Managing hypertension and meeting targets

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Despite constantly updated guidelines and a wide choice of drugs for hypertension only 37 per cent of patients have their blood pressure (BP) adequately controlled. This article gives practical tips on how best to achieve the targets for BP control using current guidelines.

The ultimate goal of identifying and treating patients with hypertension is to reduce the potential morbidity and premature mortality associated with the condition. Despite constantly updated evidence-based guidelines and a wide choice of potent, effective and usually well-tolerated antihypertensive drugs, only 37 per cent of patients have their blood pressure (BP) adequately controlled.1 While perfect control does not prevent cardiovascular disease (CVD), compared to normotensive subjects there is a 37 per cent greater lifetime risk of developing CVD in those with a BP >140/90mmHg, which will develop on average five years earlier.2

The current BP targets are not under dispute, but to achieve greater accuracy you need to: have a clear understanding of the long-term life and death implications of failure; concentrate on achieving the goal; achieve a balance of effort (neither too quick nor too slow) and know when to call it a day; focus on the details; and remain personally responsible for the equipment and methods you use. There is no big secret to success; it results from a combination of good theoretical and practical preparation, experience, good equipment and methodology, excellent teamwork, continually learning from others and not giving in until the best possible outcome has been achieved.

Accurate BP assessment is the basis of diagnosis and subsequent monitoring

The NICE guideline for hypertension (CG127) defines it as a clinic BP reading of ≥140/90mmHg combined with an ambulatory daytime or home BP average of ≥135/85mmHg (for those patients aged 80 years and over, the threshold clinic BP for diagnosis is ≥160/100mmHg with a home or ambulatory daytime mean of ≥150/95mmHg). Unless clinic BP readings are consistently ≥180/110mmHg, all patients under 80 years with repeated BP readings of ≥140/90mmHg should have home (HBPM) or ambulatory BP monitoring (ABPM) before...
starting treatment to avoid unnecessary drug medication. This begs the question of ensuring proper and accurate BP measurement and in this respect it is essential to use properly maintained equipment.

Only use BP machines that are validated for use in the particular type of patient either by the British Hypertension Society (BHS) or other validating body eg dabl Educational Trust. Always ensure that the appropriate cuff size is used whether in clinic or with home or ambulatory machines such that the bladder of the cuff circumscribes 80–100 per cent of the circumference of the mid upper arm and make sure that all staff measuring BP have up-to-date training on doing this with the equipment provided.

If healthcare practitioners are using auscultation, then validation of their auscultatory ability to detect Korotkoff sounds – including knowing that diastolic BP is measured at the disappearance of sounds (the fifth Korotkoff sound) is essential, as some clinicians have undetected hearing loss that can be exacerbated by using a poor quality stethoscope). It is important that the patient is rested for five minutes, should not talk immediately before and during measurement, that their arm is supported at heart height and that the BP is recorded clearly to the nearest 2mmHg with at least one repeated reading (and often more if the BP is failing or the patient has a slow or irregular pulse), whether the reading is by the patient or healthcare practitioner.

This approach is as important in the initial assessment and diagnosis of hypertension as it is in subsequent monitoring. Wrongly labelling a subject as having hypertension has significant long-term consequences, such as falsely reassuring the patient that their BP is “all right” when the target has not been achieved. If white coat hypertension has been diagnosed, based on clinic BP ≥140/90mmHg with home and/or ambulatory daytime BP <135/85mmHg (nighttime ABPM should also be <120/70mmHg and 24 hour mean ABPM <130/80mmHg), subsequent follow-up should still be arranged within two to five years because of the significant possibility of subsequently developing sustained hypertension. A further complication is when “masked hypertension” is present. In this condition, clinic BP appears within target ie <140/90mmHg but home or mean ambulatory daytime BP exceeds target ie ≥135/85mmHg. In this situation cardiovascular risk is dictated by the home or ambulatory readings and therefore patients will have to depend on their own BP readings or ambulatory readings.

Since validated home BP monitors with appropriate cuffs now cost less than a year of drug therapy, it is inappropriate to assess BP control solely on clinic readings and I would advocate every patient purchasing their own home BP recorder. For those who genuinely might find this prohibitive, it would be advantageous for these to be eventually available on prescription. Staff and patients should be tutored in the use of home BP monitoring. To this end, resources are available on the BHS website. Thus an accurate diagnosis and subsequent assessment of achieved BP and whether targets have been achieved is a sine qua non prior to any therapeutic intervention.

[Table 1. Non-pharmacological methods to reduce BP]

### Clear targets

NICE guidance sets out clear targets for BP control: <140/90mmHg for those <80 years of age and <150/90mmHg for those aged 80 and over, as well as suggesting HBPM and daytime ABPM targets of <135/85 and <145/85mmHg for the same groups respectively if white coat effect has been identified. In fact outcome is so much better predicted by HBPM and ABPM than clinic readings and patient interaction and target achievement improved by HBPM that self-monitored HBPM targets should become the routine where possible.

### Achieving adherence

To gain maximum adherence, it is important to clarify why BP needs reducing. Many patients are poorly motivated to take lifestyle advice or medication because they have not understood the long-term consequences of uncontrolled hypertension. Adequate time taken and directing patients to resources, literature or other support can improve concordance and BP control.

### Give lifestyle advice (see Table 1)

The benefits of salt and alcohol restriction on BP reduction should be clearly explained. Anything over two alcoholic drinks per day has been shown to elevate BP11 and reduced alcohol intake is associated with a concomitant and related BP reduction. Just modest alcohol reduction reduces BP by 2–4mmHg. The Dietary Approaches to Stop Hypertension (DASH) diet has been shown to give an average BP reduction of 7–12mmHg, weight reduction lowers BP by approximately 1mmHg/kg and physical activity by 3–5mmHg. At the same time all these interventions have metabolic benefits, which are better than would occur if the same BP reduction were achieved by medication alone.

### Investigate before treating

There is no substitute for taking a history and examining patients before prescribing for hypertension. A family history

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1. Inform patients
   - what their BP is
   - what their ideal BP should be
   - what are the risks if untreated
   - what are the benefits of BP control
2. Diet and drink
   - reduce weight where necessary
   - recommend DASH diet (including low salt, more potassium)
   - reduce alcohol to a maximum of two drinks per day
3. Encourage regular aerobic exercise
4. Minimise potentially hypertensive agents eg NSAIDs, steroids, licorice, venlafaxine
5. Consider possibility of sleep apnoea – refer if suspected
6. Self-monitoring
   - improves motivation
   - is the best index of risk and success
deterioration in renal function requires reduction in dose and consideration of underlying renal or renovascular disease. A history of renal trauma or irradiation may predispose to hypertension, which might be more sensitive to ACE inhibition, and renal tract stones may be associated with hypercalciuria, which may benefit from thiazide/thiazide-like drugs or investigation of possible hyperparathyroidism. Initial tests should always include urinalysis for protein and blood, plasma glucose, creatinine and electrolytes, cholesterol and HDL, and an ECG.

Consider elimination of hypertensive factors
The hypertensive effects of the following should all be considered and addressed before adding antihypertensive therapy: sleep deprivation, anxiety, licorice, the oral contraceptive pill, obstructive sleep apnoea, pain, sympathomimetics including phenylephrine, amphetamines, and cocaine, ciclosporin, tacrolimus, NSAIDs, busprione, venlafaxine, steroids, erythropoetin, herbal preparations containing ginseng, ginger and yohimbine, capsicum, aniseed, St John’s wort, black cohosh, guarana, cola alkaloids and ephedra. Although not in current guidelines, assessment of aldosterone and renin prior to starting treatment may avoid subsequent problems in interpreting results where hyperaldosteronism is a potential cause of hypertension.

Pharmacological treatment (see Table 2)
Step 1: initiating drug therapy
• Give medication to patients who, after lifestyle advice still have a sustained clinic BP ≥140/90mmHg and HBPM/ABPM ≥135/85mmHg who also have established CVD, target organ damage, renal disease, diabetes or a 10-year CVD risk ≥20 per cent and/or who are <80 years old.
• For others with no risk factors or aged ≥80 years, give lifestyle advice alone and start treatment when BP reaches ≥160/100mmHg and HBPM/ABPM ≥150/95mmHg.

Initiation with ACE inhibitors in patients >55 years (except in black people of African descent and females contemplating pregnancy) can start at low dose and will take into account initial renal function and requires creatinine and electrolyte reassessment preferably within the first month and after subsequent titrations, which can be in doubling doses. Sudden deterioration in renal function requires reduction in dose and consideration of underlying renal or renovascular disease. A modest elevation of urea but not creatinine caused by reduced renal filtration fraction is expected. Long-acting ACE inhibitors, eg perindopril and lisinopril, have the advantage of better 24-hour control and should normally be given in the morning rather than at night since there is evidence of better potency. Ramipril is shorter acting and may need twice daily dosing.

Although cough resulting from ACE inhibitor occurs in around 15 per cent patients, many fail to complain and put up with it. Nevertheless this sort of reaction should be sought out and a change to an angiotensin-II receptor blocker (ARB) is recommended. The ARB dose would usually start at an equivalent point within the dose range as the preceding ACE inhibitor. Where target BP has not been achieved by reaching half-way up the dose range for any single drug or where renal function has shown some signs of significant change, a calcium-channel blocker (CCB) should then be added by preference.

In those of black African descent and patients aged 55 and over, treatment should start with a long-acting CCB. Those with faster resting heart rates may benefit from using modified-release diltiazem or verapamil providing they do not develop constipation, heart failure or heart block. Nifedipine as monotherapy is more likely than other CCBs to induce tachycardia and flushing, while amlodipine, which has the advantage of an extremely long half-life, is more prone than most to induce oedema (this may be less likely when given in combination with an ACE inhibitor or ARB). Other long-acting CCBs such as lercanidipine may not so easily induce flushing or oedema.

There is marked variability in patients’ ability to tolerate CCBs. Some experience excessive diuresis, flushing, itching and oedema even at low doses especially with dihydropyridines. A

<table>
<thead>
<tr>
<th>Table 2. Pharmacological options for hypertension management</th>
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<tbody>
<tr>
<td>• Follow NICE guidelines</td>
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<tr>
<td>• Titrate drugs to achieve target BP at intervals of no more than 2–3 months</td>
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<td>• Consider early combination treatment</td>
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<td>– 2 drugs are up to 5 times more effective than doubling a single agent</td>
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<td>– if a single drug at half top-dose has not improved BP</td>
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<td>• Monitor BP response preferably using home or ambulatory measurements</td>
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<td>• Check sitting and standing BP responses in clinic – especially in the elderly</td>
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<tr>
<td>– where patients complain of dizziness or feeling unwell with medication</td>
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<tr>
<td>– where patients are taking drugs with alpha-blocking activity eg doxazosin</td>
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<tr>
<td>• Schedule checks of U&amp;E before titrating ACE inhibitor, ARB or diuretics</td>
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<td>• Ask patients about adverse reactions proactively to reduce covert non-adherence, eg female stress incontinence with doxazosin, erectile dysfunction</td>
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<td>• Consider medicine review by a third party, eg pharmacist, to discuss adherence where BP is not improving despite 3 or more drugs</td>
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<td>• Always check home and/or ABPM where resistance is present to exclude white coat effects</td>
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<td>• If true 3-drug resistance is present – refer to a hypertension specialist</td>
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switch to a rate-limiting CCB or addition of an ACE inhibitor may reduce these symptoms but not always. The use of a combination of a dihydropyridine with a rate-limiting CCB (eg amlodipine, nifedipine) may help to reduce adverse reactions caused by higher doses of any one agent. The problem is that any adverse reactions tend to reduce long-term adherence, so monitoring both the efficacy and tolerability of all antihypertensive drugs is essential.

Thiazide-like diuretics (indapamide and chlortalidone) should be used as an alternative when CCBs are not tolerated, or where oedema or possible heart failure is present. Some patients, especially those of African descent, are often especially sensitive to reduced salt intake as well as to diuretics so it is always worth giving detailed advice on the DASH diet or salt restriction alone before prescribing thiazide-like diuretics, which may be associated with adverse metabolic changes such as hyponatraemia, increasing glucose intolerance, gout, hypokalaemia and deteriorating renal function. Reduction of sodium may result from changes in renal biochemistry as well as in patients inadvertently increasing their fluid intake, and may respond to advice on modest fluid restriction. Any sustained reduction of potassium below the normal range suggests the need to check for low plasma renin as a possible indicator of hyperaldosteronism. If this is the case, further specialist investigation is warranted. If diuretics are necessary but induce gout, then the introduction of long-term allopurinol under temporary low-dose colchicine cover should be considered (rather than NSAIDs, which may increase BP).

If monotherapy is ineffective in achieving target or is not tolerated, even after swapping to an alternative agent (ACE inhibitor – CCB – diuretic) for no more than two to three months, then continue to the next step.

Step 2: dual therapy
Combining an ACE inhibitor (or ARB) with a CCB should begin when target BP has not been achieved with the mid-point of ACE or ARB dosing or with usual top tolerated doses of a CCB. Combining drugs of two different classes can achieve a five-fold greater reduction in BP than doubling the dose of one drug. Primary initiation of combination therapy achieves target BP more frequently and rapidly and reduces CV events or death by 34 per cent compared with switching from initial monotherapy to combination treatment, so should be considered as a possible starting strategy in patients with systolic BP >160mmHg.

Step 3: triple therapy
It is worth titrating drugs at intervals of no greater than two months, by which time most of the major BP-lowering benefits have been realised. Reassessment of BP achieved in clinic and by HBPM/ABPM (where clinic BP is still greater than target) as well as checking with the patient for adverse physical and, where appropriate, biochemical reactions is essential at each titration. The cost of the extra workload is offset by reduced non-adherence and better outcomes.

The failure to add an appropriate dose of a thiazide-like diuretic, if target BP has not been achieved with an ACE/CCB or ARB/CCB combination, is one of the greatest causes of apparent drug resistance. Always check for metabolic and physical adverse reactions and also for postural hypotension, especially with triple combinations. Some patients’ intolerance of treatment is because of unsuspected postural BP drop when sitting BP is apparently normal or elevated. This may be exacerbated by concomitant therapy with SSRIs and any drug having alpha-blocking activity such as tricyclic antidepressants, tamsulosin, doxazosin and phenothiazines.

The greater the number of drugs co-prescribed, the greater the chance of non-adherence; therefore, single tablet combinations may be economically more effective in the long run. Always check creatinine and electrolytes, not only prior to starting therapy but also at intervals, especially after adding or increasing doses of diuretics, ACE inhibitors or ARBs.

Resistance to three-drug combinations
If target BP has not been achieved with three complementary agents, including a thiazide-like diuretic at optimal dose, then a secondary cause for the hypertension or non-adherence should be suspected. The presence of a low potassium (≤3.5mmol/L) on a diuretic, especially in the presence of ACE inhibitor or ARB, should alert to the possibility of hyperaldosteronism and justify a check for low renin levels. Indeed low renin due to hyperaldosteronism should always be checked if

| Ensure BP is checked at least annually, preferably with HBPM or ABPM and continue to encourage long-term healthy lifestyles |
| - if target has been achieved |
| - in women with a history of pre-eclampsia who are at significantly increased risk of developing hypertension |
| - in “white coat hypertensives” – 50 per cent may eventually develop sustained hypertension |
| - in borderline hypertensives |

| Encourage patients to home monitor if possible and clarify method, targets and frequency (eg duplicate home BP morning and evening for 5 days with target average BP <135/85, if <80 years) |
| - every 6 months if BP controlled |
| - after not less than one week of new therapy or after a dose titration and before next clinical review |
| - all patients with “masked hypertension” (normal clinic BP, raised home or ABPM) need to home monitor or have assessment by ABPM to ensure control to target |

| Patients on diuretics, ACE inhibitor, ARBs and with known renal dysfunction should have U&E checks at least annually |
| If there are unexpected elevations of BP has |
| - adherence changed? |
| - medication been stopped? |
| - new medication been added eg oral contraceptive pill? |
| - renal function changed? |
| - weight changed? |

| Remember hypertensives are at increased risk of developing AF and heart failure – check annually |

Table 3. Long-term monitoring of hypertension
three-drug resistance has been demonstrated as 5 per cent or more of hypertensives may have a removable aldosterone producing adenoma.\textsuperscript{18}

Non-adherence can be checked by:
- examining prescribing records
- in-depth interview, often with a specialist nurse or pharmacist
- getting the patient to take all their medication under observation with subsequent BP check every 30 minutes for four hours in surgery (BP drops more than observed during normal checks)
- urine analysis for antihypertensive drugs.\textsuperscript{19}

At this point referral to a specialist is advisable, although the addition of a fourth drug could be considered such as spironolactone or doxazosin. For very resistant hypertensives, minoxidil can be a very potent add-on but usually concomitant loop diuretic and beta-blockade are required to counteract its tendency to induce tachycardia and fluid retention. Its tendency to induce excess hair growth may be advantageous to folliculally-challenged men but is unacceptable to many women.

Consideration of interventions such as renal angioplasty,\textsuperscript{20} renal artery nerve ablation,\textsuperscript{21} carotid sinus stimulation\textsuperscript{22} and creation of a femoral artery-venous anastomosis\textsuperscript{23} are reserved for rare cases usually under research conditions as their routine safety and effectiveness have not yet been proven beyond doubt.

**Conclusion**

Strict adherence to the NICE guidelines should result in improved success in BP control as well as reduced morbidity and mortality. Attention to detail at each step including dealing with obstacles to lowering BP such as obesity, sleep apnoea, reduction of excess salt and alcohol, regular motivation and review with upward titration of therapy from one to three or four drugs and avoidance of non-adherence are simple but powerful means of more easily achieving BP targets in a majority of patients. Long-term monitoring of patients with hypertension is outlined in Table 3.

**References**


**Declaration of interests**

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