# Get with the guidelines: Stroke prevention 2018


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CSC CNC
Canadian Stroke Consortium
Consortium Neurovasculaire Canadien

Canadian Stroke Best Practices

Centre universitaire de santé McGill
McGill University Health Centre

# Disclosure

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- **Honoraria:** Boehringer Ingelheim**,** Bayer, Allergan, Pfizer, Merz, Servier, Ipsen
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- **Consulting Fees:** Allergan Inc., Boehringer Ingelheim., Bayer, Servier, Ipsen.
- **Investments:** None ☹
- **Guideline Committees:**
  1. CHEP 2017 -
  2. Canadian Cardiovascular Society
  3. Canadian Best Practice Recommendations for Stroke Care –
     1. Co Chair Prevention Guidelines 2014-2017
     2. Committee Member Rehabilitation Guidelines 2012 -2014
     3. Steering Committee 2018-
- **Board of Directors**:
  1. Canadian Stroke Consortium
  2. Quebec Heart and Stroke Foundation

# Objectives

1. Be aware of the new Risk Stratification paradigm and Management following minor stroke or TIA

2. Update on the role of dual antiplatelets following minor stroke or TIA

3. Know the criteria required for Patent Foramen Ovale closure.

4. Effectively manage lipids in the setting of ischemic stroke.

5. Understand the consequences of delay to Cartoid endarterectomy after a TIA/Minor stroke.




RECOMMENDATIONS:

- Overview, Methods and Knowledge Exchange
- Recognition of Stroke
- Prevention of Stroke
- Acute Stroke Management
- Rehabilitation
- Transitions
- Mood, Cognition & Fatigue
- Telestroke
- Stroke in Pregnancy
- Pediatric Stroke
- Appendices

QUALITY & PERFORMANCE


2018 Stroke Report


2017 Stroke Report


2016 Stroke Key Quality Indicators and Case Definitions


2016 Stroke Report

## New release for Canadian Stroke Best Practice Recommendations

Updated recommendations for Acute Stroke Management and a new consensus statement for Acute Stroke Management during Pregnancy.

Read more

Canadian Stroke Best Practices

**Acute Stroke Management**
**&**
**Acute Stroke Management during Pregnancy**

TRANSITIONS OF CARE

Public Awareness | Prevention of Stroke | Hyper Acute Stroke Management | Acute Stroke Management | Rehabilitation | Community Reintegration

TELESTROKE

RESOURCES:


Core Elements of Delivery of Stroke Prevention Services


Stroke Assessment and Prevention Pocket Cards


Taking Action for Optimal Community and Long-Term Stroke Care

my Heart&Stroke Risk ASSESSMENT

ACT F A S T BECAUSE THE QUICKER YOU ACT, THE MORE OF THE PERSON YOU SAVE.

World Stroke Organization

UPCOMING EVENTS:

**Oct. 17-20, 2018**
**World Stroke Congress**
Montreal, Quebec, Canada
Visit Website

**Dec. 7-8, 2018**
**Heart & Stroke Clinical Update**
Toronto, Ontario, Canada
Visit Website

PATIENT & FAMILY TOOLS:

- Your Stroke Journey
- Post-Stroke Checklist
- TIA: Transient ischemic attack Fact Sheet
- Digital Tool Kit for Patients with Atrial Fibrillation
- A Family Guide Pediatric Stroke

International Journal of Stroke WSO

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SAGE

# Canadian stroke best practice recommendations: Secondary prevention of stroke, sixth edition practice guidelines, update 2017

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## Abstract

The 2017 update of The Canadian Stroke Best Practice Recommendations for the Secondary Prevention of Stroke is a collection of current evidence-based recommendations intended for use by clinicians across a wide range of settings. The goal is to provide guidance for the prevention of ischemic stroke recurrence through the identification and management of modifiable vascular risk factors. Recommendations include those related to diagnostic testing, diet and lifestyle, smoking, hypertension, hyperlipidemia, diabetes, antiplatelet and anticoagulant therapies, carotid artery disease, atrial fibrillation, and other cardiac conditions. Notable changes in this sixth edition include the development of core elements for delivering secondary stroke prevention services, the addition of a section on cervical artery dissection, new recommendations regarding the management of patent foramen ovale, and the removal of the recommendations on management of sleep apnea. The Canadian Stroke Best Practice Recommendations include a range of supporting materials such as implementation resources to facilitate the adoption of evidence to practice, and related performance measures to enable monitoring of uptake and effectiveness of the recommendations. The guidelines further emphasize the need for a systems approach to stroke care, involving an interprofessional team, with access to specialists regardless of patient location, and the need to overcome geographic barriers to ensure equity in access within a universal health care system.

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# Introduction

- There are 62,000 strokes in Canada each year.
- 80% of people survive stroke.
- There are more than 400,000 Canadians living with long-term disability from stroke and this will almost double in the next 20 years.
- There are eight million caregivers across Canada, providing at least $25 billion of unpaid care every year

http://www.strokebestpractices.ca/news/the-heart-stroke-2017-stroke-report/

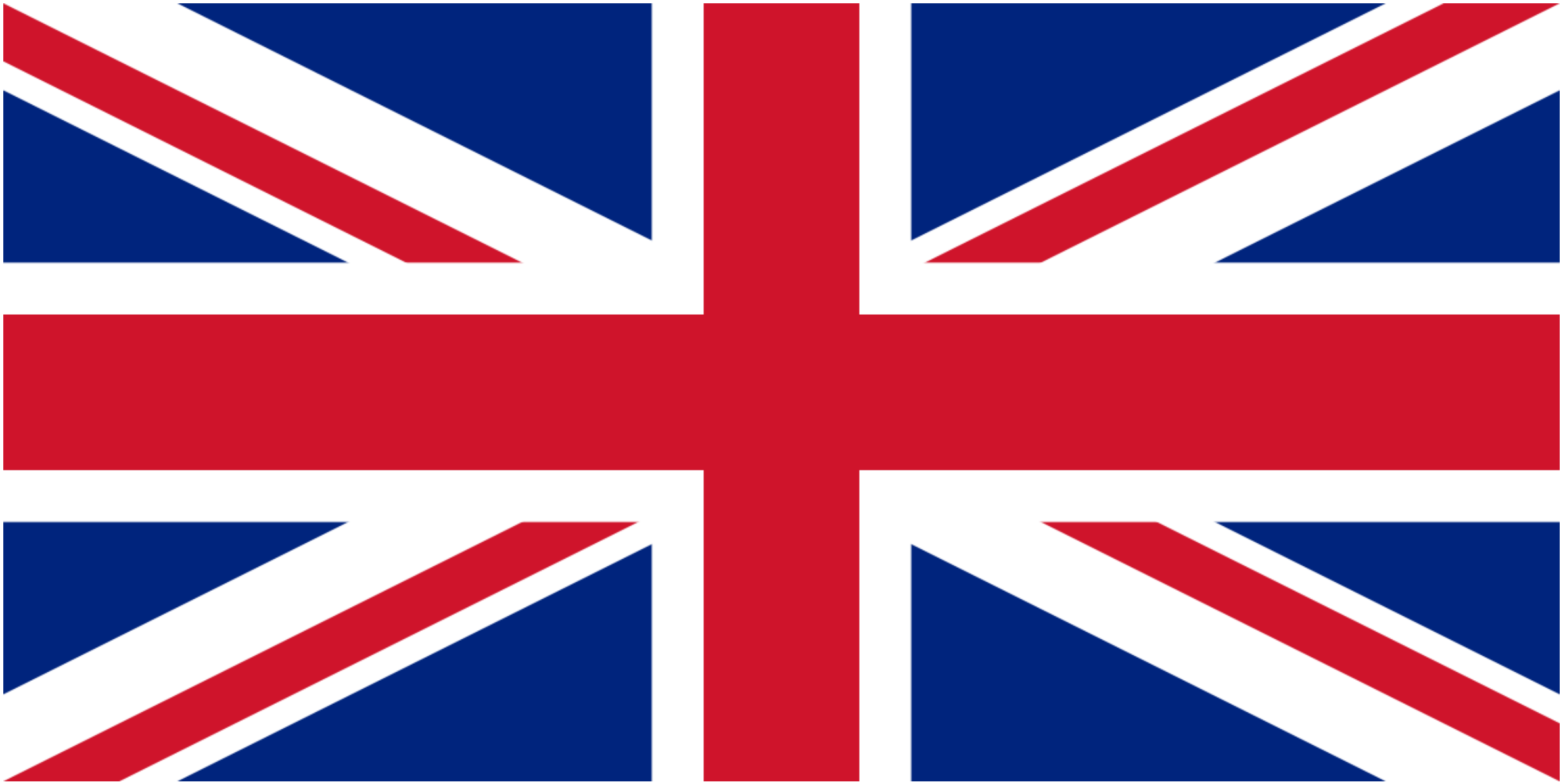
# $ABCD^2$ Lancet. 2007 Jan 27;369(9558):283-92.

- **A**ge > 60 — 1 point
- **B**lood Pressure
  - (S >140 or D > 90) — 1 point
- **C**linical
  - Unilateral weakness — 2 points
  - Speech disturbance not weak — 1 point
- **D**uration
  - > 60 minutes — 2 points
  - 10-59 min — 1 point
  - <10 min — 0 point
- **D**iabetes — 1 point

# ABCD$^2$

| | 2 days | 7 days | 90 day |
|---|---|---|---|
| 0-3 | 1.0% | 1.2% | 1.3% |
| 4-5 | 4.1% | 5.9% | 9.8% |
| 6-7 | 8.1 % | 11.7% | 17.8% |


Lancet. 2007 Jan 27;369(9558):283-92.



# Express Study : Effect of urgent treatment of TIA and minor stroke on early recurrent stroke

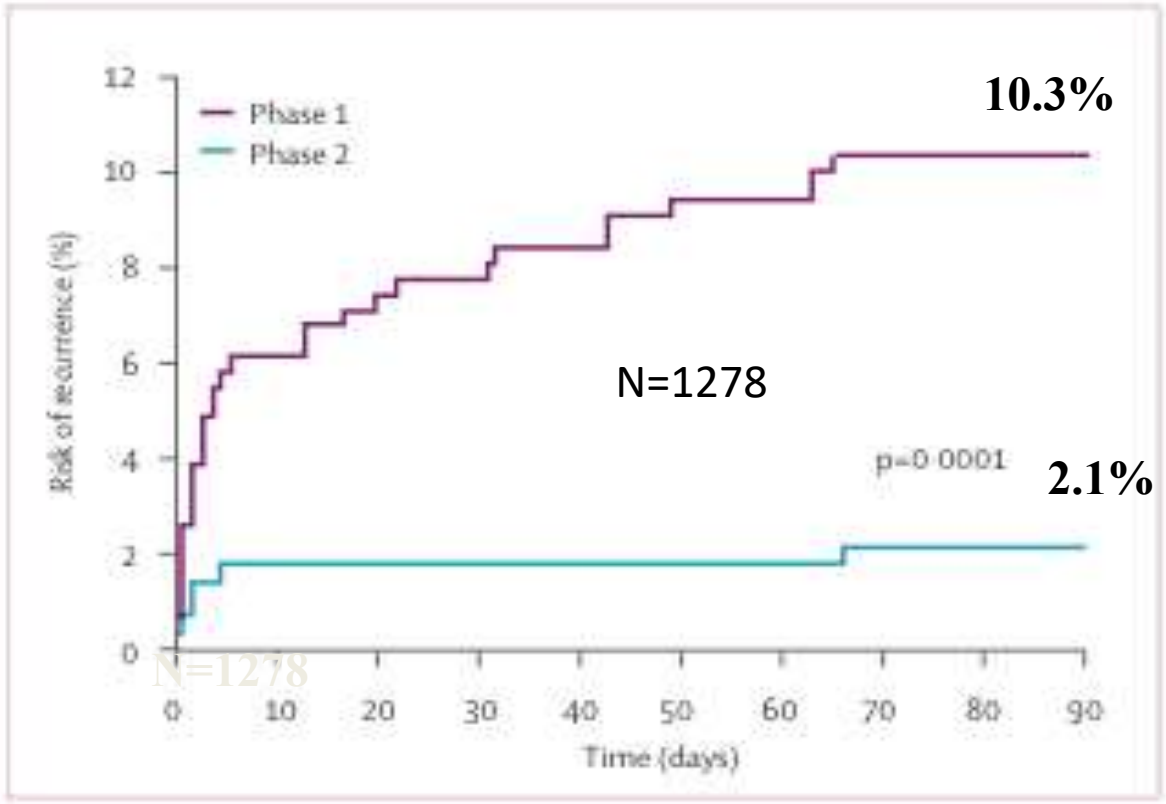
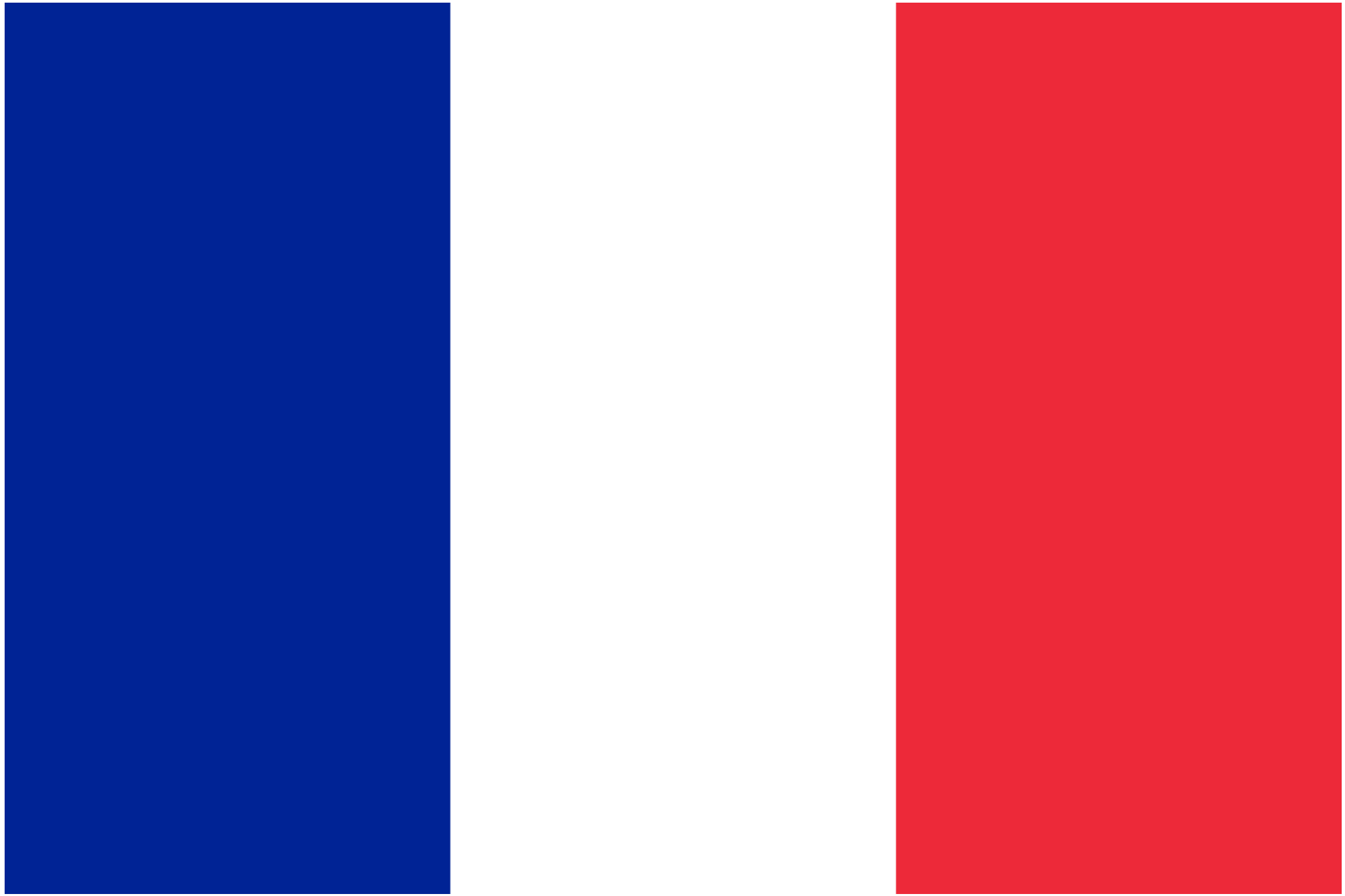



*Figure 2:* Risk of recurrent stroke after first seeking medical attention in all patients with TIA or stroke who were referred to the study clinic

•Early initiation of existing treatment after TIA associated with reduction of **80%** **(NNT= 12)** risk of stroke at 90 days.

***Lancet 2007;370:1432 -42***



# A transient ischaemic attack clinic with round-the-clock access (SOS-TIA): feasibility and effects

*Philippa C Lavallée, Elena Meseguer, Halim Abboud, Lucie Cabrejo, Jean-Marc Olivot, Olivier Simon, Mikael Mazighi, Chantal Nifle, Philippe Niclot, Bertrand Lapergue, Isabelle F Klein, Eric Brochet, Philippe Gabriel Steg, Guy Lesèche, Julien Labreuche, Pierre-Jean Touboul, Pierre Amarenco*

## Summary

**Background** Diagnosis and treatment of cerebral and retinal transient ischaemic attacks (TIAs) are often delayed by the lack of immediate access to a dedicated TIA clinic. We evaluated the effects of rapid assessment of patients with TIA on clinical decision making, length of hospital stay, and subsequent stroke rates.

**Methods** We set up SOS-TIA, a hospital clinic with 24-h access. Patients were admitted if they had sudden retinal or cerebral focal symptoms judged to relate to ischaemia and if they made a total recovery. Assessment, which included neurological, arterial, and cardiac imaging, was within 4 h of admission. A leaflet about TIA with a toll-free telephone number for SOS-TIA was sent to 15 000 family doctors, cardiologists, neurologists, and ophthalmologists in Paris and its administrative region. Endpoints were stroke within 90 days, and stroke, myocardial infarction, and vascular death within 1 year.

**Findings** Between January, 2003, and December, 2005, we admitted 1085 patients with suspected TIA; 574 (53%) were seen within 24 h of symptom onset. 701 (65%) patients had confirmed TIA or minor stroke, and 144 (13%) had possible TIA. 108 (17%) of the 643 patients with confirmed TIA had brain tissue damage. Median duration of symptoms was 15 min (IQR 5–75 min). Of the patients with confirmed or possible TIA, all started a stroke prevention programme, 43 (5%) had urgent carotid revascularisation, and 44 (5%) were treated for atrial fibrillation with anticoagulants. 808 (74%) of all patients seen were sent home on the same day. The 90-day stroke rate was 1·24% (95% CI 0·72–2·12), whereas the rate predicted from ABCD² scores was 5·96%.

**Interpretation** Use of TIA clinics with 24-h access and immediate initiation of preventive treatment might greatly reduce length of hospital stay and risk of stroke compared with expected risk.

*Lancet Neurol* 2007; 6: 953–60

Published Online
October 9, 2007
DOI:10.1016/S1474-4422(07)70248-X

See **Reflection and Reaction** page 940

See **Articles** page 961

See *Lancet* 2007;
DOI:10.1016/S0140-6736(07)61448-2

**Department of Neurology and Stroke Centre** (P C Lavallée MD, E Meseguer MD, H Abboud MD, L Cabrejo MD, J-M Olivot MD, O Simon MD, M Mazighi MD, C Nifle MD, P Niclot MD, B Lapergue MD, J Labreuche BS, P-J Touboul MD, P Amarenco MD), **Neuroradiology Unit, Department of Radiology** (I F Klein MD), **Department of Cardiology** (E Brochet MD, P G Steg MD), **and Department**

# Limitations of the $ABCD^2$

**CASE 1**

60 year old female with with a 5 minute history of left face/arm/leg numbness. BP 145/91. 2 days previously had right monocluar visual loss “like a shade coming over my eye” **$ABCD^2$: 2**

**Case 2**

70 year old female with a 5 minute history of diplopia, ataxia, and hemibody numbness. **$ABCD^2$: 1**

**Are these really low risk patients?**

| Risk For Recurrent Stroke | Time from Stroke Symptom Onset to Healthcare Presentation | Presenting Symptoms | When Patients Should be Seen by Healthcare Professional | Where Patients Should be Seen | Tests to be Done on Initial Assessment |
|---|---|---|---|---|---|
| Very HIGH RISK | Within 48 hours | - Transient, fluctuating or persistent unilateral weakness (face, arm and/or leg)<br>- Transient, fluctuating or persistent speech disturbance/aphasia.<br>- Fluctuating or persistent symptoms **without motor weakness or speech disturbance** (e.g. hemibody sensory symptoms, monocular visual loss, hemifield visual loss, ± other symptoms suggestive of posterior circulation stroke such as diplopia, dysarthria, and/or ataxia). | Immediately | Emergency Department [ideally ED with brain imaging onsite and access to alteplase (tPA)] | CT/CTA or MRI/MRA (aortic arch to vertex), ECG, Lab Work (Table 3) |
| HIGH RISK | Between 48 hours and 2 weeks | - Transient, fluctuating or persistent unilateral weakness (face, arm, and/or leg), or speech disturbance/aphasia | As soon as possible, ideally within 24 hours | Stroke Prevention Clinic with Neurologist or Stroke Specialist, Nurse Practitioner | CT/CTA or MRI/MRA (aortic arch to vertex), ECG, Lab Work (Table 3) |
| Moderate (INCREASED) RISK | Between 48 hours and 2 weeks | - Fluctuating or persistent symptoms ***without motor weakness*** or speech disturbance (e.g., hemibody sensory symptoms, monocular vision loss, binocular diplopia, hemifield vision loss, or ataxia) | As soon as possible, ideally within 2 weeks | Stroke Prevention Clinic with Neurologist or Stroke Specialist, Nurse Practitioner | CT/CTA or MRI/MRA (aortic arch to vertex), ECG, Lab Work (Table 3) |
| LOWER RISK | More than 2 weeks | - Any typical or atypical symptoms of stroke or transient ischemic attack | Ideally within 1 month | Ambulatory Clinic with access to Neurologist or Stroke Specialist, Nurse Practitioner | As appropriate based on assessment by health care team |

**Table 2. Summary of HSF recurrent stroke risk levels and initial management (based on CSBPR Secondary Prevention of Stroke, Section 1: Initial Risk Stratification and Management)**

Published in: Theodore Wein; M Patrice Lindsay; Robert Côté; et al. *International Journal of Stroke* 13, 420-443.DOI: 10.1177/1747493017743062 . 

ORIGINAL ARTICLE

# Clopidogrel and Aspirin in Acute Ischemic Stroke and High-Risk TIA

S. Claiborne Johnston, M.D., Ph.D., J. Donald Easton, M.D., Mary Farrant, M.B.A., William Barsan, M.D., Robin A. Conwit, M.D., Jordan J. Elm, Ph.D., Anthony S. Kim, M.D., Anne S. Lindblad, Ph.D., and Yuko Y. Palesch, Ph.D., for the Clinical Research Collaboration, Neurological Emergencies Treatment Trials Network, and the POINT Investigators*

## ABSTRACT

### BACKGROUND

Combination antiplatelet therapy with clopidogrel and aspirin may reduce the rate of recurrent stroke during the first 3 months after a minor ischemic stroke or transient ischemic attack (TIA). A trial of combination antiplatelet therapy in a Chinese population has shown a reduction in the risk of recurrent stroke. We tested this combination in an international population.

### METHODS

In a randomized trial, we assigned patients with minor ischemic stroke or high-risk TIA to receive either clopidogrel at a loading dose of 600 mg on day 1, followed by 75 mg per day, plus aspirin (at a dose of 50 to 325 mg per day) or the same range of doses of aspirin alone. The dose of aspirin in each group was selected by the site investigator. The primary efficacy outcome in a time-to-event analysis was the risk of a composite of major ischemic events, which was defined as ischemic stroke, myocardial infarction, or death from an ischemic vascular event, at 90 days.

### RESULTS

A total of 4881 patients were enrolled at 269 international sites. The trial was halted after 84% of the anticipated number of patients had been enrolled because the data and safety monitoring board had determined that the combination of clopidogrel and aspirin was associated with both a lower risk of major ischemic events and a higher risk of major hemorrhage than aspirin alone at 90 days. Major ischemic events occurred in 121 of 2432 patients (5.0%) receiving clopidogrel plus aspirin and in 160 of 2449 patients (6.5%) receiving aspirin plus placebo (hazard ratio, 0.75; 95% confidence interval [CI], 0.59 to 0.95; P=0.02), with most events occurring during the first week after the initial event. Major hemorrhage occurred in 23 patients (0.9%) receiving clopidogrel plus aspirin and in 10 patients (0.4%) receiving aspirin plus placebo (hazard ratio, 2.32; 95% CI, 1.10 to 4.87; P=0.02).

### CONCLUSIONS

In patients with minor ischemic stroke or high-risk TIA, those who received a combination of clopidogrel and aspirin had a lower risk of major ischemic events but a higher risk of major hemorrhage at 90 days than those who received aspirin alone. (Funded by the National Institute of Neurological Disorders and Stroke; POINT ClinicalTrials.gov number, NCT00991029.)

From the Dean's Office, Dell Medical School, University of Texas at Austin, Austin (S.C.J.); the Department of Neurology, University of California, San Francisco, San Francisco (J.D.E., M.F., A.S.K.); the Department of Emergency Medicine, University of Michigan, Ann Arbor (W.B.); the Division of Clinical Research, National Institute of Neurological Disorders and Stroke, Bethesda (R.A.C.), and Emmes, Rockville (A.S.L.) — both in Maryland; and the Data Coordination Unit, Department of Public Health Sciences, Medical University of South Carolina, Charleston (J.J.E., Y.Y.P.). Address reprint requests to Dr. Johnston at Dell Medical School, University of Texas at Austin, 1501 Red River St., Austin, TX 78701, or at clay.johnston@utexas.edu.

*A complete list of the POINT Investigators is provided in the Supplementary Appendix, available at NEJM.org.

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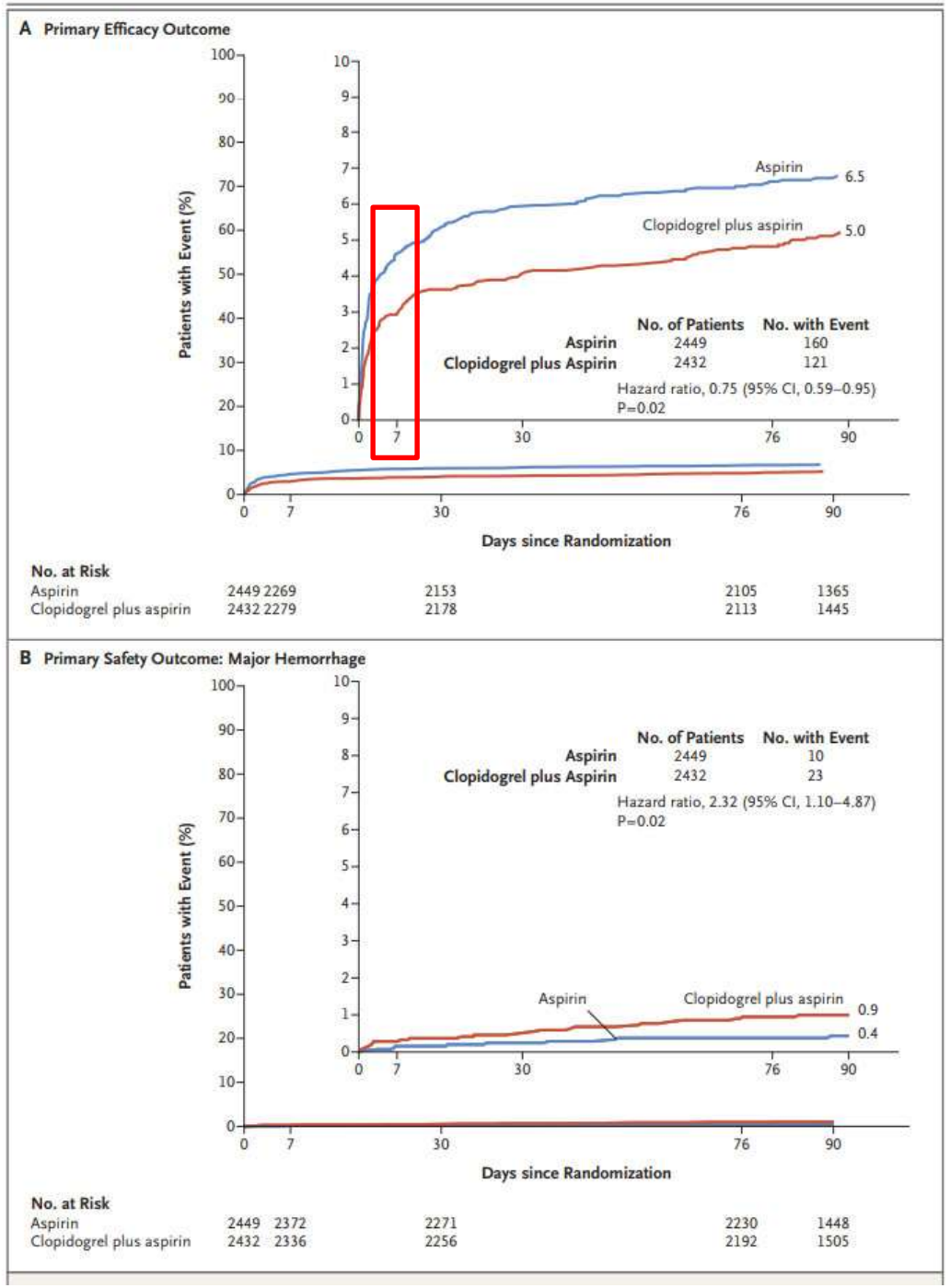
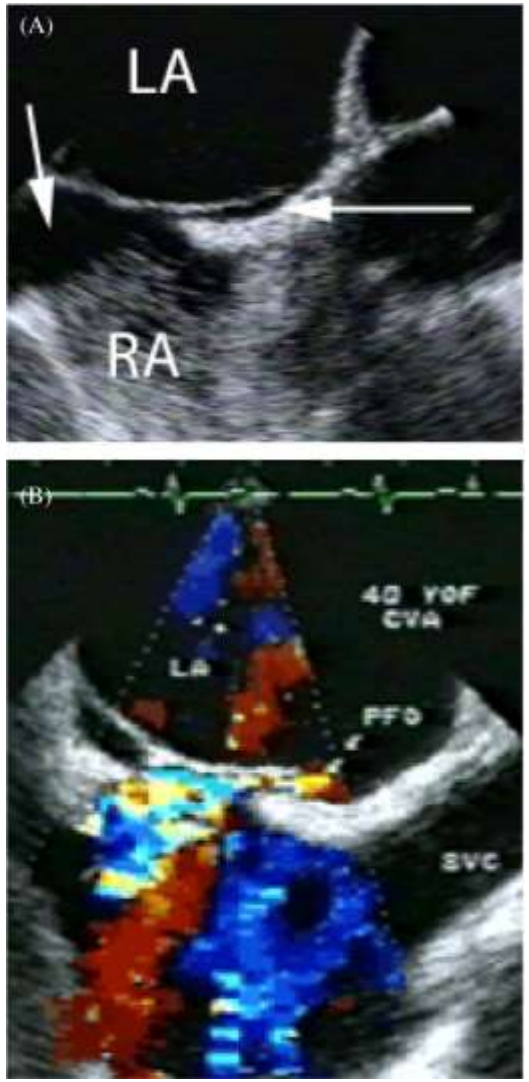

A Primary Efficacy Outcome
Patients with Event (%)
Aspirin
6.5
Clopidogrel plus aspirin
5.0
No. of Patients
No. with Event
Aspirin
2449
160
Clopidogrel plus Aspirin
2432
121
Hazard ratio, 0.75 (95% CI, 0.59–0.95)
P=0.02
Days since Randomization
No. at Risk
Aspirin
2449 2269
2153
2105
1365
Clopidogrel plus aspirin
2432 2279
2178
2113
1445
B Primary Safety Outcome: Major Hemorrhage
Patients with Event (%)
No. of Patients
No. with Event
Aspirin
2449
10
Clopidogrel plus Aspirin
2432
23
Hazard ratio, 2.32 (95% CI, 1.10–4.87)
P=0.02
Aspirin
Clopidogrel plus aspirin
0.9
0.4
Days since Randomization
No. at Risk
Aspirin
2449 2372
2271
2230
1448
Clopidogrel plus aspirin
2432 2336
2256
2192
1505

**Table 2. Efficacy and Safety Outcomes.**

| Outcome | Clopidogrel plus Aspirin (N=2432) | Aspirin (N=2449) | Hazard Ratio (95% CI) | P Value |
|---|---|---|---|---|
| | *number (percent)* | | | |
| **Primary efficacy outcome** | | | | |
| Composite of ischemic stroke, myocardial infarction, or death from ischemic vascular causes | 121 (5.0) | 160 (6.5) | 0.75 (0.59–0.95) | 0.02 |
| **Secondary efficacy outcomes** | | | | |
| Ischemic stroke | 112 (4.6) | 155 (6.3) | 0.72 (0.56–0.92) | 0.01* |
| Myocardial infarction | 10 (0.4) | 7 (0.3) | 1.44 (0.55–3.78) | 0.46* |
| Death from ischemic vascular causes | 6 (0.2) | 4 (0.2) | 1.51 (0.43–5.35) | 0.52* |
| Ischemic or hemorrhagic stroke | 116 (4.8) | 156 (6.4) | 0.74 (0.58–0.94) | 0.01* |
| Composite of ischemic stroke, myocardial infarction, death from ischemic vascular causes, or major hemorrhage | 141 (5.8) | 167 (6.8) | 0.84 (0.67–1.05) | 0.13* |
| **Primary safety outcome** | | | | |
| Major hemorrhage | 23 (0.9) | 10 (0.4) | 2.32 (1.10–4.87) | 0.02 |
| **Other safety outcomes** | | | | |
| Hemorrhagic stroke | 5 (0.2) | 3 (0.1) | 1.68 (0.40–7.03) | 0.47 |
| Symptomatic intracerebral hemorrhage | 2 (0.1) | 2 (0.1) | 1.01 (0.14–7.14) | 0.99 |
| Other symptomatic intracranial hemorrhage | 2 (0.1) | 0 | | 0.16 |
| Major hemorrhage other than intracranial hemorrhage | 17 (0.7) | 7 (0.3) | 2.45 (1.01–5.90) | 0.04 |
| Minor hemorrhage | 40 (1.6) | 13 (0.5) | 3.12 (1.67–5.83) | <0.001 |
| Death from any cause | 18 (0.7) | 12 (0.5) | 1.51 (0.73–3.13) | 0.27 |

* Post hoc correction for multiple testing of five secondary end points by the Bonferroni method resulted in a P value of 0.01 to indicate a significant difference between groups.

# Identification of candidates for PFO closure in the echocardiography laboratory




Identification of candidates for PFO closure in the echocardiography laboratory, Volume: 35, Issue: 11, Pages: 1860-1867, First published: 10 October 2018, DOI: (10.1111/echo.14154)

# Six Trials of Patent Foramen Ovale Closure

Ropper AH. N Engl J Med 2017;377:1093-1095.

**Table 1. Six Trials of Patent Foramen Ovale Closure for Stroke with Results Published in the *Journal*.***

| Trial Name (Year of Publication) | No. of Patients | Mean or Median No. of Years of Follow-up | Comparator | Primary Outcome | Hazard Ratio† | P Value† |
|---|---|---|---|---|---|---|
| Trials with negative findings | | | | | | |
| CLOSURE I (2012)[2] | 909 | 2 | Antiplatelet therapy, warfarin, or both | Composite of stroke or transient ischemic attack at 2 years, death from any cause during the first 30 days, or death from neurologic causes between 31 days and 2 years after randomization | 0.78 | 0.37 |
| PC (2013)[3] | 414 | 4.1 (PFO closure group), 4.0 (medical-therapy group) | Antiplatelet therapy or anticoagulation‡ | Composite of death, stroke, transient ischemic attack, or peripheral embolism | 0.63 | 0.34 |
| RESPECT (2013)[4] | 980 | 2.1 | Antiplatelet therapy or warfarin | Composite of recurrent nonfatal ischemic stroke, fatal ischemic stroke, or early death after randomization | 0.49 | 0.08 |
| Trials with positive findings | | | | | | |
| Gore REDUCE (2017)[5] | 664 | 3.2 | Antiplatelet therapy | Ischemic stroke and new brain infarction on imaging | 0.23 | 0.002 |
| CLOSE (2017)[6] | 663 | 5.3 | Antiplatelet therapy or anticoagulation‡ | Stroke | 0.03 | <0.001 |
| RESPECT extended follow-up (2017)[7] | 980 | 5.9 | Antiplatelet therapy or warfarin | Composite of recurrent nonfatal ischemic stroke, fatal ischemic stroke, or early death after randomization | 0.55 | 0.046 |

* CLOSE denotes Patent Foramen Ovale Closure or Anticoagulants versus Antiplatelet Therapy to Prevent Stroke Recurrence, CLOSURE I Evaluation of the STARFlex Septal Closure System in Patients with a Stroke and/or Transient Ischemic Attack due to Presumed Paradoxical Embolism through a Patent Foramen Ovale, Gore REDUCE Gore HELEX Septal Occluder and Antiplatelet Medical Management for Reduction of Recurrent Stroke or Imaging-Confirmed TIA in Patients with Patent Foramen Ovale (PFO), PC Clinical Trial Comparing Percutaneous Closure of Patent Foramen Ovale Using the Amplatzer PFO Occluder with Medical Treatment in Patients with Cryptogenic Embolism, and RESPECT Randomized Evaluation of Recurrent Stroke Comparing PFO Closure to Established Current Standard of Care Treatment.

† The hazard ratio and P value are for the expected probability of stroke or other primary outcome after closure of the PFO versus medical treatment in the intention-to-treat analysis.

‡ Anticoagulation refers to any form of anticoagulation.

***Note: These recommendations are applicable to ischemic stroke and transient ischemic attack.***

**9.1 Patent Foramen Ovale (PFO) *(Revised 2017)***

i. Patients with a recent ischemic stroke or TIA attributed to a PFO should have an evaluation by a clinician with stroke and cardiovascular expertise [Evidence Level C].

ii. For carefully-selected patients with a recent ischemic stroke or TIA attributed to a PFO, PFO device closure plus long-term antiplatelet therapy is recommended over long-term antithrombotic therapy alone provided all the following criteria are met. [Evidence Level A]:

   a. Age 18-60 years;

   b. The diagnosis of the index stroke event is confirmed by imaging as a non-lacunar embolic ischemic stroke or a TIA with positive neuroimaging or cortical symptoms;

   c. The patient has been evaluated by a neurologist or clinician with stroke expertise, and the PFO is felt to be the most likely cause for the index stroke event following a thorough etiological evaluation to exclude alternate etiologies.

iii. For patients requiring long-term anticoagulation, the decision regarding PFO closure remains unclear, and decisions should be based on individual patient characteristics and risk versus benefit profile [Evidence C].

iv. For patients with a recent ischemic stroke or TIA attributed to a PFO who do no undergo PFO closure and are aged 60 years or younger, either antiplatelet or anticoagulant therapy is recommended for secondary stroke prevention, unless there is a separate evidence-based indication for chronic anticoagulant therapy[Evidence Level B].

v. There is insufficient evidence to make a recommendation regarding the comparative effectiveness of PFO closure vs. anticoagulant therapy.

# Case Presentation

45 year old diabetic male presents with a transient pure motor hemiparesis that lasted for 10 minutes. As part of his stroke investigation he is found to have a large PFO with right to left shunt. His vascular imaging is unremarkable and a holter monitor shows no evidence of PAF.

A. This man should be sent for PFO closure based on the the recent CLOSE, RESPECT and REDUCE trials.
B. This man should have his PFO closed only if a thrombophelia work up is negative.
C. More information is required regarding the size of the PFO, the number of bubbles present on TEE and whether an atrial septal aneurysm is present
D. This man is not a candidate for PFO closure

# Case of Brother Darryl

- 75 year old male seen in stroke prevention clinic. He is here for his 6 month post stroke follow-up. His LDL-C today is **2.3** mmol/L. At the time of his event it was 3.5 mmol/L and he was placed on Atorvastatin 80mg.

- PMHx: Stroke, HTN, hyperlipidemia

Question:

1) Are you satisfied with this LDL level?
2) Should it be lowered even more?

# Case of other brother Darryl

- 73 year old male seen in stroke prevention clinic. He is her for his 6 month post stroke follow-up. His LDL-C today is **2.0** mmol/L (77mg/dl). At the time of his event it was 3.5mmol/L (135mg/dl) 2.8 and he was placed on Atorvastatin 80mg.

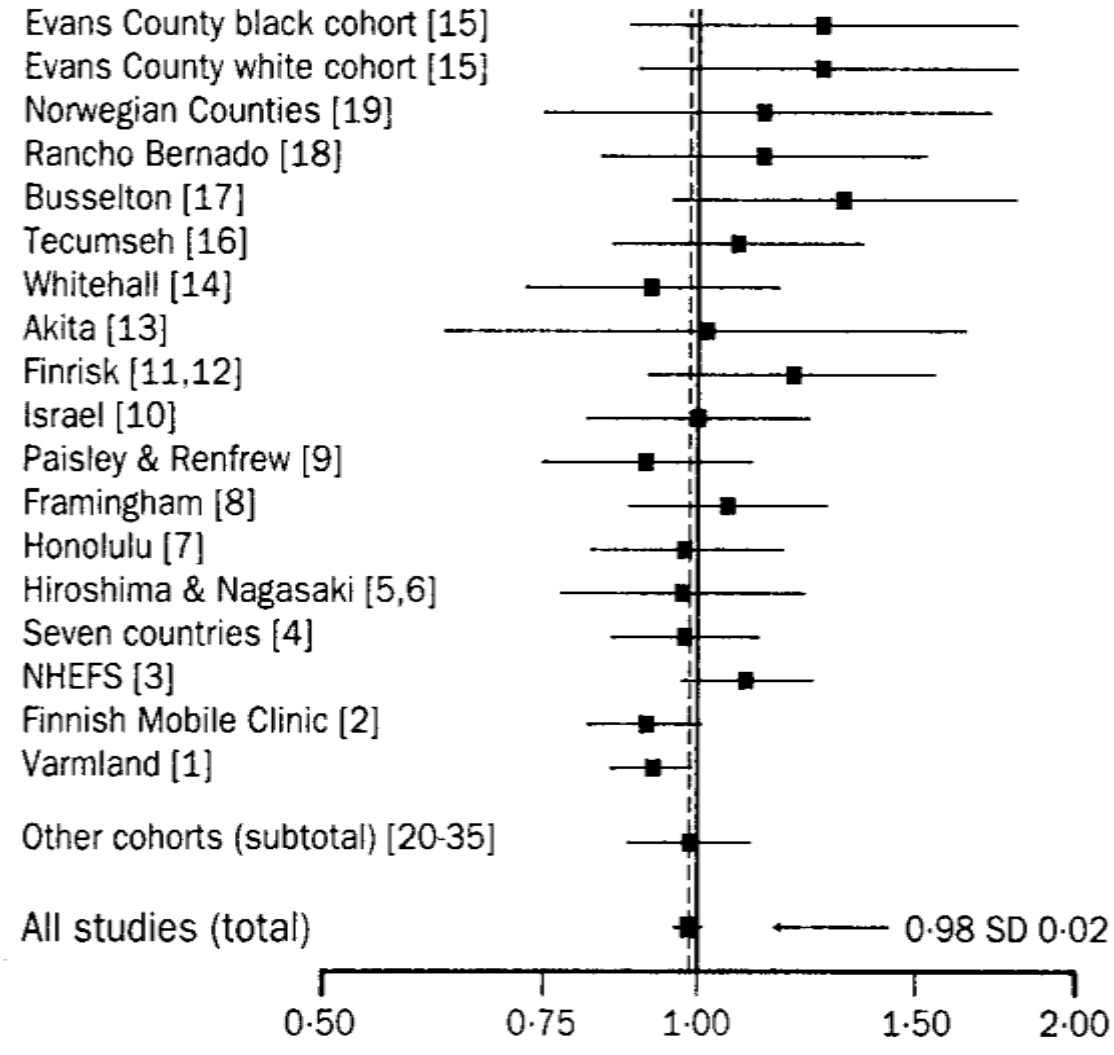
- PMHx: Stroke, HTN, hyperlipidemia, stable CAD.

Question:

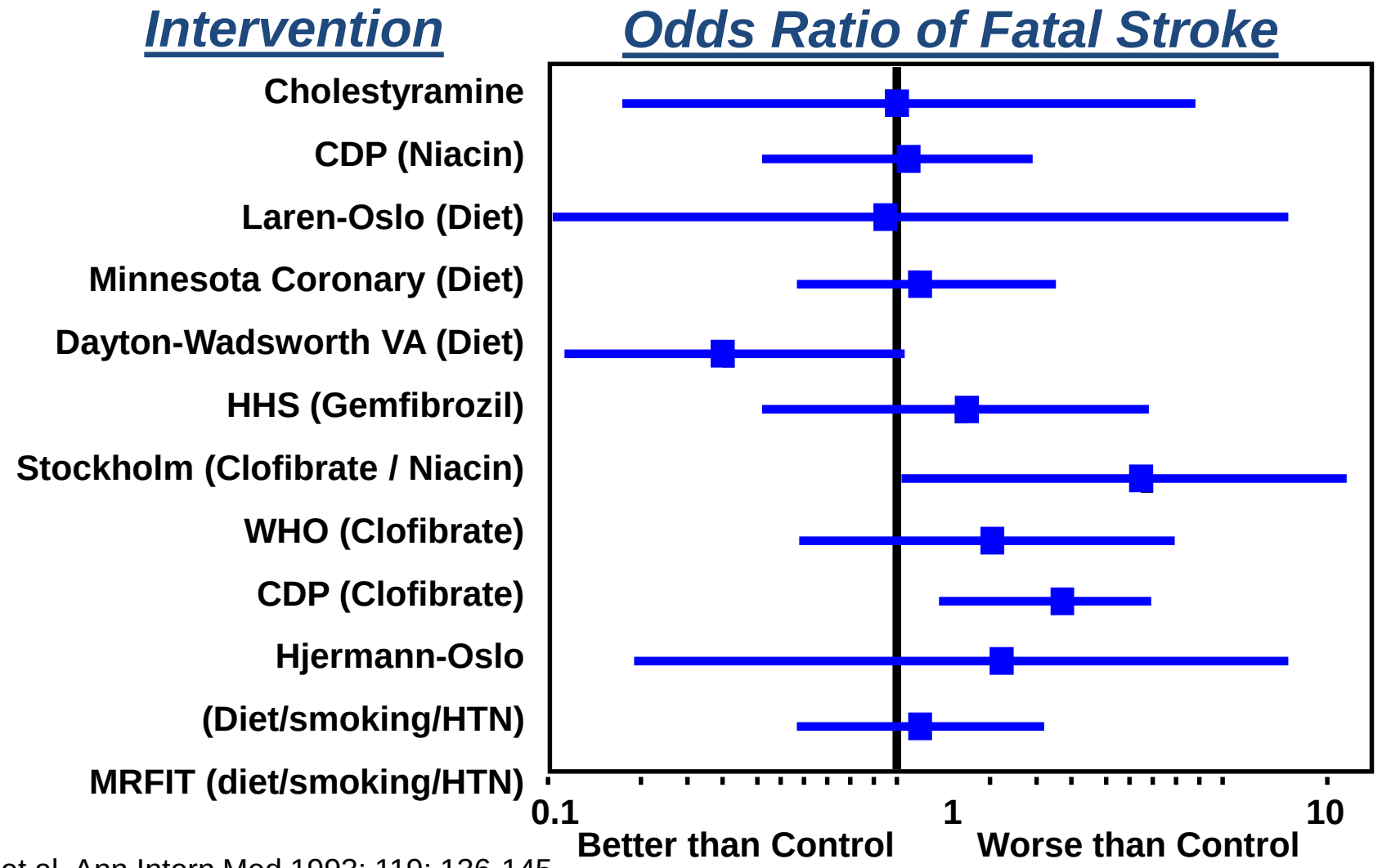
1) Are you satisfied with this LDL level?
2) Should it be lowered?

# Cholesterol and Stroke Risk

LANCET 1995; 346: 1647-1653.



# Cholesterol Reduction and the Risk for Stroke in Men: Non-Statin Trials




Atkins et al, Ann Intern Med 1993; 119: 136-145.

# Inverse association of dietary fat with development of ischemic stroke in men.

**Gillman MW, Cupples LA, Millen BE, Ellison RC, Wolf PA.**

JAMA:1997;2145-50

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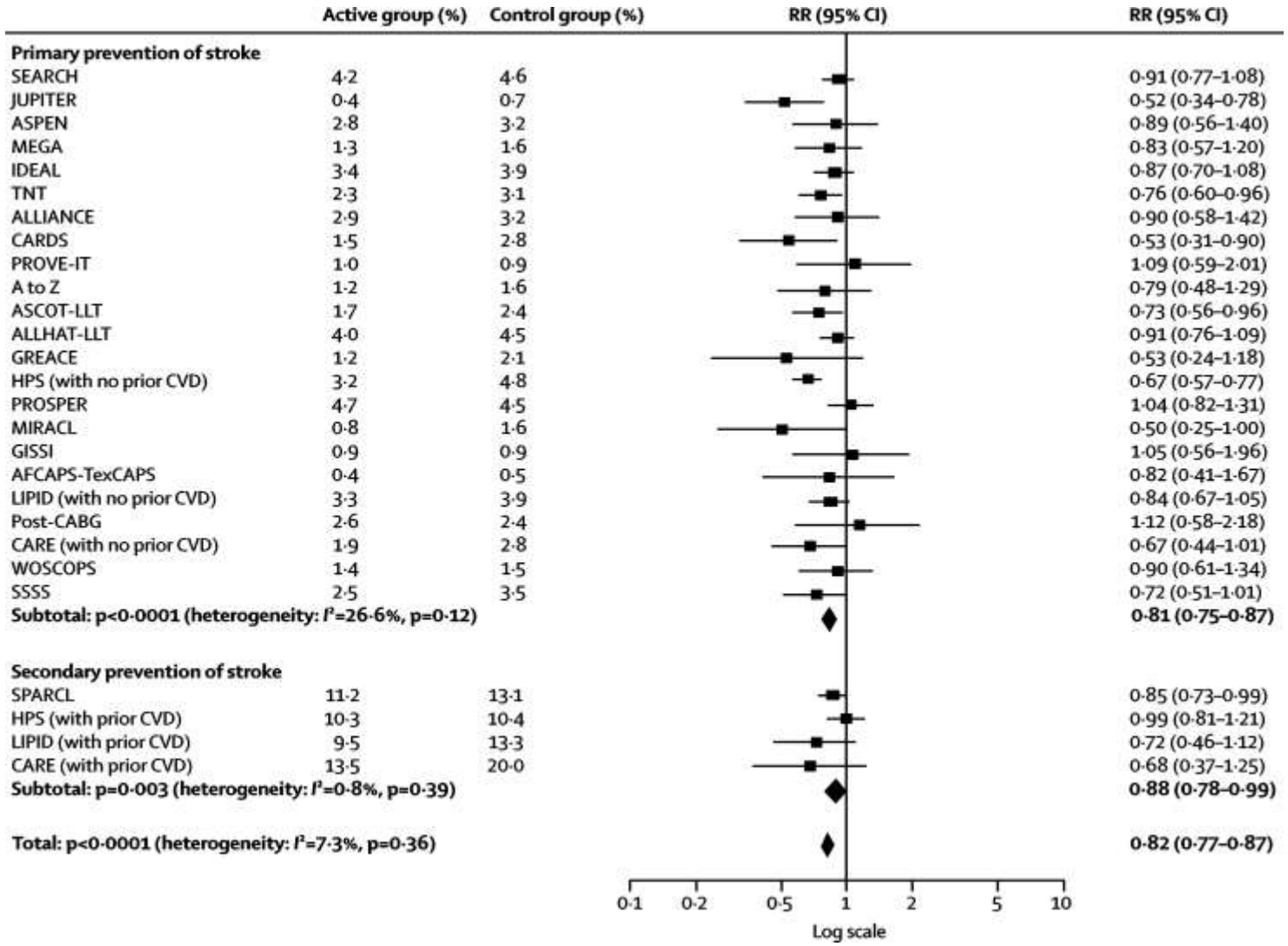
CONTEXT: A few ecological and cohort studies in Asian populations suggest an inverse association of the intake of both fat and saturated fat with risk of stroke. However, data among western populations are scant. OBJECTIVE: To examine the association of stroke incidence with intake of fat and type of fat among middle-aged US men during 20 years of follow-up. DESIGN AND SETTING: The Framingham Heart Study, a population-based cohort study. PARTICIPANTS: A total of 832 men, aged 45 through 65 years, who were free of cardiovascular disease at baseline (1966-1969). MEASUREMENTS AND DATA ANALYSIS: The diet of each subject was assessed at baseline by a single 24-hour dietary recall, from which intakes of energy and macronutrients were estimated. In Kaplan-Meier analyses, we calculated age-adjusted cumulative incidence rates of stroke. Using Cox regression, we estimated stroke incidence relative risks during 20 years of follow-up. MAIN OUTCOME MEASURE: Incidence of ischemic stroke, which occurred in 61 subjects during the follow-up period. RESULTS: Mean intakes were 10975 kJ for energy; 114 g (39% of energy) for total fat; 44 g (15%) for saturated fat; 46 g (16%) for monounsaturated fat; and 16 g (5%) for polyunsaturated fat. Risk of ischemic stroke declined across the increasing quintile of total fat (log-rank trend P=.008), saturated fat (P=.002), and monounsaturated fat (P=.008) but not polyunsaturated fat (P=.33). The age- and energy-adjusted relative risk for each increment of 3% of energy from total fat was 0.85 (95% confidence interval [CI], 0.78-0.94); for an increment of 1% from saturated fat, 0.91 (95% CI, 0.85-0.98); and for 1% from monounsaturated fat, 0.89 (95% CI, 0.83-0.96). Adjustment for cigarette smoking, glucose intolerance, body mass index, blood pressure, blood cholesterol level, physical activity, and intake of vegetables and fruits and alcohol did not materially change the results. Too few cases of hemorrhagic stroke (n=14) occurred to draw inferences. CONCLUSION: Intakes of fat, saturated fat, and monounsaturated fat were associated with reduced risk of ischemic stroke in men.

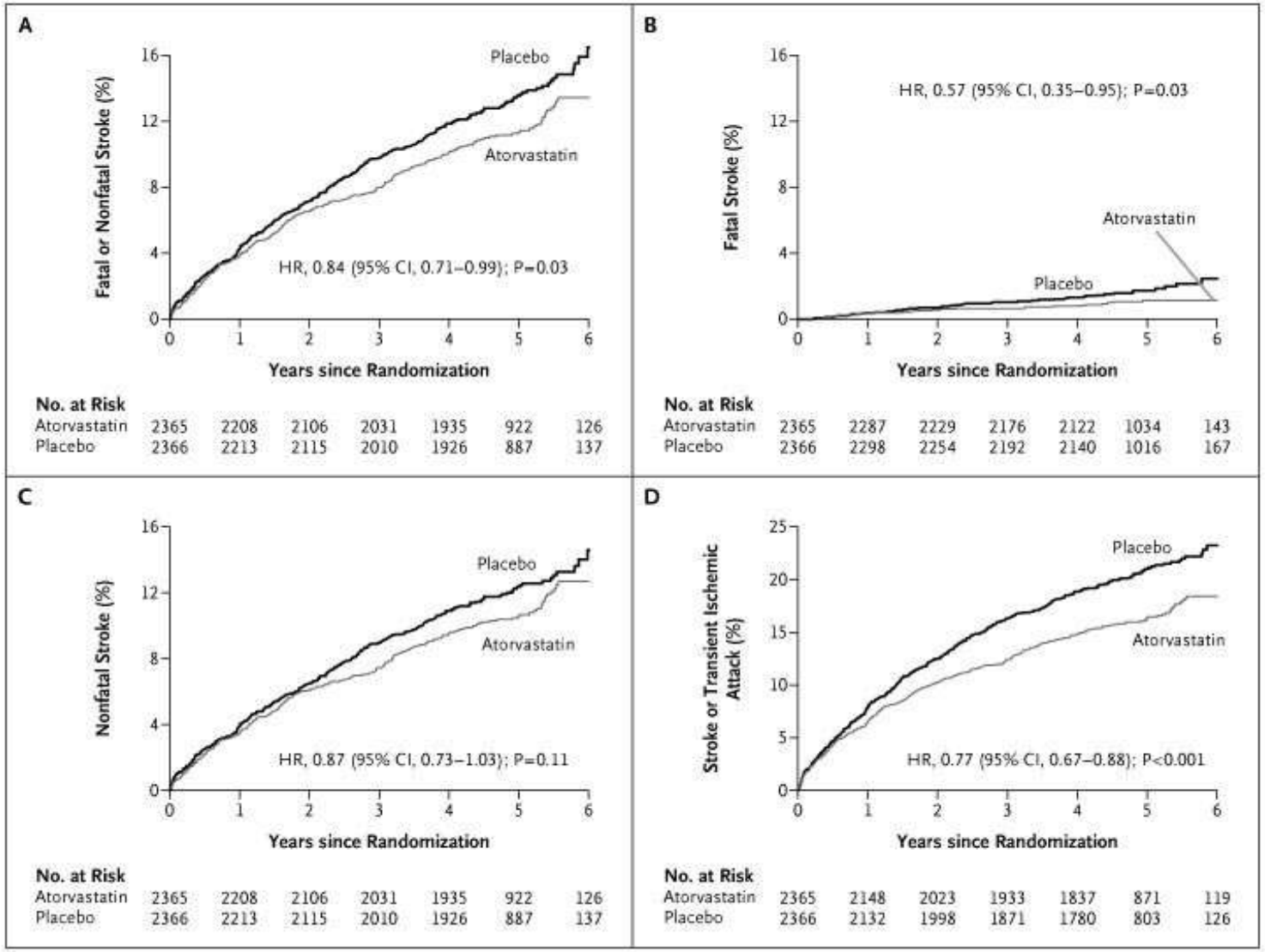
# Meta-analysis of major statin trials that assessed the effect of statins on fatal and non-fatal stroke




Amarenco et al Lancet Neurol. 2009,8:453-464

# SPARCL TRIAL

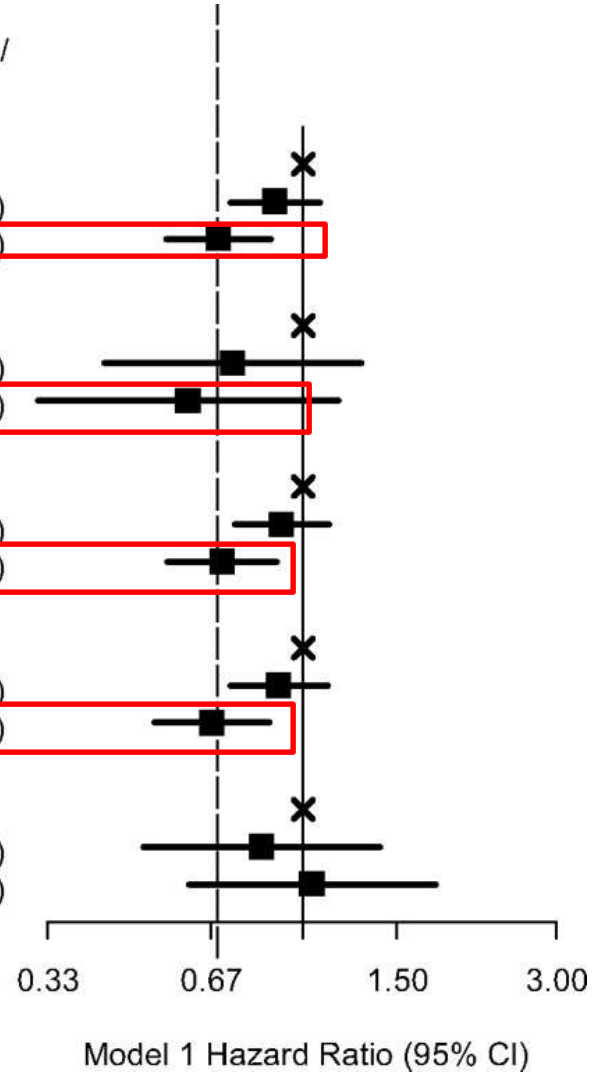
Mean LDL 1.9mmo/L




559.

# Who Benefited the Most in SPARCL
# Relationship between change in LDL-C and risk of stroke.

| | Events | Model 1: p-value/ HR (95% CI) | Model 2: p-value/ HR (95% CI) | Model 3: p-value/ HR (95% CI) |
|---|---|---|---|---|
| All Stroke | | | | |
| >=0% Increase | 210 | 0.0063 | 0.0122 | 0.0009 |
| <50% Decrease | 237 | 0.89 (0.73, 1.08) | 0.90 (0.74, 1.09) | 0.87 (0.71, 1.06) |
| >=50% Decrease | 129 | 0.69 (0.55, 0.87) | 0.71 (0.57, 0.89) | 0.65 (0.52, 0.81) |
| Fatal Stroke | | | | |
| >=0% Increase | 23 | 0.2967 | 0.3391 | 0.2385 |
| <50% Decrease | 27 | 0.74 (0.42, 1.29) | 0.75 (0.43, 1.31) | 0.73 (0.42, 1.28) |
| >=50% Decrease | 15 | 0.61 (0.32, 1.17) | 0.63 (0.33, 1.20) | 0.58 (0.30, 1.11) |
| Non-Fatal Stroke | | | | |
| >=0% Increase | 192 | 0.0130 | 0.0224 | 0.0020 |
| <50% Decrease | 218 | 0.91 (0.74, 1.12) | 0.92 (0.75, 1.13) | 0.89 (0.72, 1.09) |
| >=50% Decrease | 117 | 0.70 (0.55, 0.89) | 0.72 (0.57, 0.92) | 0.66 (0.52, 0.83) |
| Ischemic Stroke | | | | |
| >=0% Increase | 182 | 0.0063 | 0.0111 | 0.0010 |
| <50% Decrease | 204 | 0.90 (0.73, 1.12) | 0.92 (0.74, 1.13) | 0.88 (0.71, 1.09) |
| >=50% Decrease | 106 | 0.67 (0.52, 0.86) | 0.69 (0.54, 0.89) | 0.63 (0.49, 0.81) |
| Hemmorhagic Stroke | | | | |
| >=0% Increase | 26 | 0.6536 | 0.6390 | 0.6928 |
| <50% Decrease | 34 | 0.84 (0.50, 1.40) | 0.85 (0.51, 1.41) | 0.84 (0.50, 1.40) |
| >=50% Decrease | 28 | 1.04 (0.61, 1.78) | 1.07 (0.62, 1.82) | 1.02 (0.60, 1.75) |




Pierre Amarenco et al. Stroke. 2007;38:3198-3204

# Stroke Event based on LDL results in SPARCL

**Table 3. Time-Varying Nominal Value in LDL-C Results for First Event in Composite**

| | | Events | Hazard Ratio (95% CI) | *P* Value |
|---|---|---|---|---|
| | Stroke | | | |
| | ≥2.6 mmol/L | 336 | 1.00 | NA |
| | 1.8 to <2.6 mmol/L | 104 | 1.01 (0.81 to 1.27) | 0.9076 |
| <69.6mg/dl | <1.8 mmol/L | 136 | 0.72 (0.59 to 0.89) | 0.0018 |
| | Fatal stroke | | | |
| | ≥2.6 mmol/L | 40 | 1.00 | NA |
| | 1.8 to <2.6 mmol/L | 11 | 1.08 (0.52 to 2.22) | 0.8456 |
| | <1.8 mmol/L | 14 | 0.63 (0.31 to 1.26) | 0.1867 |
| | Nonfatal stroke | | | |

Amarenco et al Stroke. 2007,38:3198-3204

# New Canadian Stroke Best Practice Recommendations

**4.0** Patients who have had an ischemic stroke or transient ischemic attack should have their serum lipid levels assessed and aggressively managed [Evidence level A].

**4.1 Lipid assessment**

i. Lipid levels, including total cholesterol, total triglycerides, low-density lipoprotein [LDL] cholesterol, and high-density lipoprotein [HDL] cholesterol, should be measured on all patients presenting with stroke or transient ischemic attack [Evidence Level B].

**2. Lipid management**

ii. Patients with ischemic stroke or transient ischemic attack should be managed with aggressive therapeutic lifestyle changes to lower lipid levels, including dietary modification, as part of a comprehensive approach to lower risk of first or recurrent stroke unless contra-indicated[Evidence Level B]. *Refer to Prevention of Stroke Module, Section 2 for lifestyle Management recommendations.*

iii. A statin should be prescribed for secondary prevention in patients who have had an ischemic stroke or transient ischemic attack in order to achieve a target LDL cholesterol consistently less than 2.0 mmol/L or >50% reduction of LDL cholesterol, from baseline [Evidence Level B]. [35]

a. For individuals with stroke, acute coronary syndrome or established coronary disease, treatment to more aggressive targets (LDL-C <1.8 mmol/L or >50% reduction) may be considered [Evidence Level A].

iv. Adults with diabetes and ischemic stroke are at high risk of further vascular events and should also be treated with a statin to achieve a low-density lipoprotein cholesterol ≤2.0 mmol/L [Evidence Level B].

v. Statin therapy is not indicated for prevention of intracerebral hemorrhage [Evidence Level B].

# Question

Which individuals showed the greatest risk reduction in stroke recurrence in the SPARCL trial?

A. Individuals whom had treatment LDL's of < 2.0 mmol/L
B. Individuals whom had 50% reductions in LDL's
C. Individuals whom had treatment LDL's of < 1.3 mmol/L
D. A and B
E. None of the above

# Following a TIA - Did you know

- Carotid stenosis > 50% is linked with high risk of early recurrence!

  HR **2.6** (95% CI 1.28-5.2)

- > 70% stenosis HR 3.3 (95% CI 1.5-7.4)

- NASCET 90-day risk of stroke **>25%** for those pts with non-retinal TIA attributable to 70-99% ICAS

- In pts with medically treated high-grade ICAS, 43.5% of those presenting with a hemispheric TIA had a stroke within 2 years
  - Half of the strokes occurred **within the first month**

Sheehan et al. Stroke 2010;41:844-845

# Time Frame of Benefit for CEA

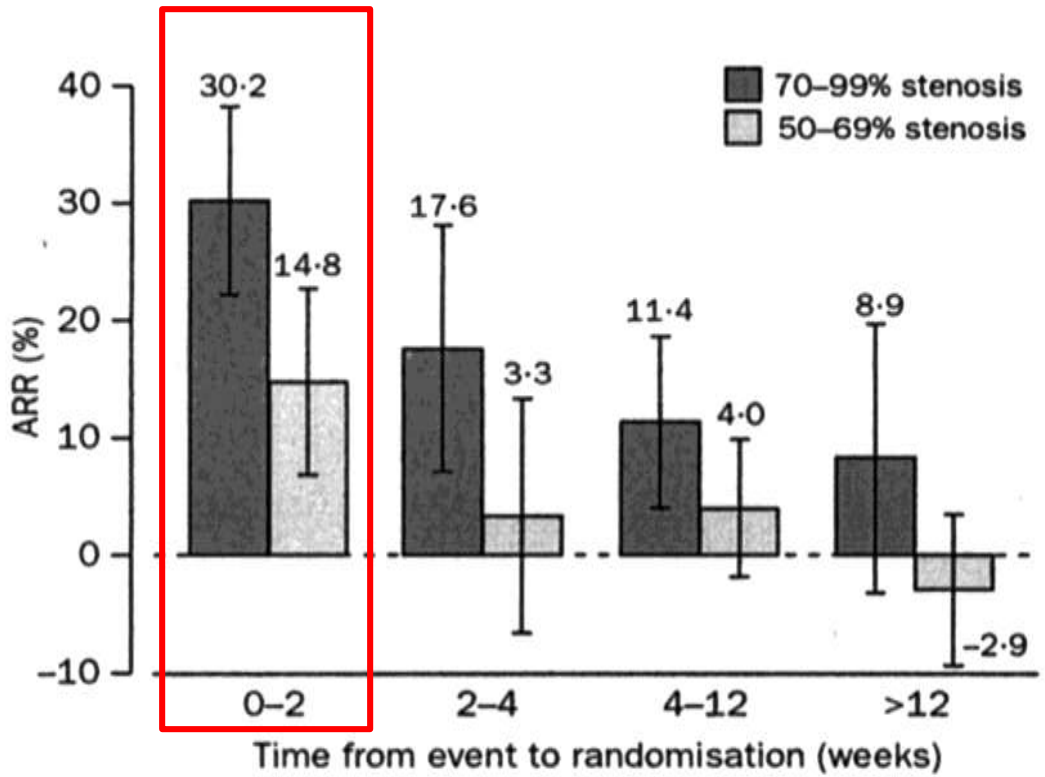



Figure 5: **Absolute reduction with surgery in the 5-year cumulative risk of ipsilateral carotid ischaemic stroke and any stroke or death within 30 days after trial surgery in patients with 50–69% stenosis and ⩾70% stenosis without near-occlusion stratified by the time from last symptomatic event to randomisation**

*Lancet,2004*

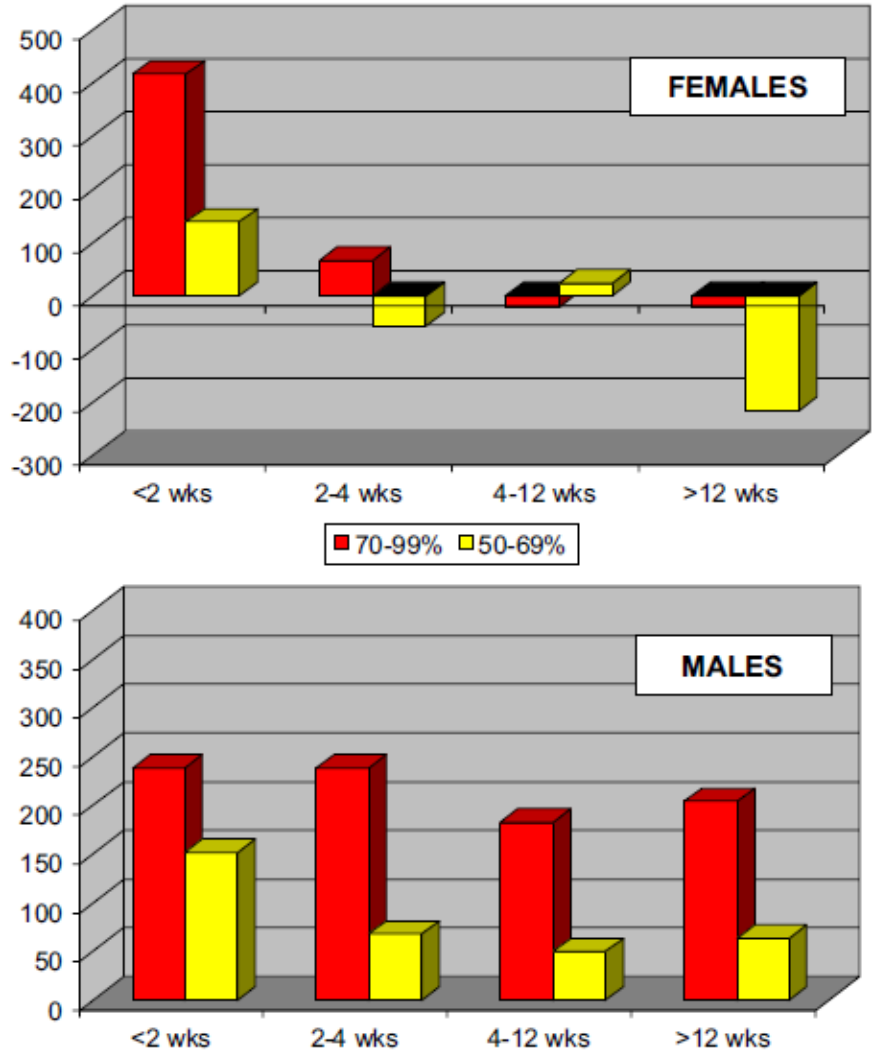
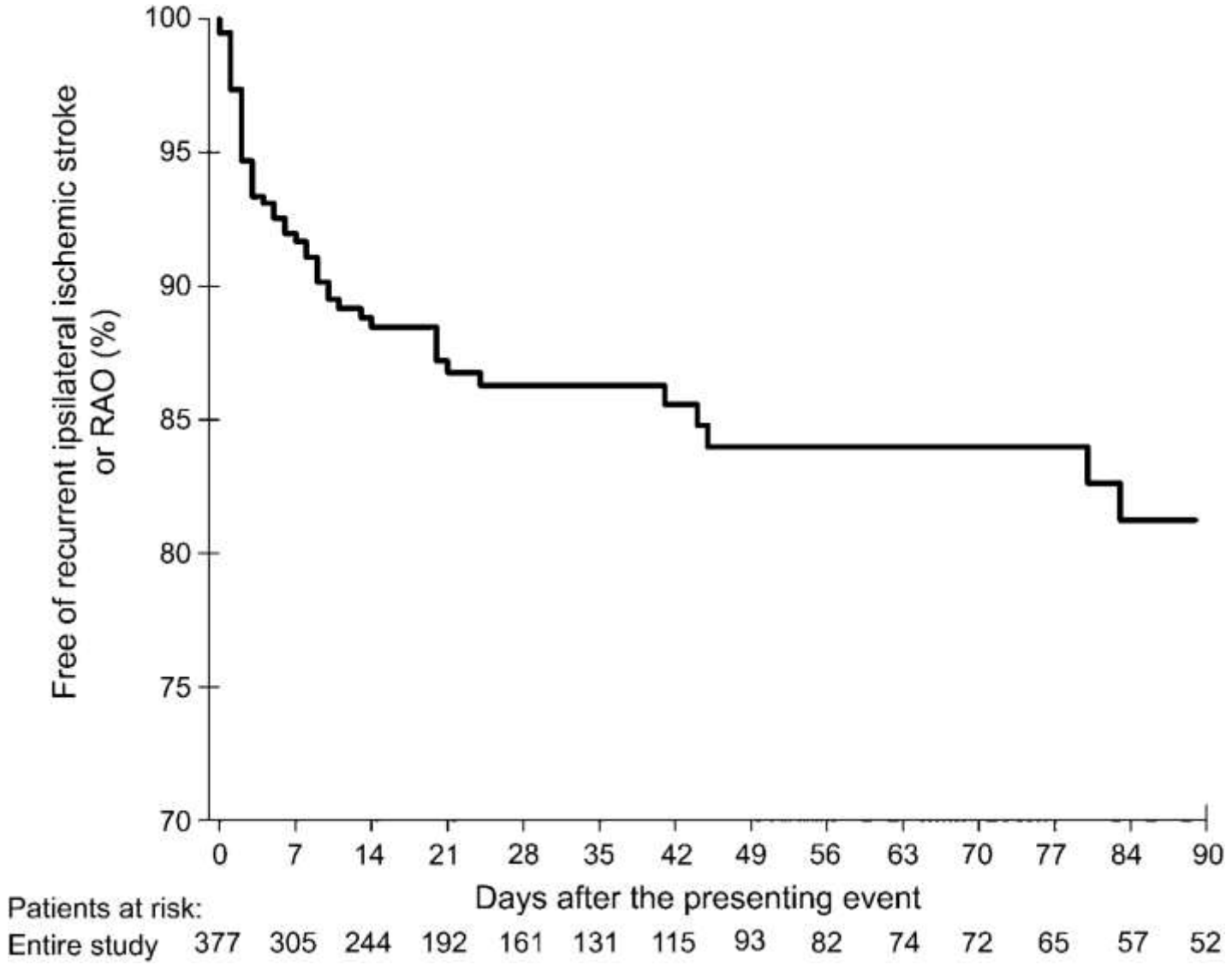



**Fig. 2.** Number of strokes prevented at 5 years by performing 1000 CEAs. Effect of gender and timing from event to CEA on prevention of late stroke relative to degree of stenosis *(recalculated from CETC data[10–12] and reproduced with permission from AR Naylor).*[4]

# Risk of recurrent ipsilateral ischemic stroke or retinal artery occlusion (RAO) within 90 days of the presenting event, prior to CEA or CAS




Elias Johansson et al. Neurology 2016;86:498-504

# Carotid Endarterectomy

- NNT=5 to prevent 1 ipsilateral stroke in 5 years treated within 2 weeks
- NNT 125 if after 12 weeks
- Patients with symptomatic carotid stenosis represent **10-15%** of patients but **account for ~50% or recurrences.**

Chimowitz M. N Engl J Med 2011;365:993-1003

# Conclusions

- TIA's should be managed on an urgent basis.
- Dual anti-platelets are recommended following a TIA for 21-30 days.
- Lipid lowering of LDL < 2.0 mmol/L or 50% reduction in LDL should be targets for stroke prevention.
- PFO closure beneficial in select patient under the age of 60
- Carotid Endarterectomy should be performed ASAP following TIA.


**Thank you for your time.**