The State of Hypertension in NZ in 2010

personal view

Patient referred to medical clinic

“Dear Dr,

Please see this man with resistant hypertension…”

50 year old European male

Blood Pressure on current meds **160/ 95**, heart rate 55BPM,BMI 30

Renal function normal
Urine ACR 6mg/mmol
Fasting glucose 5.7mmol/l
Cholesterol 5.2 HDL 0.9 LDL 3.9 Trig 2.4
ECG shows electrical LVH

Meds
Inhibace Plus 1 daily
Metoprolol CR 95mg daily
Felodipine ER 10mg daily
Simvastatin 20mg nocte
Aspirin 100mg daily

How will you manage this patient and what advice will you give the GP?

Where is hypertension in NZ in 2010?


£15.67
SHIT BOX

Why is hypertension poorly managed in New Zealand?

Colleague feigning interest in hypertension

Voice Crying in the Wilderness

FO Simpson

Graeme Campbell

Kevin O’Brien

Robin Briant

Gavin Kellaway

Gary Nicholls

Mark Richards

Eric Espiner

And Others…

- A generation of hypertension specialists has retired or died

- Management of high blood pressure was deemed to be a GP/ primary care problem (circa 1990)

- Their hypertension clinics were disestablished

- Teaching of registrars and medical students is poor

- Skills have been lost across the board

“Those who cannot remember the past are doomed to repeat it”

George Santayana, philosopher
(1863-1952)

What are we left with?

2009 Edition

MINISTRY OF HEALTH
MANATŪ HAUORA

New Zealand Cardiovascular Guidelines Handbook

A summary resource for primary care practitioners

Cardiovascular risk assessment and diabetes screening

Cardiovascular risk factor management

Smoking cessation

Atrial fibrillation

Coronary heart disease

Stroke and transient ischaemic attack

Rheumatic fever

Prevention of infective endocarditis

Heart failure

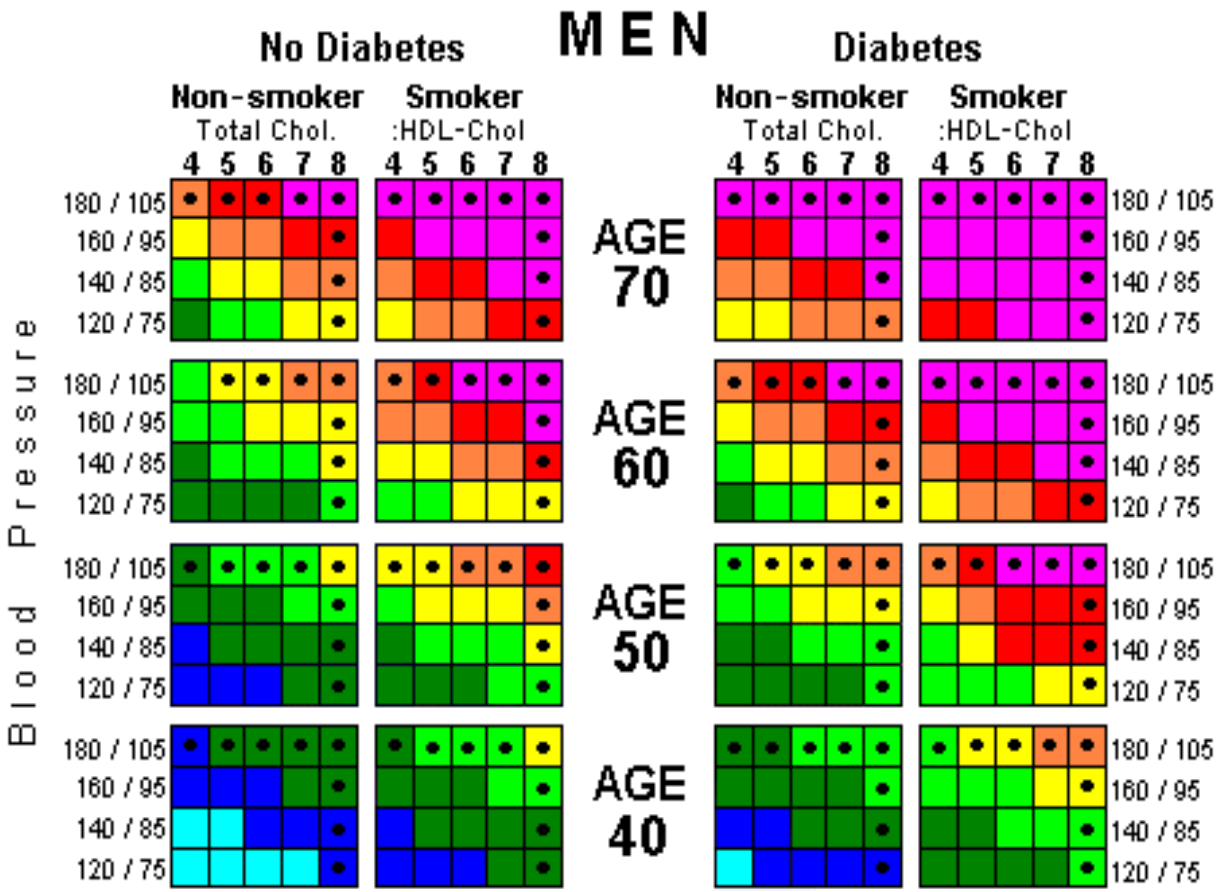
Kidney Health NEW ZEALAND

STROKE FOUNDATION OF NEW ZEALAND INC

diabetes new zealand

Heart Foundation

New Zealand GUIDELINES GROUP
Te Rōpū Rarangi Tohutohu
Promoting Effective Health and Disability Services


MEN
No Diabetes
Diabetes
Non-smoker
Smoker
Total Chol.
:HDL-Chol
4 5 6 7 8
Blood Pressure
180 / 105
160 / 95
140 / 85
120 / 75
AGE 70
AGE 60
AGE 50
AGE 40

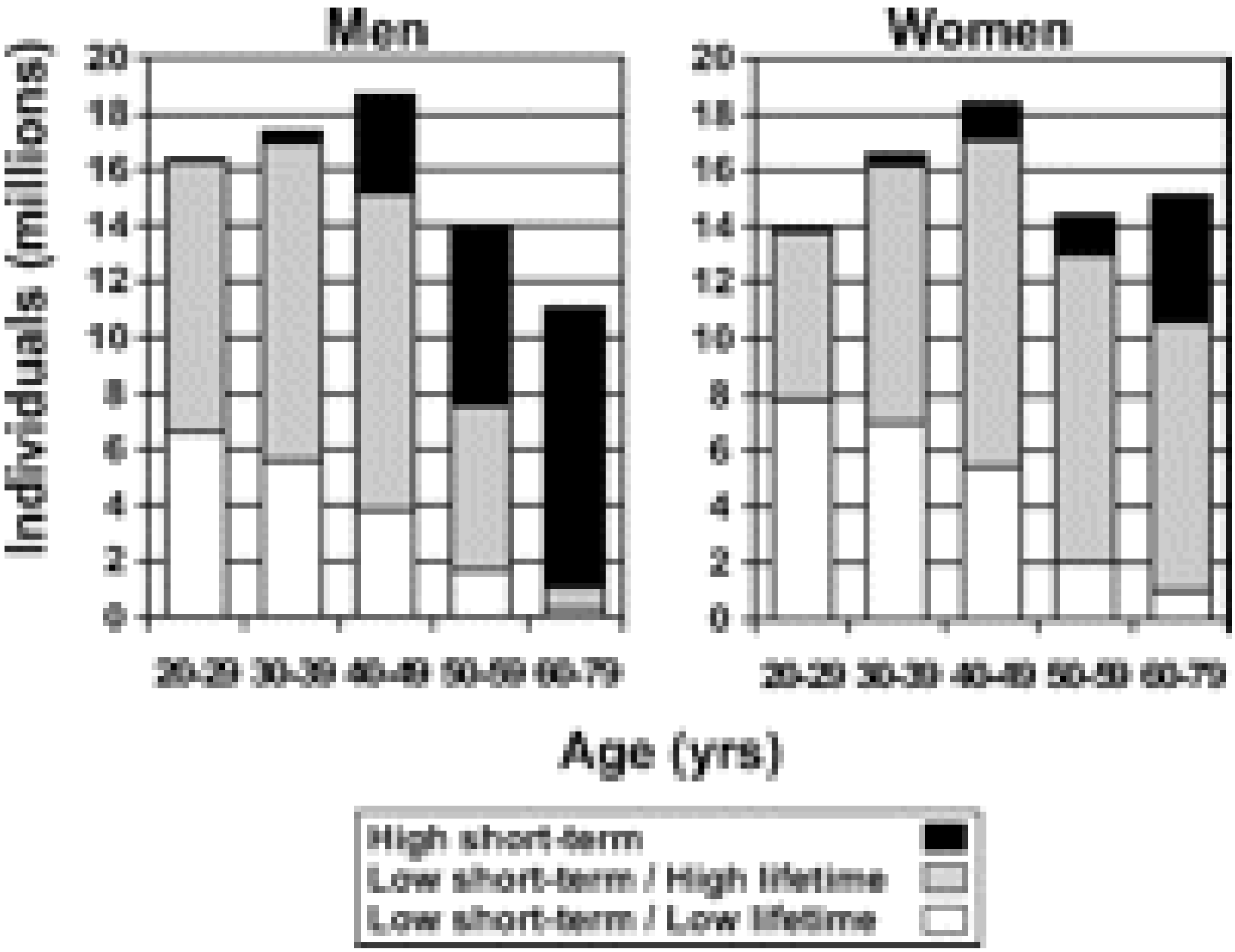
Basis for this is that active (pharmacological) treatment is suggested if 5 year risk of cardiovascular event is > 15-20%

But

“Isolated single risk factors” do not mandate therapy unless extremely abnormal
(BP > 170/100, total cholesterol > 8mmol/l etc)

So for example a 49 year old woman with normal lipids and a sustained BP 165/95 does not warrant antihypertensive therapy

A 40 year old man with a total cholesterol of 7.5 and normal blood pressure does not warrant statin therapy


Men
Women
Individuals (millions)
0
2
4
6
8
10
12
14
16
18
20
20-29
30-39
40-49
50-59
60-79
Age (yrs)
High short-term
Low short-term / High lifetime
Low short-term / Low lifetime

Framingham Risk and MI in Young Women

- Young women < 65 y presenting with MI

- None had a calculated risk of 20% (10 year)

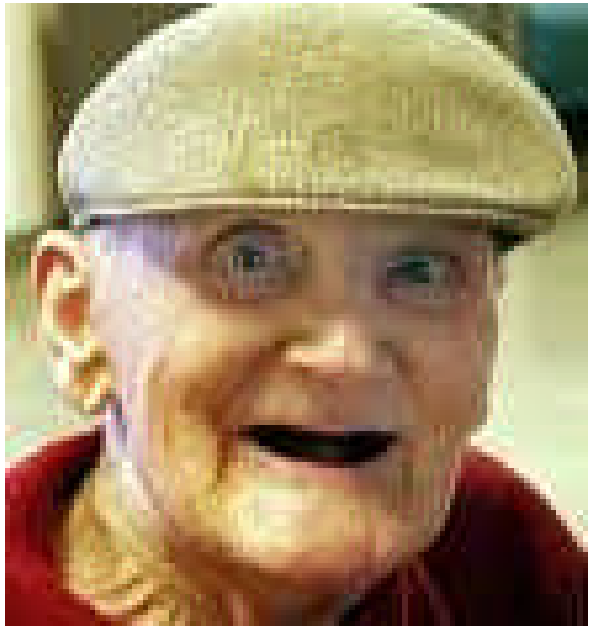
Akosah et al. JACC.2003

What the Guideline doesn't tell you is that although the 49 year old with a BP of 165/95 or a cholesterol of 7.5mmol/l is at low short term risk,

Long term risk is extremely high

And the NZ Cardiovascular Risk Guideline can thus be described as"

"Old Men Making Rules to Treat Themselves"

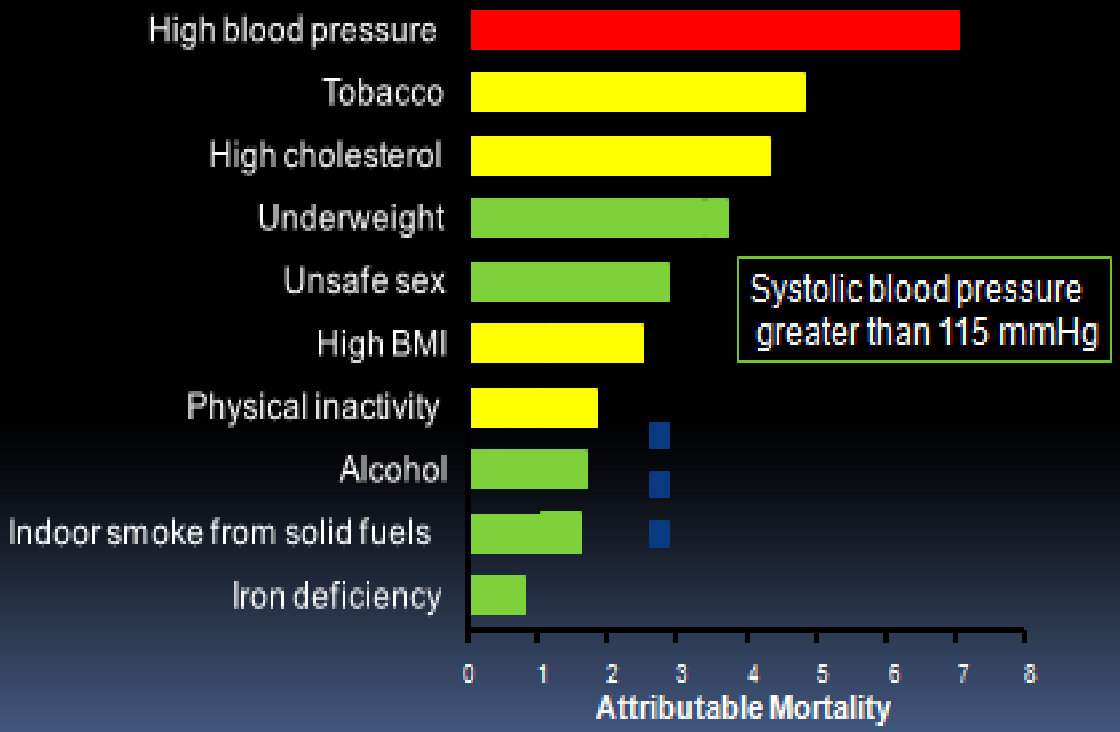


And worse…

Nowhere in the 92 page document is there any sensible information on how to treat high blood pressure (particularly at the difficult end of the spectrum)

So What?

Proportion of deaths attributable to leading risk factors worldwide (2000)



WHO 2000 Report. *Lancet*. 2002;360:1347-1360

Slide Source
Hypertension Online
www.hypertensiononline.org

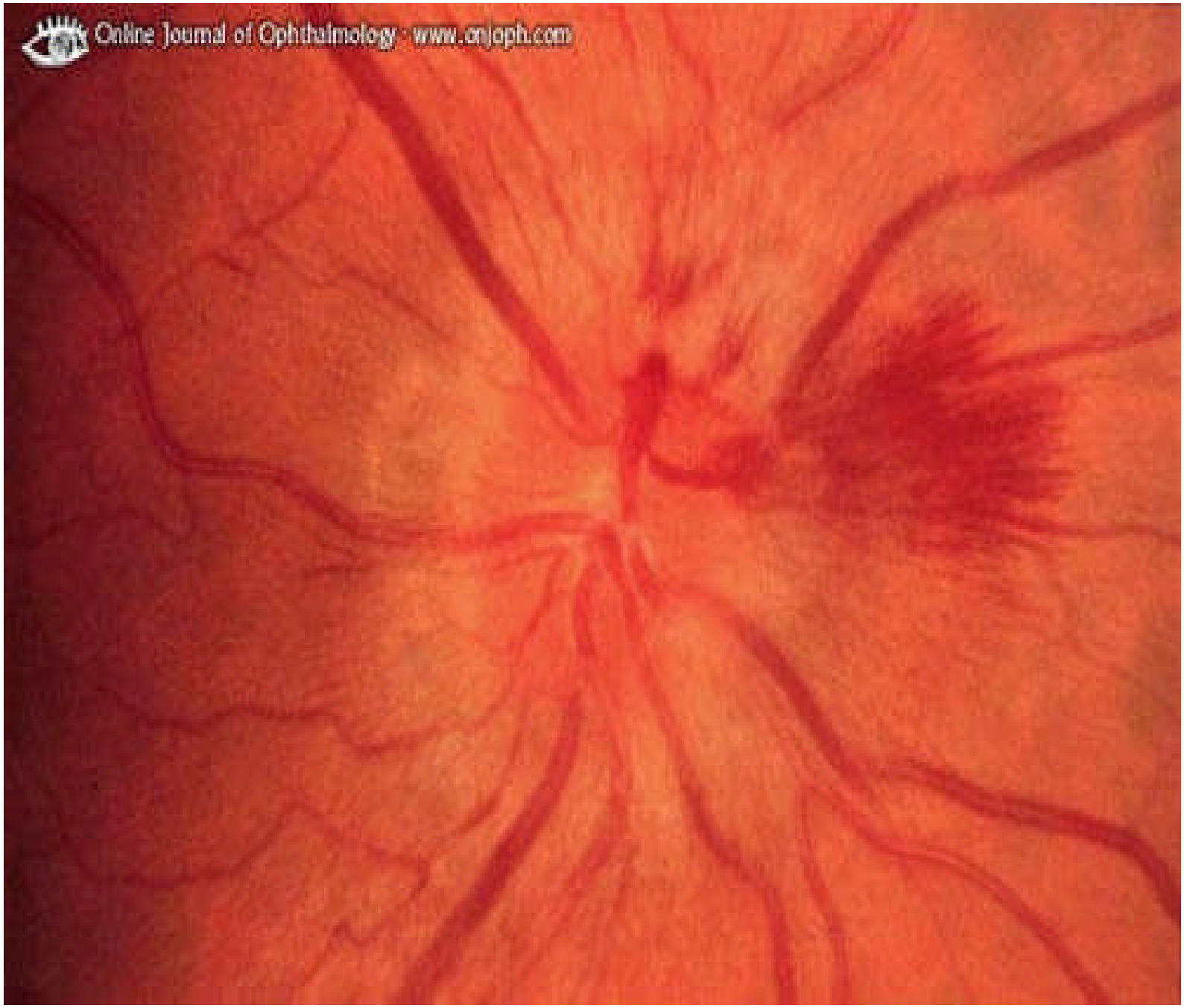
The coronary care units are still full

The stroke units are still full

High blood pressure is the commonest cause of chronic kidney disease

High Blood pressure will soon take over from diabetes as the commonest cause of end stage renal failure requiring dialysis

And from my point of view, in some ways most distressing of all…


Online Journal of Ophthalmology · www.onjoph.com

Waitemata Hypertension Clinic Risk Factor Management Guideline

- No smoking at any time

- Antihypertensive drug treatment of all (irrespective of age, gender, smoking or lipid status) with sustained BP >= 140/90, and > =130/80 for diabetes, CKD,or history of MI, stroke or PVD

- Statins for all (irrespective of age, gender, BP or smoking status) with LDL-C > 2.5mmol/l (or non-HDL-C > 3.3), and irrespective of lipid profile in diabetics, CKD,or history of MI, stroke or PVD

- Low dose aspirin in all over 50 on treatment for hypertension or dyslipidaemia, and and irrespective of age in all individuals with a history of MI, stroke, or PVD

So how do we treat high blood pressure specifically?

Compelling indications for individual drug classes

Compelling Indication	Initial therapy options
Heart failure	Thiaz/BB/ACEI/ARB/Aldo Ant
Post myocardial infarction	BB/ACEI/Aldo Ant
High CVD Risk	Thiaz/BB/ACEI/ARB/CCB
Diabetes	Thiaz/BB/ACEI/ARB/CCB
CKD	ACEI/ARB
Recurrent Stroke Prevention	Thiazide/ACEI

In large randomised trials best cardiovascular outcomes associated with

Thiazide Diuretics

ACE-inhibitors

Calcium channel blockers

Most hypertensives require combination therapy to achieve BP target

But as a rough general rule when using monotherapy

Drugs which block the renin-angiotensin system (ACE-inhibitors, ARB's, and beta blockers) work better in individiuals younger than 60 years

Drugs which cause natriuresis (diuretics and calcium channel blockers) work better in individuals over 60 years (and people of black African descent)

Stage 1 hypertension (140/90 – 159/99 or 130/80 – 149/89 in DM, CKD, or CVD)

Start with 1 drug
- ACE-I or ARB if < 60 years
- Thiazide or CCB if > 60 years

Stage 2 hypertension in individuals under 75 years (>= 160/100 or 150/90 in DM, CKD, or CVD)

Start with 2 drugs
- ACE-I or ARB + Thiazide *or* CCB (all ages)

Stage 2 hypertension in individuals over 75 years (>= 160/100 or 150/90 in DM, CKD, or CVD) – treat as for stage 1 hypertension (starting with 1 drug)

Then optimise doses and add additional classes of medication until target BP achieved

Aim to reach target BP within 3 months

4th Drug after ACE-I/ CCB/ Thiazide?

Choice of:

Spironolactone
Alpha blocker
Beta Blocker
Combined Alpha-Beta Blocker

Aldosterone – New Paradigm

Aldosterone is elaborated at many sites apart from the adrenal, including the heart, vascular smooth muscle and kidney where it interacts directly with mineralocorticoid receptors to promote endothelial dysfunction and reduce vascular compliance. It is increasingly recognised as a direct mediator of vascular damage (separate from A2)

Apart from causing sodium and water retention, Aldosterone

- *Reduces A and V compliance*
- *Increases peripheral vascular resistance*
- *Promotes myocardial hypertrophy + fibrosis*
- *Increases baroreflex dysfunction*

All of these effects potentially reversed by Spironolactone

Aldosterone an important mediator of resistant hypertension in the metabolic syndrome

ASCOT Spironolactone Substudy

(*Chapman et al Hypertension 2007;49(4):839-845*)

Spironolactone or moxonodine optional add-ons for participants with uncontrolled BP on 3 drugs

1790 received SPTN, but 212 for non-BP reasons and 167 insuff. data so 1411 available for analysis.

Mean dose 25mg; mean BP starting SPTN (on ave 2.9 other drugs) 156.9/85.3

Mean BP fall 18/11.5 (to 135.1/75.8) / effect independent of gender, diabetic status, or concomitant use of thiazides or ACE-inhibitor.

Gynaecomastia or breast discomfort – 6% of men (leading to discontinuation in ½)

4% serum K > 5.5mmol/l 2% > 6mmol/l

1% serum Na < 130

Cessation of SPTN due to biochem abnormalities – 2%

Largest and best study to date evaluating SPTN use in resistant hypertension

Smaller studies show equivalent results -
Calhoun et al (Hypertension 2002;40:892-6)
Ouzam et al (AJH 2002)

2006 BHS guidelines suggest SPTN as 4th drug in RH

Beta Blockers as Initial Therapy in Hypertension?

Large studies showing inferior cardiovascular outcome with beta blockers vs diuretic, ARB, ACE-inhibitor, CCB

MRC Trial of hypertension in Older Adults (*BMJ 1992;304:405-412*)
LIFE (*Lancet 2002;359:995-1010*)
HOPE (*Circulation 2001;104:52-6*)
ASCOT (*Lancet 2005;366:895*)

Meta-analysis (Lancet 2005;366:895)

13 RCT's, 106 000 pts

All beta blockers associated with worse stroke outcome

Atenolol, but not non-atenolol beta blockers (principally metoprolol) associated with increased risk of MI or all-cause death.

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How will you manage this patient and what advice will you give the GP?

Definition of Resistant Hypertension

Blood pressure not at target (<140/90 or < 130/80 in diabetes, CKD or CVD)

Despite

- optimal doses of
- a minumum of three
- complementary drugs
- one of which is a

diuretic

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How will you manage this patient and what advice will you give the GP?

Hydrochlorothiazide 12.5mg daily is an *often* ineffective dose which has never been associated with beneficial cardiovascular outcome in clinical trials

Inhibace Plus (cilazapril 5mg + HCTZ 12.5mg)

combines a usually adequate dose of ACE-inhibitor with and often inadequate dose of thiazide…

And thus can be described as…

“The Work of the Devil”

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Meds
~~**Inhibace Plus 1 daily**~~
Cilazapril (Inhibace) 5mg daily
Chlorthalidone 12.5-25mg daily – subsequently add Spironolactone25mg daily if required
Metoprolol CR 95mg daily
Felodipine ER 10mg daily
Simvastatin 20mg nocte
Aspirin 100mg daily

The surgery is scheduled for a month’s time.

What advice do you give the GP to optimise his blood pressure in the interim?

Tip:

(By far) the commonest cause of difficult hypertension relates to diuretic use:

- no diuretic
- not enough diuretic
- wrong diuretic

Optimal combination therapy

ACE inhibitor + Thiazide

or

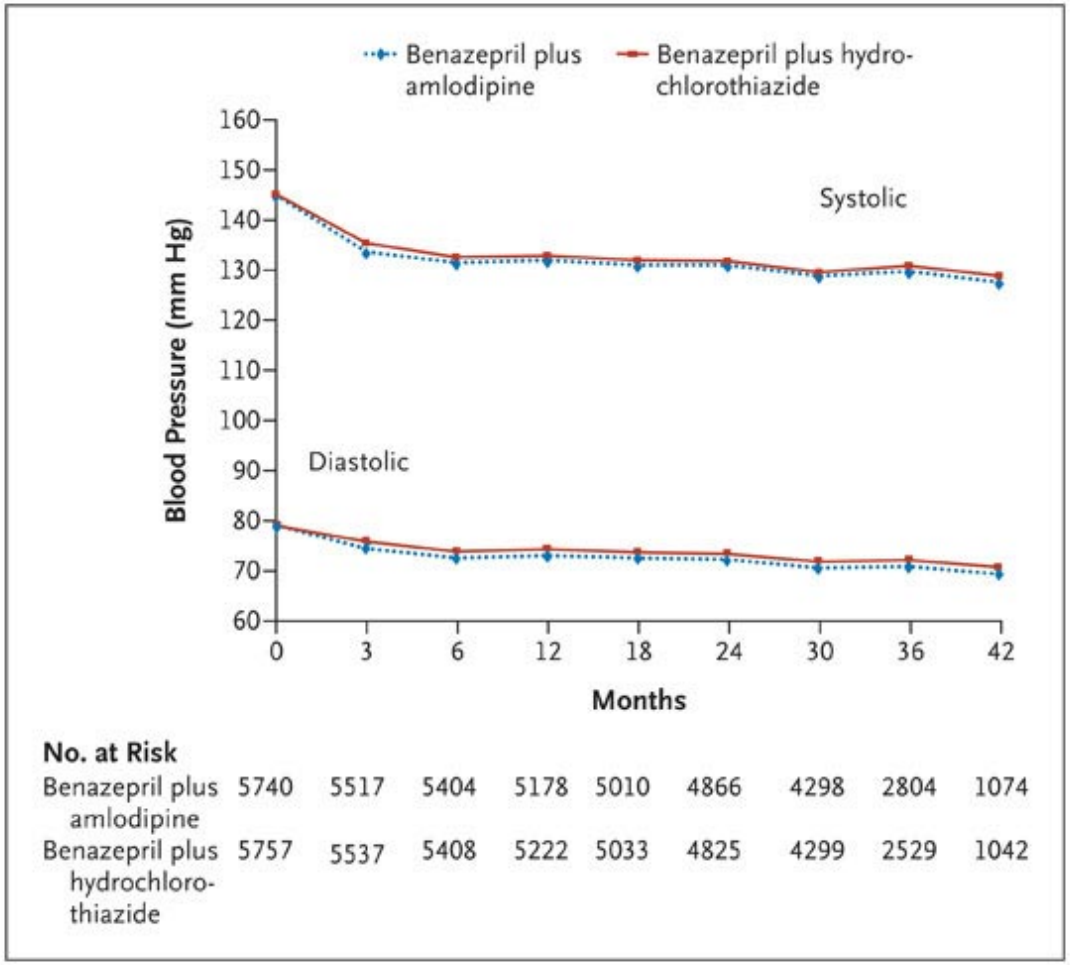
ACE inhibitor + CCB?

ACCOMPLISH (*NEJM 2008;359:2417-2428*) was a large (11 400) outcome study of high risk hypertensives > 55 yrs and SBP > 160 . Many obese and 60% diabetic. Pts randomised to Benazepril/HCTZ or Benazepril/Amlodipine combinations.

Primary endpoint – composite of death from cardiovascular causes, nonfatal MI, nonfatal stroke, hospitalisation for angina, resuscitation after cardiac arrest, and coronary revascularisation

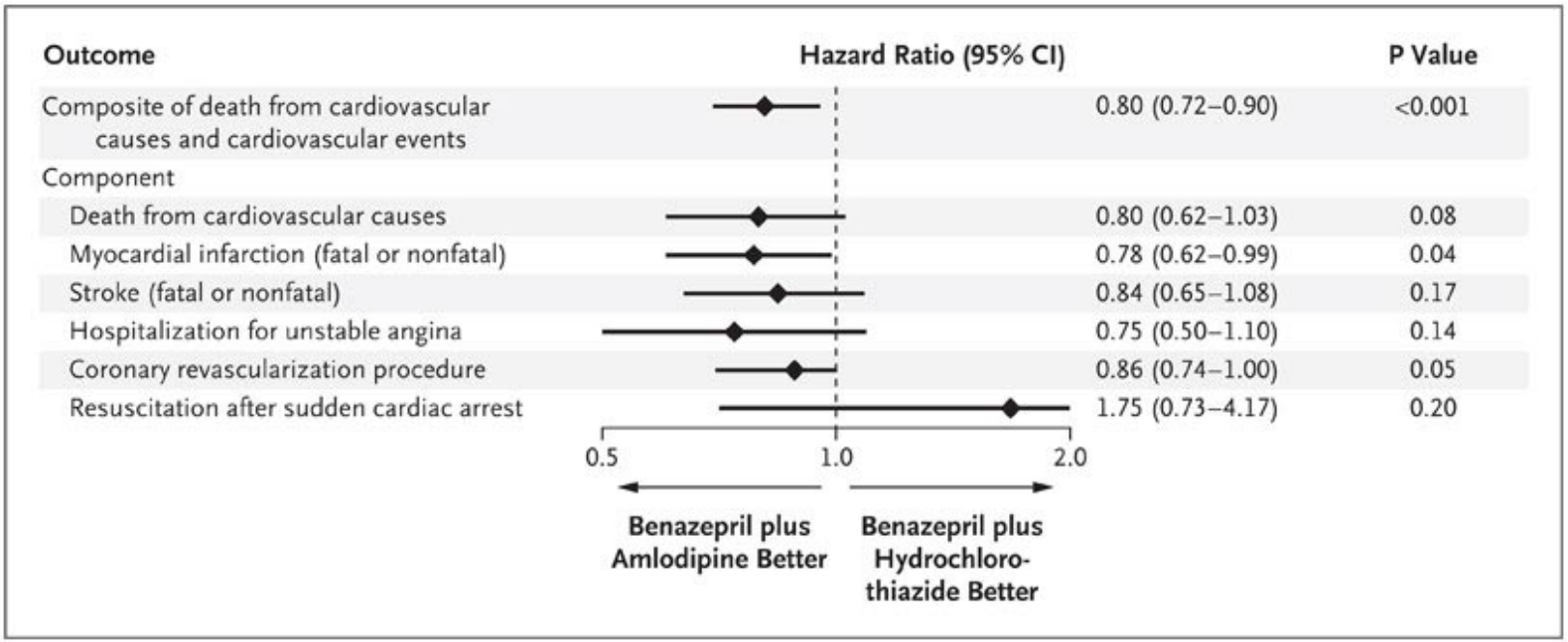
Pts randomised from 2003.

Excellent BP control with 76% having BP at target at 18 months and few dropouts for side effects. 50% obese 60% diabetes mellitus



No. at Risk

Benazepril plus amlodipine	5740	5517	5404	5178	5010	4866	4298	2804	1074
Benazepril plus hydrochlorothiazide	5757	5537	5408	5222	5033	4825	4299	2529	1042



Trial stopped early in October 2007 by data safety and monitoring committee following interim analysis of 60% of expected information from the trial.

Over a mean f/u of 39 months, cardiovascular morbidity/mortality was reduced by 20% with the ACEI/CCB compared with the ACEI/HCTZ

“The benazepril-amlodipine combination was superior to the benazepril hydrochlorothiazide combination in reducing cardiovascular events in patients with hypertension who were at high risk for such events”

Treatment of Hypertension in Patients 80 years of Age or Older (HYVET Study)

N.Engl.J.Med.2008;358:1887-98

- In this study, patients 80 years of age or older with sustained systolic hypertension were randomly assigned to receive either the diuretic indapamide, with or without the angiotensin-converting-enzyme inhibitor perindopril, or matching placebos, for a target blood pressure of 150/80 mm Hg

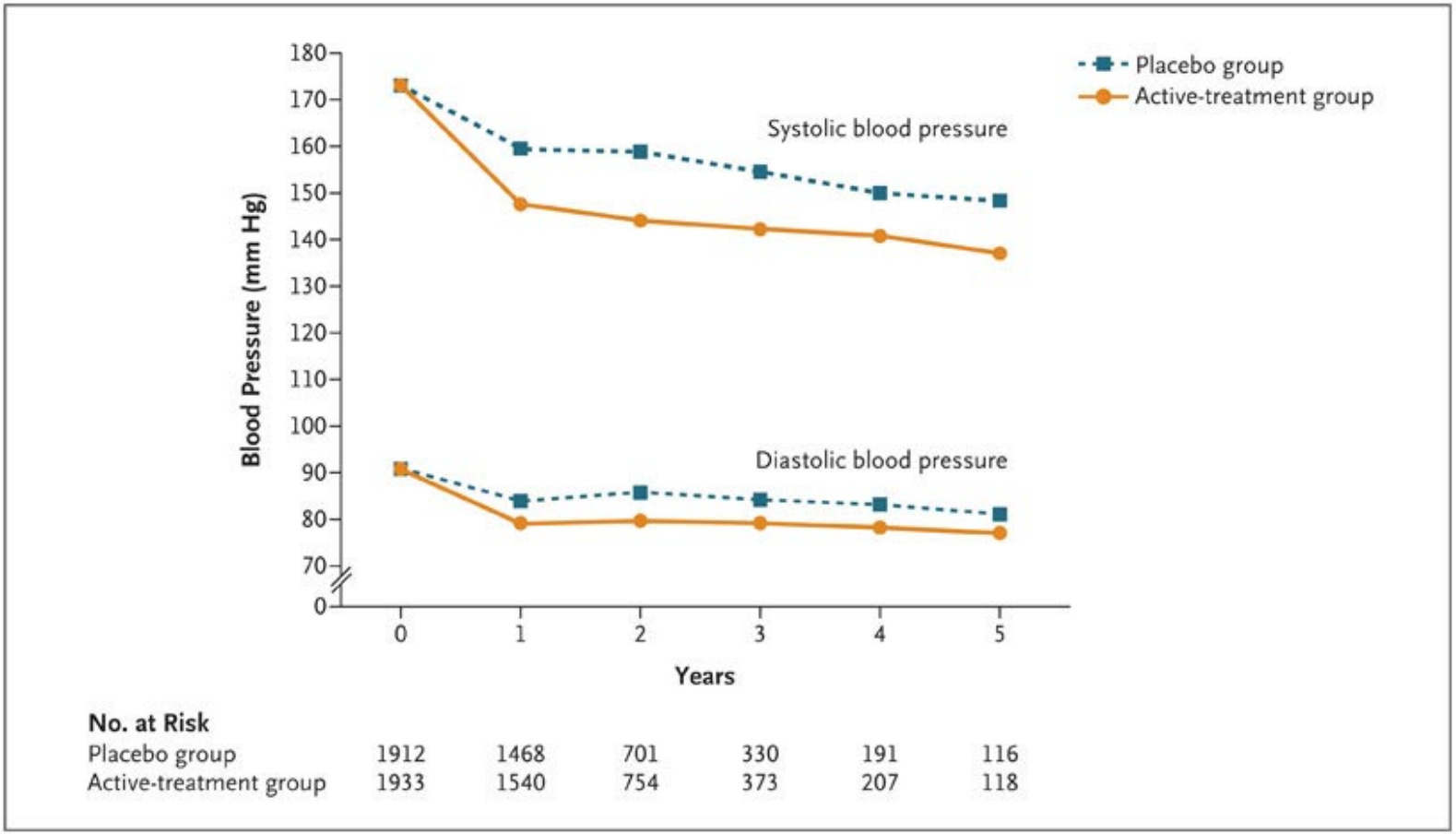
1933 patients on active treatment and 1912 placebo

Mean age 83.6 years (both groups)

Mean seated BP 173/90 (both groups)

Mean BP reduction in treatment group 15/6.1

Followed for mean 4 years

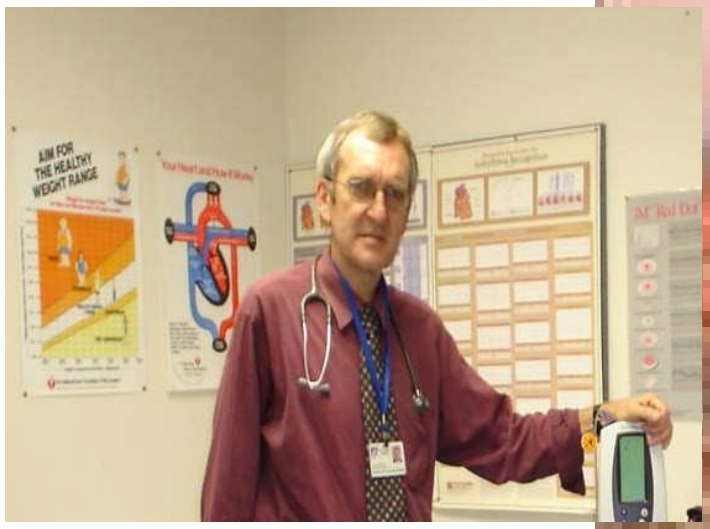


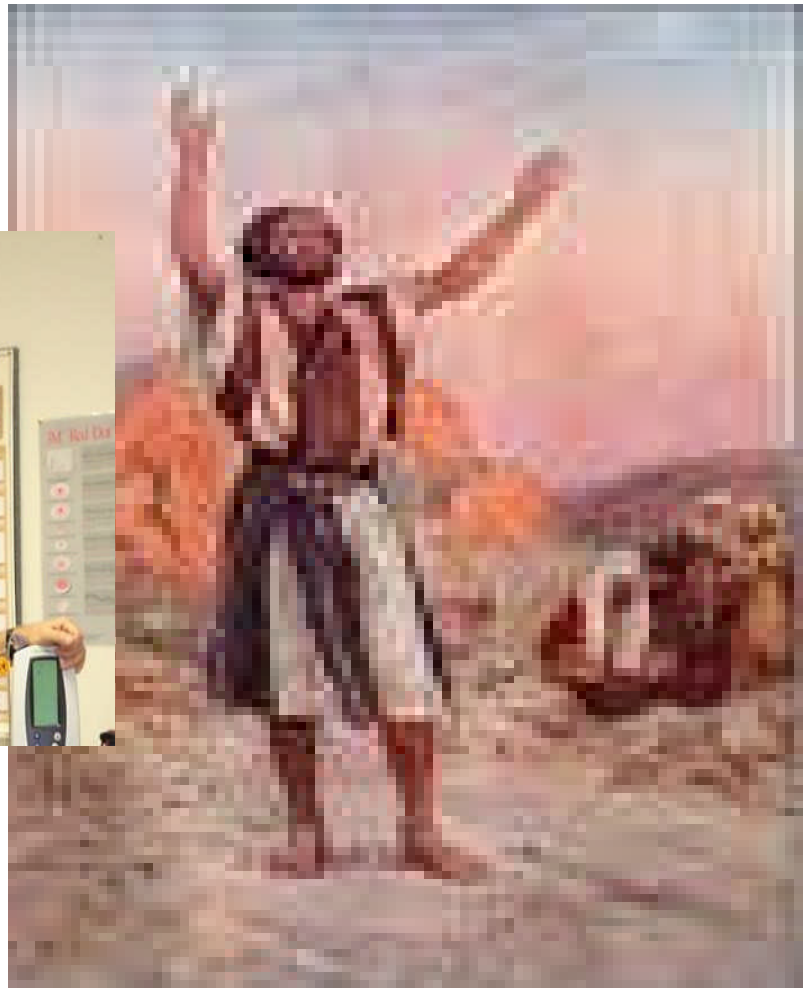
Treatment Group had:

- 30% reduction in in rate of fatal or non-fatal stroke
- 39% reduction in rate of death from stroke
- 21% reduction in rate of death from any cause
- 23% reduction in rate of death from cardiovascular causes
- 64% reduction in rate of heart failure

BP should be measured measured at every medical consultation

Treat short term and long term cardiovascular risk





Inhibace Plus is the work of the devil

Please tell GP’s to refer their patients with difficult hypertension to the Waitemata Hypertension Clinic

Aim is primordial disease prevention