

Achieving Blood Pressure Targets

**Setting Expectations to Achieve Blood
Pressure Control –**

**Applying a Business Principle to
Hypertension Management**



Car cost \$50 000

Just over 3 years old

Warranty has expired

What will repair cost?

Has engine already been damaged?

Check oil level and drive slowly to the dealer

Explain problem to smiling service manager



“Oil leak in this model can be serious
Often hard to get to the leak
May need it in the workshop for several days
May cost over \$1000”

But

“Don’t worry, I know we can find the problem. We’ll take you to the hospital and I’ll call you later once we know what’s going on”

The service manager calls back at 2pm

“Great news...we fixed the leak and it only cost \$150. Also, we washed your car and we will bring it to the hospital”

The service manager exceeded your expectations by:

- Lower than expected repair cost
- Unexpected free car wash
- Time saved by returning the car

Business Principle – Meet and Exceed Customer Expectations with the aim of retaining existing customers and attracting new ones

How can this be applied to hypertension management?

Referral to Medical Outpatients

“Dear Colleague,

Please see this 50 year old man with uncontrolled hypertension

New pt to me 6 months ago with untreated hypertension. Blood pressure at that time 180/100

Blood Pressure on current meds 160/ 95, 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

Meds

Inhibace Plus 1 daily

Metoprolol CR 95mg daily

Simvastatin 20mg nocte

Aspirin 100mg daily

Yours Sincerely...”

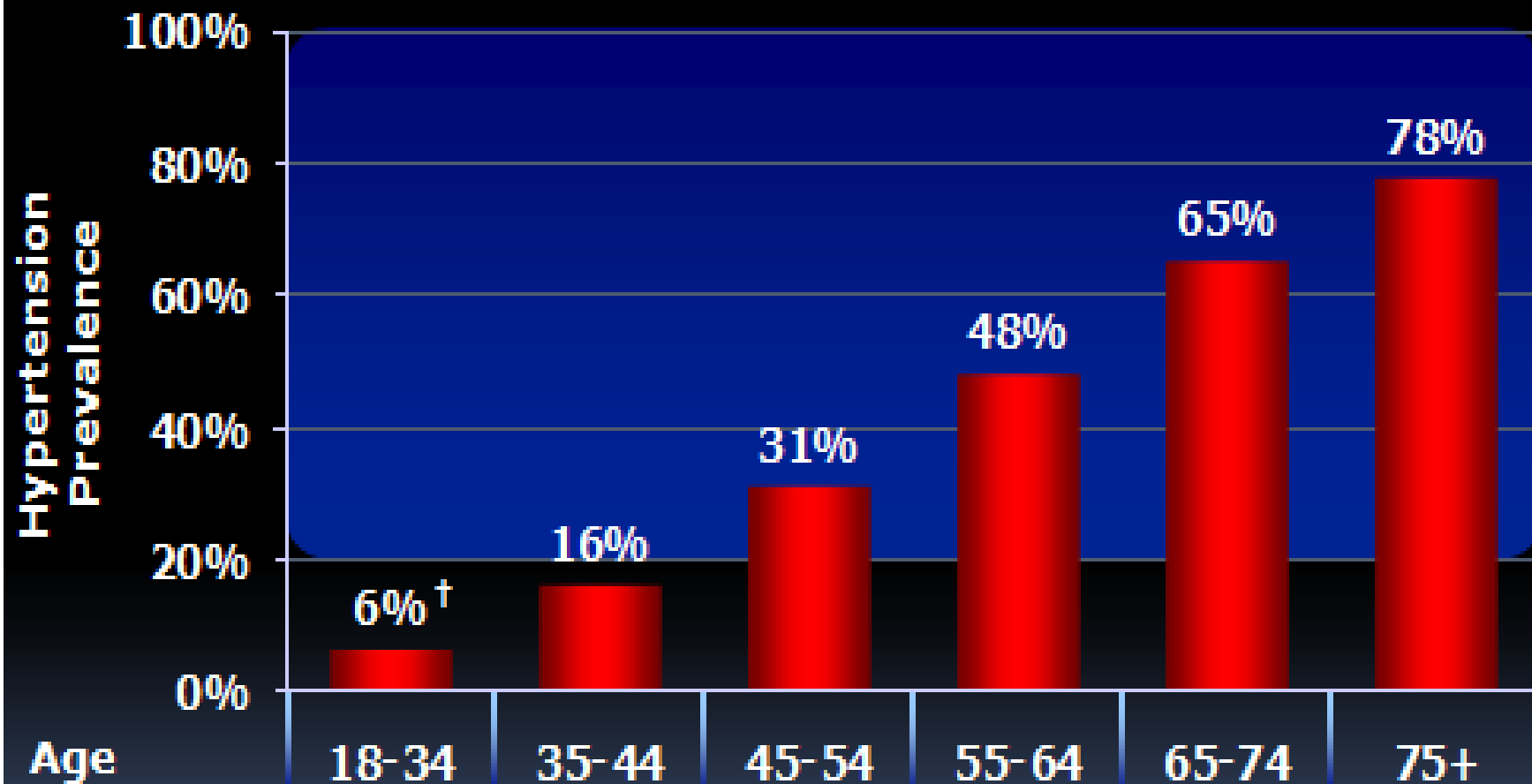
Some difficulties GP's have with hypertension management

- How to persuade an individual that they need to take medication (often several) lifelong, for a condition that is asymptomatic, and where the medication may have significant side effects.
- Patients' knowledge and expectations of their blood pressure treatment and what is their role in achieving blood pressure target.
- How to counter patients' negative expectations about what is necessary to control their blood pressure?

What information does the patient require to make the (sometimes) long and arduous task of achieving blood pressure control acceptable to him/her?

(1) Hypertension is
common

Prevalence of Hypertension in the United States by Age Group*



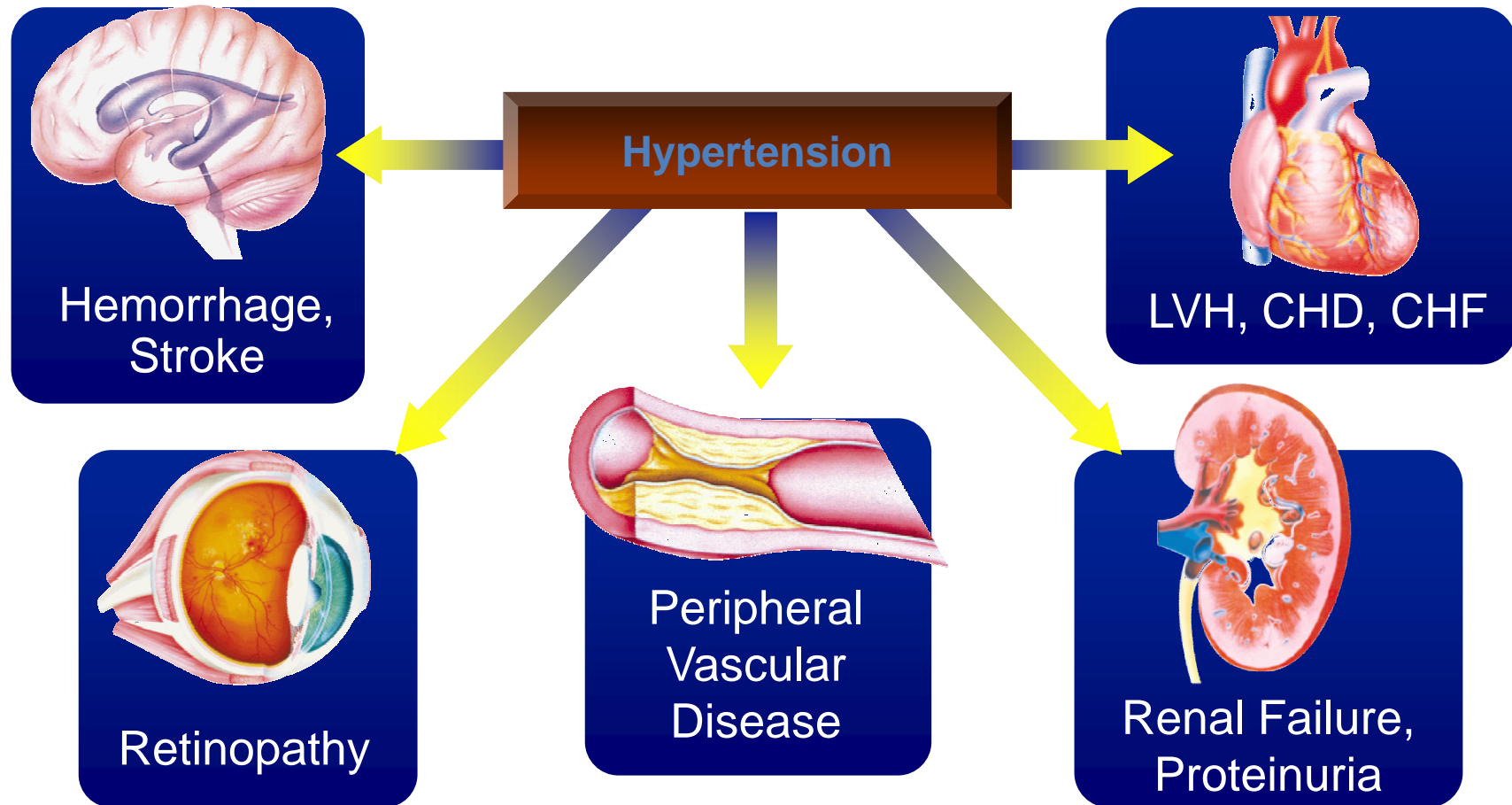
*Based on data from the 1999–2000 National Health and Nutrition Examination Survey. Hypertension is defined as blood pressure $\geq 140/90$ mm Hg or as receiving antihypertensive treatment.

[†]Low reliability due to large relative error.

Fields LE, et al. *Hypertension*. 2004;44:398-404.

Slide Source
Hypertension Online
www.hypertensiononline.org

(2) Hypertension is
serious



CHD = coronary heart disease
CHF = congestive heart failure
LVH = left ventricular hypertrophy

Chobanian AV, et al. *JAMA*. 2003;289:2560-2572.

Untreated hypertension
reduces life expectancy by ~ 5
years

(3) Much of the excess cardiovascular morbidity and mortality can be prevented by adjusting blood pressure values to the recommended goals.

This has been demonstrated conclusively in large clinical trials

Unequivocal Benefits of Lowering BP:

Relative risk reduction – constant

Absolute risk reduction – varies

Average % Reduction

Stroke incidence	35-40%
Myocardial Infarction	20-25%
Heart Failure	50%

(4) Antihypertensive drug therapy is (almost) always required to achieve blood pressure targets

Lifestyle modification, including the DASH diet, sodium restriction, and weight reduction for the overweight patient, can assist in hypertension control and reduce the number of classes of antihypertensive agents needed to achieve blood pressure goals

Exercise initially increases systolic blood pressure and it is *unrealistic for a patient to believe that he or she can exercise his or her way to normotension.*

(5) Most people require a combination of several classes of antihypertensive medication to achieve BP target

In stage 1 hypertension , 2 classes of antihypertensive medications may be needed to reach blood pressure goals. (Only 30% of stage 1 controlled on monotherapy)

In stage 2 hypertension, in particular in individuals with chronic kidney disease, diabetes, or the metabolic syndrome ≥ 3 classes of antihypertensive medication may be needed to reach blood pressure goals (and need for 4, 5 or even 6 drugs is not unusual).

(6) On average each medication will reduce blood pressure 10/5 (“Rule of 10/5”)

The patient should know their starting blood pressure and goal blood pressure to gain insight in to how many medications they are likely to require.

(7) Each medication may require 2-3 dose adjustments

(8) The recommended interval between medication adjustments (new or dose increase) is 2 weeks, and only 1 adjustment can be made per visit

(9) All classes of antihypertensive drug have side effects – these need to be explained in detail and that if an unacceptable side effect occurs with a particular drug, an alternative will be found

(10) Using an antihypertensive treatment algorithm rather than a random selection of of antihypertensive agents is more likely to achieve blood pressure goals.

So...Advice for this
particular patient...

“You are at significant risk of heart attack, stroke and other cardiovascular complications. Your risk cardiovascular death is 8x higher than someone with optimal blood pressure”

“This risk can be significantly reduced by reducing your BP to target level”

“Your target blood pressure is 140/90 (or less)”

“To achieve this you are likely to require a minimum of 4 medications”

“You will start on 2 medications simultaneously, and need to visit for medication adjustment fortnightly”

“Each individual medication may require dose adjustment 2 or 3 times and we can only make 1 dose-adjustment per visit”

“ You may not tolerate a particular class of drug, in which case we will replace it with a different class (there are always additional options). Before adding any new drug I will discuss the potential side effects with you in detail.”

“ You may require up to 12 fortnightly visits to get your blood pressure to target”

“You can monitor you progress with a home BP monitor”

“ Lifestyle measures are a very important adjunct but will not avoid the need for (several) antihypertensive drugs”

Which 4-drug combination is likely to be most efficacious (BP-lowering and cardiovascular outcome)?

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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

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”

JNC-7 Blood Pressure Treatment (2003)

Treat to BP < 140/90 or < 130/80 in pts with diabetes or CKD

Start with lifestyle modifications

Without Compelling Indications

Stage 1

Thiazide for most

Stage 2

Thiazide + ACE-I ARB, BB, or CCB

With Compelling Indications

Drug(s) for compelling indications



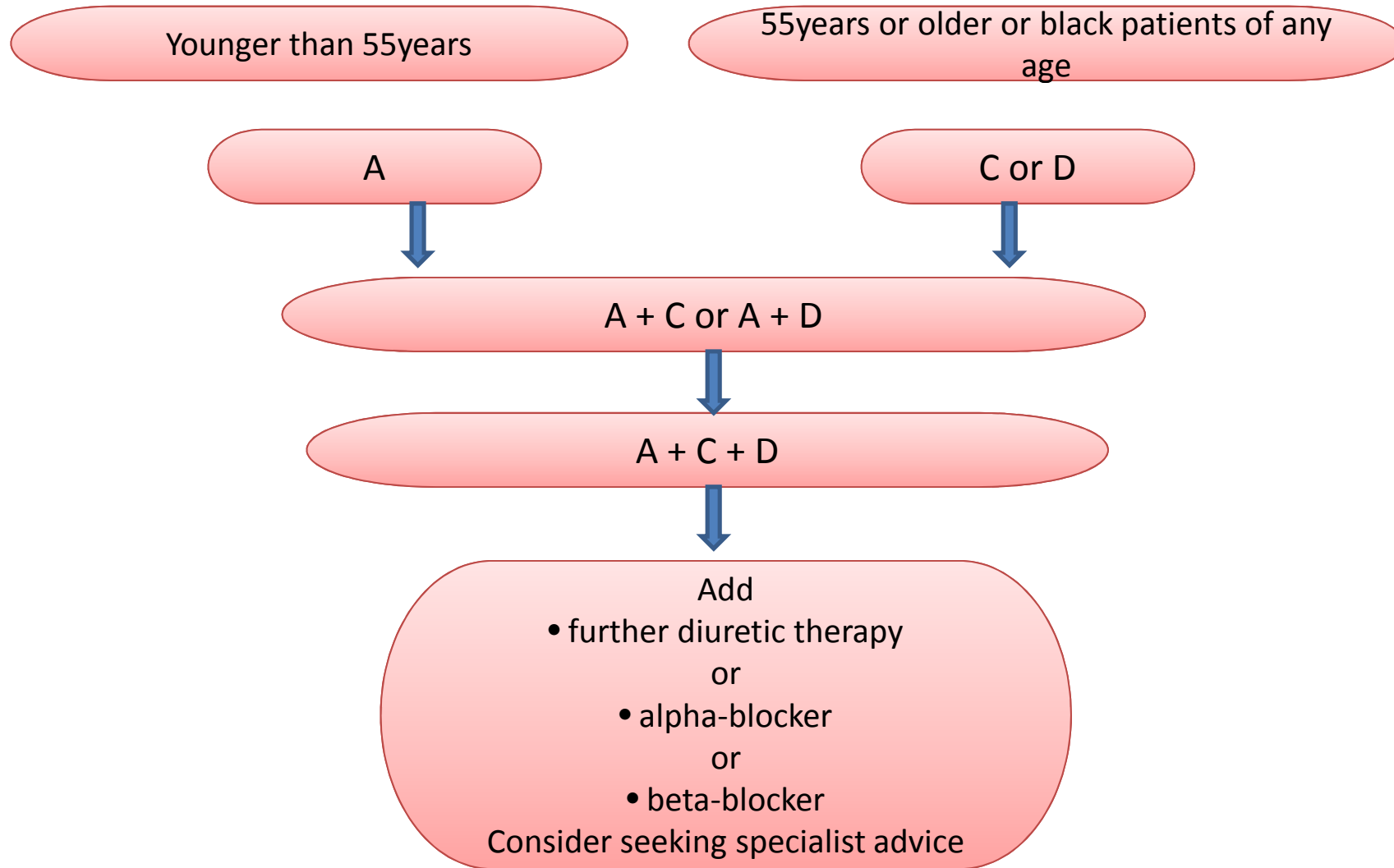
Not at goal BP

Optimise dosages or add additional drugs until goal BP achieved

Most people will require at least 2 drugs

BHS/NICE Guideline 2006

Choosing drugs for patients newly diagnosed with hypertension



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.

In large randomised trials best cardiovascular outcomes associated with

Thiazide Diuretic

ACE-inhibitor

Calcium channel blocker

In 2009 for a patient with stage 2 hypertension starting combination therapy – which 2-drug combination is likely to be most effective?

ACE inhibitor + Thiazide

vs

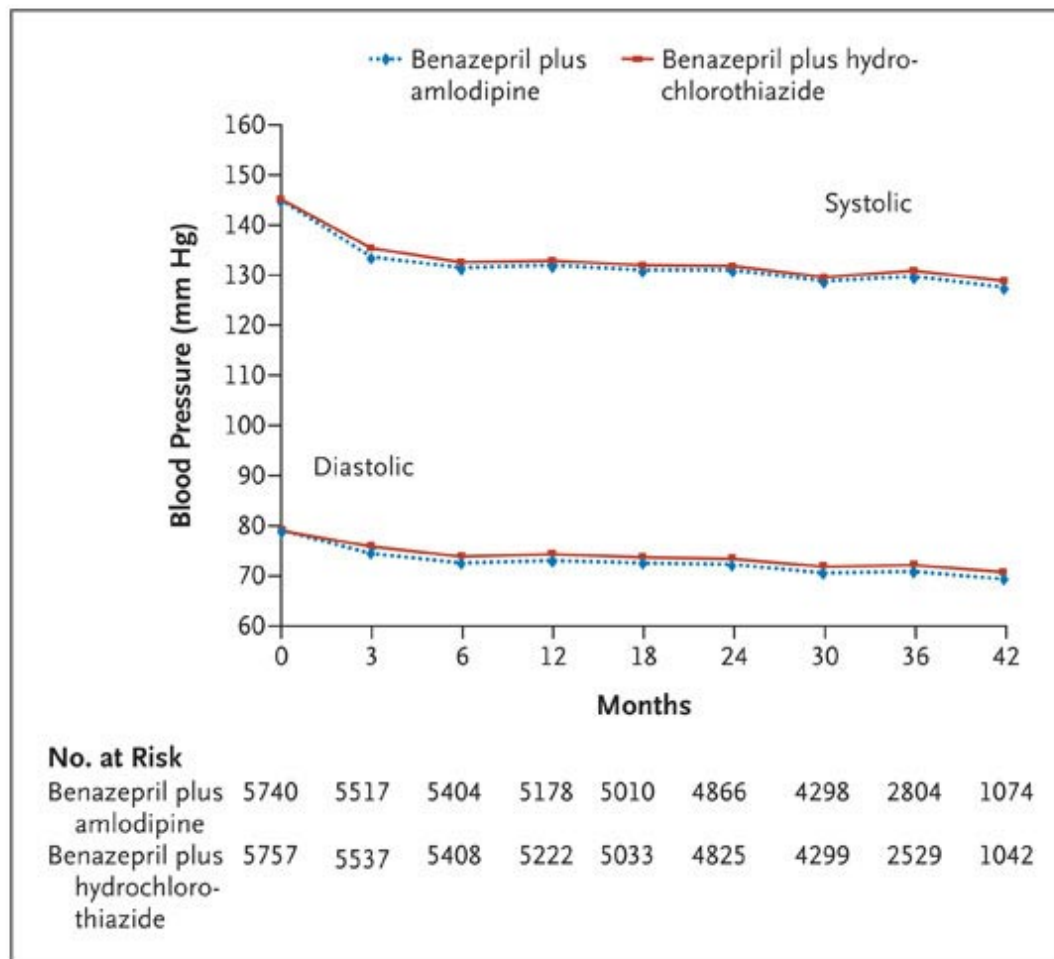
ACE inhibitor + CCB

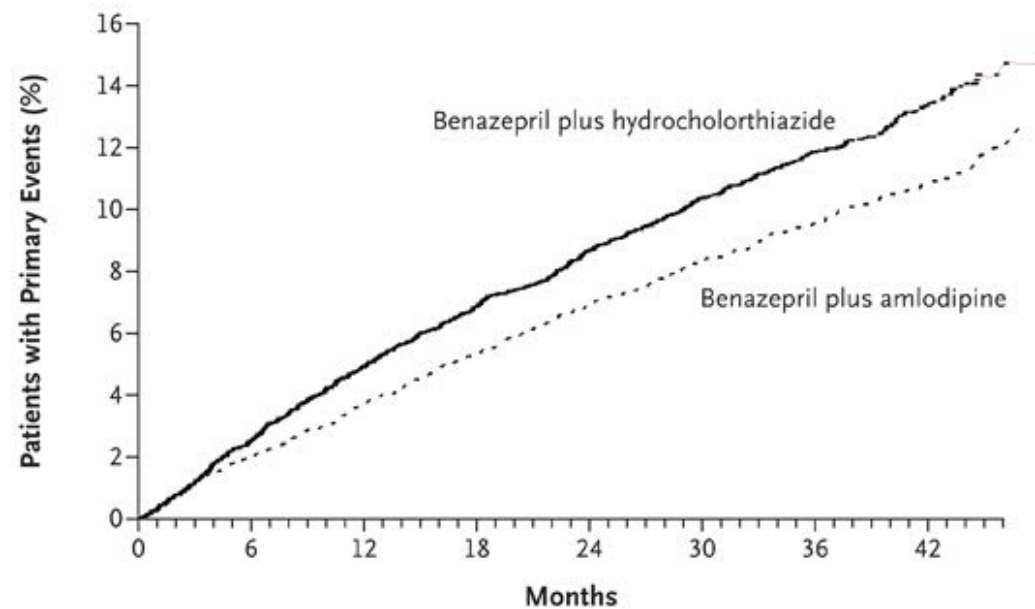
ACCOMPLISH (*NEJM* 2008;359:2417-2428) was a large (11 400) outcome study of high risk hypertensives > 55 yrs and SBP > 160 . Many obese and 60% diabetic. Pts randomised to Benazepril/HCTZ or Benazepril/Amlodipine combinations.

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

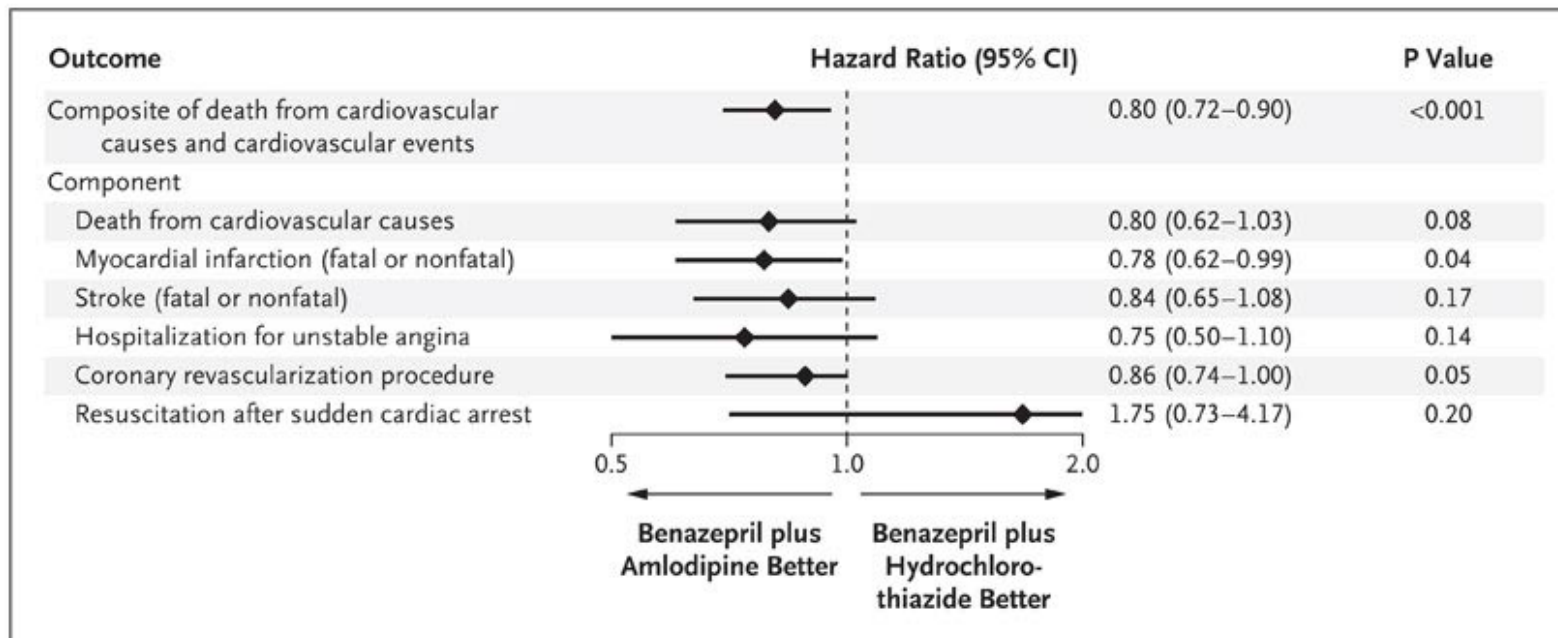




No. at Risk

Benazepril plus amlodipine	5512	5317	5141	4959	4739	2826	1447
Benazepril plus hydrochlorothiazide	5483	5274	5082	4892	4655	2749	1390





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”

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

Lisinopril 10mg mane + amlodipine 5mg mane



Lisinopril 20mg mane + amlodipine 5mg mane



Lisinopril 40mg mane + amlodipine 5mg mane



Lisinopril 40mg mane + amlodipine 10mg mane



Lisinopril 40mg mane + amlodipine 10mg mane + chlorthalidone 12.5mg mane



Lisinopril 40mg mane + amlodipine 10mg mane + chlorthalidone 25mg mane



Lisinopril 40mg mane + amlodipine 10mg mane + chlorthalidone 25mg mane + spironolactone 12.5mg mane

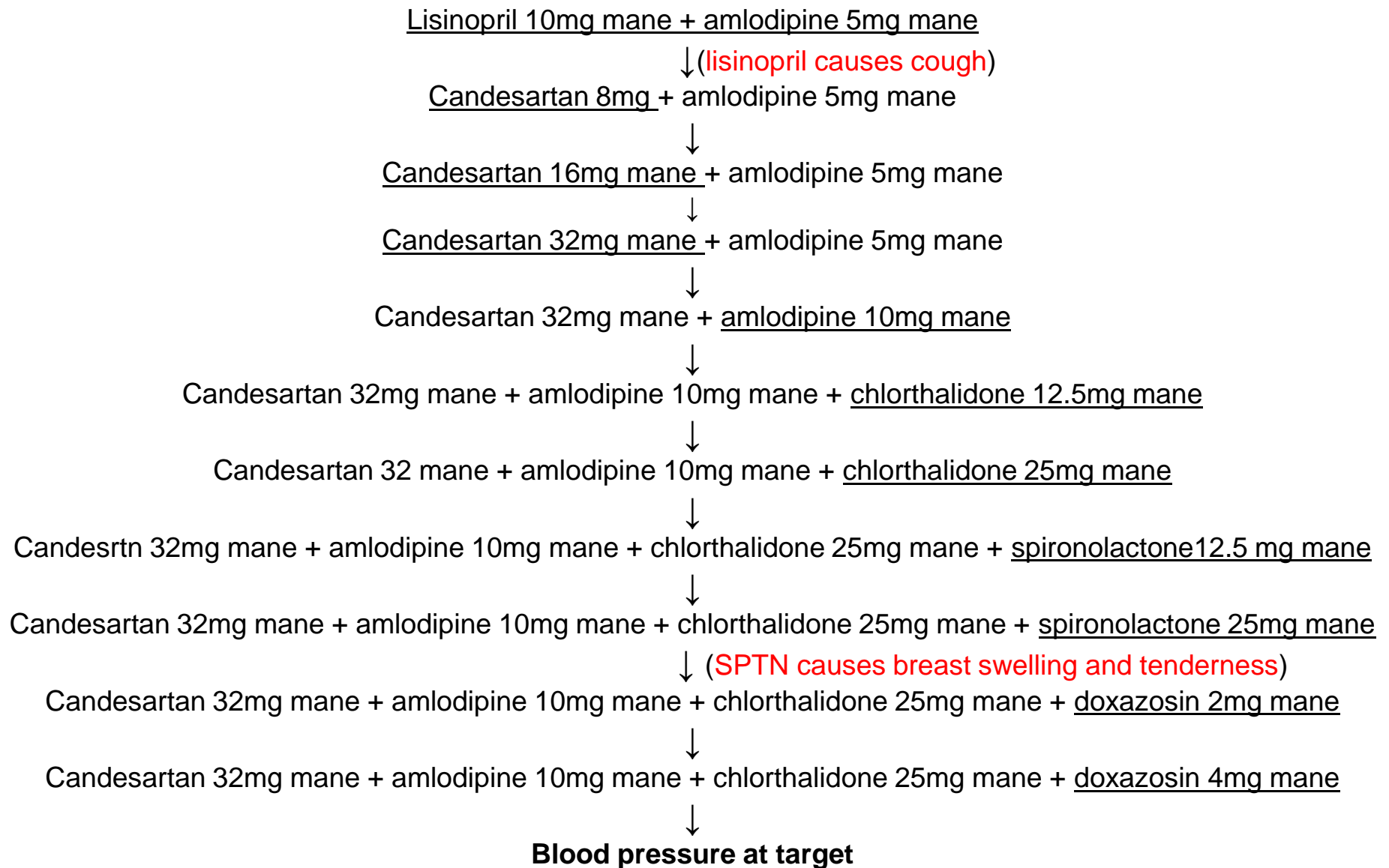


Lisinopril 40mg mane + amlodipine 10mg mane + chlorthalidone 25mg mane + spironolactone 25mg mane



Blood pressure at target

**8 fortnightly visits
(exceeded patient expectation)**



2 drug intolerances have increased fortnightly visits to 11 (in line with patient expectation from the beginning)

SUMMARY

Patient needs

to know that untreated hypertension carries significant risks of premature cardiovascular events and death

to know that most of this excess risk can be obviated by reducing blood pressure to target levels

to understand that treatment is complex and the drugs are not magic bullets

to understand that lifestyle change is important but is (almost) never sufficient on its own

to understand that few patients get to target with < 2 drugs, and most require more

to understand that treatment will be time-consuming and multiple visits for medication adjustment will be required

to feel in control of the process and to be part of the solution

- If target BP is achieved with fewer visits than estimated, the patient is impressed and grateful
- If target BP takes the estimated time (or longer) to achieve – they have been given reasonable expectations from the start and have felt in control of the process, so are unlikely be unhappy and will respect your expertise and perseverance on their behalf.
- Treatment is evidence-based within the limits of our current knowledge