

## Postural Hypotension

Artaza Gilani (0000-0002-5385-8524)<sup>1,2</sup>, Stephen P Juraschek<sup>3</sup>, Matthew J Belanger<sup>3</sup>, Julie E Vowles<sup>4</sup>, S Goya Wannamethee<sup>1</sup>

1. University College London Research Department of Primary Care and Population Health, Upper Third Floor, University College London Medical School (Royal Free Hospital Campus), Rowland Hill Street, London, NW3 2PF.

Artaza Gilani Honorary Lecturer

S Goya Wannamethee Professor of Epidemiology

2. North West London

Artaza Gilani General Practitioner

3. Harvard Medical School, Beth Israel Deaconess Medical Center, Division of General Medicine, Section for Research, 330 Brookline Avenue, CO-1309, #216 Boston, MA 02215.

Stephen P Juraschek Assistant Professor of Medicine

Matthew J Belanger Senior Resident Physician

4. The Hillingdon Hospitals NHS Foundation Trust, Pield Heath Road, Uxbridge, UB8 3NN.

Julie E Vowles Consultant in Acute and Geriatric Medicine

Correspondence to: Artaza Gilani, University College London Research Department of Primary Care and Population Health, Upper Third Floor, University College London Medical School (Royal Free Hospital Campus), Rowland Hill Street, London, NW3 2PF, e-mail

artaza.gilani@ucl.ac.uk, telephone: 0208 0168 021

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Postural hypotension, also called orthostatic hypotension, is an abnormal drop in blood pressure on standing. It impairs quality of life and increases risk of falls, cardiovascular disease, depression, dementia and death(1-4).

### Box: Sources and Selection Criteria

We searched Embase, Medline, The Cochrane Central Register of Controlled Trials and Web of Science using the terms, “orthostatic hypotension”, “postural hypotension”, “orthostatic intolerance” and “postural intolerance”. We also used personal archived references, which included our published work and National Institute for Health and Care Excellence (NICE) guidelines.

### **How common is it?**

The prevalence of postural hypotension increases with age: two large population-based studies in the US suggest it is found in <5% of people aged 45-49 years, almost 15% in those aged 65-69 years and over 25% of those >85 years(5). One in five community-dwelling adults over the age of 60 years and one in four persons in long-term residential care have postural hypotension, as per a systematic review and meta-analysis (26 studies, >25000 people)(6).

Postural hypotension is likely to be common in geriatric inpatients(7, 8). Factors such as clinical settings, encouragement to mobilize, and frequency of testing may affect prevalence in hospitals (8-10).

### **How is it caused?**

Normally when we stand, gravity causes blood to pool below the level of the diaphragm. There is reduced venous return so cardiac output falls. The body usually responds to these changes through a coordinated response of the autonomic nervous system to maintain blood pressure. In postural hypotension, there is an inadequate, or delayed, response to the fluid shifts that occur with standing. This leads to an exaggerated drop in systolic blood pressure ( $\geq 20$  mmHg) and/or

diastolic blood pressure ( $\geq 10$  mmHg) that occurs within three minutes of standing upright(9)(Figure 1).

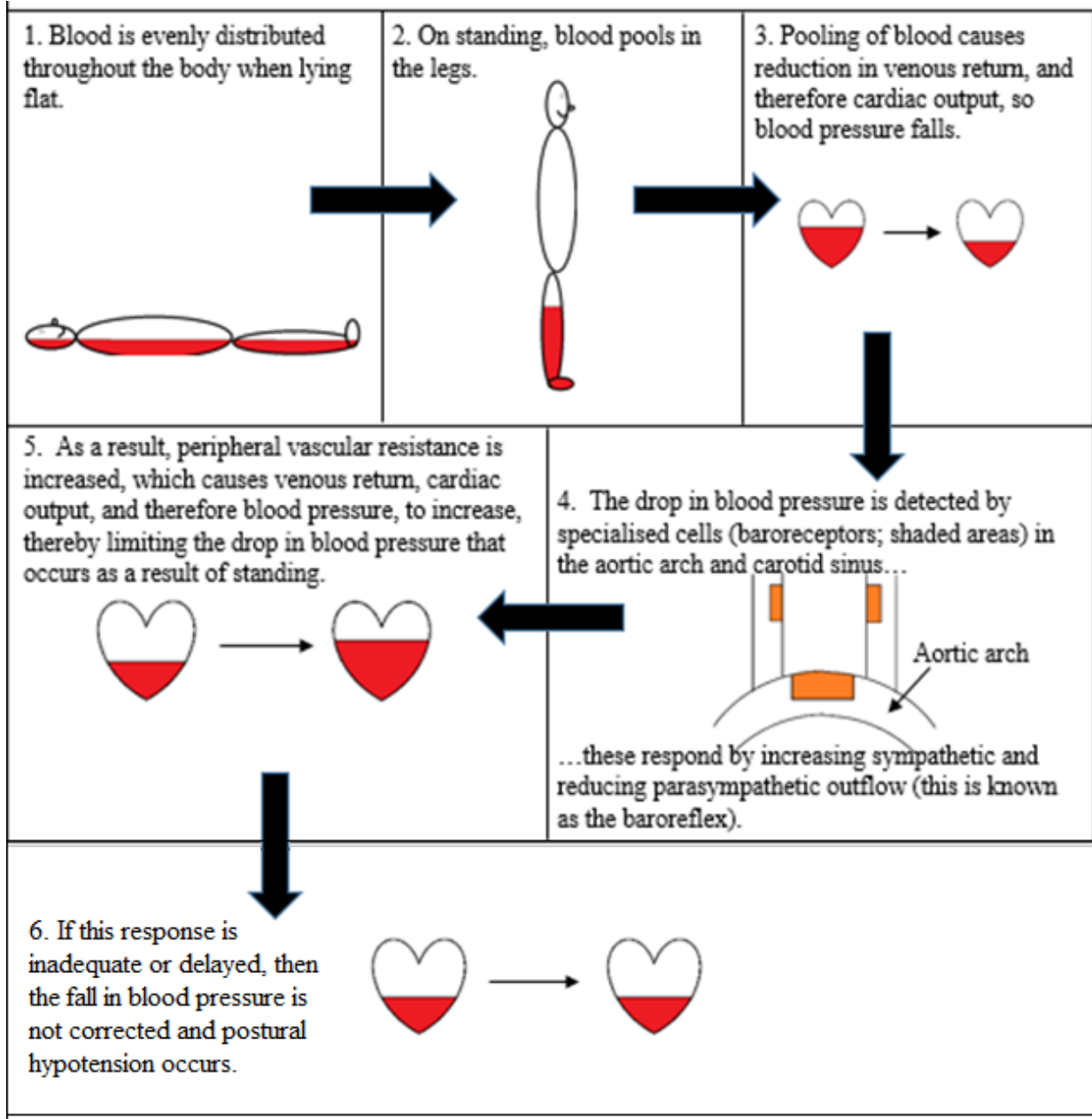


Figure 1: The normal physiological response that occurs when we change position from lying to standing. The response is coordinated through neuronal and non-neuronal mechanisms. If this response is inadequate, or delayed, postural hypotension occurs. Postural hypotension may be caused by problems with the nervous system (neurogenic causes) and/or problems independent of the nervous system (non-neurogenic causes); there may be overlap between the two types of

*causes i.e. some factors cause postural hypotension through both neurogenic and non-neurogenic mechanisms. An example of a neurogenic cause of postural hypotension is Parkinson's disease, which causes autonomic dysfunction. An example of a non-neurogenic cause of postural hypotension is anaemia, which causes volume depletion. Some causes of postural hypotension may be permanent, such as Parkinson's disease, causing recurring symptoms, while others may be transient, such as anaemia, which if then corrected, causes transient or isolated symptoms.*

### **How do patients present?**

Patients may present with light-headedness (feeling faint or woozy), or dizziness (spinning symptoms or feeling off balance) triggered by changes in posture. These symptoms usually resolve with lying down or sitting. Symptoms may occur first thing in the morning, as the patient gets up from bed, or throughout the day, as they change position from lying to standing, sitting to standing or even lying to sitting. Less well-recognised symptoms of postural hypotension, which are also transient and resolve with lying or sitting down, are shown in Box 1(11). It is not known how diagnostic or common these symptoms are, but if they occur in relation to changes in posture, they should prompt clinicians to check for postural hypotension. Some patients have no symptoms: in a small observational study, about a third had postural hypotension but were asymptomatic with it(12, 13), while other patients may present with transient loss of consciousness or falls.

#### **Box 1: Non-specific symptoms of postural hypotension**

- Blurry vision
- Visual field deficits
- Difficulty concentrating
- Cognitive slowing
- Weakness
- Fatigue
- Shortness of breath
- Chest pain
- Backache
- Lower extremity pain
- “Coat-hanger” headache (headache in the sub-occipital region and neck pain in the posterior cervical and shoulder regions).

## Who gets postural hypotension?

Postural hypotension may be caused by problems with the nervous system (neurogenic causes) and/or problems independent of the nervous system (non-neurogenic causes – these are more common than neurogenic causes)(14) (Table 1). The causes may overlap. It is common in patients with medical conditions such as diabetes and Parkinson’s disease. About a quarter of patients with diabetes have postural hypotension, as per a systematic review and meta-analysis (21 studies, 13722 patients)(15). High HbA1c, hypertension, and diabetic neuropathy increase its likelihood. About a third of patients with Parkinson’s disease have postural hypotension(16).

*Table 1: Examples of causes of postural hypotension and conditions in which it is found(14). Medications and cardiovascular disease may result in postural hypotension through both neurogenic and non-neurogenic mechanisms. Besides its diuretic effect, short term alcohol consumption may contribute to postural hypotension by impairment of vasoconstriction(17). Alcohol is a neurotoxin so chronic consumption may also contribute to postural hypotension through neurogenic mechanisms.*

<b>Neurogenic causes</b>
Neurodegenerative disease e.g. Parkinson’s disease, Parkinson’s Plus Syndromes
Peripheral neuropathy e.g. Diabetes mellitus, B12 deficiency, renal failure, amyloidosis, rheumatological, autoimmune, and paraneoplastic conditions
<b>Non-neurogenic causes</b>
<b>Volume depletion:</b> Medications (alpha-blockers, antihypertensives, nitrates, diuretics, SSRIs, TCAs, antipsychotics, beta-blockers), dehydration, haemorrhage, hyperglycaemia, alcohol
<b>Cardiovascular Disease:</b> Aortic stenosis, hypertension, heart failure, atherosclerosis/vascular stiffening, arrhythmias
<b>Other:</b> Adrenal insufficiency, physical deconditioning, ageing

## Idiopathic

Medications can cause postural hypotension as an adverse reaction, but it is not known which drug classes are most likely to cause it. Individual susceptibility, age, comorbidities and polypharmacy determine whether a patient develops postural hypotension(18, 19) and the number of antihypertensive drugs prescribed may be more predictive of postural hypotension than an individual class of drug(14).

### **What to cover on clinical assessment?**

The purpose of the history and examination is to identify the cause(s) of postural hypotension, which may be multifactorial. Clarify the nature of symptoms, their onset in relation to changes in posture and if they are persistent/recurrent or isolated. Ask about factors such as diurnal variability, food intake, hydration, ambient temperature, prolonged recumbency and deconditioning, as these can affect symptoms(9). Consider drug-induced causes by reviewing the drug history. Clinical features to look for will depend on the history of the patient suspected to have postural hypotension – a patient with palpitations may have a murmur suggestive of structural abnormality of the heart, while a patient who describes slowness of movement and tremor may have hypomimia and rigidity, suggestive of Parkinson's.

### **Who to test for postural hypotension?**

NICE advises assessing for postural hypotension in patients who are symptomatic or those who present with a fall(20). We do not recommend screening for it in the general population but routine screening may be considered in certain groups of patients. For example, NICE advise checking for postural hypotension in patients who have hypertension alongside type 2 diabetes or who have hypertension and are aged 80 and over(20). Similarly, The American Diabetes Association recommends an assessment for postural hypotension during initial evaluation of hypertension, in all patients, and periodically at follow-up even in the absence of symptoms of postural hypotension(21). Expert consensus(22) also suggests screening for postural hypotension

in patients suspected of, or diagnosed with any neurodegenerative condition associated with autonomic dysfunction (such as Parkinson's disease) and in patients with peripheral neuropathies known to be associated with autonomic dysfunction (such as diabetes) but these recommendations are not currently in NICE guidelines.

“Classic” postural hypotension occurs within three minutes of standing; “delayed” postural hypotension occurs after three minutes. It will be important to take postural blood pressure measurements beyond three minutes of standing, if patients report symptoms occurring after this point in time, else a diagnosis of postural hypotension may be missed. The overwhelming majority of studies have investigated classic postural hypotension, rather than delayed, and less is known about this type of postural hypotension(23).

Some patients may not meet the defined criteria for a diagnosis of postural hypotension despite having symptoms of it and home postural measurements showing a postural drop in blood pressure. Other causes of postural hypotension should be considered and if there remains a high index of suspicion, these patients may be managed as those with postural hypotension.

### *Blood pressure measurement*

Take lying and standing blood pressure measurements and check for a drop in systolic blood pressure  $\geq 20$  mmHg and/or diastolic blood pressure  $\geq 10$  mmHg within three minutes of standing. Sitting and standing, and occasionally lying and sitting, measurements are sometimes used for convenience or because of practical reasons. The optimal thresholds for a diagnosis based on these measurements are not known(24-26). If these measurements are used and an exaggerated drop in blood pressure is not found, it may not be possible to confidently exclude postural hypotension and lying and standing measurements should be taken (this repeat measurement can be done without delay). Tilt-table testing (a diagnostic procedure used in patients with syncope of uncertain origin and during which a patient is put under positional/orthostatic stress in a controlled and monitored setting) is a specialist cardiology investigation that requires referral to secondary care. It can also be used for the diagnosis of postural hypotension but is uncommon.

There is wide variation between guidelines on how to take postural blood pressure measurements (Table 2). NICE recommends measuring blood pressure with the person either lying or sitting down and then measuring blood pressure again once the person has been standing for at least 1 minute(20). Take multiple lying and standing measurements, rather than just one lying and one standing measurement. For example, The Royal College of Physicians recommends taking the first blood pressure measurement after lying for at least five minutes, the second after standing in the first minute and the third after standing for three minutes(27). Repeat measurements at a later point in time, rather than rely on a one-off clinic measurement, as this will increase detection rates(10). In practical terms, this may mean taking serial home postural blood pressure measurements (morning and evening), either by patients themselves or their carer(s). This may only be feasible in those who are sufficiently mobile. It may be inappropriate in patients with severe symptoms at high risk of falls who cannot be supported while taking measurements.

Make note of changes in heart rate when taking lying and standing blood pressure measurements. If postural hypotension is found and there is an accompanying increase of the heart rate that is  $< 15$  beats per minute, this may suggest a neurogenic cause of postural hypotension(22). On the other hand, if postural hypotension is found and there is an increase of the heart rate of  $> 15$  beats



per minute, this may suggest a non-neurogenic cause(22). However, heart rate is only a general indicator of underlying cause, which may be multifactorial, and it may not be an accurate measure if the patient is on a beta-blocker, for example.

The measurement process can be time-consuming in a busy practice. It may be appropriate to involve allied healthcare professionals in taking postural measurements on the day of the appointment, prior to consultation with a doctor, as is done in falls clinics.

Table 2: Guidelines regarding the measurement of blood pressure to detect postural hypotension

<b>Guideline/ Source</b>	<b>Drop in blood pressure to diagnose postural hypotension</b>	<b>Specific Measurement Instructions*</b>
Updated Consensus Statement (2011)(9) Endorsed by the American Autonomic Society, the European Federation of Autonomic Societies, the Autonomic Research Group of the World Federation of Neurology and the Autonomic Disorders section of the American Academy of Neurology.	≥ 20 mmHg systolic Or ≥ 10 mmHg diastolic ** ***	<ul style="list-style-type: none"> <li>• Standing measurement should be obtained within 3 minutes of standing. However, “some patients present with symptomatic orthostatic hypotension that occurs beyond 3 minutes of standing”</li> <li>• Number of standing measurement not specified, but the decrease in blood pressure should be “sustained”</li> </ul>
Hypertension Canada (2018) (see supplementary material within guideline)(28)	Not specified	<ul style="list-style-type: none"> <li>• Measure baseline blood pressure in seated position after 5 minutes of sitting (obtain 3 measurements, discard the first and average the last 2)</li> <li>• For baseline blood pressure, “supine blood pressure measurements may also be helpful in the assessment of elderly and diabetic patients”</li> <li>• Measure standing blood pressure 2 minutes after standing and at times when symptoms of postural hypotension are reported</li> </ul>
NICE: Transient loss of consciousness in over 16s (2010) (29)	“Marked fall in blood pressure”; specific thresholds not specified	<ul style="list-style-type: none"> <li>• Obtain baseline measurement in the supine position, followed by “repeated measurements” while standing for 3 minutes</li> </ul>
NICE: Hypertension in adults: diagnosis and management (2019) (20)	≥ 20 mmHg systolic	<ul style="list-style-type: none"> <li>• Obtain at least one measurement in the supine or sitting position followed by standing blood pressure after at least one minute of standing</li> </ul>

NICE: Postural hypotension in adults: fludrocortisone (2013) (30)	$\geq 20$ mmHg systolic Or $\geq 10$ mmHg diastolic	<ul style="list-style-type: none"> <li>• Obtain standing blood pressure within 3 minutes of standing</li> </ul>
European Society of Hypertension/ European Society of Cardiology (2018)(31)	$\geq 20$ mmHg systolic Or $\geq 10$ mmHg diastolic	<ul style="list-style-type: none"> <li>• Baseline blood pressure may be obtained in the seated position after sitting for 5 minutes (measure 3 times, discard first and average the last 2).</li> <li>• Supine measurements should be “considered in subsequent visits in older people, people with diabetes, and people with other conditions in which postural hypotension may frequently occur”</li> <li>• Measure blood pressure 1 min and 3 min after standing</li> </ul>
National Heart Foundation of Australia (2016)(32)	Not specified	<ul style="list-style-type: none"> <li>• Measure baseline blood pressure after sitting for several minutes (measure at least 3 times and average the last 2)</li> <li>• Measure blood pressure once after standing for at least 2 minutes</li> </ul>
American College of Cardiology/American Heart Association (2017)(33)	$> 20$ mmHg systolic Or $> 10$ mmHg	<ul style="list-style-type: none"> <li>• Have patient relax in a seated position (with feet flat on the floor and back supported) for <math>&gt; 5</math> min prior to obtaining baseline blood pressure</li> <li>• Measure blood pressure in the seated position, immediately after rising, and again 1-2 minutes after standing****(34)</li> </ul>
Royal College of Physicians (United Kingdom) (2017)(27)	$\geq 20$ mmHg systolic Or “A drop to below 90 mmHg on standing even if the drop is less than 20 mmHg” Or $\geq 10$ mmHg diastolic	<ul style="list-style-type: none"> <li>• Measure baseline blood pressure in the supine position after lying for at least 5 minutes (one measurement)</li> <li>• After standing, obtain one measurement “in the first minute”; second measurement “after standing for three minutes”</li> </ul>

		• Repeat standing measurements “if the blood pressure is still falling”
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*NICE - The National Institute for Health and Care Excellence (United Kingdom)*

*\* Salient instructions from each guideline are highlighted*

*\*\* Diagnosis can also be made based on these thresholds using a head-up tilt to at least 60 degrees on a tilt table(9)*

*\*\*\* In patients with supine hypertension, a decrease  $\geq 30$  mmHg systolic blood pressure “may be a more appropriate criterion”(9)*

*\*\*\*\* From the American Heart Association 2019 Scientific Statement on Measurement of Blood Pressure in Humans(34)*

### **What differential diagnoses to consider?**

With post-prandial hypotension(35), patients may experience similar symptoms to postural hypotension that are triggered by meals, rather than changes in posture. Vaso-vagal syncope (commonly referred to as a “faint”), like postural hypotension, may be accompanied by an acute drop in blood pressure when standing, but tends to occur in younger, otherwise healthy adults. There may be prodromal symptoms before the transient loss of consciousness, including sweating, nausea and pallor. It is usually precipitated by emotional stress, pain, heat, dehydration or a period of prolonged sitting or standing(36). Carotid sinus syndrome causes syncope, near-syncope or unexplained falls due to carotid sinus hypersensitivity, and like postural hypotension, is more common in older people(37). It is difficult to distinguish carotid sinus syndrome from postural hypotension clinically, because there is overlap between the two conditions (they may coexist) and because they cause similar symptoms. Tilt-table testing may help in differentiating the two.

### **What are its complications?**

Postural hypotension worsens physical function, impairing balance and ability to perform activities of daily living(38). Postural hypotension is associated with an increased risk of falls (odds ratio 1.73, 95% CI 1.50–1.99(1)), heart failure (hazard ratio 1.34, 95% CI 1.17–1.52(39)), coronary heart disease (hazard ratio 1.44, 95% CI 1.18–1.75(39)), stroke (hazard ratio 1.64, 95% CI 1.13–2.37(2)), atrial fibrillation (hazard ratio 1.51, 95% CI 1.28–1.79(39)) and all-cause mortality (relative risk 1.50; 95% CI 1.24–1.81(2)), as per evidence from large meta-analyses. Small studies point to an increased risk of cognitive impairment, dementia and depression(3,4).

It is unclear if risk differs between symptomatic and asymptomatic patients and between age groups.

### **How is it managed?**

Treatment for postural hypotension is generally only initiated in symptomatic patients. The clinical significance of postural hypotension that is asymptomatic is unclear.

### *Address reversible causes*

Address reversible causes of postural hypotension (such as drugs, infection, dehydration and anaemia). Further investigations to find out why a patient has postural hypotension will need to be chosen on a case-by-case basis. A one-size-fits-all approach is not suggested – because of the wide range of possible causes of postural hypotension – but examples of tests that may be appropriate in primary care include bloods (the exact ones will depend on the history, but may include FBC, UEs, HbA1C, B12, for example), ECG (if an arrhythmia is suspected) and echocardiogram (if a structural heart problem is suspected). If drug-related causes are suspected, further investigations may be unnecessary. Stopping or reducing the dose of an offending drug or using a modified-release preparation and re-assessing the patient after an appropriate wash-out period should address the symptoms. The wash-out period will depend on the pharmacokinetics of the specific drug in question. Ensure the withdrawn drug is either replaced by another drug or the underlying condition is adequately managed without drugs.

Once postural hypotension has been identified, empower patients to manage their condition through education about their diagnosis (Box 2). Help them understand what postural hypotension is, why it occurs, what causes it and what may make it worse. Things that can worsen symptoms include prolonged standing, eating large meals, drinking alcohol, deconditioning, becoming dehydrated, being in hot environments, taking hot baths/showers and straining(9, 11).

#### **Box 2: What patients need to know**

- What is postural hypotension? Postural hypotension is a drop in blood pressure that happens after standing or changing position. If you feel lightheaded or dizzy when you stand up, or if you have fallen or fainted after getting up from a sitting or lying position, you may have

postural hypotension. Some people with postural hypotension also feel fatigue, weakness, or trouble concentrating when changing positions.

- Postural hypotension is common. It affects about 1 in 5 (20%) of older adults. Your GP can help diagnose it and discuss how best to treat your symptoms.
- Simple lifestyle changes can be incorporated into your daily routine and may help relieve some of the symptoms of postural hypotension, and keep you from feeling dizzy or lightheaded. This includes avoiding sudden and quick movements when changing position from sitting to standing or lying to standing.
- If lifestyle changes aren't enough to control the symptoms, prescription medication may be helpful. Choosing the right medication for you depends on your symptoms, your overall health, and other medications you may be taking.
- There is much uncertainty about which treatment options work best for postural hypotension because little research has been done to show how well they improve symptoms. The studies that have been done are small in number, but they indicate that certain medications (called fludrocortisone, midodrine and droxidopa) might relieve your symptoms.
- If you choose to take a medication, your doctor will closely monitor your health to make sure you are benefiting from the medication, while avoiding its troublesome side effects.
- Depending on what's causing it, postural hypotension may not be eliminated or cured completely. The goal of treatment will be to alleviate your symptoms and lower the risk of having a fall.

### *Treat symptoms*

The aim of treatment is to reduce symptoms and risk of injury. The aim is not to try to normalise the magnitude of the postural fall in blood pressure, because its correlation with symptoms<sup>(13)</sup> and the risk of complications is not established. Asymptomatic postural hypotension is not currently treated.

Box 3 lists common non-pharmacological measures that may be suggested in practice. However, recent systematic reviews highlight that there is no high-quality evidence on their benefit to support their efficacy(11, 40, 41). The studies are limited in number and most are small with a short period of follow-up. Lower limb and abdominal compression therapy may offer some benefit, but the evidence is of very low quality(40).

**Box 3: Non-pharmacological treatments for postural hypotension**

- Change position slowly and in stages from lying to sitting to standing, rather than lying to standing in a swift motion
- Maintain adequate hydration
- Avoid alcohol, large meals, very warm environments and hot showers/baths
- Sleep with the head of the bed elevated
- Exercise programmes
- Various physical manoeuvres (such as crossing the legs while standing and tensing the muscles in the legs/buttocks after standing)
- Lower limb compression
- Abdominal binders

Pharmacological treatment (Table 3) may be needed if symptoms are not well-controlled by conservative measures. It is usually started by a specialist (or after discussion with a specialist) but can be modified in primary care. Which specialist a patient is referred to will depend on what the referring clinician suspects the underlying cause of the postural hypotension is. For example, a young patient with repeated unexplained syncopal symptoms and palpitations would most appropriately be referred to a cardiologist, an older patient who has bradykinesia and a shuffling gait to a neurologist and a frail patient with multi-morbidity and polypharmacy with recurrent falls to a geriatrician. When or if a patient is referred will depend on whether a cause can be identified and corrected in primary care or whether postural hypotension is unexplained and occurring persistently and frequently (this will require more urgent referral or discussion with a specialist than postural hypotension that has a transient cause which has been corrected). Patients



will need to be reviewed regularly to monitor for side effects (including standing and supine hypertension) and to up-titrate doses if symptoms remain poorly controlled. If side-effects worsen a patient's quality of life more than the symptoms of postural hypotension, consider stopping the drug. Note that prescribing practices may vary and be dictated by local guidelines. In the UK, for example, NICE advises that fludrocortisone for postural hypotension is off-label, while midodrine is indicated only for people with postural hypotension due to autonomic dysfunction (use for other types of postural hypotension is off-label)(42). Droxidopa does not yet have market authorization for use in postural hypotension in the UK.

Systematic reviews and meta-analyses of small randomized controlled trials with short durations of follow-up indicate fludrocortisone, midodrine and droxidopa may each reduce some of the symptoms of postural hypotension but, as is the case with non-pharmacological treatment options, the evidence is weak so the efficacy of these drugs in improving symptoms remains uncertain (43-45). Because studies with longer follow up have not yet been done, it is not known how long patients should try treatment before they can expect to see benefit from it.

*Table 3: Summary of pharmacological treatment options for postural hypotension; based on information from the NICE fludrocortisone and midodrine evidence summaries(30, 42) and the 2017 joint American Autonomic Society and National Parkinson Foundation consensus panel recommendations(22). The drugs listed in this table have been highlighted over other possible drugs because they have been evaluated in systematic reviews and meta-analyses but the evidence supporting their use is currently weak.*

<b>Medication</b>	<b>Mechanism of Action</b>	<b>Dose</b>	<b>Adverse reactions</b>	<b>Other considerations</b>
Fludrocortisone	Synthetic adrenocortical steroid that increases plasma volume by promoting sodium reabsorption	Initial dose: 100 micrograms OD; may be increased to 200 micrograms OD (maximum dose of 400 micrograms OD not typically used due to significant increase in side effects without additional therapeutic benefit)	<ul style="list-style-type: none"> <li>• Hypokalemia, oedema, congestive heart failure, hypertension, headache</li> </ul>	<ul style="list-style-type: none"> <li>• Monitor electrolytes closely during initiation and periodically during maintenance therapy</li> <li>• Use cautiously in patients with heart failure or hypertension</li> </ul>
Midodrine	Prodrug of a sympathomimetic agent which increases vasoconstriction and arterial resistance	Initial dose: 2.5 mg three times daily; may be increased weekly up to 10 mg three times daily	<ul style="list-style-type: none"> <li>• Piloerection, scalp itching, dysuria, supine hypertension, headache, paraesthesias, nausea</li> </ul>	<ul style="list-style-type: none"> <li>• Avoid concomitant use of other sympathomimetics (e.g., TCAs, antihistamines)</li> <li>• Use cautiously in patients with heart failure or renal disease</li> </ul>

				<ul style="list-style-type: none"> <li>• Last dose should be taken 4 hours before bedtime to prevent supine hypertension</li> </ul>
Droxidopa	Prodrug of noradrenaline; the exact mechanism of action for the treatment of postural hypotension is not known, but may be through increased circulating noradrenaline	Initial dose: 100 mg three times daily; may be increased every 24 to 48 hours to max dose of 600 mg three times daily	<ul style="list-style-type: none"> <li>• Headache, nausea, dizziness, supine hypertension</li> </ul>	<ul style="list-style-type: none"> <li>• Use cautiously in patients with heart failure or renal disease</li> <li>• Last dose should be taken 4 hours before bedtime to prevent supine hypertension</li> </ul>

### *Special considerations in hypertensive patients with postural hypotension*

Clinicians usually worry that tight control of blood pressure in a hypertensive patient may cause, or worsen, postural hypotension(46). This is another area of controversy and clinical guidelines for this scenario have not yet been developed, but approaches have been suggested in the literature(46). It may help keeping the following in mind:

(i) different antihypertensive drug classes (such as alpha-blockers, beta-blockers, calcium channel blockers, diuretics, ACE-inhibitors and angiotensin II antagonists) confer different risk of postural hypotension(14) but there is inconsistency between reports that link particular antihypertensive drugs to it(18). In other words, it is not known which class of drug is most likely to cause postural hypotension.

(ii) the number of drugs may be more predictive of postural hypotension than individual drug classes(14) so in a case where a patient has postural hypotension and is on multiple drugs that may be causing it, discontinuing any one of them is likely to reduce symptoms of postural hypotension. Which one to discontinue first will depend on the individual circumstances of a particular patient. For example, if a patient with heart failure develops postural hypotension and is on a beta-blocker, ACE-inhibitor and alpha-blocker, (all of which may cause postural hypotension) it would be reasonable to either reduce the dose (or stop altogether) the alpha-blocker in the first instance, because the beta-blocker and ACE-inhibitor are more likely to be cardioprotective (and therefore important prognostically for a patient with heart failure) than the alpha-blocker.

(iii) uncontrolled hypertension may worsen postural hypotension(46). In a large randomised controlled trial, more intensive blood pressure targets (systolic blood pressure  $\leq 120$  mmHg) were not more likely to cause postural hypotension, compared to standard targets (systolic blood pressure  $\leq 140$  mmHg) – in this particular study, postural hypotension was observed less frequently in the intensive target group, compared to the standard target group, but syncope was more common (47). A recent systematic review and meta-analysis supports this, showing that lower blood pressure treatment goals decreased the risk of postural hypotension(48). An implication of this is that tighter blood pressure control may not necessarily make postural hypotension more likely and it may not be necessary to compromise blood pressure targets in people with postural hypotension.

(iv) When an anti-hypertensive drug is thought to be causing postural hypotension, management options include stopping that drug, using it at a lower dose or substituting it for a different class of drug to see if this resolves the symptoms of postural hypotension. If a drug is stopped or its dose reduced, after an appropriate wash-out period (which will depend on that pharmacokinetics of an individual drug class), reassess patients for symptoms of postural hypotension and for the development of uncontrolled hypertension by monitoring their blood pressure, either through home blood pressure readings or 24-hour blood pressure monitoring. If postural hypotension persists despite removal of the suspected offending drug, consider whether the drug was truly causative and whether it should be re-started, or replaced by another class of drug.

(v) ensure that decisions regarding continuing and/or discontinuing medications are reviewed regularly by asking patients about symptoms of postural hypotension and monitoring their blood pressure, and be mindful that this may require close and co-ordinated partnership between primary and secondary care.

### **Box: Postural hypertension**

Less commonly, patient's blood pressure may rise on standing(49). Postural hypertension remains an under-appreciated clinical finding and there is no consensus on what defines an "exaggerated" increase in blood pressure. and. Most studies consider it an increase in systolic blood pressure  $\geq 20$  mmHg More recent definitions mirror the thresholds for postural hypotension and include an increase in diastolic blood pressure  $\geq 10$  mmHg as well(49). Its prevalence ranges from 1.1% to almost 40%, depending on the cohort studied and definition used(49). Some observational studies suggest it may increase risk of cardiovascular morbidity, including myocardial infarction and stroke, cardiovascular-related mortality and all-cause mortality(49). Further research is needed on the clinical relevance of postural hypertension and the risk of adverse health outcomes to determine if postural variability of blood pressure (regardless of whether it is an increase or decrease) is a worrying clinical sign.

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## Boxes

### What you need to know

1. Postural hypotension is common and usually defined as a drop in systolic blood pressure  $\geq 20$  mmHg and/or diastolic blood pressure  $\geq 10$  mmHg that occurs within three minutes of standing; test for it in people who are symptomatic or present with an unexplained fall.



2. There is no consensus on how postural blood pressure measurements should be taken but home-based monitoring, or multiple measurements over different days, may improve detection rates.
3. Postural hypotension increases risk of falls, cardiovascular diseases and mortality; there is growing, but less strong, evidence that links it to increased risk of dementia and late-life depression, also.
4. It is not known which specific drug classes increase risk of postural hypotension most, but when it comes to antihypertensive medications, the number of drugs is more predictive of postural hypotension than a particular antihypertensive drug class.
5. The aim of treatment, rather than trying to reduce the magnitude of the postural drop in blood pressure, is to reduce symptoms (including risk of injury) and improve quality of life.
6. Current evidence for both non-pharmacological and pharmacological interventions is poor, making it even more important to think about why a patient has postural hypotension in the first place and to re-assess patients following interventions, including when medications have been stopped, to see if there has been any effect on symptoms.

#### Questions for future research

1. What are the health implications of delayed vs classic postural hypotension and what are the most effective treatment options?
2. Is there a difference in adverse health outcomes between symptomatic and asymptomatic postural hypotension?
3. What is the best way to measure/detect postural hypotension?
4. Is there correlation between improvement in the magnitude of the drop in postural blood

pressure and symptoms, and does this translate into reduced risk of complications?

5. What is more important for patients – reducing symptoms of postural hypotension, its complications, or both, and which treatments best meet these criteria?

6. What non-pharmacological management options are best at reducing symptoms of postural hypotension and reducing the risk of a fall?

7. Which classes and combinations of drugs are most likely to cause postural hypotension?

#### Additional educational resources

Review Article: Magkas N, Tsioufis C, Thomopoulos C, Dilaveris P, Georgiopoulos G, Doulas M, et al. Orthostatic hypertension: From pathophysiology to clinical applications and therapeutic considerations. *The Journal of Clinical Hypertension*. 2019;21(3):426-33 (open access)

Review Article: Ricci F, De Caterina R, Fedorowski A. Orthostatic Hypotension: Epidemiology, Prognosis, and Treatment. *Journal of the American College of Cardiology*. 2015;66(7):848-60 (open access)

#### Information resources for patients

Patient information leaflet on postural hypotension and how to manage it, written by the Centre for Disease Control and Prevention. [https://www.cdc.gov/stedi/pdf/Postural\\_Hypotension-print.pdf](https://www.cdc.gov/stedi/pdf/Postural_Hypotension-print.pdf) (free)

#### Education into practice

What is the protocol for taking postural blood pressure measurements at your clinic?

If a patient has suspected drug-induced postural hypotension, and the drug is discontinued, what is your approach to monitoring for improvement in postural hypotension and ensuring that stopping the drug has not worsened another medical problem? If a drug has been stopped in a secondary care setting, how do you effectively and clearly communicate the need for a specific medication review to colleagues in primary care?

#### How patients were involved in the creation of this article

A patient partner through the Patient and Family Advisory Council at Beth Israel Deaconess Medical Center, Tobie Atlas, reviewed the manuscript and provided feedback on sections related to education, management, and goals of therapy for postural hypotension. Tobie was instrumental in the creation of Box 2 (What patients need to know), a patient-centred summary of essential information that doctors can provide to patients with postural hypotension.

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We have read and understood the BMJ policy on declaration of interests and have no relevant interests to declare.

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#### Contributorship statement and guarantor

AG had the idea for the article, performed the literature search and wrote the article. All authors then reviewed and revised the content. All authors approved the final version to be published.

AG is the guarantor.

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