

CV Update 2011

**Dr Sandy Gupta, MD FRCP
Consultant Cardiologist
Whipps Cross and St Bartholomews Hospitals
London, UK**

Lower (but not too low) **is better**

LDL-Cholesterol

BP

Blood sugar

BMI

Salt intake

Calories

Waist circumference

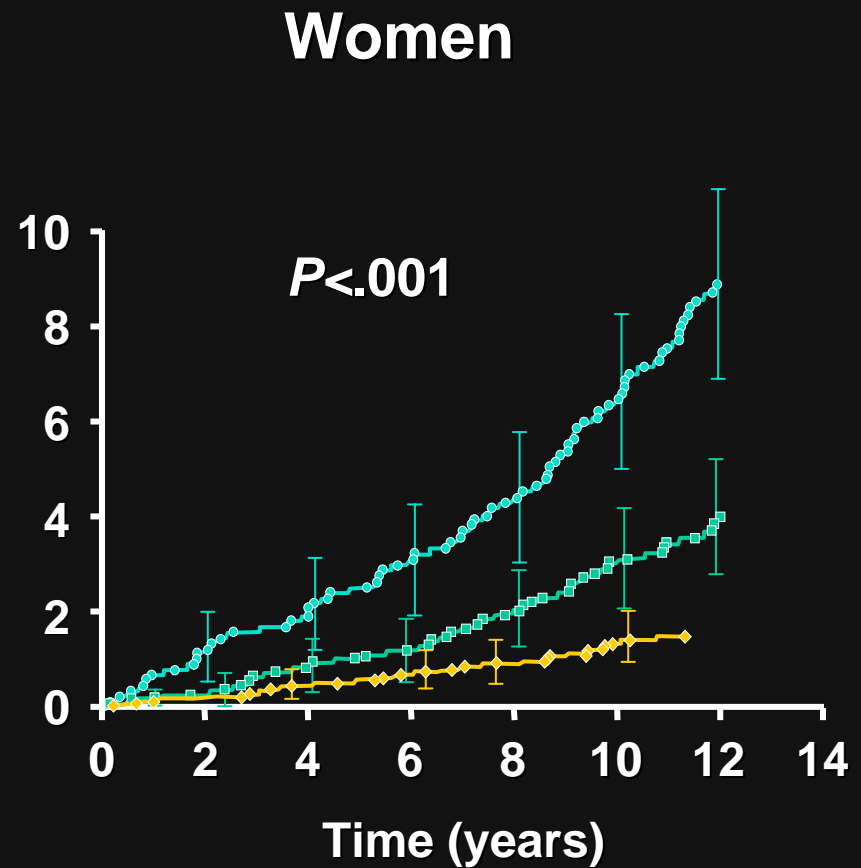
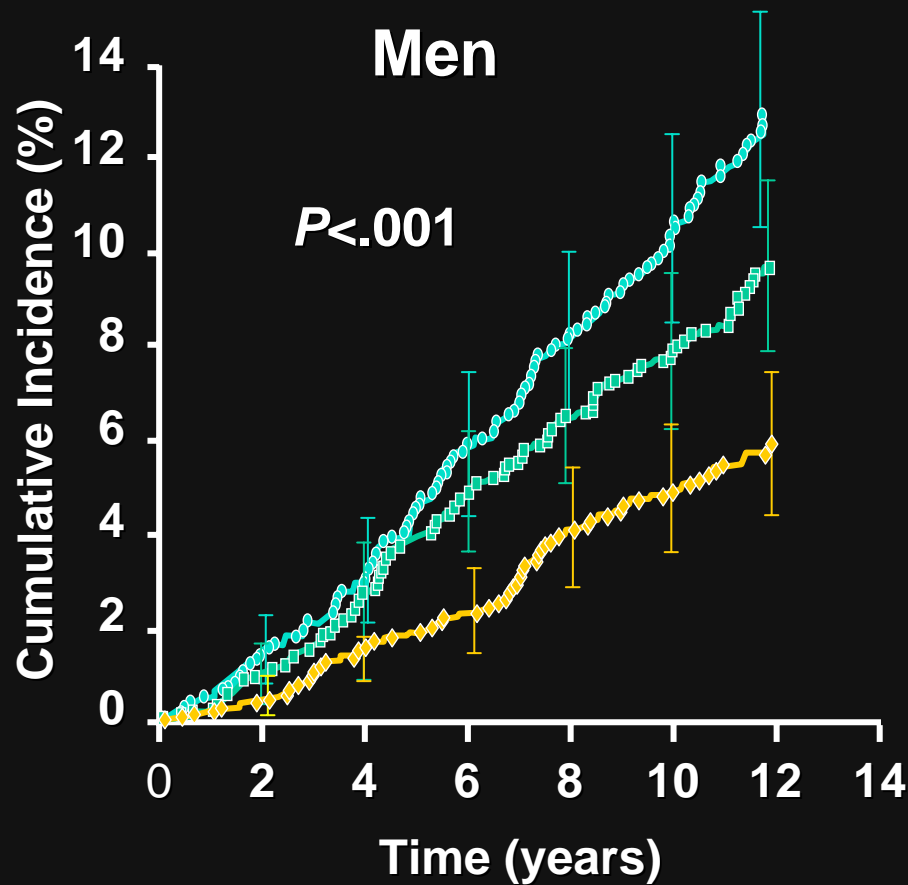
HbA1c

Proteinuria

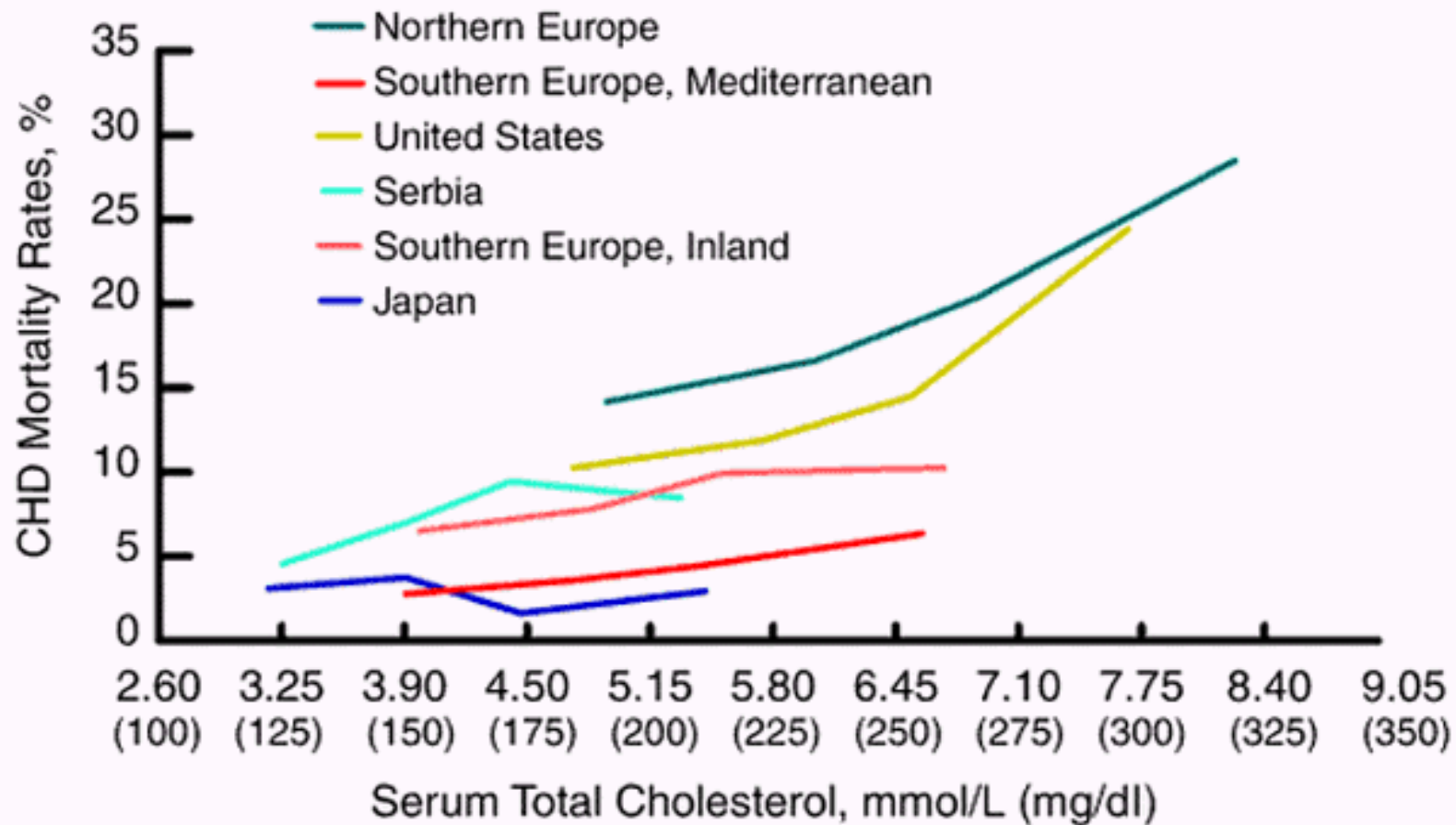
Heart Rate

High-Normal BP and CVD Risk

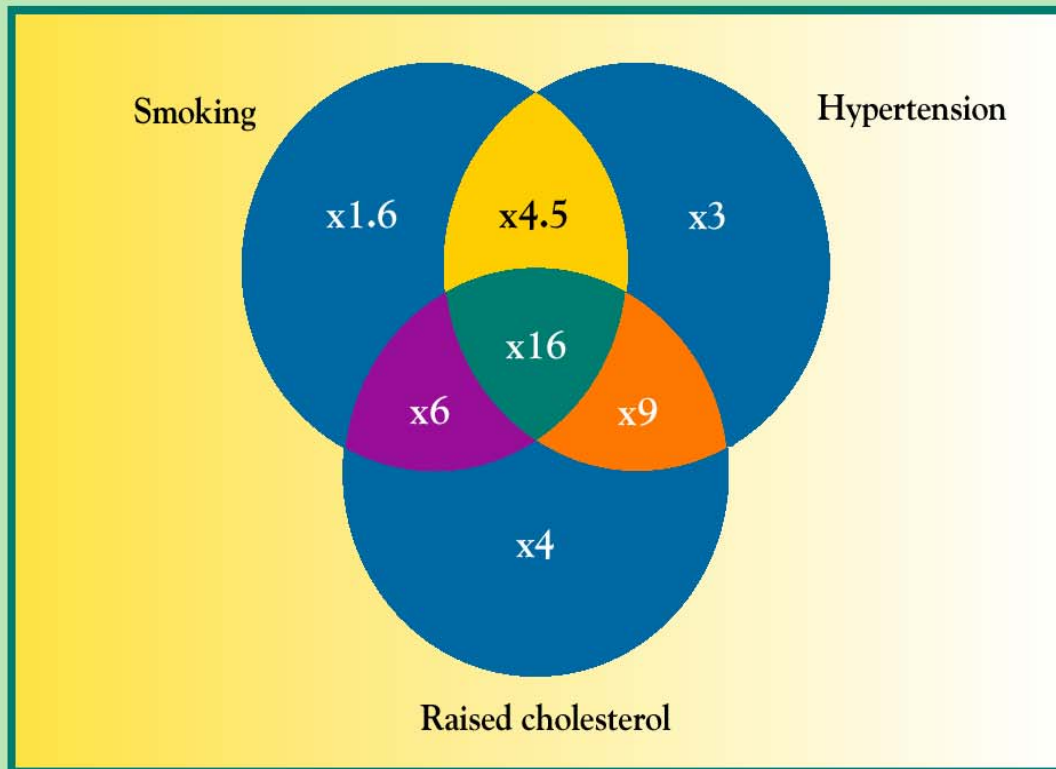
- High normal 130-139/85-89 mm Hg } Prehypertension
- Normal 120-129/80-84 mm Hg }
- ◆ Optimal <120/80 mm Hg



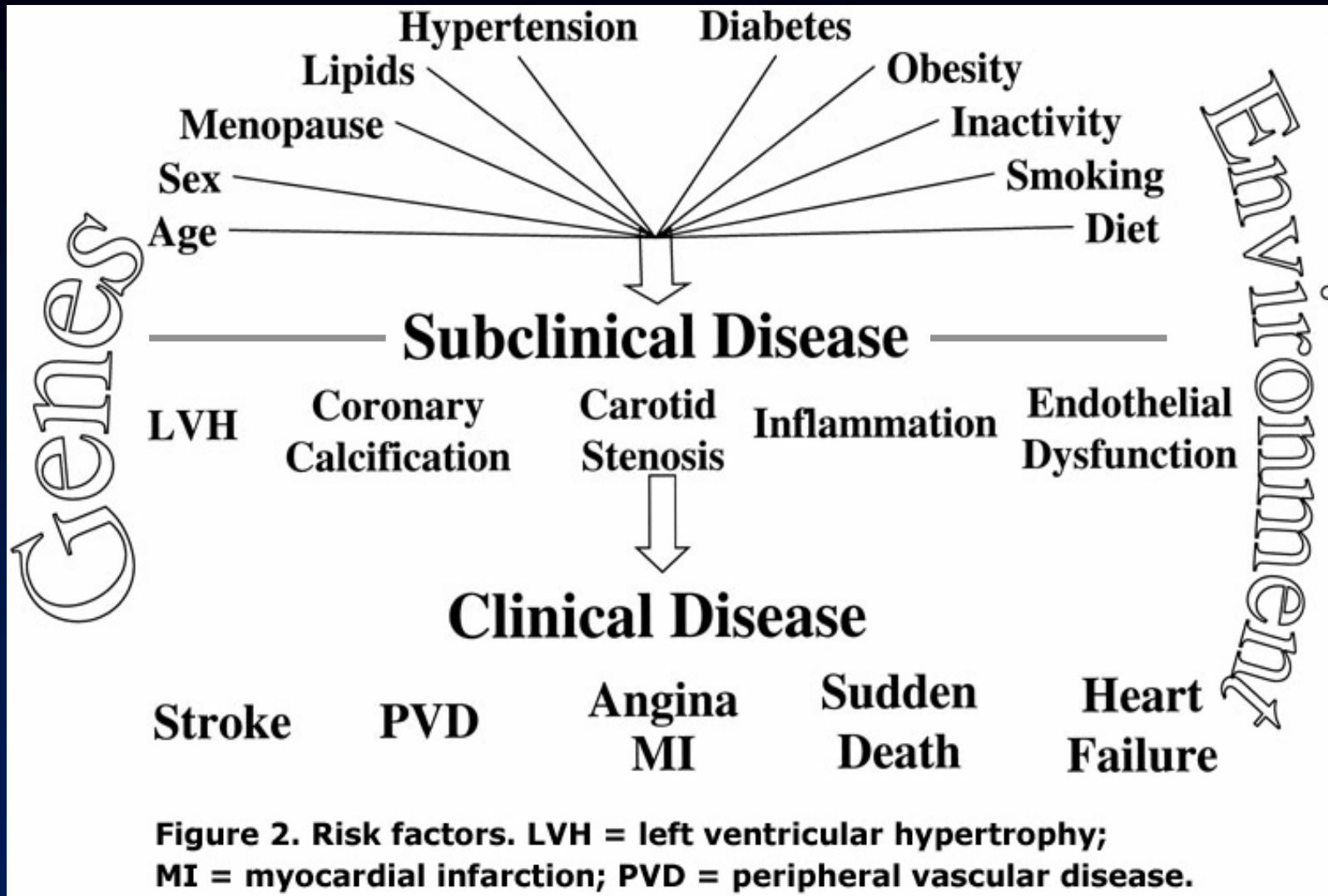
Vasan et al. *N Engl J Med.* 2001



Framingham interaction of risk factors³



- Cholesterol as a single risk factor raises chances of CHD by 4 times³



Source: Fletcher et al., 33rd Bethesda Conf: Preventive Cardiology: How Can We Do Better? JACC 2002;40:4:579-651., Wilson et al. Abdominal aortic calcific deposits are an important predictor of vascular morbidity and mortality. Circulation 2001;103:1529-34., Jaffer et al. Age and Sex Distribution of Subclinical Aortic Atherosclerosis - A Magnetic Resonance Imaging Examination of the Framingham Heart Study Art, Thromb, Vasc Biol 2002;22:849.

Effect of potentially modifiable risk factors associated with myocardial infarction in 52 countries (the INTERHEART study): case-control study

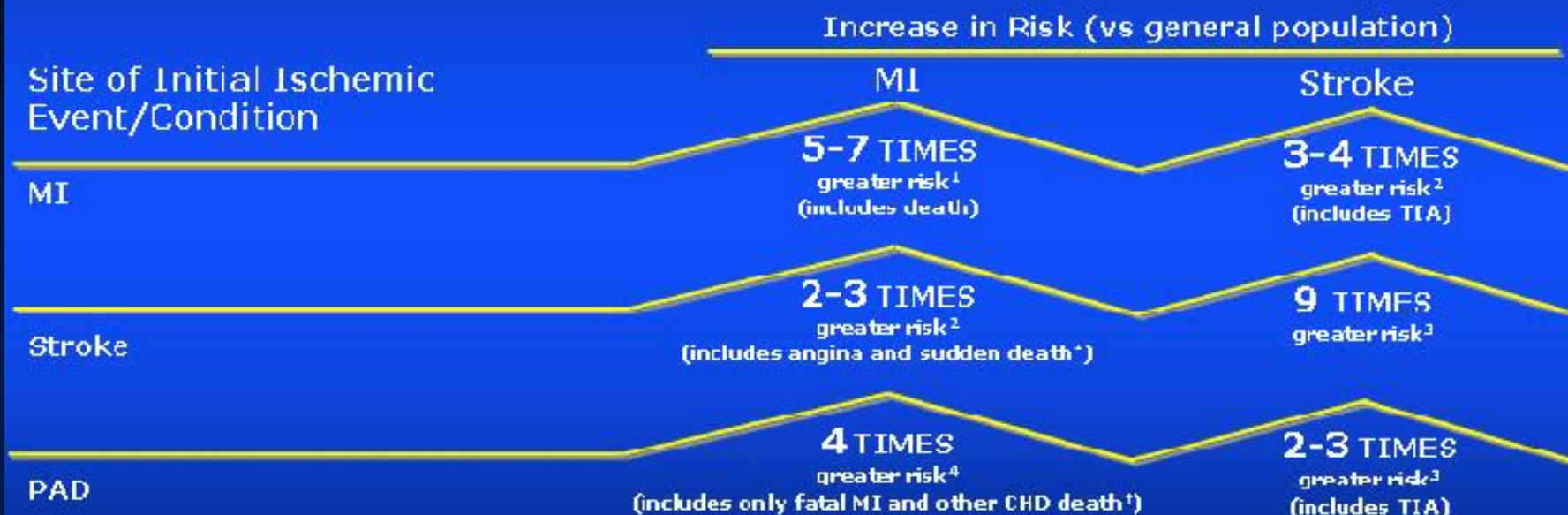
Salim Yusuf, Steven Hawken, Stephanie Ôunpuu, Tony Dans, Alvaro Avezum, Fernando Lanas, Matthew McQueen, Andrzej Budaj, Prem Pais, John Varigos, Liu Lisheng, on behalf of the INTERHEART Study Investigators*

Lancet, Sept 2004

	Cases (n=12 461)	Controls (n=14 637)
Geographic region		
Western Europe	664	767
Central and eastern Europe	1727	1927
Middle East	1639	1786
Africa	578	789
South Asia	1732	2204
China and Hong Kong	3030	3056
Southeast Asia and Japan	969	1199
Australia and New Zealand	589	681
South America and Mexico	1237	1888
North America	296	340
Ethnic origin		
European	3314	3710
Chinese	3130	3167
South Asian	2171	2573
Other Asian	871	1073
Arab	1306	1479
Latin American	1141	1834
Black African	157	369
Coloured African	311	339
Other	60	93

Risk of Ischemic Events in Atherosclerotic Clinical Syndromes

Epidemiologic data show patients with atherosclerosis are at increased risk of both MI and stroke¹⁻³



*Sudden death defined as death documented within 1 hour and attributed to coronary heart disease (CHD).

[†]Includes only fatal MI and other CHD death; does not include nonfatal MI.

¹Adult Treatment Panel II. *Circulation*. 1994;89:1333-1435.

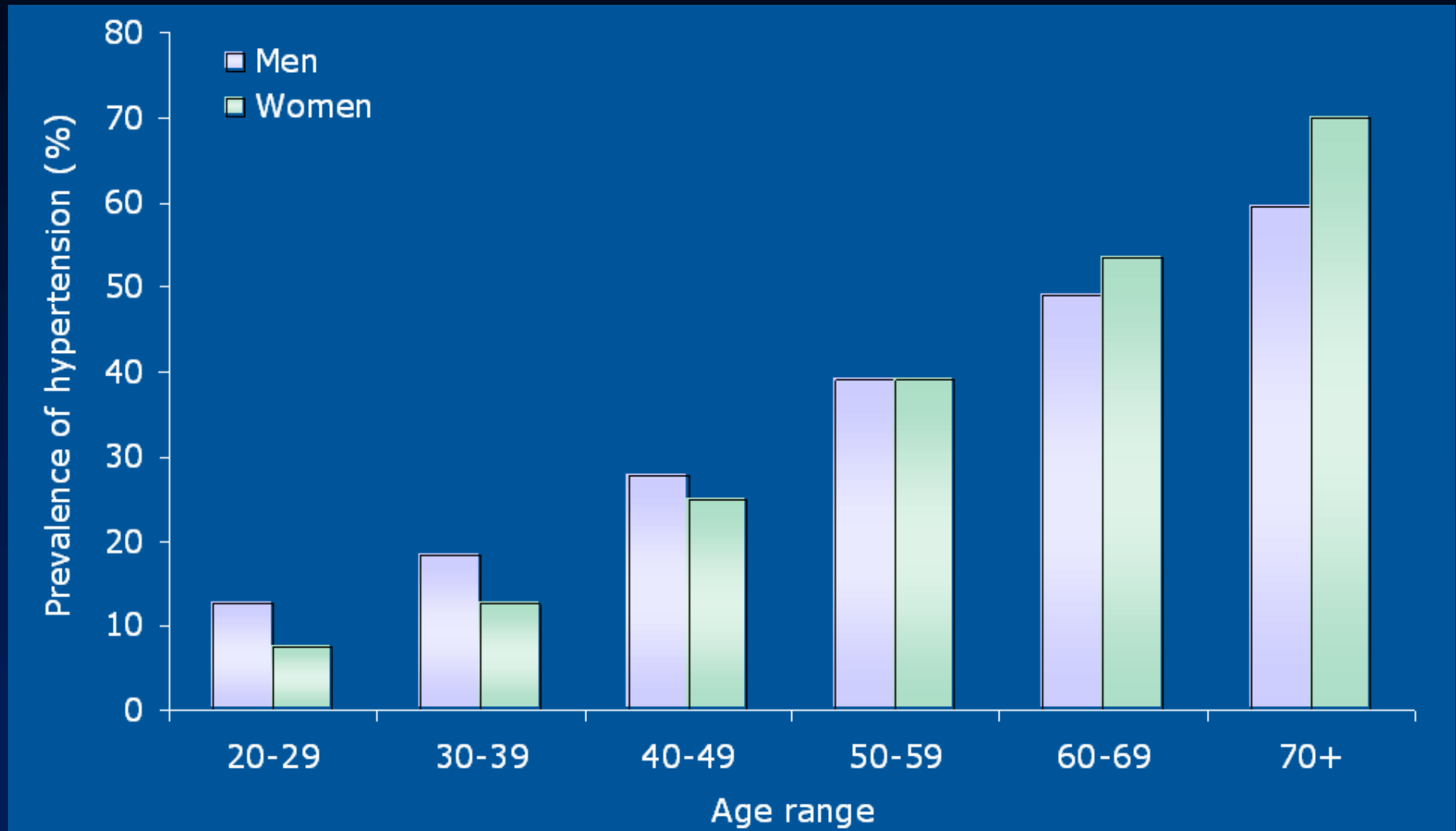
²Kannel WB. *J Cardiovasc Risk*. 1994;1:333-339.

³Willerdink JJ, Easton JD. *Arch Neurol*. 1992;49:857-863.

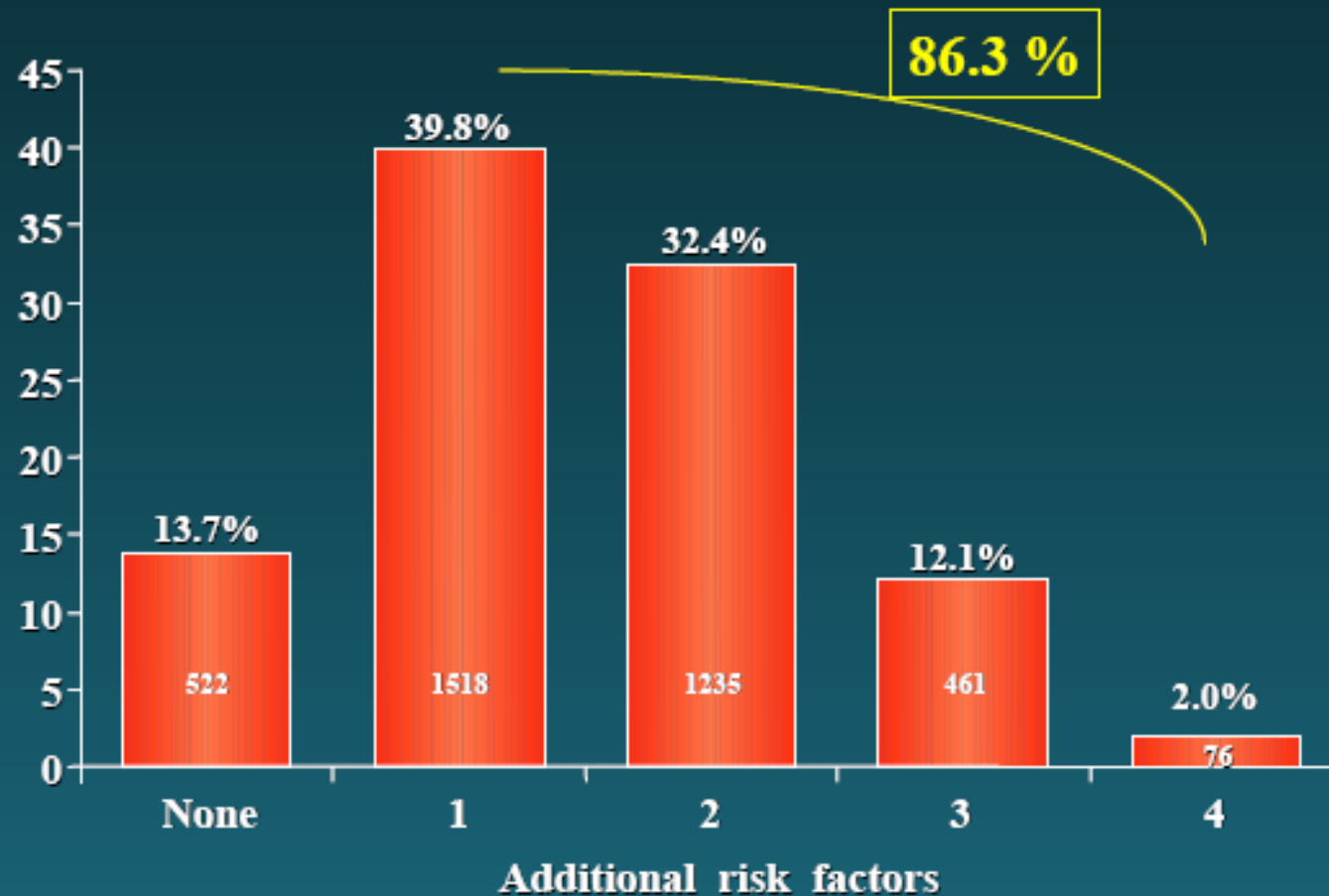
⁴Criqui MH et al. *N Engl J Med*. 1992;326:381-386.

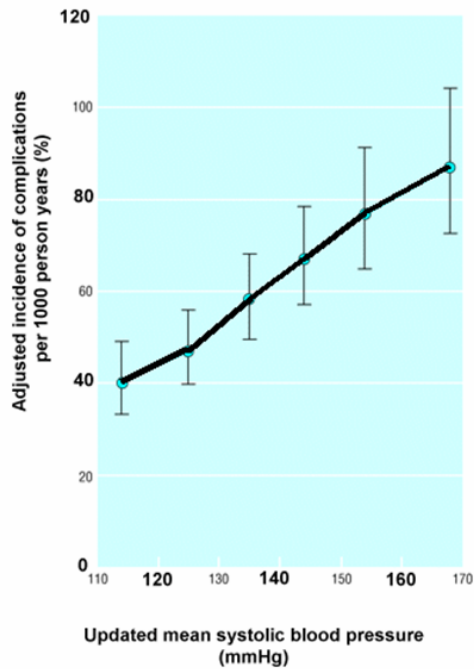
**Estimated 1 billion
people with
hypertension
worldwide**

BP and increasing age



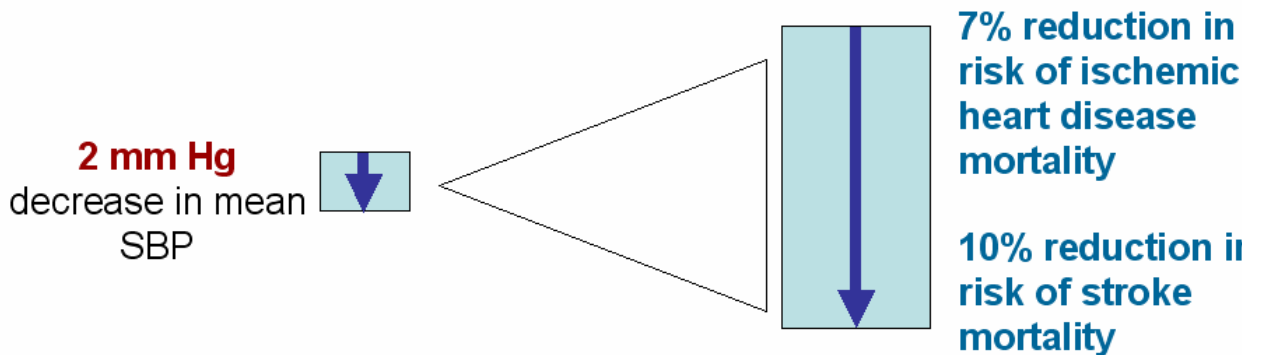
Percentage of hypertensive patients with CV risk factors



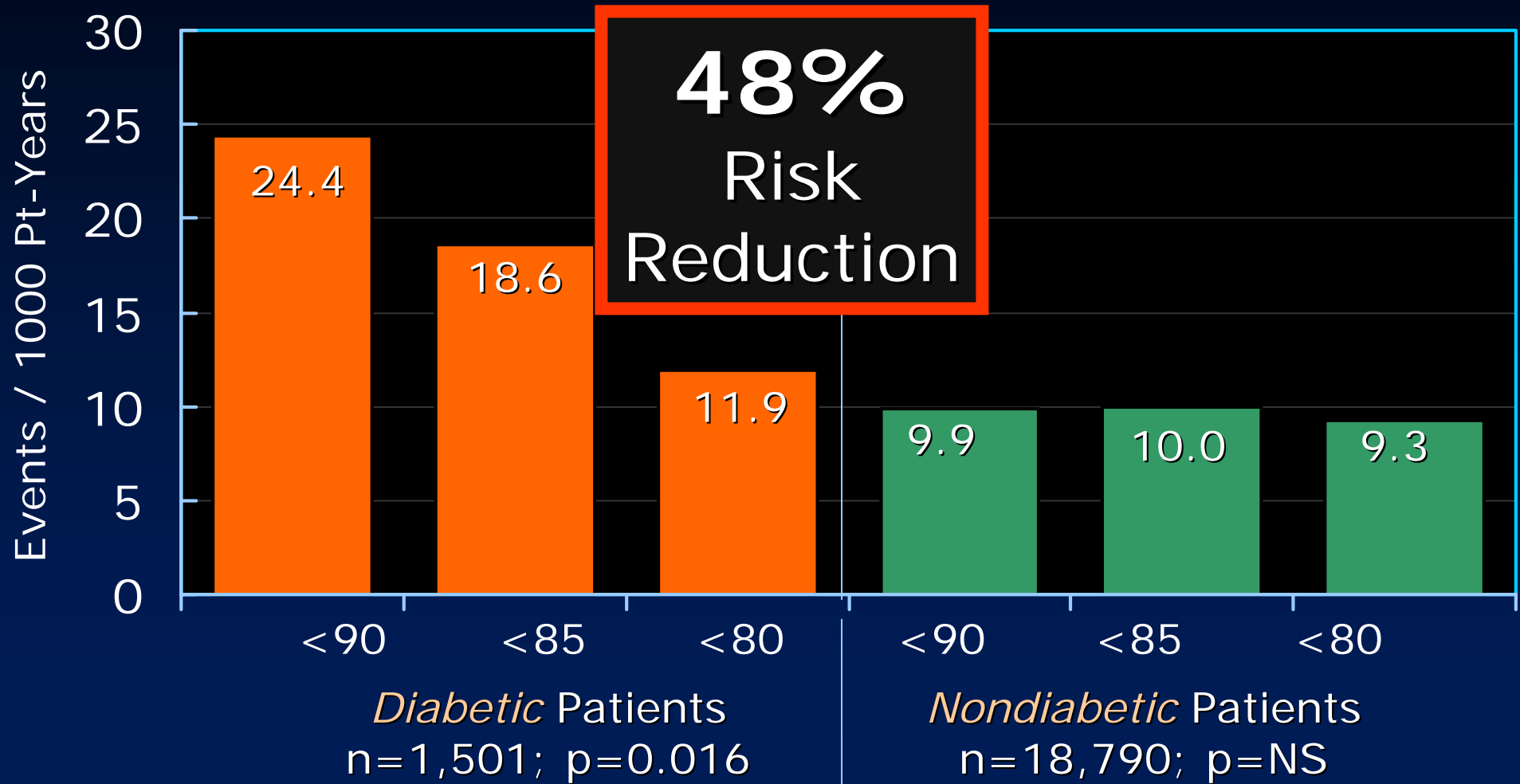


Each 1 mmHg in systolic BP gives rise to 1.2% of complications

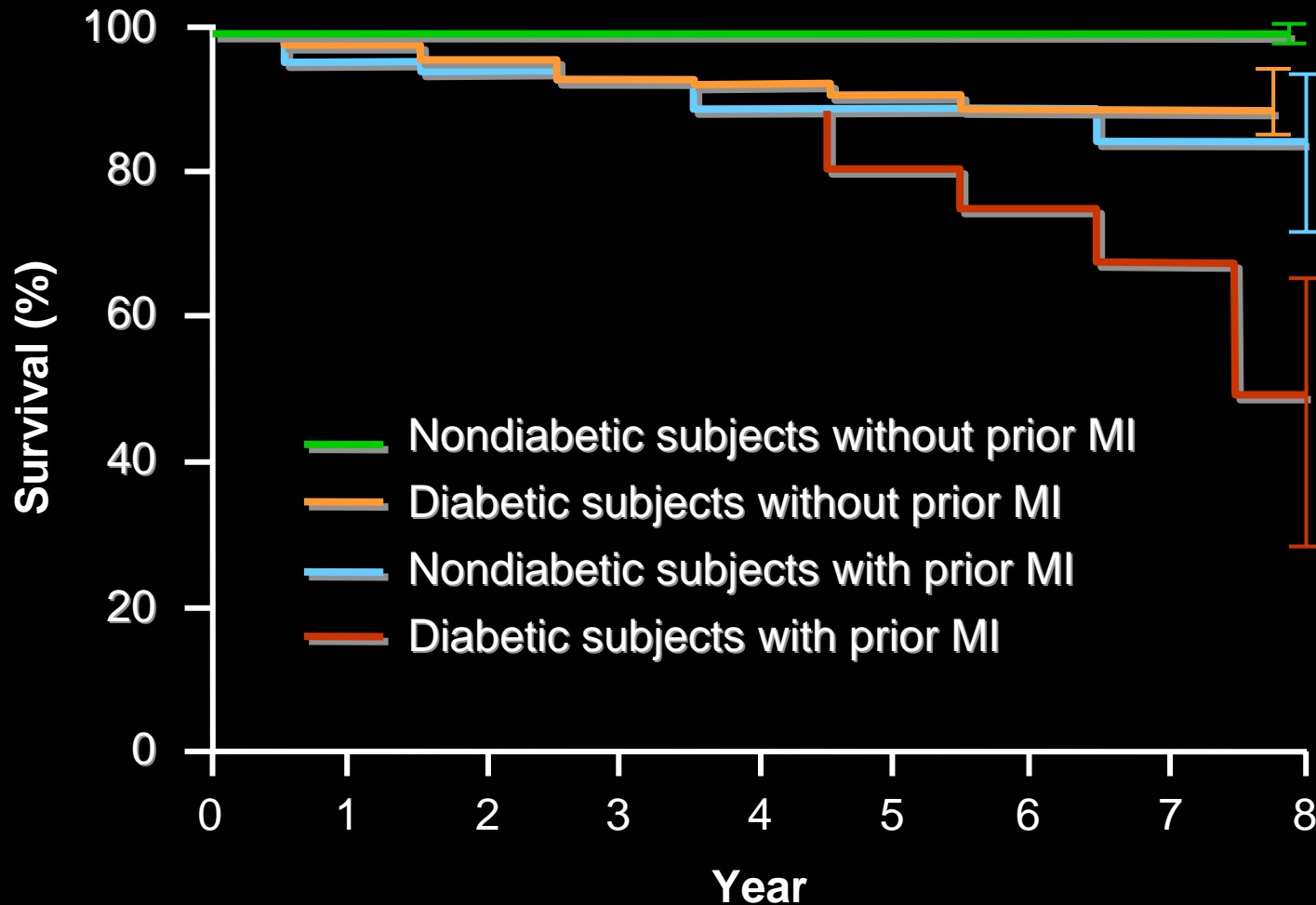
- Meta-analysis of 61 prospective, observational studies
- 1 million adults
- 12.7 million person-years



HOT study



DM, MI and survival



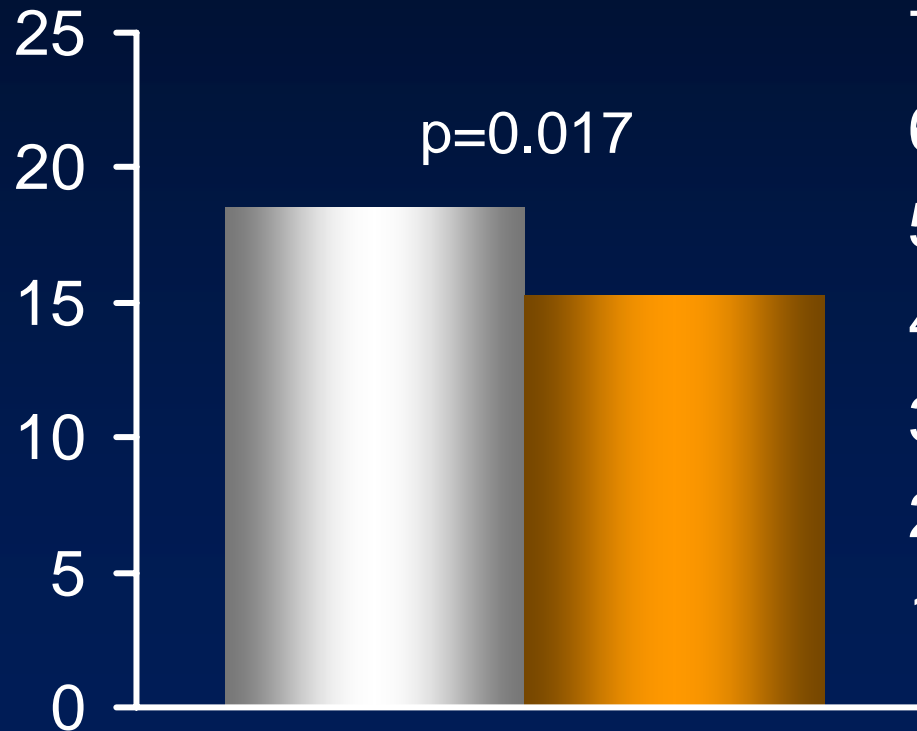
CHARM

Candesartan in Heart failure
Assessment of Reduction
in Mortality and morbidity

CHARM-Preserved

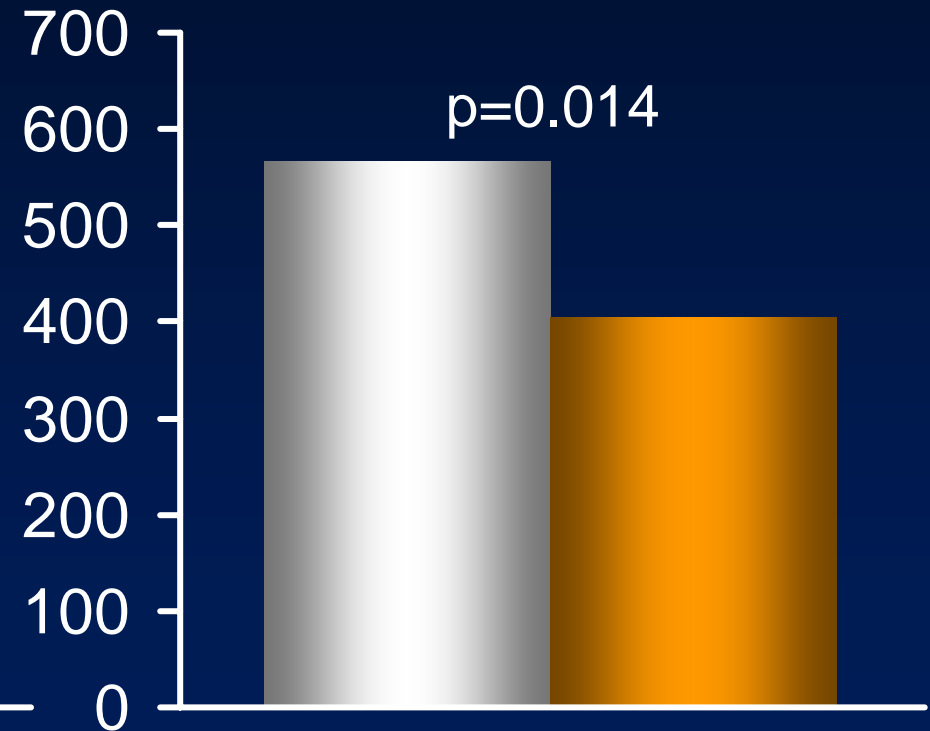
Placebo
Candesartan

Proportion of patients (%)



Patients hospitalised

Number of episodes



Hospitalisations

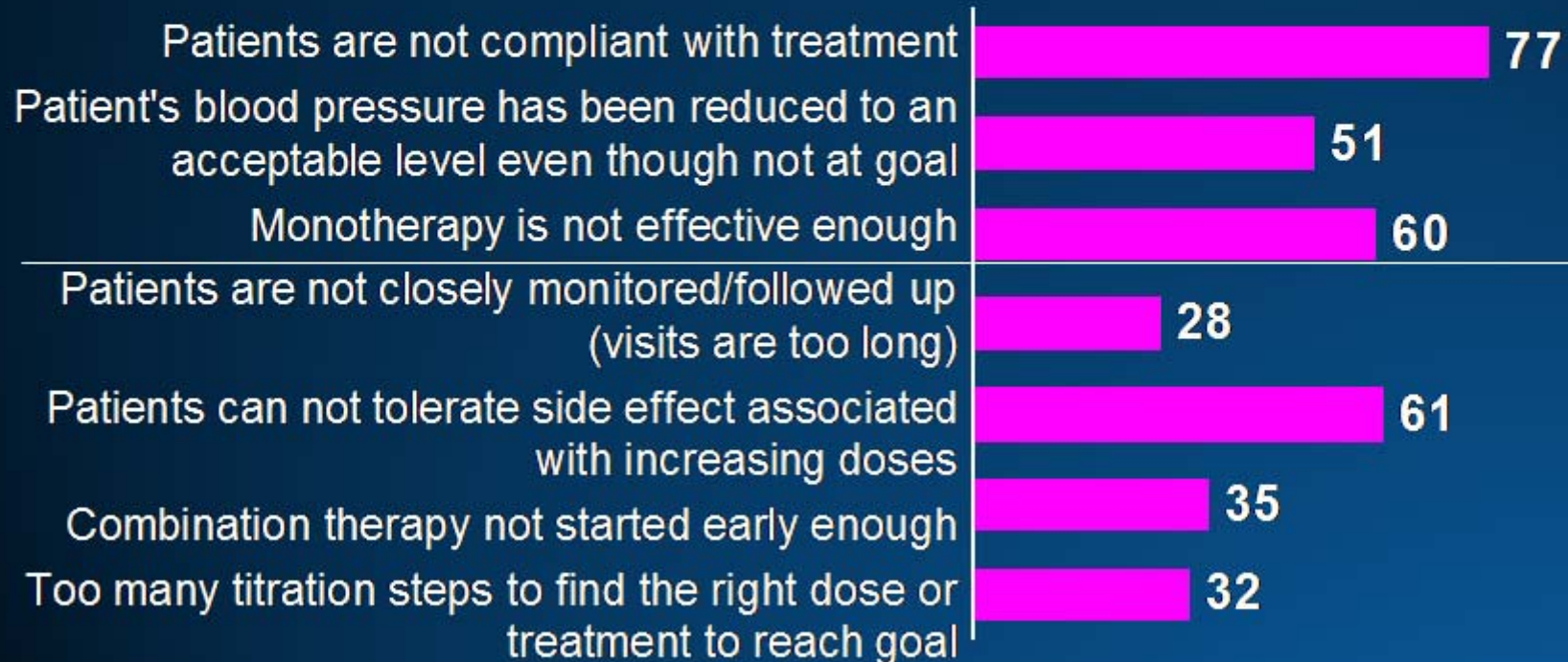
CHARM-Overall

Development of new diabetes

Number of cases (%)		HR	p-value
Candesartan n=2715	Placebo n=2721	(CI)	
163 (6)	202 (7)	0.78 (0.64-0.96)	0.020

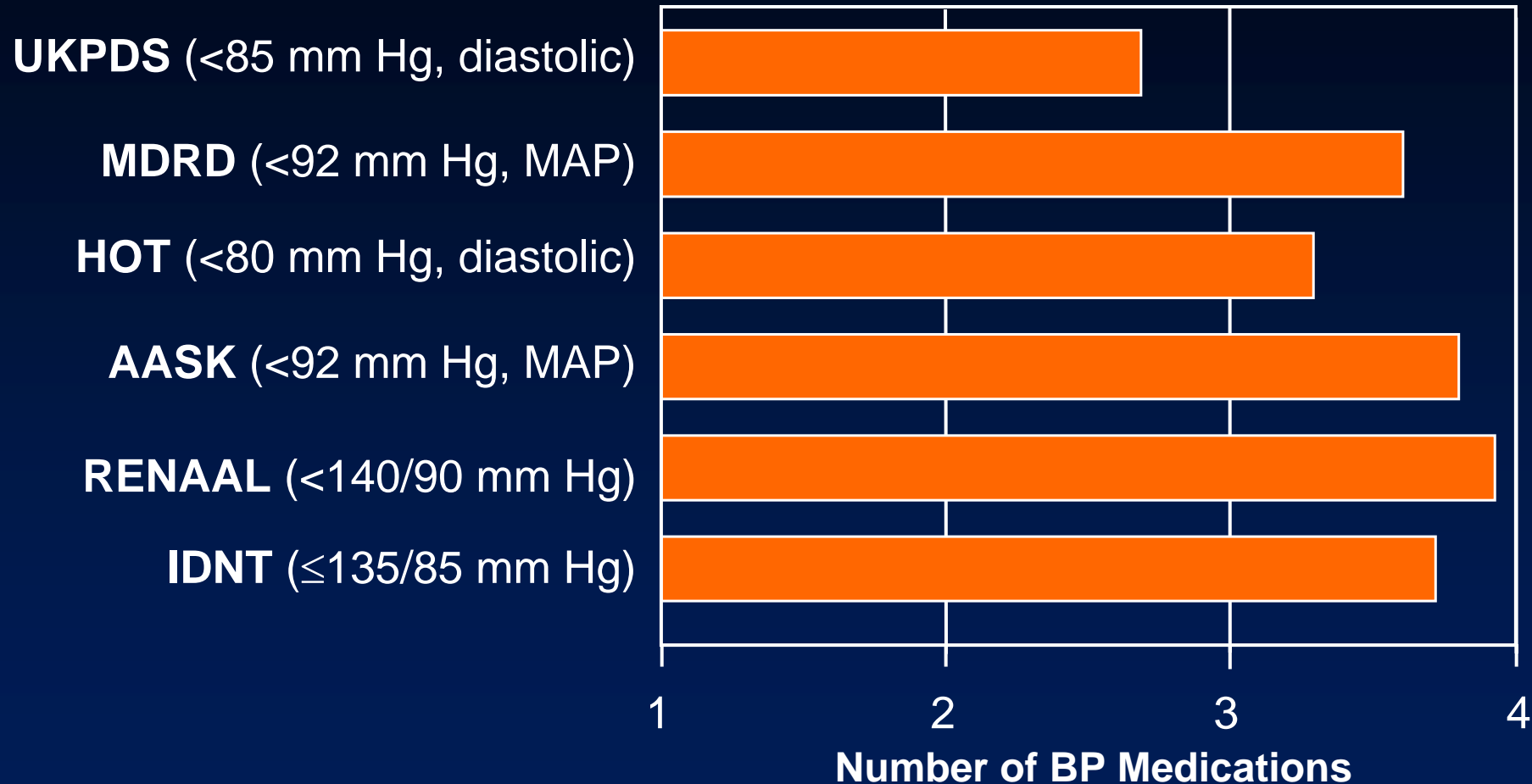
Reasons for not achieving blood pressure goals

Why in your opinion do no more than 50% of treated hypertensive patients achieve their blood pressure goals? (more than one answer)



Remaining responses: Insufficient GP knowledge, cultural, social issue, medication too expensive, obesity / lifestyle, not applied, don't know (n=4)

Antihypertensive Therapy: Number of Agents Required to Achieve BP Goal



Bakris et al. *Am J Kidney Dis.* 2000;36:646-661; Bakris et al. *Arch Intern Med.* 2003;163:1555-1565; Lewis et al. *N Engl J Med.* 2001;345:851-860.

Joint NICE/British Hypertension Society Guidelines: Recent update to management algorithm in essential hypertension

**Released
June 2006**

Younger than
55 years

55 years or older or black**
patients of any age

Step 1

ACEi/ARB*

CCB or Diuretic

Step 2

ACEi/ARB* & CCB or ACEi/ARB* & Diuretic

Step 3

ACEi/ARB* & CCB & Diuretic

Step 4

Add in:
• further diuretic therapy or
• alpha blocker or
• beta blocker or
Consider seeking specialist advice

***if an ACE inhibitor is not
tolerated**

****Black patients are
defined as those of
African or Caribbean
descent only**

RAS Blockade Across the CV Continuum

Hypertension

- LIFE
- SCOPE
- VALUE
- KYOTO HEART
- CAPP
- ANBP-2
- ALLHAT
- CASE-J

Heart Failure

- ELITE II
- Val-HeFT
- CHARM
- CONSENSUS I
- SOLVD
- PEP-CHF
- I-PRESERVE

Vascular

- ELITE II
- Val-HeFT
- CHARM
- CONSENSUS I
- SOLVD
- PEP-CHF
- I-PRESERVE

Diabetes - Renal

- RENAAL
- IDNT
- ABCD-2V
- AASK
- MARVAL
- ADVANCE
- DETAIL
- DIRECT
- ROADMAP

Pre-Diabetes

- NAVIGATOR
- DREAM

MI

- OPTIMAAL
- VALIANT
- CONSENSUS II
- ISIS-4
- GISSI-3
- SMILE
- SAVE
- AIRE
- TRACE

CAD

- EUROPA
- PEACE
- IMAGINE

2° Stroke Prevention

- ACCESS
- PROGRESS
- PRoFESS
- SCAST

Initial Comparative Studies in Hypertensive Patients

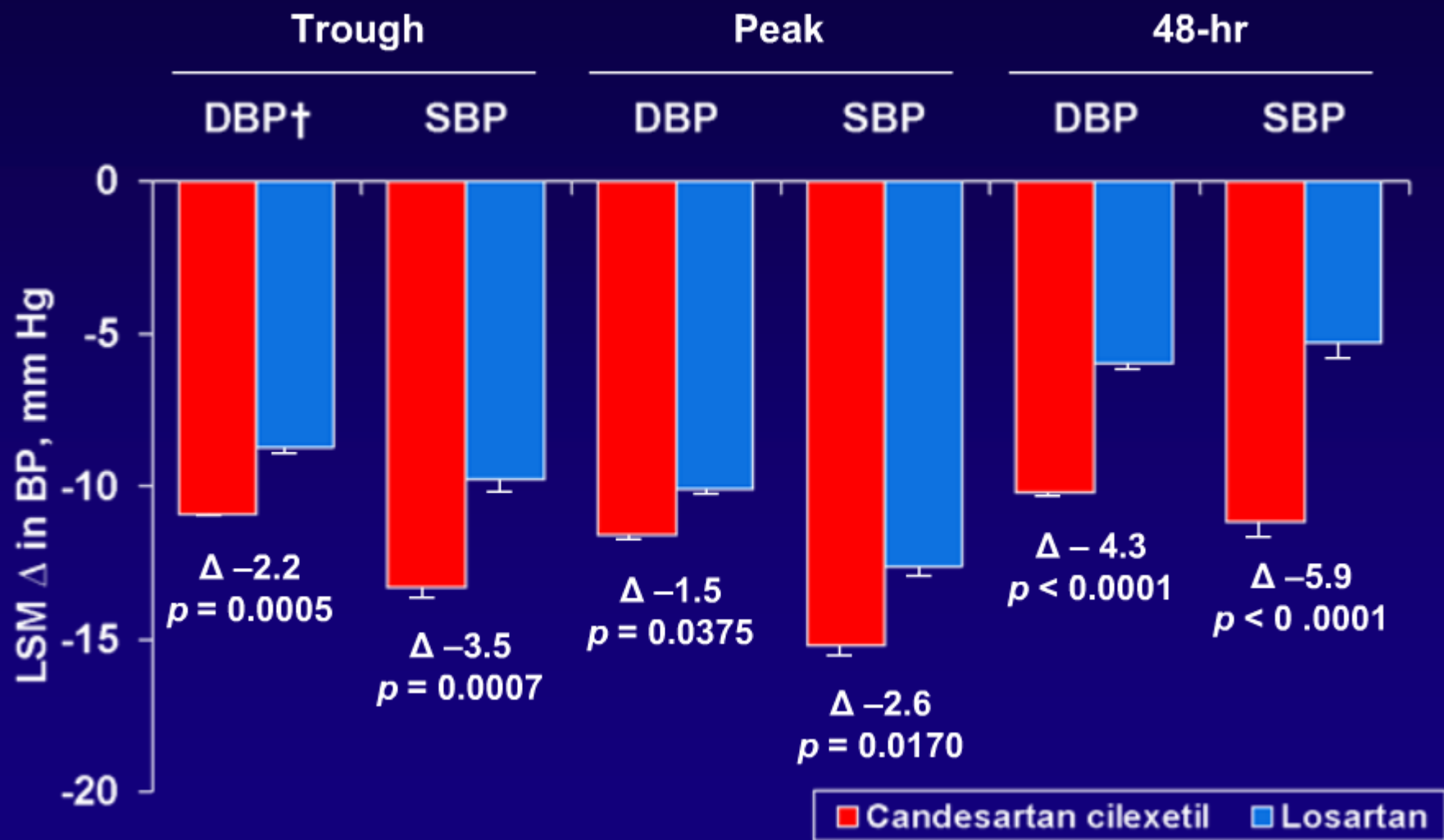
Two randomized, double-blind, multicenter, controlled, parallel-group, 8-wk studies in patients with a mean sitting DBP of 95 to 114 mm Hg

SH-AHM-0001 (n = 337)

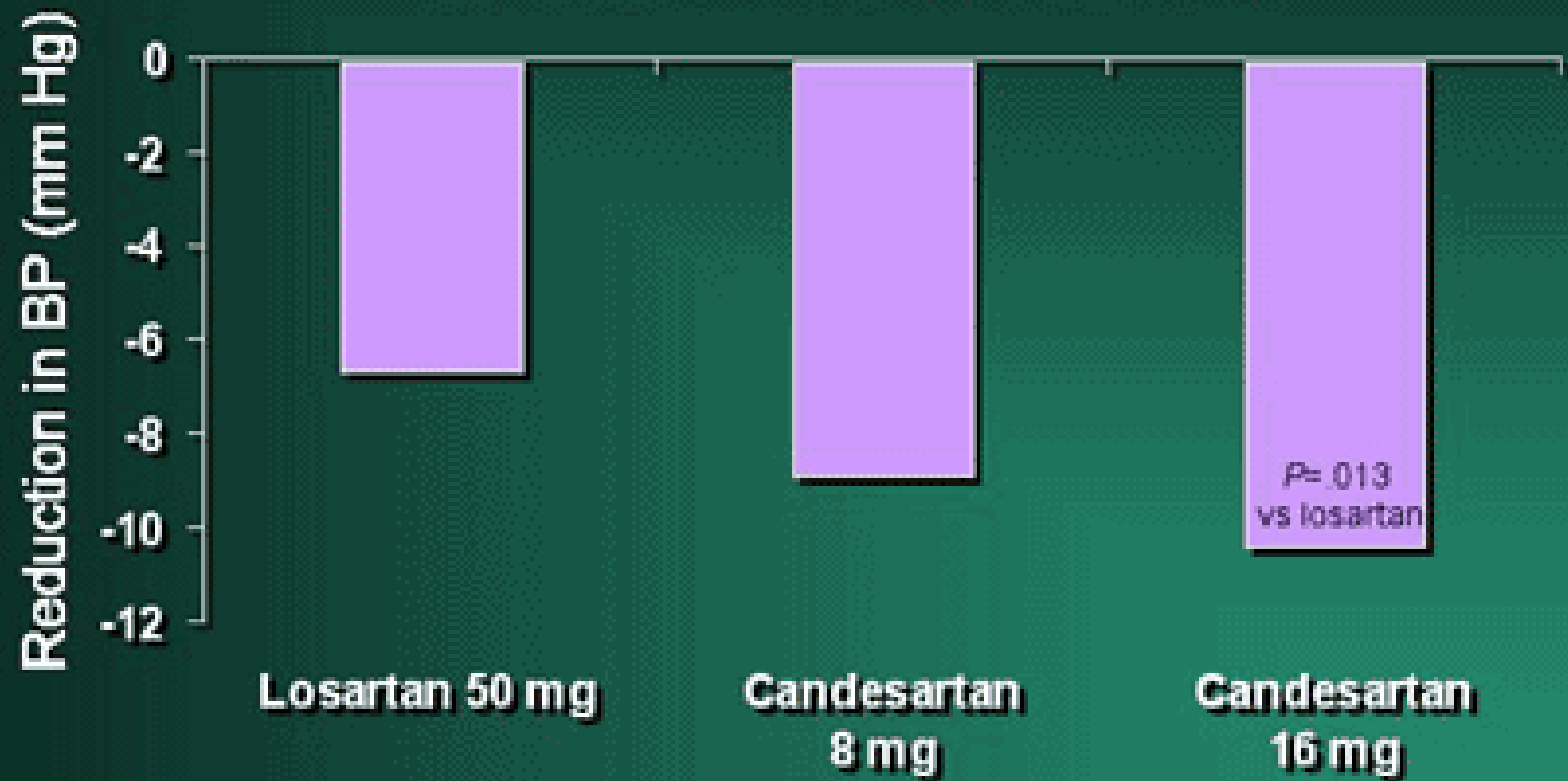
- Candesartan cilexetil
 - 8 mg QD
- Candesartan cilexetil
 - 16 mg QD
- Losartan 50 mg QD
- Placebo QD

Study 175 (n = 332)

- Candesartan cilexetil 16 mg titrated as needed[†] to 32 mg QD
- Losartan 50 mg titrated as needed[†] to 100 mg QD

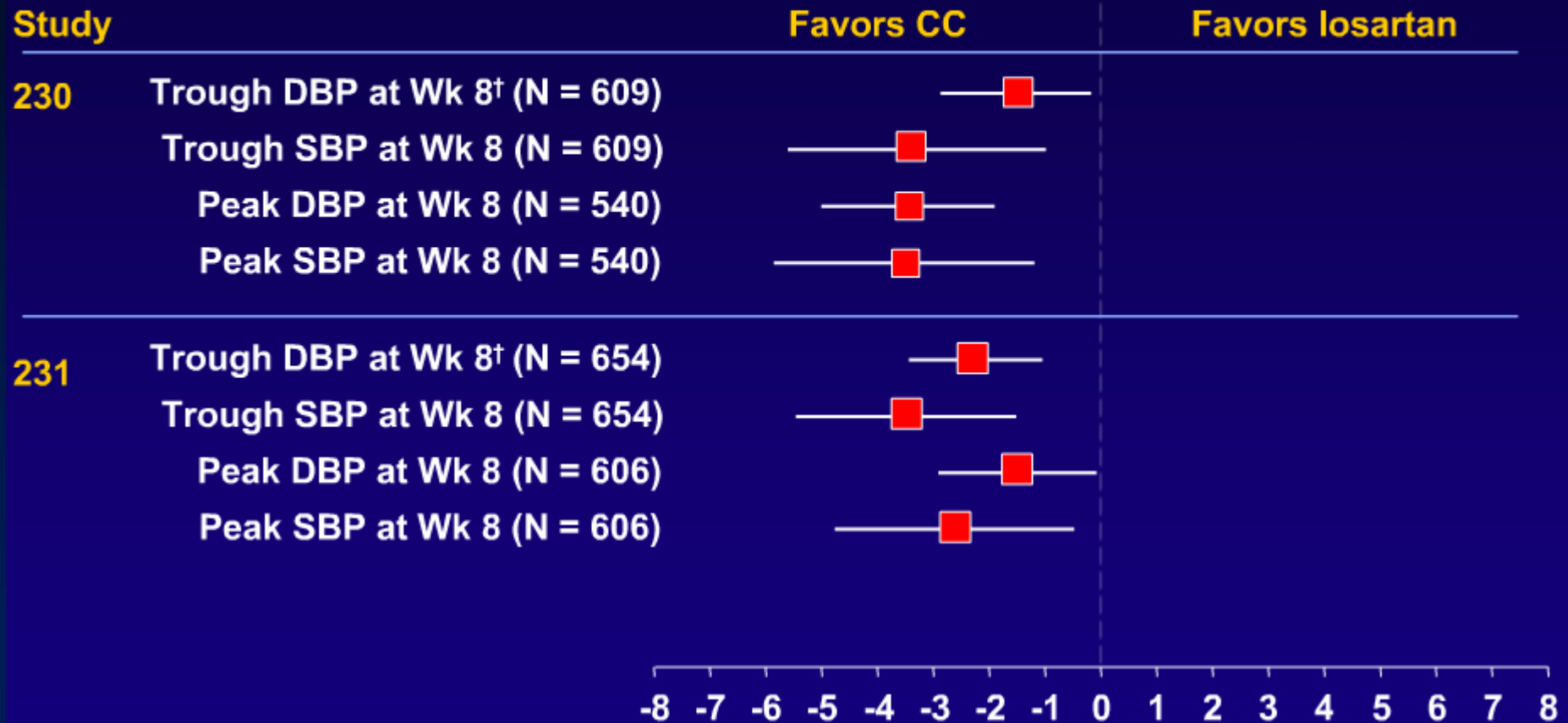


Trough Diastolic Blood Pressure

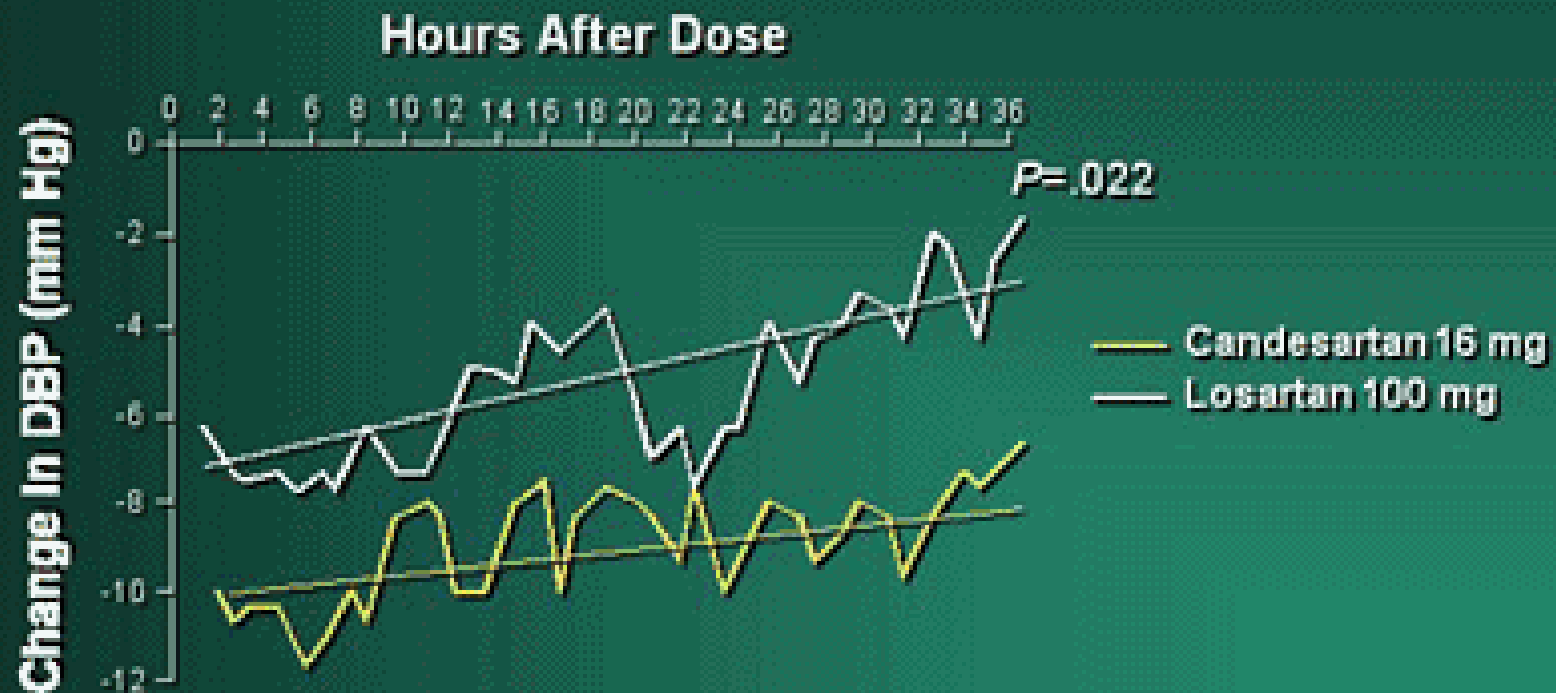


Andersson OK, et al. *Blood Press.* 1998;7:53-9.

Efficacy Data for 2 CLAIM Trials (230, 231)

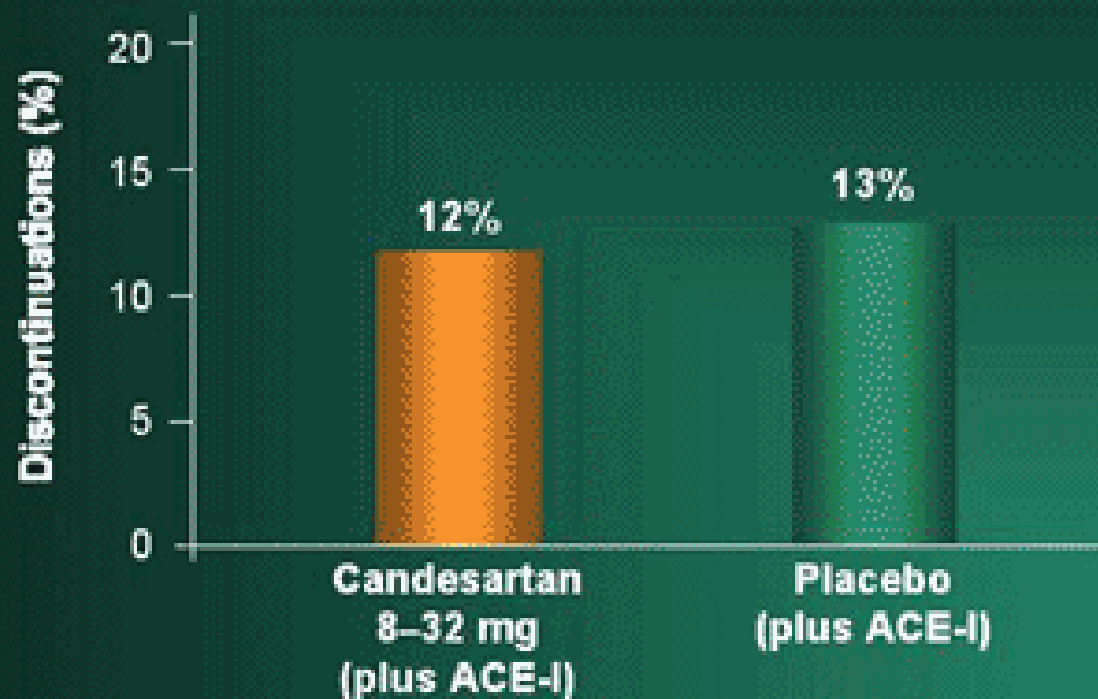


36-hour Control of Blood Pressure Mean Change in DBP from Baseline to Week 8 (Missed Dose Study)



Lacourcière Y for The GHAMP Study

Tolerability and Safety of High Dose Candesartan in Combination with ACE-I in Heart Failure



n=98 patients, randomized 2:1 on candesartan vs placebo

Gradman AH, et al. *Circulation* 1999;100[abstract]:1-783

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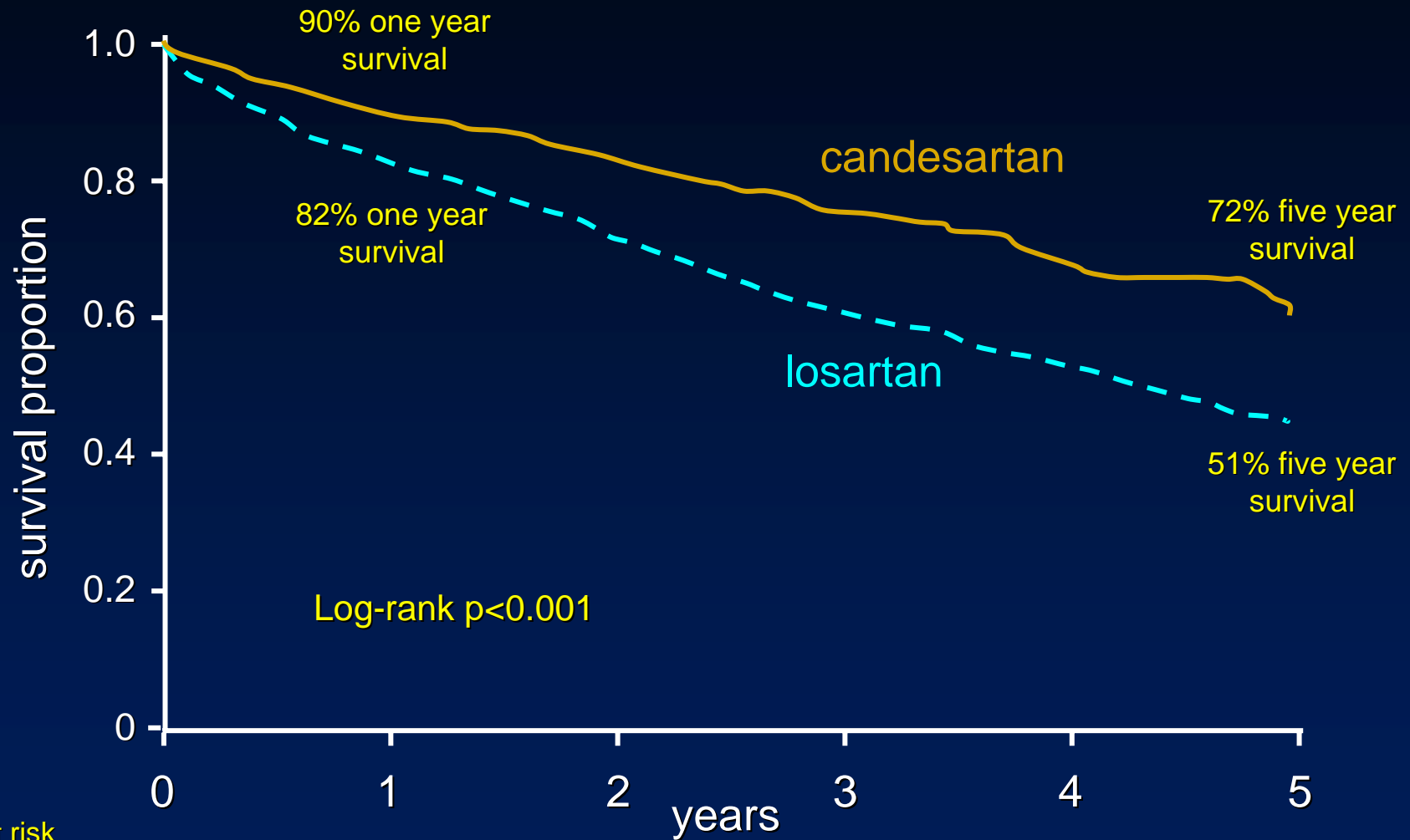
Association of Candesartan vs Losartan With All-Cause Mortality in Patients With Heart Failure

Maria Eklind-Cervenka, MD; Lina Benson, MSc; Ulf Dahlström, MD, PhD;
Magnus Edner, MD, PhD; Mårten Rosenqvist, MD, PhD; Lars H. Lund, MD, PhD

They gathered and examined data from the Swedish Heart Failure Registry, involving 30,254 patients registered from 60 outpatient clinics and 62 patients from the beginning of 2000 through 2009. 2,639 patients received candesartan and 2,500 received losartan.

- 90% of the candesartan patients survived for at least one year
- 83% of the losartan patients survived for at least one year
- 61% of the candesartan patients survived for at least five years
- 44% of the losartan patients survived for at least five years

Candesartan v Losartan: Mortality in Heart Failure Patients



Number at risk
Candesartan
Losartan

2639
2500

1739
1692

957
1097

426
646

125
359

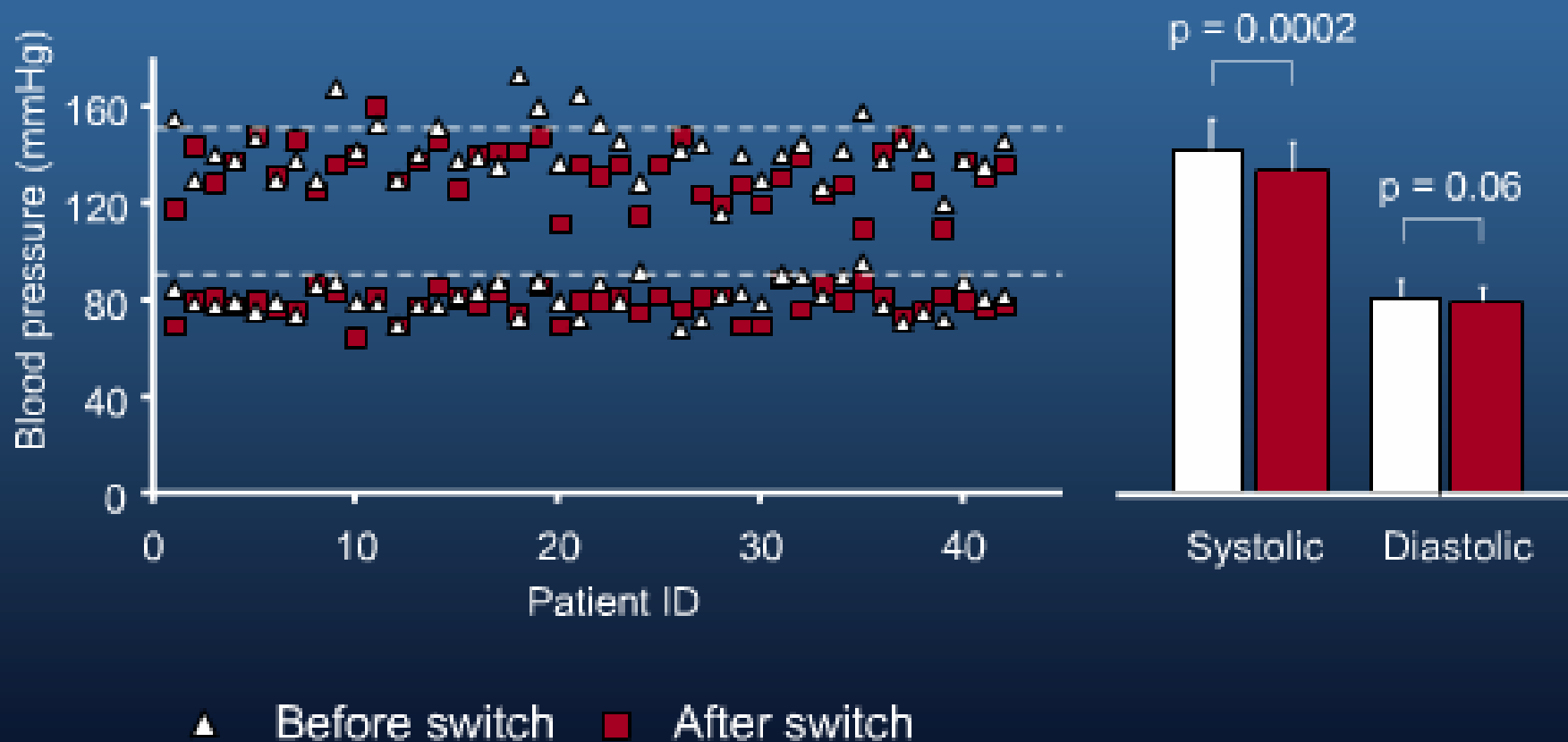
30
178

Switching patients from
atorvastatin to simvastatin and
losartan to candesartan in a
primary care setting

Dr Juliet Usher-Smith

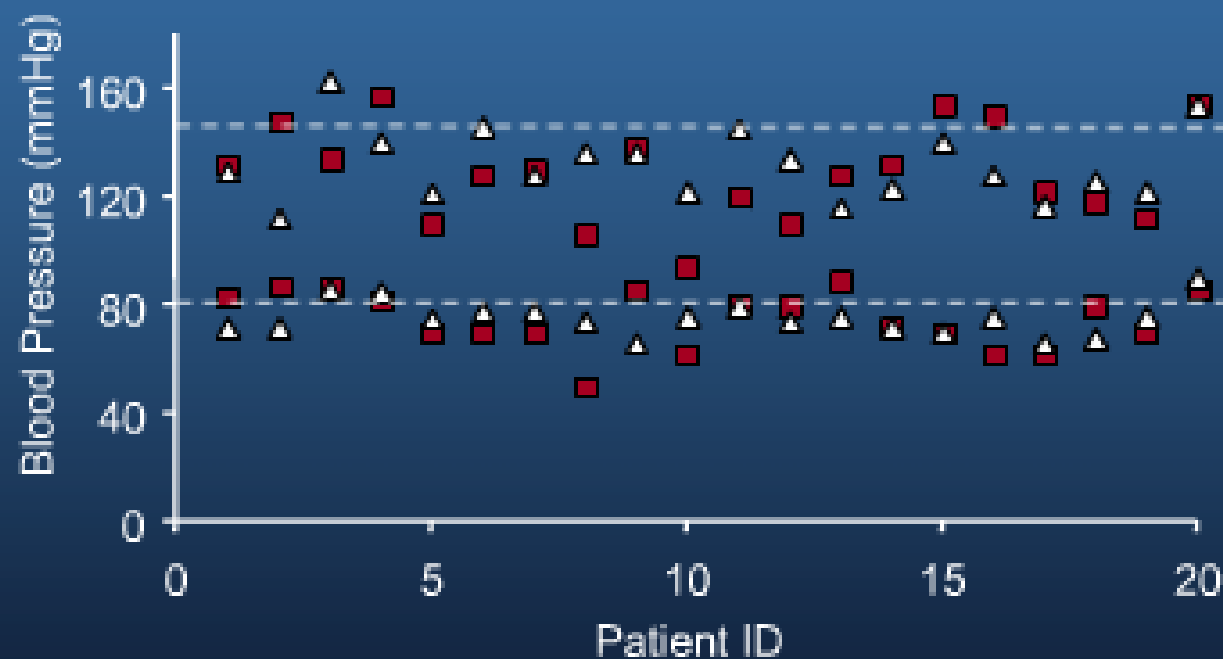
SARTAN SWITCH - CLINICAL OUTCOME

PATIENTS WITHOUT DIABETES OR CVD

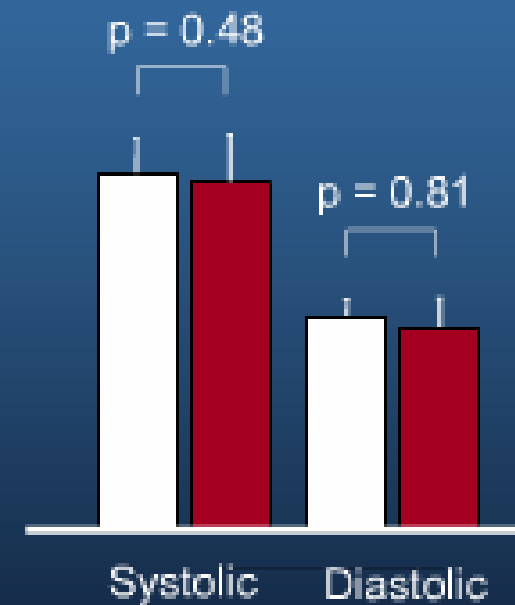


SARTAN SWITCH - CLINICAL OUTCOME

PATIENTS WITH CARDIOVASCULAR DISEASE

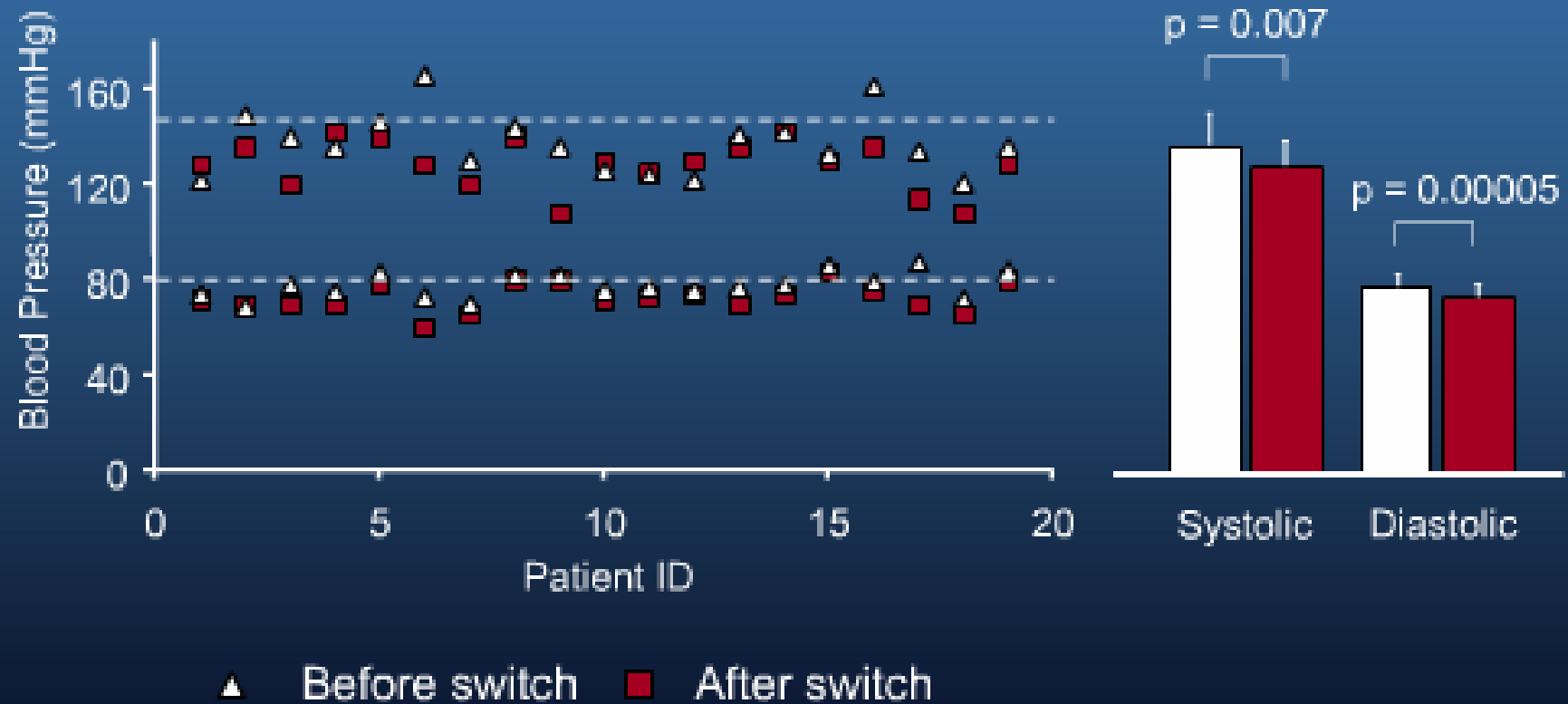


▲ Before switch ■ After switch



SARTAN SWITCH - CLINICAL OUTCOME

PATIENTS WITH DIABETES



LVH



Patients reaching blood pressure and blood cholesterol goals during treatment

Percentage of people aged 70 years or below with established CVD who achieve blood pressure goal of less than 140/90 mmHg, or blood cholesterol goal of less than 5.0 mmol/l
2001

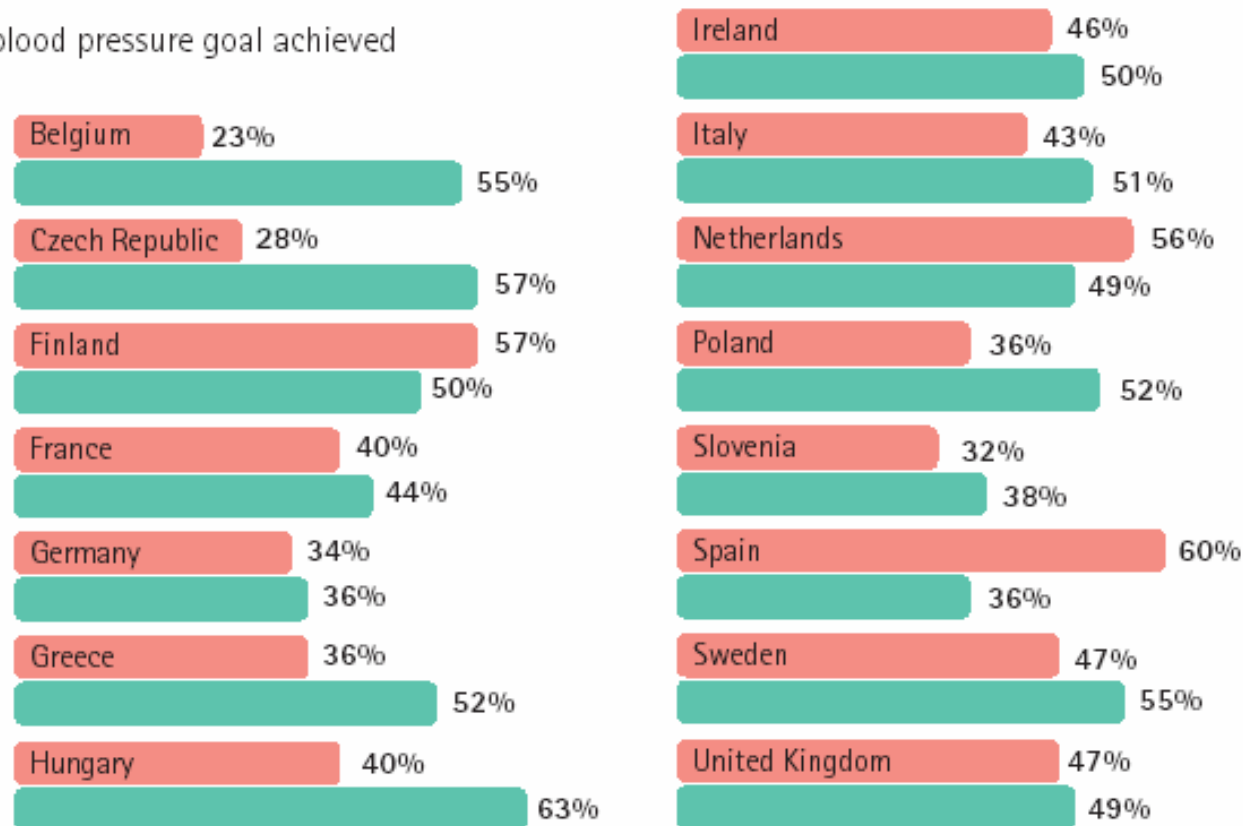
selected European countries



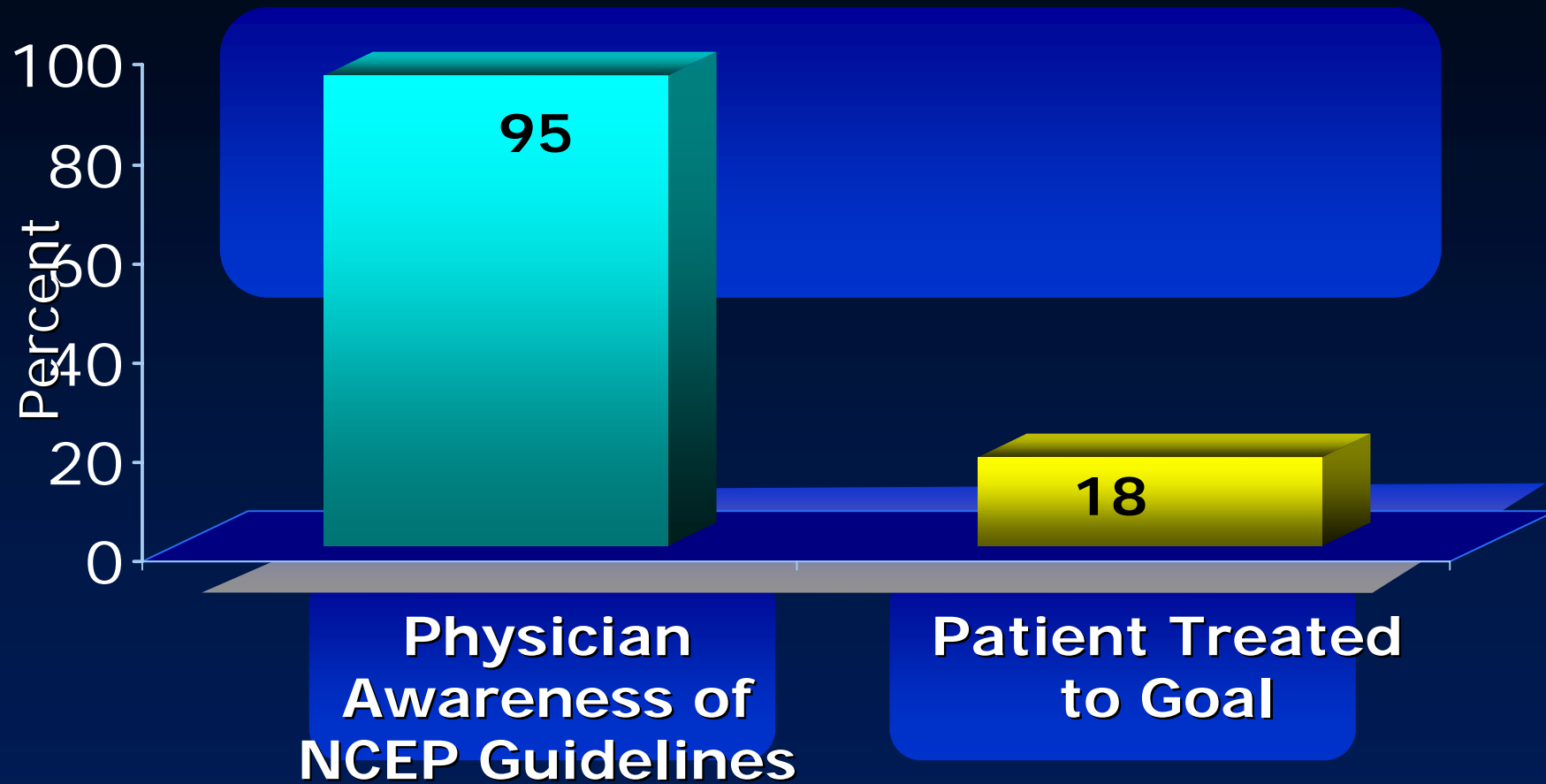
blood cholesterol goal achieved



blood pressure goal achieved



CHD Patient Treatment Gap



Provider awareness does not equal successful implementation

Fat in food

This table shows the amount of fat there is in one serving of some foods, along with the fat content of some lower fat alternative choices.

STARCHY FOODS

Potatoes (140 g or 5 oz serving)

thin-cut chips	17 g	
thick-cut chips	8 g	
oven chips	7 g	
roast potatoes	8 g	
baked potatoes	0.1 g	
boiled potatoes	0.1 g	

Rice (85 g or 3 oz raw weight)

fried	8 g	
boiled	1 g	

Chapattis

made with fat	8 g	
made without fat	0.5 g	

DAIRY PRODUCTS

Milk (284 ml or 1/2 pint)

whole	11 g	
semi-skimmed	5 g	
skimmed	0.3g	

Cheese (60 g or 2 oz serving)

Cheddar	20 g	
Edam	14 g	
low fat Cheddar	8 g	

Cream (30 g or 1 oz serving)

double cream	14 g	
single cream	6 g	
yoghurt (low fat plain)	0.3 g	
fromage frais (low fat)	0.3 g	

FISH

Cod (85 g or 3 oz serving)

fried in batter	9 g	
poached	1 g	

Fish fingers (3)

fried	11 g	
grilled	6 g	

MEAT AND MEAT PRODUCTS

Pork chop (85 g or 3 oz serving)

fried with fat left on	16 g	
grilled with fat removed	6 g	

Sausages (2 large)

ordinary	21 g	
'low fat'	11 g	

Beefburgers, grilled (2)

ordinary	18 g	
'low fat'	9 g	

POULTRY

Roast chicken (85 g or 3 oz serving)

skin left on	12 g	
skin removed	5 g	

FATS AND OILS

Spreads (10 g or 1/2 oz serving)

butter	8 g	
margarine (all types)	8 g	
low fat spread	4 g	

ghee

10 g

oil (all types)

10 g

SWEET SNACKS

small chocolate bar

15 g

halva

11 g

sevyaan

7 g

burfi

5 g

2 digestive biscuits

6 g

SAVOURY SNACKS

1 samosa

26 g

crisps (small bag)

ordinary

9 g

'low fat'

7 g

Peanuts (small bag)

12 g

Chinese pastry with

bean filling

6 g

"Polypill" to fight cardiovascular disease

A strategy to reduce cardiovascular disease by more than 80%

N J Wald, M R Law

BMJ VOLUME 326 28 JUNE 2003

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Researchers: 'Polypill' could cut heart attacks, strokes

Friday, June 27, 2003 Posted: 10:18 AM EDT (1418 GMT)

LONDON, England -- British researchers say a four-part pill containing aspirin, folic acid and other drugs could cut heart attacks and strokes by more than 80 percent.

The "Polypill" -- which would include drugs to lower cholesterol and blood pressure -- would help prevent disease in the Western world more than any other single treatment, the



A strategy to reduce cardiovascular disease by more than 80%

N J Wald, M R Law

A strategy to reduce cardiovascular disease by more than 80%

N J Wald, M R Law

Abstract

Objectives To determine the combination of drugs and vitamins, and their doses, for use in a single daily pill to achieve a large effect in preventing cardiovascular disease with minimal adverse effects. The strategy was to simultaneously reduce four cardiovascular risk factors (low density lipoprotein cholesterol, blood pressure, serum homocysteine, and platelet function) regardless of pretreatment levels.

Design We quantified the efficacy and adverse effects of the proposed formulation from published meta-analyses of randomised trials and cohort studies and a meta-analysis of 15 trials of low dose (50-125 mg/day) aspirin.

Outcome measures Proportional reduction in ischaemic heart disease (IHD) events and strokes; life years gained; and prevalence of adverse effects.

Results The formulation which met our objectives was: a statin (for example, atorvastatin (daily dose 10 mg) or simvastatin (40 mg)); three blood pressure lowering drugs (for example, a thiazide, a β blocker, and an angiotensin converting enzyme inhibitor), each at half standard dose; folic acid (0.8 mg); and aspirin (75 mg). We estimate that the combination (which we call the Polypill) reduces IHD events by 88% (95% confidence interval 84% to 91%) and stroke by 80% (71% to 87%). One third of people taking this pill from age 55 would benefit, gaining on average about 11 years of life free from an IHD event or stroke. Summing the adverse effects of the components observed in randomised trials shows that the Polypill would cause symptoms in 8-15% of people (depending on the precise formulation).

Conclusion The Polypill strategy could largely prevent heart attacks and stroke if taken by everyone aged 55 and older and everyone with existing cardiovascular disease. It would be acceptably safe and with widespread use would have a greater impact on the prevention of disease in the Western world than any other single intervention.

Introduction

Heart attacks, stroke, and other preventable cardiovascular diseases kill or seriously affect half the population of Britain. Western diet and lifestyle have increased the population levels of several of the causal "risk factors," and their combined effects have made

the diseases common. Cardiovascular disease can be avoided or delayed, but the necessary changes to Western diet and lifestyle are not practicable in the short term. Randomised trials show that drugs to lower three risk factors—low density lipoprotein (LDL) cholesterol,¹ blood pressure,^{2,3} and platelet function (with aspirin)⁴⁻⁶—reduce the incidence of ischaemic heart disease (IHD) events and stroke. Evidence that lowering serum homocysteine (with folic acid) reduces the risk of these diseases is largely observational but still compelling.⁷⁻¹⁰

Drug treatment to prevent IHD events and stroke has generally been limited to single risk factors, to targeting the minority of patients with values in the tail of the risk factor distribution, and to reducing the risk factors to "average" population values. This policy can achieve only modest reductions in disease.¹¹ A large preventive effect would require intervention in everyone at increased risk irrespective of the risk factor levels; intervention on several reversible causal risk factors together; and reducing these risk factors by as much as possible.¹²

We describe a strategy to prevent cardiovascular disease based on these three principles¹² and quantify the overall preventive effect. We show that a daily treatment, the Polypill, comprising six components, each lowering one of the above four risk factors, would prevent more than 80% of IHD events and strokes, with a low risk of adverse effects. This strategy would be suitable for people with known cardiovascular disease and for everyone over a specified age (say 55), without requiring risk factors to be measured.

Methods

We identified categories of drugs or vitamins used to modify LDL cholesterol, blood pressure, homocysteine, and platelet function. For LDL cholesterol, statins are the drugs of choice.^{13,14} For lowering blood pressure, we considered all five main categories of drugs: thiazides, β blockers, angiotensin converting enzyme (ACE) inhibitors, angiotensin II receptor antagonists, and calcium channel blockers.¹⁵ Serum homocysteine is most effectively reduced by folic acid; vitamins B-6 and B-12 have relatively small effects.¹² Aspirin is the most widely used and least expensive antiplatelet agent.

The choices of statin and of the categories and doses of blood pressure lowering drugs were

Editorial by Rodgers

Department of Environmental and Preventive Medicine, Wotton Institute of Preventive Medicine, Barts and the London, Queen Mary's School of Medicine and Dentistry, University of London, London EC1M 6BQ
N J Wald
professor
M R Law
professor

Correspondence to:
N J Wald
nj.wald@qmul.ac.uk

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appear on bmj.com