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

“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 you car and we will bring 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 meds160/ 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 ≥140/90 mm Hg or as receiving antihypertensive treatment.

†Low reliability due to large relative error.

(2) Hypertension is serious
Peripheral Vascular Disease

Hemorrhage, Stroke

Retinopathy

LVH, CHD, CHF

Renal Failure, Proteinuria

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

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

<table>
<thead>
<tr>
<th>Condition</th>
<th>Average % Reduction</th>
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<tbody>
<tr>
<td>Stroke incidence</td>
<td>35-40%</td>
</tr>
<tr>
<td>Myocardial Infarction</td>
<td>20-25%</td>
</tr>
<tr>
<td>Heart Failure</td>
<td>50%</td>
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</table>
(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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Yours Sincerely…”
Definition of Resistant Hypertension

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

Despite

- optimal doses of
- a minimum 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

- Younger than 55 years
  - A
- 55 years or older or black patients of any age
  - C or D
    - A + C or A + D
      - A + C + D
        - Add
          - further diuretic therapy
            - or
              - alpha-blocker
                - or
                  - beta-blocker
        - Consider seeking specialist advice
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
Effects of Treatment on Systolic and Diastolic Blood Pressure over Time


[Graph showing blood pressure changes over time for different treatments.]

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
### Hazard Ratios for the Primary Outcome and the Individual Components


<table>
<thead>
<tr>
<th>Outcome</th>
<th>Hazard Ratio (95% CI)</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Composite of death from cardiovascular causes and cardiovascular events</td>
<td>0.80 (0.72–0.90)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Component</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Death from cardiovascular causes</td>
<td>0.80 (0.62–1.03)</td>
<td>0.08</td>
</tr>
<tr>
<td>Myocardial infarction (fatal or nonfatal)</td>
<td>0.78 (0.62–0.99)</td>
<td>0.04</td>
</tr>
<tr>
<td>Stroke (fatal or nonfatal)</td>
<td>0.84 (0.65–1.08)</td>
<td>0.17</td>
</tr>
<tr>
<td>Hospitalization for unstable angina</td>
<td>0.75 (0.50–1.10)</td>
<td>0.14</td>
</tr>
<tr>
<td>Coronary revascularization procedure</td>
<td>0.86 (0.74–1.00)</td>
<td>0.05</td>
</tr>
<tr>
<td>Resuscitation after sudden cardiac arrest</td>
<td>1.75 (0.73–4.17)</td>
<td>0.20</td>
</tr>
</tbody>
</table>

**Graphical Representation**

- **Benazepril plus Amlodipine Better**
- **Benazepril plus Hydrochlorothiazide Better**
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)
Lisinopril 10mg mane + amlodipine 5mg mane
↓ (lisinopril causes cough)
Candesartan 8mg + amlodipine 5mg mane
↓
Candesartan 16mg mane + amlodipine 5mg mane
↓
Candesartan 32mg mane + amlodipine 5mg mane
↓
Candesartan 32mg mane + amlodipine 10mg mane
↓
Candesartan 32mg mane + amlodipine 10mg mane + chlorthalidone 12.5mg mane
↓
Candesartan 32 mane + amlodipine 10mg mane + chlorthalidone 25mg mane
↓
Candesartan 32mg mane + amlodipine 10mg mane + chlorthalidone 25mg mane + spironolactone 12.5 mg mane
↓
Candesartan 32mg mane + amlodipine 10mg mane + chlorthalidone 25mg mane + spironolactone 25mg mane
↓ (SPTN causes breast swelling and tenderness)
Candesartan 32mg mane + amlodipine 10mg mane + chlorthalidone 25mg mane + doxazosin 2mg mane
↓
Candesartan 32mg mane + amlodipine 10mg mane + chlorthalidone 25mg mane + doxazosin 4mg mane
↓
**Blood pressure at target**

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.