

Managing hypertension in diabetes: Updated NICE guidance

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Article points

1. There is good evidence documenting the greater benefits of blood pressure control compared with reductions in HbA_{1c} and cholesterol in people with diabetes.
2. The updated NICE guideline suggests the use of ambulatory blood pressure monitoring in preference to repeated clinic measurements.
3. The treatment algorithm has changed significantly in the updated guidance; the popular ABCD (now ACD) algorithm has been updated.
4. Recent evidence suggests that patients aged ≥80 years with hypertension gain immediate benefit from treatment.

Key words

- Blood pressure
- Hypertension
- Older people
- Salt intake

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NICE published an updated guideline on the management of hypertension in association with the British Hypertension Society in August 2011. This article summarises the changes to the guidance and looks at its implications for people with diabetes. The treatment of hypertension in older people is explored in the light of recently published evidence from the Hypertension in the Very Elderly Trial; the author also looks at the pharmacological management of hypertension and lifestyle advice for people with diabetes.

There is good evidence documenting the greater benefits of blood pressure control compared with reductions in HbA_{1c} and cholesterol in people with diabetes. Consider treating 1000 people with diabetes for 5 years; lowering blood pressure by 10/5 mmHg will prevent 29 cardiovascular events compared with the prevention of 23 events by lowering total cholesterol by 1 mmol/L and eight cardiovascular events for a 9.8 mmol/mol (0.9 percentage points) reduction in HbA_{1c} level (Yudkin et al, 2010). It is generally accepted that treating hypertension confers more benefit than the treatment of other cardiovascular risk factors and is also probably easier to control in the long term than dysglycaemia. DM 31 was a new blood pressure indicator introduced in the most recent revision of Quality and Outcomes Framework (QOF) indicators – “the percentage of patients with diabetes in whom the last blood pressure is 140/80 or less in the previous 15 months” (British Medical Association and NHS Employers, 2011). This was a tighter indicator, replacing DM 12, which had a blood pressure target of ≤145/85 mmHg.

Evidence base for treating hypertension in people with diabetes

The treatment of hypertension in research and guidance does not distinguish between

people with type 1 or type 2 diabetes. People with type 1 diabetes are also at a higher risk of developing hypertension and in those with type 2 diabetes the management of hypertension is of huge importance. The blood pressure segment of the UKPDS (UK Prospective Diabetes Study) was designed to determine whether tight control of blood pressure prevented macrovascular and microvascular complications in people with type 2 diabetes (UKPDS Group, 1998). A total of 1148 hypertensive people with type 2 diabetes were recruited with a mean blood pressure at entry of 160/94 mmHg; 758 people were allocated to tight control of blood pressure and 390 to less tight control, with a median follow-up of 8.4 years. Mean blood pressure during follow-up was significantly reduced in the group assigned tight blood pressure control (144/82 mmHg versus 154/87 mmHg; $P<0.0001$).

Over 9 years there was a 32% reduction in diabetes-related deaths, a 44% reduction in fatal and non-fatal strokes and a 37% reduction in microvascular complications in those people assigned to the tight arm. The UKPDS post-trial monitoring results showed that the risk reductions of intensive control are lost as soon as control was relaxed. Unlike glycaemic control, there is no legacy effect (Holman et al, 2008).

Page points

1. The results of the Action to Control Cardiovascular Risk in Diabetes trial showed that in people with type 2 diabetes at high risk for cardiovascular events, targeting a systolic blood pressure of less than 120 mmHg compared with less than 140 mmHg did not reduce the rate of a composite outcome of fatal and non-fatal major cardiovascular events.
2. The updated guideline on hypertension does not specifically cover the treatment of people with diabetes (nor indeed does it cover management of hypertension in pregnancy or children).

The ACCORD (Action to Control Cardiovascular Risk in Diabetes) blood pressure trial tested the effect of a target systolic blood pressure below 120 mmHg on major cardiovascular events among high-risk people with type 2 diabetes (ACCORD Study Group et al, 2010). A total of 4733 participants with type 2 diabetes were randomly assigned to intensive therapy (targeting a systolic blood pressure of less than 120 mmHg), or standard therapy (targeting a systolic blood pressure of less than 140 mmHg). The primary composite outcome was non-fatal myocardial infarction, non-fatal stroke, or death from cardiovascular causes with a mean follow-up of 4.7 years. The results showed that in people with type 2 diabetes at high risk for cardiovascular events, targeting a systolic blood pressure of less than 120 mmHg compared with less than 140 mmHg did not reduce the rate of a composite outcome of fatal and non-fatal major cardiovascular events.

The ADVANCE (Action in diabetes and Vascular disease: Preterax and Diamicon MR Controlled Evaluation) trial was the first clinical trial to demonstrate the benefits of blood pressure reduction on both microvascular and macrovascular events in both hypertensive and normotensive people with type 2 diabetes (Patel et al, 2007). The trial recruited 11 140 people worldwide who were 55 years of age and older, with type 2 diabetes plus one or

more additional risk factors for cardiovascular disease. After a mean follow-up of 4.3 years, people on active treatment with perindopril and indapamide achieved a mean 5.6/2.2 mmHg greater reduction in blood pressure. There was a significant 18% relative risk reduction in cardiovascular death and a significant 14% relative risk reduction in death from any cause. Benefits appeared to be independent of initial blood pressure (i.e. they were similar in hypertensive and normotensive patients).

Updated NICE hypertension guidance

In August 2011 NICE updated its hypertension guidance in collaboration with the British Hypertension Society. The updated guideline on hypertension does not specifically cover the treatment of people with diabetes (nor indeed does it cover management of hypertension in pregnancy or children). These guidelines have engendered debate, with some discussion surrounding the evidence base for the new guidelines (Brown et al, 2012; McManus et al, 2012). In essence there are three changes in the new guidance (Box 1). Hypertension is categorised as stage 1, stage 2 or severe hypertension (Box 2).

Ambulatory blood pressure monitoring

The updated NICE (2011) guideline suggests the use of ambulatory blood pressure monitoring (ABPM) in preference to repeated clinic measurements.

- Clinic BPM (CBPM) should first be determined by having an individual rested and relaxed with at least three measurements taken 1 minute apart. The lowest figure from either the second or third reading is usually taken. When CBPM is $\geq 140/90$ mmHg ABPM should be offered.
- For ABPM the average value of at least 14 measurements taken during the individual's usual waking hours should be used for confirmation of a diagnosis.
- Where ABPM is not available, home BPM is an alternative and in this circumstance blood pressure should be recorded twice daily and measurement should continue for 7 days. The average value of the readings,

Box 1. Key changes in updated NICE (2011) hypertension guideline.

- Ambulatory blood pressure monitoring (ABPM) is used for the initial diagnosis of hypertension in all patients.
- Specific advice on the treatment of hypertension in the elderly (aged over 80 years).
- The position of and type of diuretic alters in the treatment algorithm.

Box 2. NICE (2011) stages of hypertension.

- Stage 1 hypertension: clinic blood pressure (BP) $\geq 140/90$ mmHg and ambulatory blood pressure monitoring (ABPM) or home BPM (HBPM) average $\geq 135/85$ mmHg.
- Stage 2 hypertension: clinic BP $\geq 160/100$ mmHg and ABPM or HBPM daytime average $\geq 150/95$ mmHg.
- Severe hypertension: clinic systolic BP ≥ 180 mmHg or clinic diastolic BP ≥ 110 mmHg.

having discarded the measurements taken on the first day, should be used. For each reading measurements should be taken twice, separated by 1 minute, with the person seated.

Hypertension algorithm

The treatment algorithm has changed significantly in the updated guidance; the popular ABCD (now ACD) algorithm has been updated (NICE, 2011). People aged below 55 years should receive an angiotensin converting

enzyme inhibitor (ACE-I) or angiotensin II receptor blocker (ARB) first line. This reflects a slight change, in that the previous guideline suggested using an ARB when an ACE-I was not tolerated.

Patients aged 55 years or over or who are of African or Caribbean family origin should receive a calcium channel blocker (CCB) first-line. The second step is to combine an ACE-I with a CCB. The third step is an ACE-I plus CCB plus thiazide-like diuretic.

Page point

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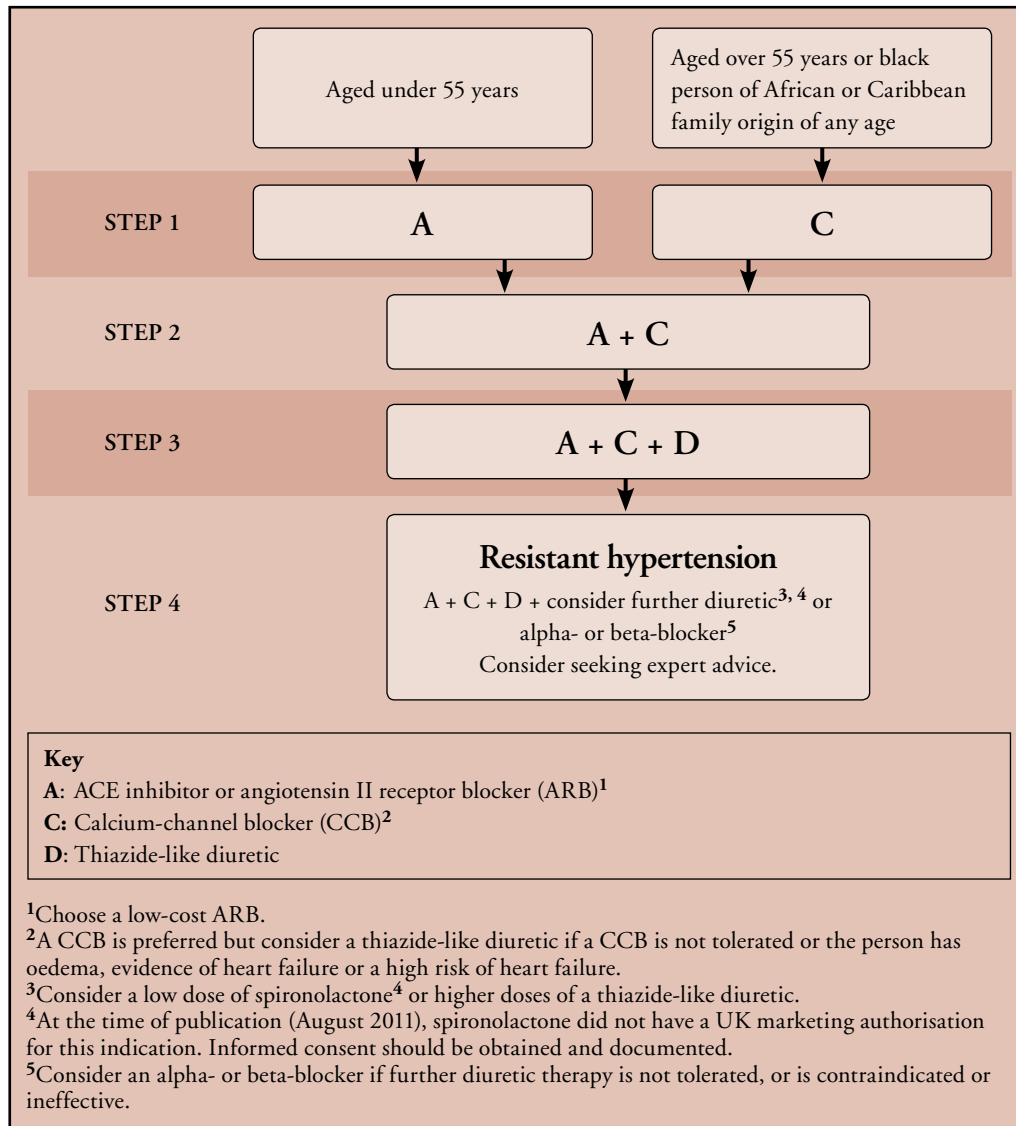


Figure 1. Summary of antihypertensive drug treatment. Reproduced with permission from the National Institute for Health and Clinical Excellence (2011) CG127 Hypertension: Clinical Management of Primary Hypertension in Adults. NICE, London. Available at www.nice.org.uk/guidance/CG127.



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Indapamide or chlortalidone should be used as opposed to bendroflumethiazide. This change reflects the fact that most endpoint trials used the former drugs although there is no recommendation to swap people from bendroflumethiazide if they are already taking it. For resistant hypertension (a notable problem in people with diabetes) spironolactone should be considered while keeping a close review of urea and electrolytes. If further diabetes therapy is contraindicated or not tolerated then a beta- or alpha-blocker should be considered. The updated algorithm is shown in *Figure 1*. Blood pressure targets for people without diabetes are shown in *Box 3*.

Hypertension in older people

Of particular interest in the updated guideline is the advice on treating hypertension in older people. An aggressive approach to managing blood pressure would often seem counter-intuitive and there are obvious practical considerations to treating older individuals. Generally speaking, evidence on treatment options are limited in elderly groups because such individuals are not regularly recruited into clinical trials. The HYVET (Hypertension in the Very Elderly Trial) addressed the important issue of hypertension in individuals aged 80 years or over (Beckett et al, 2008).

A total of 3845 people (excluding those in residential care or with dementia) who were 80 years of age or older and had a sustained systolic blood pressure of 160 mmHg or more were randomised to receive either the diuretic indapamide (sustained release, 1.5 mg) or matching placebo. The ACE-I perindopril (2 mg or 4 mg), or matching placebo, was added if necessary to achieve the target blood pressure of 150/80 mmHg. The primary endpoint was fatal or non-fatal stroke. At 2 years, the mean blood pressure while sitting was 15.0/6.1 mmHg lower in the active treatment group than in the placebo group.

In an intention-to-treat analysis, active treatment was associated with a 30% reduction in the rate of fatal or non-fatal stroke, a 39% reduction in the rate of death from stroke, a 21% reduction in the rate of death from any cause, a 23% reduction in the rate of death from cardiovascular causes and a 64% reduction in the rate of heart failure. Fewer serious adverse events were reported in the active-treatment group (358 versus 448 in the placebo group; $P=0.001$). The results provided evidence that antihypertensive treatment with indapamide (sustained release) with or without perindopril, in persons 80 years of age or older, was beneficial. As such, the updated NICE guideline recommends treatment in people aged over 80 years, but with a higher treatment target.



A more recently published HYVET extension study provides evidence that people aged 80 years or over with hypertension gain immediate benefit from treatment, and sustained differences in reductions of total and cardiovascular mortality reinforce the benefits and support the need for early and long-term treatment (Beckett et al, 2012).

Diabetes and hypertension

It is well known that approximately three-quarters of people with type 2 diabetes are hypertensive ($\geq 140/90$ mmHg) at diagnosis, which is in contrast to type 1 diabetes where blood pressure upon diagnosis does not differ from that in people without diabetes. The pathophysiology of hypertension consists of fluid and salt overload and vasoconstriction, which is mediated by renin. Resistant hypertension is common in diabetes and multiple agents acting against the various stages of the pathophysiological pathway are often required. The NICE standards for initiating treatment and treatment targets for people with diabetes are shown in *Box 4*. For people with diabetes and stage 1 hypertension, treatment should be initiated even in the absence of end-organ damage.

Lifestyle

Managing diabetes relies on doing the basics well. Seeing and treating people with hypertension and diabetes provides regular opportunities to promote a healthy lifestyle although it is accepted that education on its own is unlikely to be effective. In brief, people should be advised to take account of the interventions below, all of which have been shown to lead to modest reductions in blood pressure:

- Reduce salt intake to <2.4 g of sodium (<100 mmol/day). Simple advice of not adding salt to food and reducing the consumption of pre-packaged foods, which are often high in salt, should be given. A reduction in urinary sodium excretion of 30–45 mmol/day results only in a small reduction in blood pressure but reduced cardiovascular events by 25% in long-term follow-up (Cook et al, 2007).
- Eat a healthy low-calorie diet.
- Take aerobic exercise for 30–60 minutes three to five times each week.
- Reduce alcohol consumption.
- Avoid excessive consumption of coffee and other caffeine-rich products (five or more cups a day is associated with a small increase in blood pressure [2/1 mmHg]; NICE, 2011).

Pharmacological treatment of hypertension in people with diabetes

For people with diabetes, it is generally accepted that it is desirable first-line to opt for angiotensin blockade (such as an



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“The updated NICE hypertension guideline should lead to faster and more accurate diagnosis of hypertension. The use of ambulatory blood pressure monitoring is likely to improve patient confidence in accepting treatment.”

ACE-I or ARB) owing to the reno-protective effects of these agents. A common side effect of ACE-I is cough, which is reported to occur in approximately 10% of patients (Bangalore et al, 2010), but everyday practice would suggest it is more common than this. Renal function should be assessed 1 week after starting an ACE-I or ARB to detect a rise in serum creatinine or hyperkalaemia. It is also important to remember that both of these agents are teratogenic and should be stopped at least 3 months before conceiving and, where necessary, individuals should be swapped to safer alternatives, such as methyldopa. Discussions of the importance of adequate contraception in women taking any teratogenic medication should take place at review. Finally, it is also important to consider secondary causes of hypertension, especially where blood pressure seems resistant to treatment. In a recent general practice-based study, the prevalence of a raised aldosterone–renin ratio (necessitating a requirement for further investigation) was 20% in people with resistant

hypertension (Schmiemann et al, 2012). Other endocrine causes of hypertension and diabetes include Cushing’s syndrome and acromegaly; it is worth keeping these rarer conditions in mind.

Conclusion

In summary, the updated NICE hypertension guideline should lead to faster and more accurate diagnosis of hypertension. The use of ABPM is likely to improve patient confidence in accepting treatment. Anecdotally, the author has met many patients who have simply blamed the “white coat effect” for high clinic readings and in turn have been reluctant to start treatment. This new approach might help to convince more people to accept treatment where it is needed. ■

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Box 3. NICE (2011) treatment levels and treatment targets in people without diabetes.

- If a person aged below 80 years has stage 1 hypertension with target organ damage, established cardiovascular disease, renal disease, diabetes, or a 10-year cardiovascular risk equivalent of ≥20%, or stage 2 hypertension at any age, drug treatment should be initiated immediately.
- Response to treatment is assessed with CBPM
- Aim for <140/90 mmHg (or <135/85 mmHg if using ABPM or HBPM) for people aged under 80 years
- Aim for <150/90 mmHg (as used in HYVET [Beckett et al, 2008; 2012]) (or <145/85 mmHg if using ABPM or HBPM) for people aged over 80 years.

ABPM=ambulatory blood pressure monitoring; CBPM=clinic BPM; HBPM=home BPM; HYVET=Hypertension in the Very Elderly Trial.

Box 4. NICE (2009) treatment thresholds and blood pressure targets in people with diabetes.

Treatment threshold	>140/90 mmHg
Target	<140/80 mmHg (if no end-organ damage) <130/80 mmHg (with presence of end-organ damage)