



National Prescribing Service Limited

# **Case study 28: Managing hypertension in diabetes**

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**An Independent, Australian organisation for Quality Use of Medicines**

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The information contained in this material is derived from a critical analysis of a wide range of authoritative evidence. Any treatment decision based on this information should be made in the context of the individual clinical circumstances of each patient.

# Case study 28: Managing hypertension in diabetes

## Scenario

Brian is a 60-year old accountant who returns to have his blood pressure reviewed. When he was initially noted to be hypertensive you started ramipril 2.5 mg daily, to which he had a moderate response. You increased the dose to ramipril 5 mg daily four weeks ago. Brian has type 2 diabetes, is hypercholesterolaemic and overweight. He is otherwise well. He has never smoked, has no personal or family history of heart disease. His current medications are ramipril 5 mg daily, simvastatin 40 mg daily and metformin 1 g twice daily with meals.

## Examination results

Height: 180 cm  
Weight: 93 kg  
Body mass index: 29 kg/m<sup>2</sup>  
Waist measurement at the umbilicus: 110 cm  
BP (before initiation of ramipril): 160/95 mmHg  
BP (this visit): 145/90 mmHg

## Recent biochemical test results

Creatinine: 0.10 mmol/L (normal)  
HbA<sub>1c</sub>: 6.8%  
Ratio of total cholesterol: HDL-cholesterol: 4.4  
Total cholesterol: 6.1 mmol/L  
HDL-cholesterol: 1.4 mmol/L  
Urinary albumin creatinine ratio: normal

1 a. What was Brian's five-year risk of a fatal or non-fatal cardiovascular event when his blood pressure was 160/95 mmHg?

mild (< 10%)  moderate (10–15%)  high (15–20%)  very high (> 20%)

b. How did you determine this result?

clinical judgement  using risk calculator

2. What is Brian's target blood pressure?

\_\_\_\_\_

3. Would you change his drug regimen?

no

yes, please list all drugs below:

Drug

Dose

Frequency

Time to review

\_\_\_\_\_

4. What non-drug measures should Brian undertake?

\_\_\_\_\_

5. What strategies would you use to encourage Brian to comply with his medication and lifestyle changes and when would you review implementation of these strategies?

\_\_\_\_\_

# Summary of results

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At the time of publication 1155 responses had been received from doctors and 200 of these have been compiled for feedback.

## **Risk of a cardiovascular event**

- 47% of respondents correctly identified Brian's five-year risk of a cardiovascular event as high (15–20%) when his blood pressure was 160/95 mmHg.

## **Estimation method for cardiovascular risk**

- 53% of respondents estimated Brian's risk by using clinical judgement.
- 43% used a risk calculator.

## **Target blood pressure**

- 44% of respondents set the target blood pressure level at < 130/85 mmHg, consistent with current guidelines.<sup>1</sup>

## **Changes to drug regimen**

- 91% of respondents would change the drug regimen. Of these:
  - 54% would double the dose of ramipril to 10 mg per day
  - 42% would add a low-dose thiazide diuretic
  - 39% would increase the dose of simvastatin
  - 10% would add aspirin.

## **Non-drug measures**

- All respondents would recommend some form of lifestyle modification. Of these:
  - 95% would encourage regular physical activity
  - 85% would encourage weight reduction
  - 70% would encourage healthy eating
  - 47% would discourage excessive dietary sodium intake.

## **Strategies to encourage compliance with medication/lifestyle changes**

- 98% of respondents specified strategies to encourage Brian to comply with his medication and lifestyle changes. Of those:
  - 47% would discuss cardiovascular risk with Brian and the benefits of risk reduction
  - 27% would suggest regular patient follow-up
  - 20% would refer to a dietitian.
- Of those who specified a time to review implementation of above strategies:
  - 60% of respondents would review in one to two months.
  - 34% would review in three to six months.

## Key points

- Assess cardiovascular risk and manage hypertension along with other risk factors.<sup>2</sup>
- Non-drug measures to reduce both blood pressure and cardiovascular risk should be introduced in all patients with hypertension.<sup>2</sup>
- Diabetes is one of many risk factors that place people at high or very high cardiovascular risk.<sup>3</sup>
- ACE inhibitors, thiazides and beta-blockers are suitable drug choices in people with both hypertension and diabetes.<sup>2,4</sup>
- Target blood pressure in people with diabetes should be < 130/85 mmHg (lower if there is proteinuria).<sup>1</sup>
- Tight blood pressure control with an aim to reach target level should be a key goal for people with diabetes.<sup>5</sup>
- Always institute lifestyle modifications in parallel with drug treatment in people at high and very high cardiovascular risk.<sup>4</sup>

# Results in detail

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## Question 1a. What was Brian's five-year risk of a fatal or non-fatal cardiovascular event when his blood pressure was 160/95 mmHg?

- 47% of respondents correctly identified Brian's risk as high (15–20%).
- 29% identified it as very high (> 20%).
- 21% identified it as moderate (10–15%).
- 4% identified it as mild (< 10%).

## Question 1b. How did you determine this result?

- 53% of respondents estimated Brian's risk by using clinical judgement.
- 43% used a risk calculator.
- 3% used both methods.



### Practice points

- The decision to introduce antihypertensive drug treatment should be based on a person's absolute cardiovascular risk and blood pressure.<sup>4</sup>
- To assess the absolute risk of a cardiovascular event, use a tool such as the New Zealand Guidelines Group's Cardiovascular Risk Calculator (available at: [www.nps.org.au/docs/pdfs/cardiovascularrisk.pdf](http://www.nps.org.au/docs/pdfs/cardiovascularrisk.pdf)).<sup>6</sup>

## Question 2. What is Brian's target blood pressure?

- 44% of respondents set the target blood pressure level at < 130/85 mmHg, consistent with current guidelines.<sup>1</sup>
- 45% indicated a target level between 130/85 and 139/89 mmHg.
- 9% indicated targets of  $\geq 140$  mmHg systolic and/or  $\geq 90$  mmHg diastolic.



### Practice points

- Diabetes is one of many other risk factors (such as symptomatic cardiovascular disease, evidence of target organ damage, and Aboriginal, Torres Strait Islander, Maori or Pacific Islander origin) that place people at high or very high cardiovascular risk.<sup>3</sup>
- Latest guidelines from the National Heart Foundation of Australia and Cardiac Society of Australia and New Zealand recommend the following target blood pressures for adults with diabetes:<sup>1</sup>

Proteinuria	Target blood pressure (mmHg)
0– 0.25 g/day	< 130/85
0.25–1 g/day	< 130/80
> 1 g/day	< 125/75

- Tight blood pressure control with an aim to reach target level should be a key goal for people with diabetes because it can substantially reduce cardiovascular risk.<sup>5</sup>
- Anyone with above-optimal blood pressure ( $\geq 120/80$  mmHg) should be encouraged to make lifestyle changes.<sup>7</sup>
- Yearly assessment of microalbuminuria, preferably in timed overnight urine collections, is recommended for people with diabetes.<sup>8</sup>

### Question 3. Would you change his drug regimen?

- 91% of respondents would change Brian’s drug regimen. Of these, 77 % considered Brian to be at high or very high cardiovascular risk.
- Of those who would increase the dose of ramipril:
  - 97% would double the dose of ramipril to 10 mg per day
  - 10% would add a thiazide simultaneously.
- Of those who would add a thiazide, 65% would use hydrochlorothiazide.

**Table 1: Medication changes**

Medication change	Time to review <sup>a</sup>	Percentage of respondents <sup>b</sup> (n=182)
Increase ramipril to 7.5–10 mg once daily	2 to 12 weeks	55.5
Add a low-dose thiazide <sup>c</sup> once daily	2 to 6 weeks	42.3
Add a high-dose thiazide once daily	2 to 6 weeks	2.2
Add amlodipine/lercanidipine/atenolol once daily	2 to 6 weeks	3.3
Replace ramipril with a fixed-dose combination product <sup>d</sup>	2 to 6 weeks	4.4
Increase simvastatin to 60–80 mg once daily	2 to 12 weeks	39.0
Replace simvastatin with another ‘statin’ <sup>e</sup>	2 to 12 weeks	3.3
Increase metformin to 2.25–3 g/day (in 3 divided doses)	4 to 12 weeks	4.4
Add 100–150 mg aspirin once daily	4 to 12 weeks	9.9

a. Not all respondents specified a time to review.

b. Respondents may have more than one response.

c. Excludes use of a fixed-dose combination product (see Appendix for low-dose thiazides).

d. Contains a different ACE inhibitor or an angiotensin II receptor antagonist plus a low-dose thiazide (see Appendix).

e. Atorvastatin or pravastatin.



### Practice points

- ACE inhibitors, thiazides and beta-blockers are suitable drug choices for people with both hypertension and diabetes.<sup>2,4</sup>
- Allow at least 4 weeks to gauge response to antihypertensive drug treatment before the next dose increment is made.<sup>4</sup>
- Aspirin (150 mg daily) is recommended in people with diabetes over the age of 50 years as they have a cardiovascular risk equivalent to people with known coronary artery disease. Weigh up the potential cardiovascular benefits versus bleeding risks.<sup>8</sup>
- If the blood pressure response to a single antihypertensive agent is inadequate, combining two agents at a low dose (generally including a low-dose thiazide) is usually preferable to higher doses of a single drug due. This provides enhanced antihypertensive effects with less likelihood of dose-related adverse effects.<sup>9</sup>

#### Question 4. What non-drug measures should Brian undertake?

- All respondents would recommend some form of lifestyle modification, and
  - 95% would encourage regular physical activity
  - 85% would encourage weight reduction
  - 70% would encourage healthy eating
  - 47% would discourage excessive dietary sodium intake
  - 28% would discourage excessive alcohol consumption.
- 7% of respondents would recommend stress management/relaxation.

#### Practice points



- Non-drug measures to reduce both blood pressure and cardiovascular risk should be introduced in all patients with hypertension.<sup>2</sup> Encourage healthy lifestyle changes in all patients with blood pressure  $\geq 120/80$  mmHg.<sup>7</sup>
- Always institute lifestyle modifications in parallel with drug treatment in people at high and very high cardiovascular risk.<sup>4</sup> Written information, such as the NPS 'Prescription' pad for dietary and lifestyle changes, is available to doctors for all patients (e-mail: [info@nps.org.au](mailto:info@nps.org.au) for your free copies). Alternatively, contact the Heart Foundation's Heartline on 1300 36 27 87 for information and aids to healthy eating for consumers.

**Question 5. What strategies would you use to encourage Brian to comply with his medication and lifestyle changes and when would you review implementation of these strategies?**

- 98% of respondents specified strategies to encourage Brian to comply with his medication and lifestyle changes (Table 2). Of these, 47% specified when to review implementation of these strategies (Table 3).

**Table 2. Strategies to encourage compliance with medication and lifestyle changes**

Strategies	Percentage of respondents <sup>a</sup> (n=195)
Education on cardiovascular risk and benefits of risk reduction	48.2
Encourage regular follow-up/review	27.7
Refer to a dietitian	20.5
Provide encouragement/motivation	14.4
Refer to a diabetes educator	13.3
Encourage participation in exercise program	11.3
Encourage patient self-monitoring (weight, blood pressure and blood sugar levels)	9.7
Involve partner/family in patient care	8.2
Provide written information	7.5
Other <sup>b</sup>	6.5

a. Respondents may have more than one response.

b. Includes referral to an ophthalmologist, use of a dosette box and pedometer.

**Table 3. When to review implementation of strategies**

Time to review	Percentage of respondents (n= 92)
Two weeks	6.5
One to two months	59.8
Three to six months	33.7

**Practice points**



- Blood pressure lowering therapy is most effective when the patient is motivated to comply with medication and lifestyle changes. Motivation improves when patients have positive experiences with their doctors. To achieve this, doctors need to develop empathy with their patients as this can both build trust and be a potent motivator.<sup>7</sup>

# Commentary 1

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## Key points

- Use of a cardiovascular (CV) risk calculator is the most accurate way of predicting CV risk, but this should be used with clinical judgement.
- Target blood pressure should take into account the presence of other conditions (e.g. diabetes).
- Medication combinations are often needed to reach target blood pressure. Combined low-dose therapy is ideal.
- Motivating patients to continue on medications and make lifestyle changes is important. The GP's approach is an important factor in determining how successful this strategy will be.

## Estimation method for CV risk

A quarter of respondents identified Brian's CV risk as only mild or moderate, these results were similar both for those reporting using risk calculators and for those using clinical judgement. This is a little disappointing given the high priority of an accurate CV risk estimate for this man and its importance in deciding the appropriate preventative measures for his care.

Clinical judgement was used more commonly than a risk calculator despite long standing recommendations to use such calculators and their ready availability. A small percentage indicated they used both methods, and this is ideal. Evidence shows that using clinical judgement alone runs a substantial risk of incorrectly identifying a patient's absolute risk of CV disease.<sup>10</sup>

I believe that identifying Brian's 5-year CV risk is an important part of his clinical management. It is not always easy to cover everything in one consultation, but it seems to be a good strategy in the context of reviewing his blood pressure, which is currently not at target. I use the New Zealand CV risk calculator<sup>6</sup>, but try to be aware

of factors not included in the tables; these include, family history and pre-existing vascular disease. Clinical judgement and looking at the individual context is an important added element of this calculation. I find this fits in easily during a consultation and keep the risk calculator at hand around my desk.

## Blood pressure targets

Less than half of the respondents correctly identified the target blood pressure for Brian, and over half of the respondents suggested a higher blood pressure target was acceptable. The current National Heart Foundation Guidelines recommend a target blood pressure of < 130/85 mmHg for patients with diabetes (targets are lower if there is proteinuria).<sup>1</sup> Anyone whose blood pressure is above the optimal level (i.e.  $\geq 120/80$  mmHg) should also be encouraged to make lifestyle changes. Evidence certainly suggests that CV risk increases from a blood pressure of 115/75 mmHg.<sup>11</sup>

Reaching targets may present problems with medication compliance, side effects and costs, and some patients are unable to reach target despite drug therapy and lifestyle changes. Therefore, the important message is that any reduction towards the target is worthwhile in terms of reduced CV risk, particularly for patients with diabetes.

## Medication changes

Most respondents planned medication changes, especially those who estimated Brian's CV risk as high/very high. Some recommended increasing the ramipril dose while others suggested adding a low-dose thiazide to an overall low-dose combination, which is more in line with guidelines. Single fixed-dose combined therapy was recommended by a small number.

Only a very small percentage of respondents suggested adding aspirin, even though this is recommended for all diabetics over the age of 50 years because of their higher absolute risk of CV disease (equivalent to a non-diabetic with established coronary heart disease).<sup>8</sup>

### **Lifestyle changes**

There was an encouraging prominence given to lifestyle measures, the majority of responses focused on physical activity, weight reduction and healthy diet, and nearly half would use CV risk reduction as a part of a strategy for motivating Brian. Having calculated the CV risk with the patient, the results can certainly be used to prioritise management strategies, monitor progress and help motivate the patient to make lifestyle changes if appropriate. In my experience, patients of all education and literacy levels, as well as those whose primary language is other than English, can all readily understand the results and find it helpful in deciding what to do.

I believe we should encourage all patients to be active in the management of their own conditions, and diabetes and hypertension are both very suitable for this. Setting goals that patients have decided on and are committed to is important. In this regard, there is evidence that the way GPs approach patients is important in developing empathy and trust, both of which are felt to directly influence blood pressure control.<sup>11</sup> The principles of motivational interviewing are also useful in the short time available in the consultation to address lifestyle issues.

### **Time to review**

Suggested review times ranged from two to twelve weeks; guidelines suggest a four-week period as appropriate to gauge effects of thiazide introduction or dose changes. It may be important to give Brian the option to return earlier should he be aware of any side effects. Earlier review may also be helpful in supporting lifestyle changes.

## Commentary 2

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### Key points

- Managing hypertension is particularly important in patients with multiple risk factors at high risk of cardiovascular (CV) disease. A risk calculator is a quick and easy way to assess absolute CV risk.
- Lifestyle changes should be introduced in all patients with hypertension and/or high CV risk with the aim of reducing not just blood pressure but overall risk.
- Achieving target blood pressure (< 130/80 mmHg) should be a key goal in patients with diabetes and hypertension, and most patients will require more than one antihypertensive.
- Thiazides, ACE inhibitors and beta-blockers are suitable first-line drugs in people with both hypertension and diabetes without renal disease.

### CV Risk

Brian has a combination of risk factors often referred to as the 'metabolic syndrome' (i.e. obesity, hypertension, dyslipidaemia and Type 2 diabetes) which indicates a high risk of CV disease. Other risk factors include cigarette smoking and family history of CV disease. Although it is reasonably straightforward in this case to assess the absolute 5-year risk of a CV event as being high using clinical judgement alone, risk calculators can significantly improve the accuracy of risk assessment in some cases and provide the patient with a graphical illustration of potential benefits of altering one or more risk factors. Only about half of the respondents accurately assessed the level of risk, but over 75% assessed it as high or very high, and the clinical outcome would have been the same. As the New Zealand CV risk calculator<sup>6</sup> is readily available on the NPS website ([www.nps.org.au/docs/pdfs/cardiovascularrisk.pdf](http://www.nps.org.au/docs/pdfs/cardiovascularrisk.pdf)), more practitioners may start using it.

It is vital in this situation to deal with the total risk factor profile and lifestyle factors are critically important in achieving this goal. Weight loss, in this case, would be particularly valuable since it would be likely to reduce Brian's blood pressure, improve control of his diabetes and dyslipidaemia.

### Target Blood Pressure

Target blood pressure levels have progressively decreased over the past few years as more evidence has become available to support the concept that the lower the blood pressure achieved, the better the clinical outcome. Almost all respondents indicated a target level of < 140/90 mmHg. Of those, nearly half chose < 130/85 mmHg, which is consistent with National Heart Foundation Guidelines<sup>1</sup>; much of the NPS material is based on these.

However, more recent guidance, including the 2003 US Joint National Committee Guidelines<sup>7</sup> (JNC 7) and an Australian review of trial evidence<sup>12</sup>, suggests that < 130/80 mmHg should be the target for hypertensive patients with diabetes. It has also become clear that the primary focus should be on reaching the systolic pressure because systolic pressure is a better predictor of outcome. Target blood pressure remains slightly higher than 'optimal' blood pressure (< 120/80 mmHg), because of the difficulty in achieving such a low pressure cost-effectively and without adverse effects.

### Changes in drug regimen

Most respondents would, appropriately, change Brian's drug regimen. Clearly, although he has responded reasonably well to the ACE inhibitor, he has not reached his blood pressure target. His lipids and diabetes could also be better controlled. Thiazides, ACE inhibitors and beta-blockers are all safe and effective and

are suitable first-line drugs in people with both hypertension and diabetes without renal disease. Calcium-channel blockers are also suitable as an add-on antihypertensive in people with diabetes. In the presence of renal disease, ACE inhibitors are the preferred agent. Angiotensin receptor antagonists seem likely to have similar benefits to those of ACE inhibitors, although the finding that they may delay progression of renal disease is solely based on a surrogate endpoint (serum creatinine).

It is known that more than half of all patients with hypertension require two or more drugs to achieve blood pressure control. The JNC 7 report<sup>7</sup> recommends starting with a combination of two drugs be considered for a patient with a starting blood pressure of more than 20/10 mmHg above their target. Brian has already had a reduction of 15/5 mmHg with ramipril, and I would suggest that the most appropriate step now would be to add a second agent, specifically a low-dose thiazide diuretic. Increasing the ramipril is an alternative approach, but it seems unlikely to achieve the additional 15/10 mmHg reduction required to reach target. He may ultimately require a third drug.

### **Non-drug measures**

All respondents were aware of the need for lifestyle modification (e.g. weight loss, exercise, salt restriction, smoking cessation, alcohol

restriction), but some aspects were slightly underemphasised. Weight reduction is critical to the management of people with 'metabolic syndrome' and will partially reverse many of the features leading to high CV risk. This needs to be stressed to patients. The possibility that a patient may be able to stop taking some of their pills if they lose weight can be a powerful incentive. We were not told what Brian's alcohol consumption is, but if he drinks more than 4 standard drinks a day then reduced consumption will also have a beneficial effect on his blood pressure.

### **Strategies to encourage compliance/adherence**

The responses to this section were a little concerning. Hypertension and many of its associated conditions are asymptomatic, and it is easy for patients to underestimate their importance and the importance of adhering to both lifestyle measures and prescribed drug therapy. Education is therefore a vital part of the overall management of such patients. Active encouragement of lifestyle changes can also be valuable in assisting patients to make changes; these can often be very difficult to achieve otherwise. A strong 'therapeutic alliance' between doctor and patient can provide emotional support and motivation.<sup>7</sup>

# Appendix

## Thiazide and thiazide-like diuretics

Generic name	Product name	Low-dose
<b>Thiazide</b>		
Bendrofluazide 5 mg	Aprinox	2.5 mg (1/2 a tab)
Hydrochlorothiazide 25 mg	Dithiazide	≤ 25 mg (1/2–1 tab)
<b>Thiazide-like diuretics</b>		
Chlorthalidone 25 mg	Hygroton	≤ 25 mg (1/2–1 tab)
Indapamide 2.5 mg	Dapa-Tabs, Indahexal, Insig, Napamide, Natrilix	Not practical
Indapamide 1.5 mg	Natrilix SR (slow release preparation)	1.5 mg (1 tab)

## Fixed-dose combination products (low-dose thiazide plus ACE inhibitor or angiotensin II receptor antagonist)

Generic name	Product name
<b>Hydrochlorothiazide-containing products</b>	
Hydrochlorothiazide 6 mg + enalapril 20 mg	Renitec Plus
Hydrochlorothiazide 12.5 mg + fosinopril 10 mg	Monoplus 10/12.5
Hydrochlorothiazide 12.5 mg + fosinopril 20 mg	Monoplus 20/12.5
Hydrochlorothiazide 12.5 mg + quinapril 10 mg	Accuretic 10/12.5
Hydrochlorothiazide 12.5 mg + quinapril 20 mg	Accuretic 20/12.5
Hydrochlorothiazide 12.5 mg + candesartan 16 mg	Atacand Plus
Hydrochlorothiazide 12.5 mg + eprosartan 600mg	Teveten Plus
Hydrochlorothiazide 12.5 mg + irbesartan 150 mg	Avapro HCT 150/12.5, Karvezide 150/12.5
Hydrochlorothiazide 12.5 mg + irbesartan 300 mg	Avapro HCT 300/12.5, Karvezide 300/12.5
Hydrochlorothiazide 12.5 mg + telmisartan 40 mg	Micardis Plus 40/12.5
Hydrochlorothiazide 12.5 mg + telmisartan 80 mg	Micardis Plus 80/12.5
<b>Indapamide-containing product</b>	
Indapamide 1.25 mg + perindopril 4 mg	Coversyl Plus

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