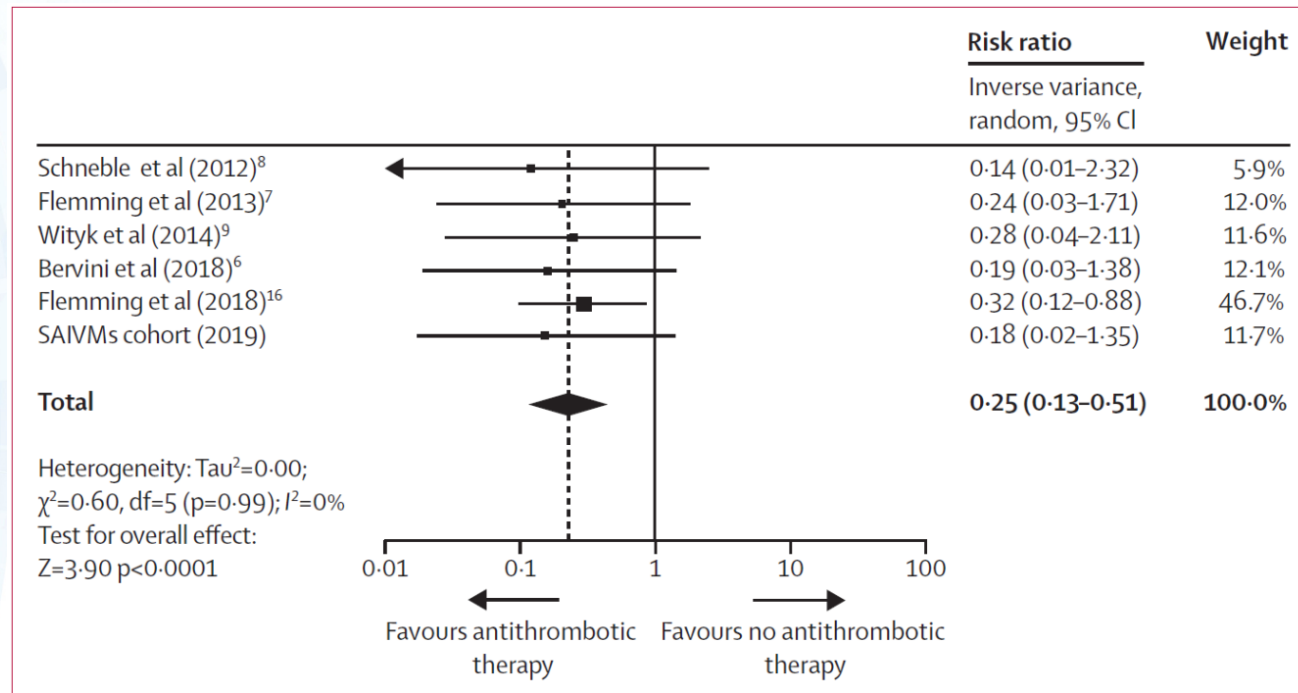


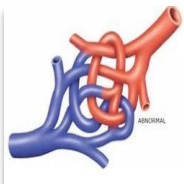
Figure 2: Meta-analysis of the association between antithrombotic therapy use and the risk of intracranial haemorrhage from cerebral cavernous malformations in cohort studies

# Cavernome: récapitulatif

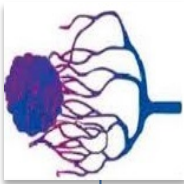
- Suivi clinique
  - Déficit focal, convulsion
  - Dépistage génétique pour lésions multiples
- Suivi radiologique
  - Probablement indiqué, fréquence incertaine
- Référence en centre de haut volume

## iC.R.A.N.I.U.M

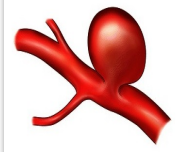
Centre Innovation de Référence des Anomalies Neurovasculaires  
Rares du Centre Hospitalier de l'Université de Montréal



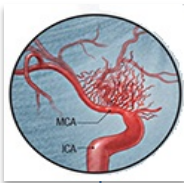
Malformation  
artérioveineuses  
Fistules dures



Cavernomes



Anévrismes familiaux



Moyamoya

### SYMPTOMATOLOGI

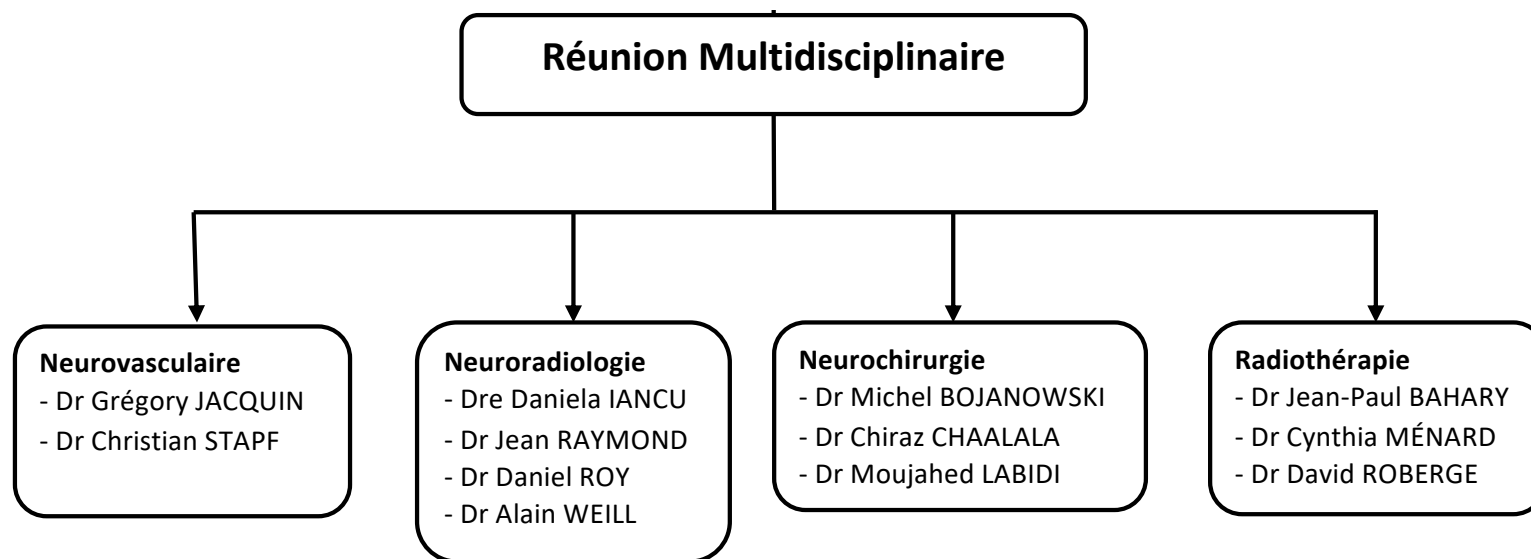
- **E** AVC hémorragique
- AVC ischémique
- Épilepsie
- Déficit neurologique
- Céphalée chronique
- Asymptomatique

### PRISE EN CHARGE

- Multidisciplinaire
- Suivi spécialisé
- Interventionnel
- Non-interventionnel

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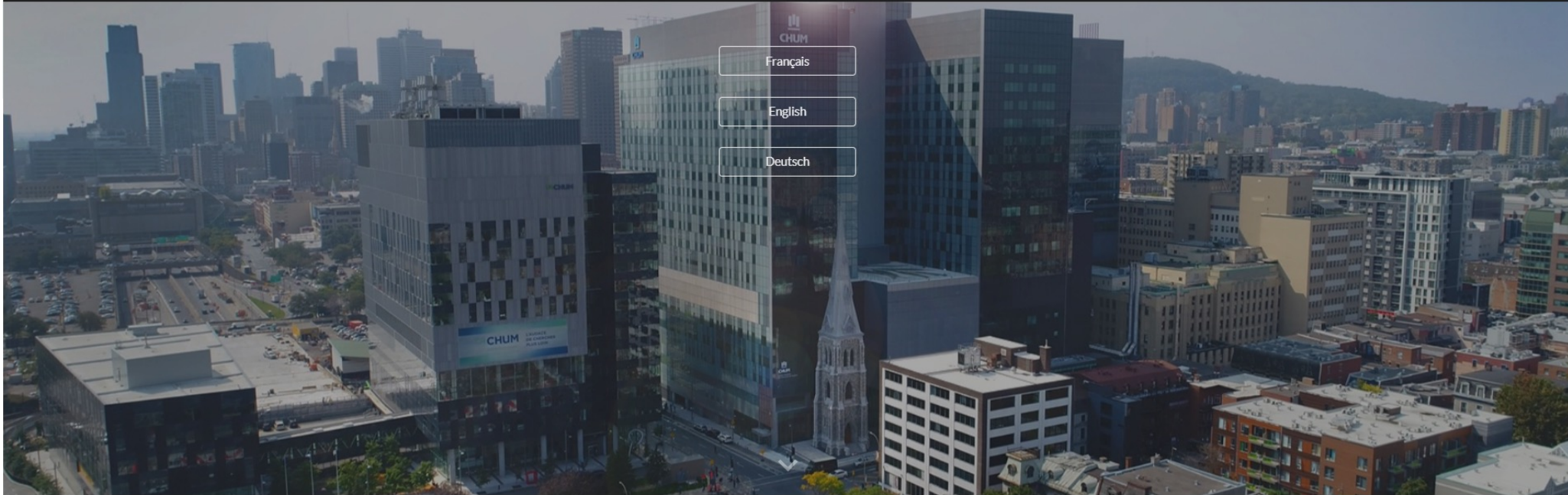


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# Trouvailles fortuites en imagerie neurovasculaires

- En résumé...
  - Rassurance: la plupart des cas de figure ne nécessitent pas d'intervention invasive
  - Instaurer les traitements de prévention primaire des maladies vasculaires (HTA, arrêt du tabac, ...)
  - Pour toute question ou incertitude
    - Référence en centre de haut volume ([montrealneurovasc.ca](http://montrealneurovasc.ca))
    - Appel au neurologue vasculaire de garde