Stroke Management and Prevention: An Evidence Based Approach

Prof. Md. Mujibur Rahman
Department of Medicine
Shaheed Suhrawardy Medical College

Acute stroke is characterized by the rapid appearance (usually over minutes) of a focal deficit of brain function, most commonly a hemiplegia with or without signs of focal higher cerebral dysfunction (such as aphasia), hemisensory loss, visual field defect or brain-stem deficit

Several terms have been used to classify strokes, often based on the duration and evolution of symptoms.

- *Transient ischaemic attack (TIA)* – Describes a stroke in which symptoms resolve within 24 hours.
- *Stroke* – This is the term reserved for those events in which symptoms last more than 24 hours.
- *Progressing stroke or stroke in evolution* – This describes a stroke in which the focal neurological deficit worsens after the patient first presents.
- *Completed stroke* – This describes a stroke in which the focal deficit persists and is not progressing.

Stroke and its impact

Approximately >690 000 people in the United States have a stroke each year, of which about 610 000 are a first attack; and 6.4 million Americans are stroke survivors

Around 240 000 US adults experience a TIA in each year

Annual risk for future ischemic stroke after an initial ischemic stroke or TIA is ≈3% to 4%

Stroke is also estimated to result in 134 000 deaths annually and is the third leading cause of death in the nation behind heart disease and cancer

- In 2010, the cost of stroke is estimated at $73.7 billion (direct and indirect costs), with a mean lifetime cost estimated at $140 048.
- Stroke is also a leading cause of functional impairments, with 20% of survivors requiring institutional care after 3 months and 15% to 30% being permanently disabled.
- Stroke is a life-changing event that affects not only stroke patients themselves but their family members and caregivers as well.

Despite the advancement of treatment strategies, effective prevention remains the best approach for reducing the burden of stroke

Primary prevention is particularly important because 77% of strokes are first events

- Though sufficient data is not available in Bangladesh, the picture is almost the same; rather worse.
- In every admission, stroke patients constitute about 10% of the admitted patients.

Management

Aim

- Management is aimed at
  - minimizing the volume of brain that is irreversibly damaged
  - preventing complications
  - reducing the patient's disability and handicap through rehabilitation, and
  - reducing the risk of recurrent stroke or other vascular events
  - With TIA there is no brain damage and disability, so the priority is to reduce the risk of further vascular events

Supportive care

- **Airway**
  - Perform bedside swallow screen and keep patient nil by mouth if swallowing unsafe or aspiration occurs
- **Breathing**
  - Check respiratory rate and oxygen saturation and give oxygen if saturation < 95%
- **Circulation**
  - Check peripheral perfusion, pulse and blood pressure and treat abnormalities with fluid replacement, anti-arrhythmics and inotropic drugs as appropriate
- **Hydration**
  - If signs of dehydration, give fluids parenterally or by nasogastric tube

Supportive care

- **Nutrition**
  - Assess nutritional status and provide nutritional supplements if necessary
  - If dysphagia persists for > 48 hrs, start feeding via a nasogastric tube
- **Medication**
  - If patient is dysphagic, consider alternative routes for essential medications

Supportive care

- **Blood pressure**
  - Unless there is heart or renal failure, evidence of hypertensive encephalopathy or aortic dissection, do not lower blood pressure in first week as it may reduce cerebral perfusion
  - Blood pressure often returns towards patient's normal level within first few days

Supportive care

- **Blood glucose**
  - Check blood glucose and treat when levels are ≥ 11.1 mmol/L (200 mg/dL) (by insulin infusion or glucose/ potassium/insulin (GKI)
  - Monitor closely to avoid hypoglycaemia
- **Temperature**
  - If pyrexic, investigate and treat underlying cause
  - Control with antipyretics, as raised brain temperature may increase infarct volume

Supportive care

- **Pressure areas**
  - Reduce risk of skin breakdown:
    - Treat infection
    - Maintain nutrition
    - Provide pressure-relieving mattress
    - Turn immobile patients regularly

Supportive care

- **Incontinence**
  - Check for constipation and urinary retention; treat appropriately
  - Avoid urinary catheterisation unless patient is in acute urinary retention or incontinence is threatening pressure areas
- **Mobilisation**
  - Avoid bed rest

Surgery & Alternatives

- Patients with cerebellar haematomas or infarcts with mass effect may develop obstructive hydrocephalus and some will benefit from insertion of a ventricular drain and/or decompressive surgery
- Some patients with large haematomas or infarction with massive oedema in the cerebral hemispheres may benefit from anti-oedema agents, such as mannitol or artificial ventilation

Thrombolysis

- Intravenous thrombolysis with recombinant tissue plasminogen activator (rt-PA) increases the risk of haemorrhagic transformation of the cerebral infarct with potentially fatal results
- If it is given within 4.5 hours of symptom onset to carefully selected patients, the haemorrhagic risk is offset by an improvement in overall outcome

Prevention

Guidelines for the Primary Prevention of Stroke

Recommendations from AHA and ASA

Non-modifiable Risk Factors

Age

Sex

Race and Ethnicity

Low birth weight

Genetic Factors

These factors are generally not modifiable but identify persons who are at increased risk of stroke and who may benefit from rigorous prevention or treatment of other modifiable risk factors

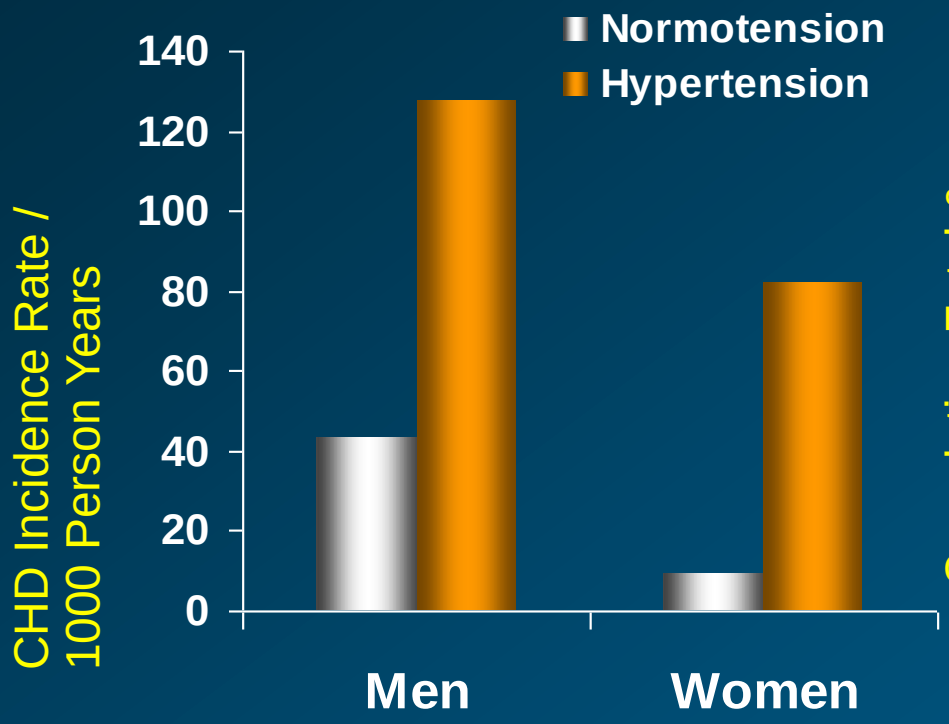
Well-Documented and Modifiable Risk Factors

Hypertension
DM
Dyslipidemia
Cigarette Smoking
Physical Inactivity
Dietary Habits
Atrial Fibrillation
Acute MI with transmural thrombosis
Prosthetic heart valves
HRT
OCP

Hypertension

Historical Lessons About Hypertension

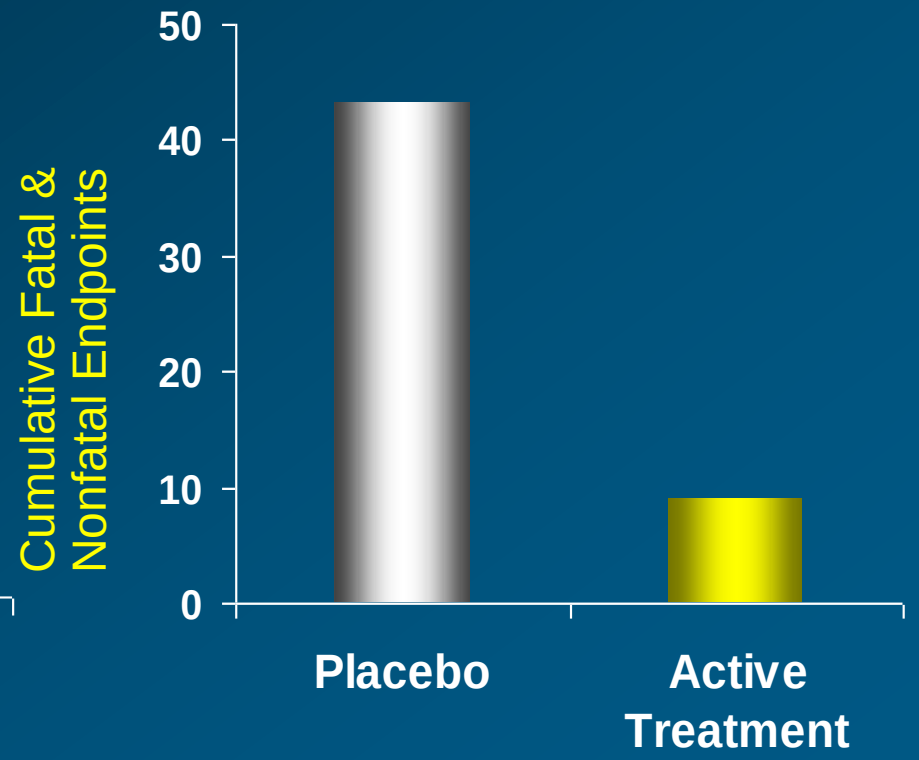
Hypertension Increases Morbidity and Mortality



THE FRAMINGHAM STUDY

Ann Intern Med. 1961;55:33-50

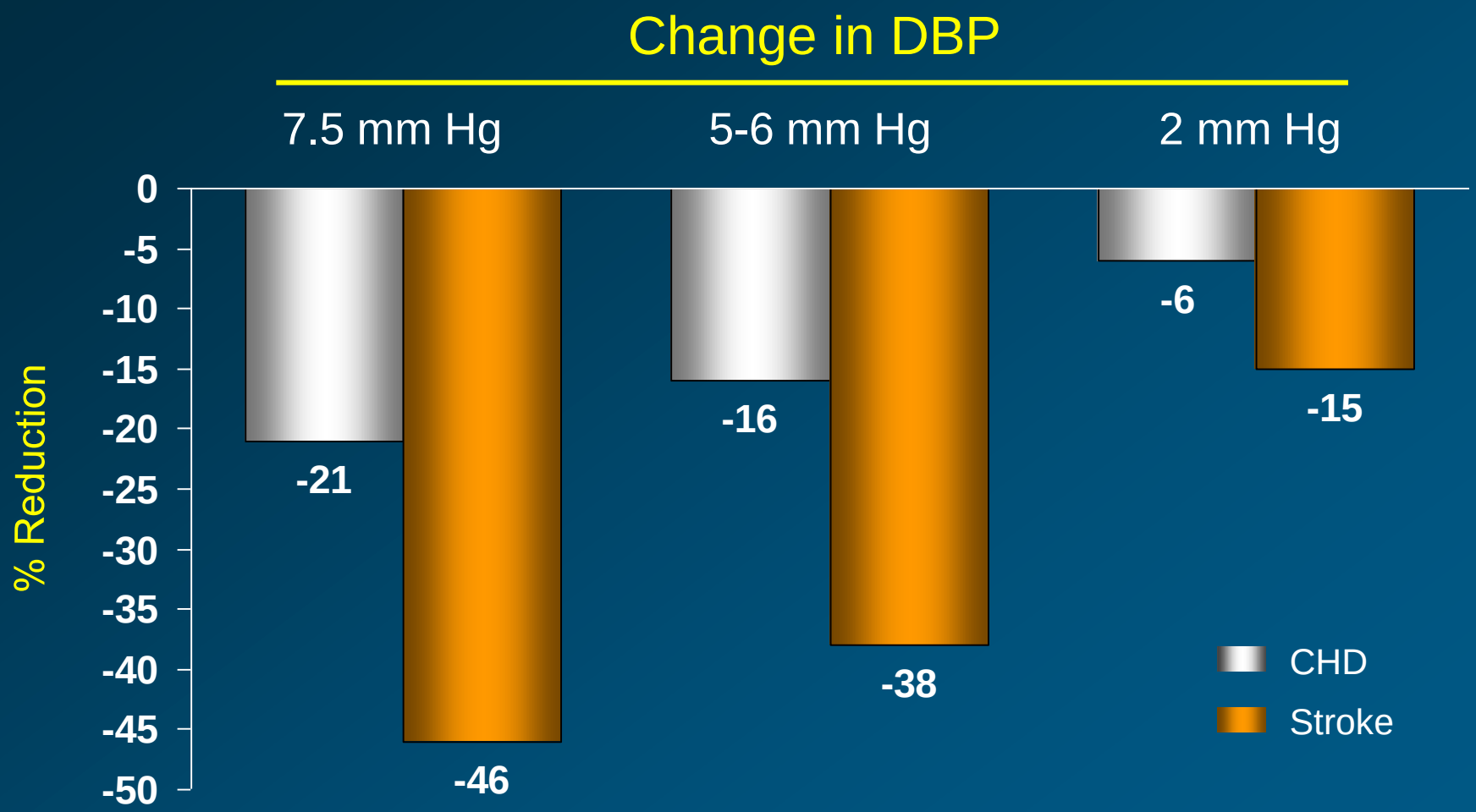
Treatment Decreases Morbidity and Mortality



THE VET. ADM. STUDY II

JAMA. 1970;213:1143-1152

Implications of Reductions in Diastolic BP for Primary Prevention



Cook, et al. *Arch Int Med*. 1995;155:701-709.

Goal BP

Systolic BP should be treated to a goal of 140 mm Hg and diastolic BP to 90 mm Hg because these levels are associated with a lower risk of stroke and cardiovascular events

(*Class I; Level of Evidence A*)

DM

Case-control studies of stroke patients and prospective epidemiological studies have confirmed that diabetes independently increases risk of ischemic stroke with a

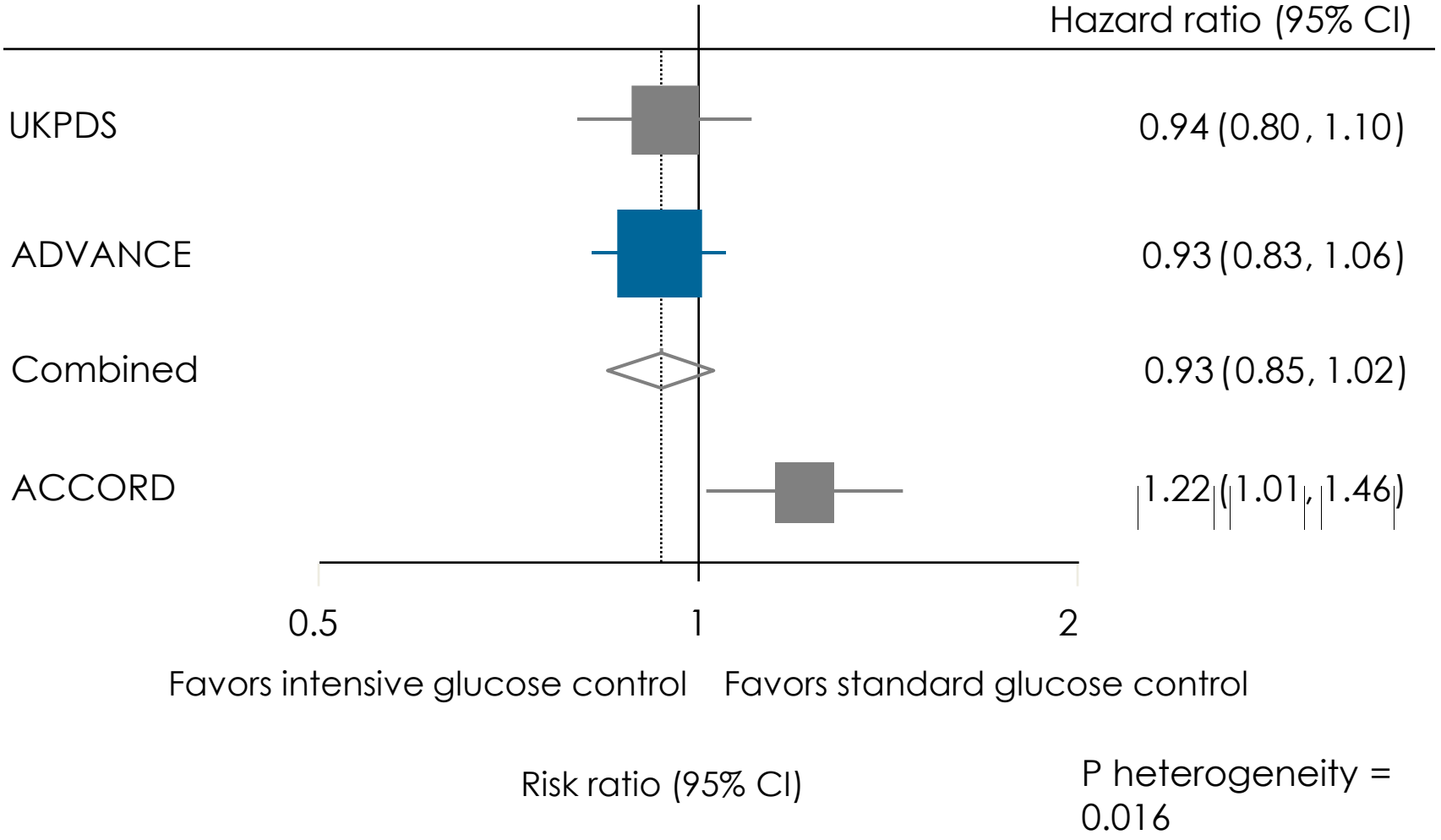
RR 1.8 - 6

Glycemic Control and Stroke

UKPDS

ACCORD

ADVANCE


Hazard ratio (95% CI)
UKPDS
0.94 (0.80, 1.10)
ADVANCE
0.93 (0.83, 1.06)
Combined
0.93 (0.85, 1.02)
ACCORD
1.22 (1.01, 1.46)
0.5
1
2
Favors intensive glucose control
Favors standard glucose control
Risk ratio (95% CI)
P heterogeneity = 0.016

HTN and DM

In patients with HTN with DM or renal disease, the BP goal is 130/80 mm Hg

(Class I; Level of Evidence A)

Treatment of HTN in adults with DM with an ACEI or an ARB is useful

(Class I; Level of Evidence A)

DM and Statin

Treatment of adults with DM with a statin, especially those with additional risk factors, is recommended

(Class I; Level of Evidence A)

The addition of a fibrate to a statin in persons with diabetes is not useful for decreasing stroke risk

(Class III; Level of Evidence B)

Diabetes Aspirin and Stroke

The benefit of aspirin for reduction of stroke risk has not been satisfactorily demonstrated for patients with diabetes;

However, administration of aspirin may be reasonable in those at high CVD risk

(*Class IIb; Level of Evidence B)*

Dyslipidemia

Most but not all epidemiological studies find an association between higher cholesterol levels and an increased risk of ischemic stroke

In the Multiple Risk Factor Intervention Trial (MRFIT), which included 350 000 men, the relative risk of death from nonhemorrhagic stroke increased progressively for each level of cholesterol

Dyslipidemia

In MRFIT the risk of death from intracranial hemorrhage was increased 3-fold in men with total cholesterol concentrations of 4.14 mmol/L (160 mg/dL) compared with higher levels.

Smoking and Stroke

Factor	Prevalence	Population Attributable risk %	Relative Risk	Risk Reduction With Treatment
Cigarette smoking	19.8	12-14	1.9 (ischemic stroke) 2.9 (SAH)	50% within 1 yr; baseline after 5 yr

AHA/ASA Guidelines for Primary Prevention of Stroke. Stroke. 2011;42:517-584

Smoking and Stroke

Abstention from cigarette smoking by nonsmokers and

Smoking cessation by current smokers are recommended

(Class I; Level of Evidence B)

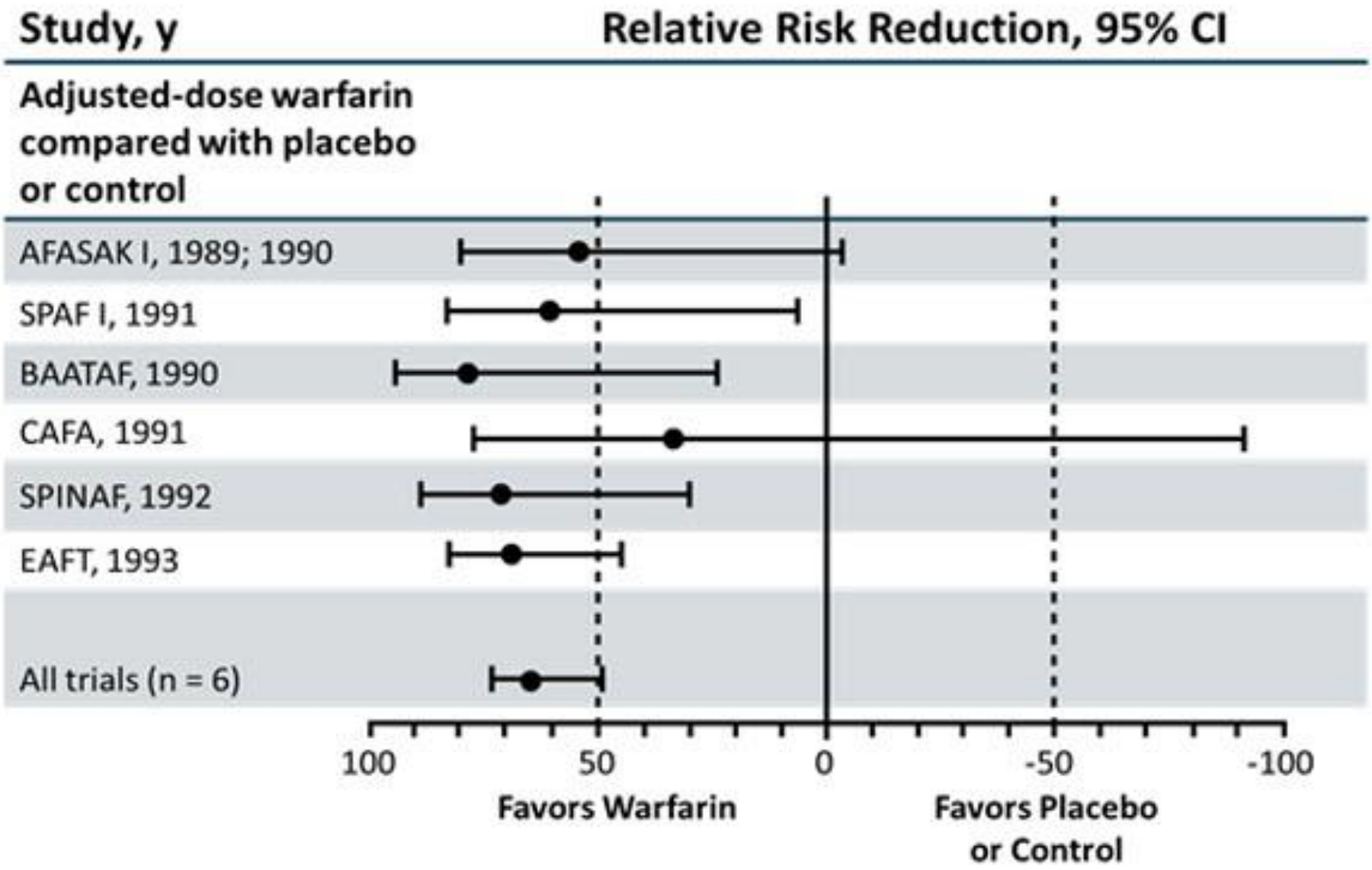
Atrial Fibrillation

Assessment of stroke risk – $CHA_2DS_2VAS_C$

CHA_2DS_2VASc	Points
Congestive heart failure	1
Hypertension	1
Age ≥75 years	2
Diabetes mellitus	1
Stroke or TIA or Thromboembolism	2
Vascular disease (MI, PAD)	1
Age 65–74 years	1
Sex Female	1
Maximum Score	9

Score	Risk	Considerations
0	Low	No anticoagulant therapy (or Aspirin)
1	Moderate	Oral anticoagulant, either NOACs or well controlled warfarin at INR 2.0-3.0 (or Aspirin 75–325 mg daily)
2	High	Oral anticoagulant, using either a NOACs (apixaban, rivaroxaban or dabigatran) or well controlled warfarin at INR 2.0-3.0

Warfarin vs Placebo



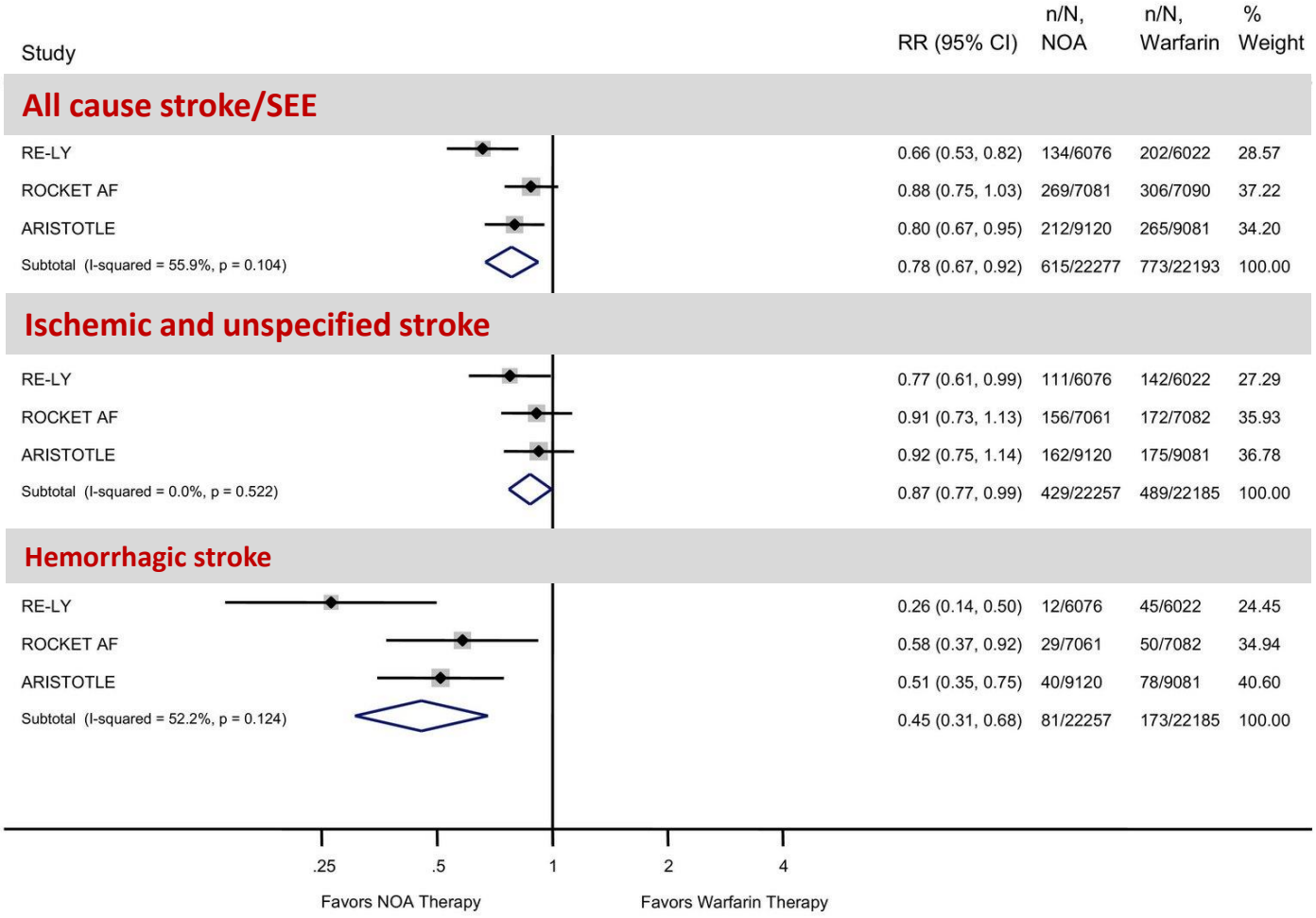
Efficacy of Warfarin & Aspirin for Stroke Prevention in Atrial Fibrillation: Meta-Analysis of RCT

comparison	no of trials	No of patient	Relative risk reduction 95%CI	Estimated NNT for primary prevention
Adjusted dose Warfarin vs Control	6	2900	64%(49-74)	40
Adjusted dose Aspirin vs Control	7	3990	19%(-1-35)	140

AHA/ASA Guidelines for Primary Prevention of Stroke. Stroke. 2011;42:517-584

Meta-analysis of Efficacy and Safety of New Oral Anticoagulants

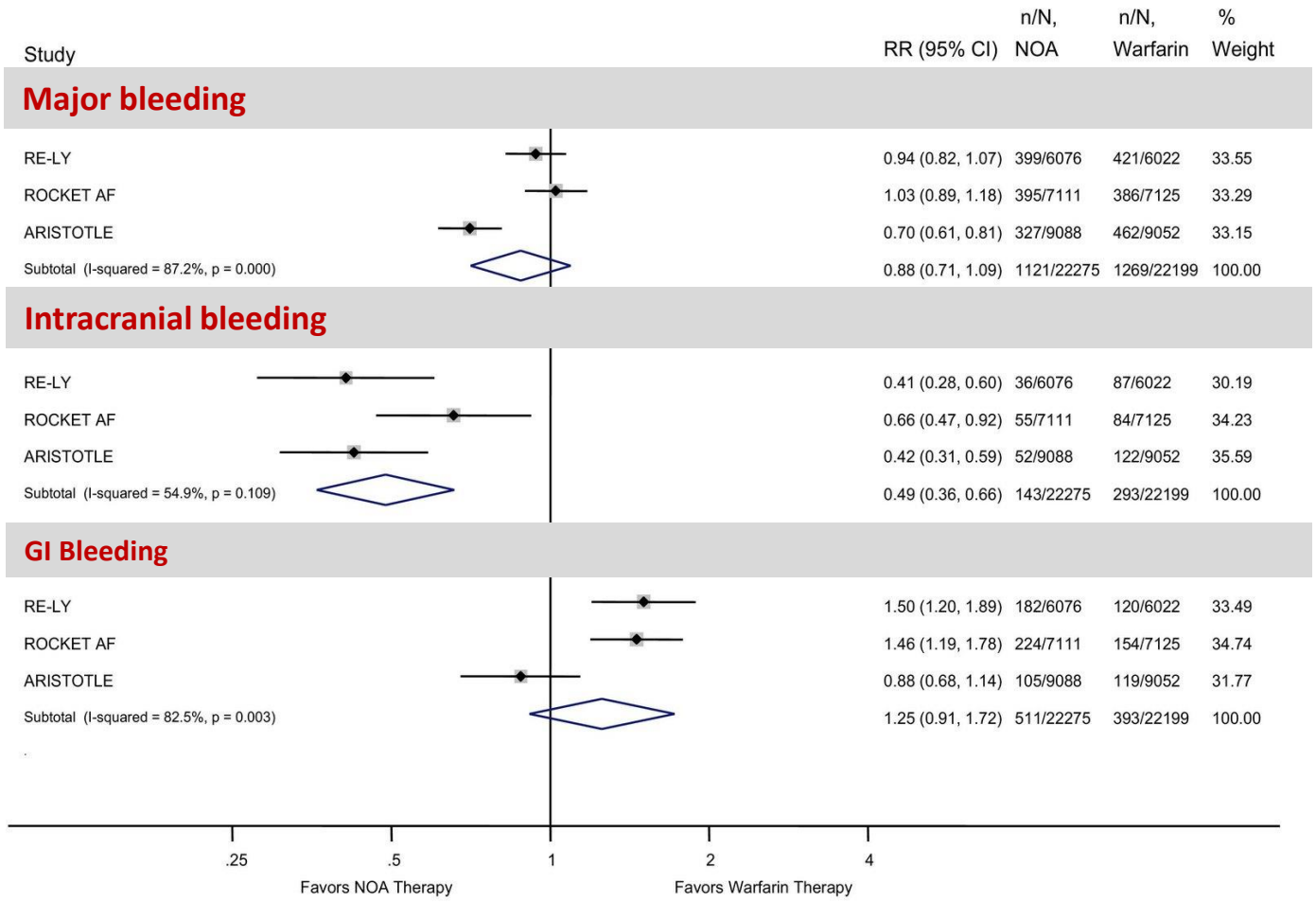
Dabigatran, Rivaroxaban, Apixaban vs. Warfarin in AF patients



Miller CS, Grandi SM, Shimony A, Filion KB, Eisenberg MJ. Am J Cardiol. 2012 Aug 1;110(3):453-60. Pub Med PMID: 22537354..

Meta-analysis of Efficacy and Safety of New Oral Anticoagulants

Dabigatran, Rivaroxaban, Apixaban vs. Warfarin in AF patients



Miller CS, Grandi SM, Shimony A, Filion KB, Eisenberg MJ. Am J Cardiol. 2012 Aug 1;110(3):453-60. Pub Med PMID: 22537354.

Acute MI and Left Ventricular Thrombus

It is reasonable to prescribe warfarin to post–ST segment elevation MI patients with left ventricular mural thrombi or an a kinetic left ventricular segment to prevent stroke

(*Class IIa; Level of Evidence A).*

Oral Contraceptive Pills

Oral contraceptive pills (OCP) may be harmful in women with additional risk factors (eg, cigarette smoking, prior thromboembolic events)

(Class III; Level of Evidence C)

For those who choose to use OCP despite the increased risk associated with their use, aggressive therapy for other stroke risk factors may be reasonable

(Class IIb; Level of Evidence C)

Physical Inactivity

- Adults should engage in at least 150 minutes (2 hours and 30 minutes) per week of moderate intensity or 75 minutes (1 hour and 15 minutes) per week of vigorous intensity aerobic physical activity

    Class I; Level of Evidence B

Among overweight and obese persons, weight reduction is reasonable as a means of reducing risk of stroke

    Class IIa; Level of Evidence B

Aspirin for Primary Stroke Prevention

- The use of aspirin for cardiovascular (including but not specific to stroke) prophylaxis is recommended for persons whose risk is sufficiently high for the benefits to outweigh the risks associated with treatment (a 10-year risk of cardiovascular events of 6% to 10%)

  (Class I; Level of Evidence A)

- Aspirin is not useful for preventing a first stroke in persons at low risk

(Class III; Level of Evidence A)

MITRAL AND AORTIC VALVE DISEASE

- For patients with ischemic stroke or TIA who have rheumatic mitral valve disease and AF, long-term VKA therapy with an INR target of 2.5 (range, 2.0–3.0) is recommended

  Class I; Level of Evidence A

- For patients with rheumatic mitral valve disease who have an ischemic stroke or TIA while being treated with adequate VKA therapy, the addition of aspirin might be considered (Class IIb; Level of Evidence C)

Secondary Stroke Prevention

HYPERTENSION

Blood Pressure

Initiation of blood pressure (BP) therapy is indicated for previously untreated patients with ischemic stroke or TIA with BP ≥140/90 mmHg

(Class I; Level of Evidence B).

Initiation of therapy for patients with BP <140/90 mm Hg is of uncertain benefit

(Class IIb; Level of Evidence C).

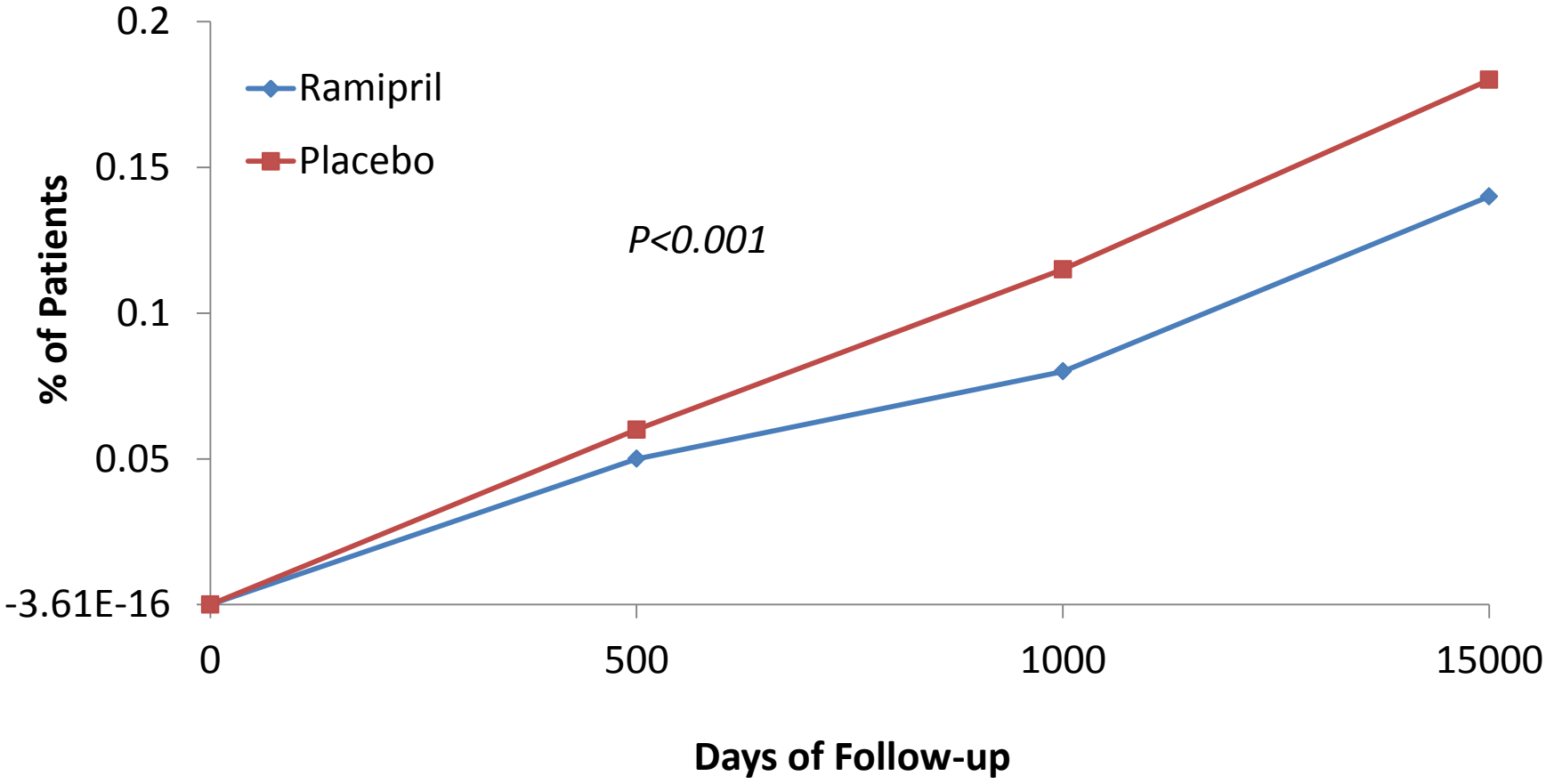
Goals for target BP level or reduction from pretreatment baseline are uncertain and should be individualized, but it is reasonable to achieve a blood pressure <140/90 mm Hg

(Class IIa; Level of Evidence B).

For patients with a recent lacunar stroke, it might be reasonable to target a systolic blood pressure of <130 mm Hg

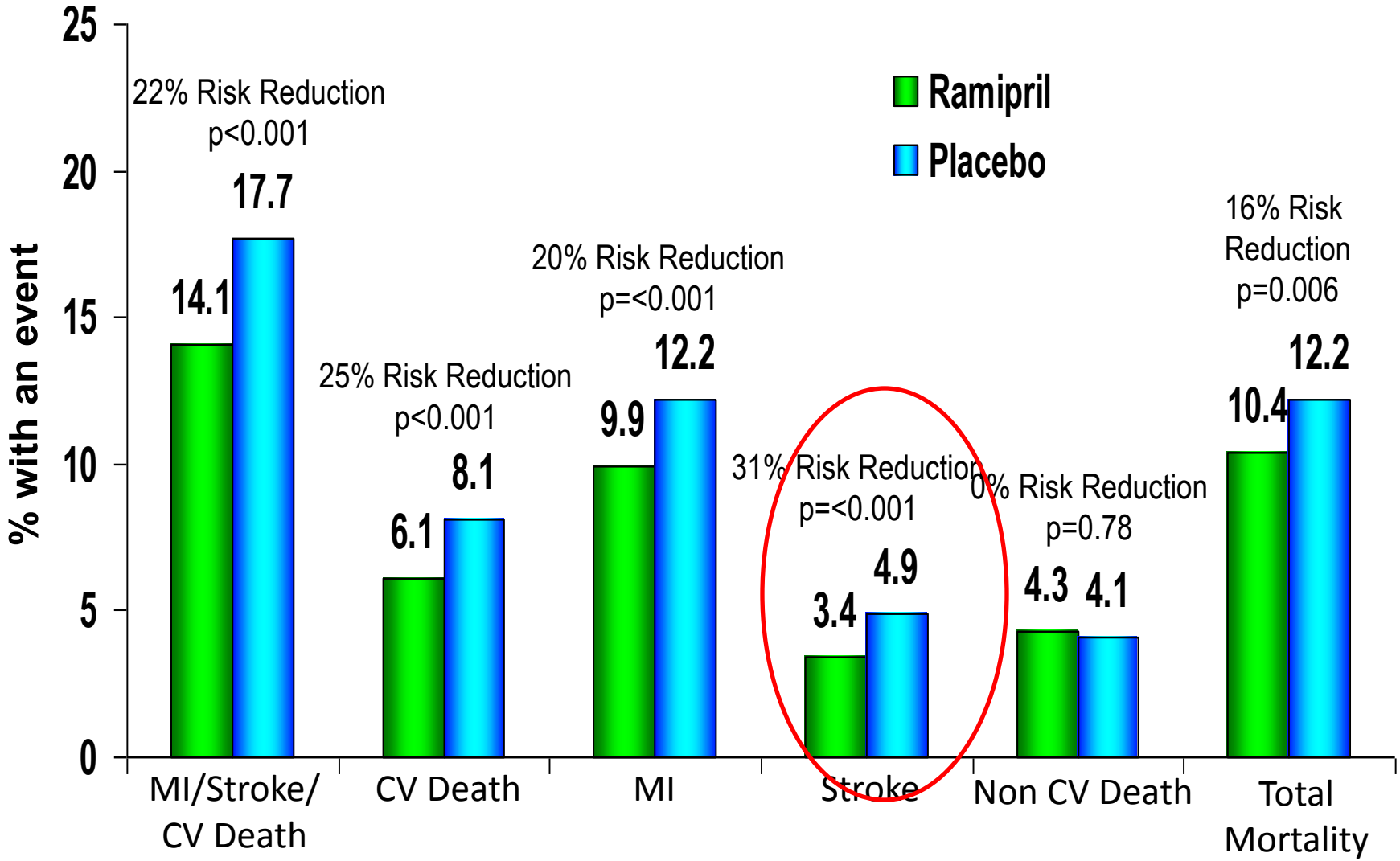
(Class IIb; Level of Evidence B).

HOPE - Kaplan-Meier Estimates of the Composite Endpoint of CV Death, MI or Stroke in the Ramipril and Placebo Groups



N Engl J Med, January 20, 2000

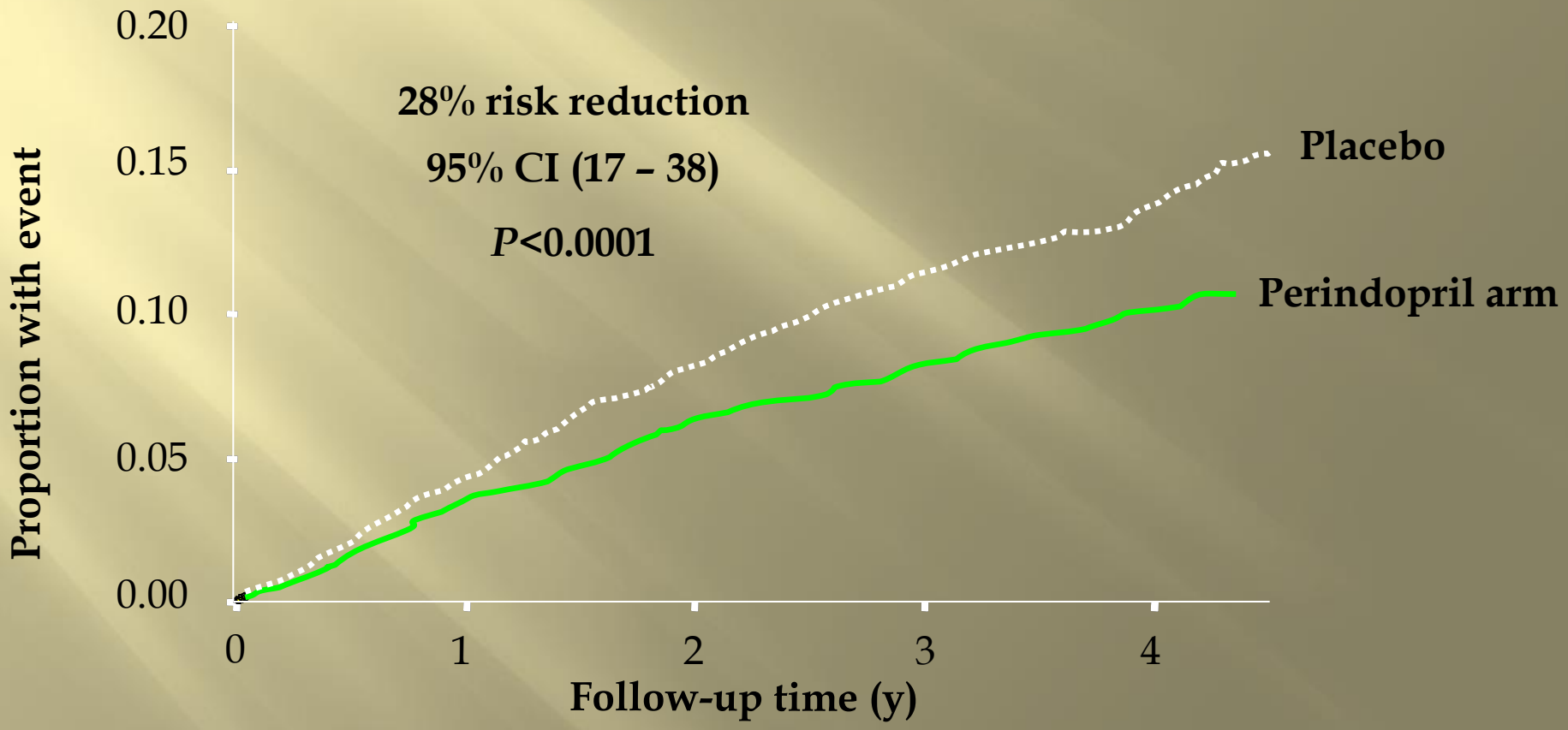
HOPE - Primary Endpoint Results



N Engl J Med, January 20, 2000

Results

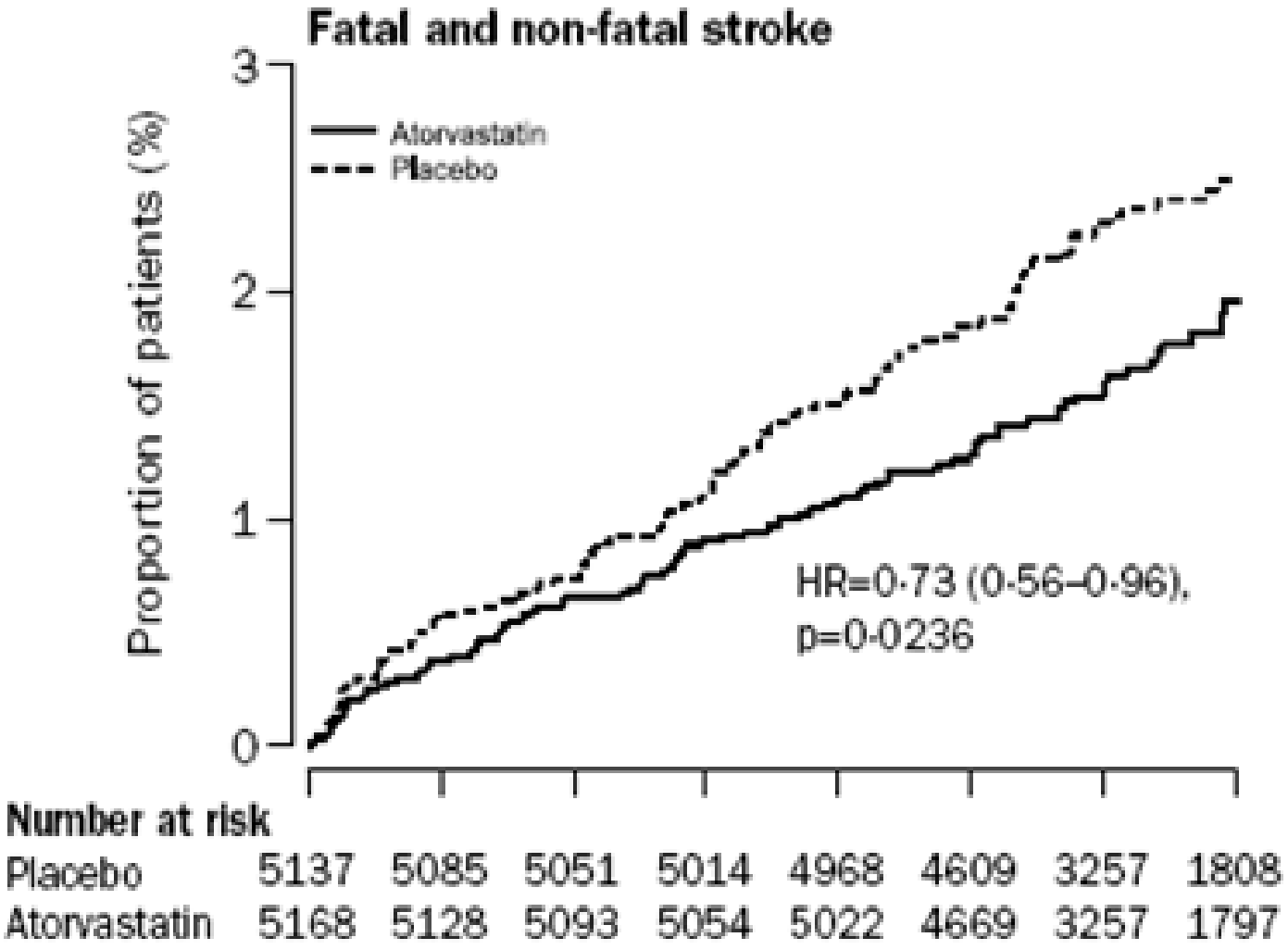
Perindopril-based regimen reduces stroke



Reference: *Lancet* 2001;358:1033-1041.

Dyslipidemia

Cumulative incidence of Fatal and non-fatal stoke



ASCOT LLA :*Lancet 2003; 361: 1149–58*

Take Home Message

- Preventive measures are always better than treatment in stroke
- There are huge evidence in favor of prevention both in primary and secondary settings of stroke
- If appropriate measures are taken a great number of strokes can be avoided

Thank You