Orthostatic Hypotension:

A Vestibular Physician's Deep Review of Mechanisms, Autonomic Subtypes, and Management

Vestibular Medicine for Vestibular Physicians

Systemic & Multisensory Balance Disorders — Module 4.2

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How to Use This Review

This literature review forms part of the Vestibular Medicine for Vestibular Physicians series published by the Australian Dizziness Clinics Education Hub. It is written for vestibular physicians, neuro-otologists, advanced ENT trainees, and vestibular physiotherapists working at the deep end of systemic and multisensory vestibular practice, where a working command of mechanism, criteria, and atypical presentations is expected rather than optional.

The review is dense by design — intended as a 30–40 minute deep read or a desktop reference. It is supported by an A4 clinician cheat sheet, short-form clinician videos, audio episodes, and a patient information leaflet within the same Education Hub module.

Callout Box Guide

□ **Key Point:** Foundational concepts and summary statements that anchor the core clinical content of each section.

□ **Clinical Insight:** Clinically relevant observations for direct application in assessment and management.

□ **Clinical Pearl:** High-yield memorable clinical points — the take-home messages most likely to change practice.

□ **Important:** Red flags, atypical presentations, and critical safety points requiring escalation or imaging.

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I. Introduction and Epidemiology

Orthostatic hypotension (OH) is defined by a sustained fall in systolic blood pressure (BP) of at least 20 mmHg or diastolic BP of at least 10 mmHg within three minutes of assuming the upright position after at least five minutes of supine rest [1,2]. This operational definition, established by consensus and codified in international guidelines, captures the haemodynamic failure of the gravitational challenge rather than any single underlying mechanism [1]. For the vestibular physician, OH matters because it generates dizziness, presyncope, and near-falls that are phenomenologically indistinguishable from vestibular causes — making it a mandatory entry in the differential diagnosis of postural dizziness [3,4].

Population-based studies establish OH as one of the most prevalent cardiovascular reflexogenic conditions in adults over 65 years. The Rotterdam Study found OH in 16.2% of a community sample aged 55 years and older, rising to 18.5% in those over 75 [5]. The Systolic Blood Pressure Intervention Trial (SPRINT) documented OH in 11.3% of high-cardiovascular-risk adults at enrolment [6]. Because most population studies apply only a two- to three-minute standing protocol, delayed OH (onset after three minutes of standing) is systematically under-counted, and true prevalence is likely higher [7,8]. In dizziness clinic populations specifically, OH and POTS combined account for 10–22% of presentations, and recognition rates improve substantially when an active stand test is performed as a routine part of the initial assessment [3,4,9].

The clinical burden of OH extends well beyond momentary dizziness. Epidemiological data link OH to a 40–70% increased risk of falls and fall-related fractures [10], a two-fold increased risk of incident dementia [11], and an independent association with cardiovascular events and all-cause mortality [12,13]. In the AGES-Reykjavik cohort, OH was associated with white matter hyperintensity burden independent of hypertension, suggesting a direct cerebrovascular injury pathway [14]. The combination of falls, syncope, cognitive change, and dizziness in an older person should always prompt a structured orthostatic evaluation before vestibular-specific investigations [4].

□ **Key Point:** OH is defined by the haemodynamic criterion alone — not by symptoms. Up to 50% of patients with confirmed OH are asymptomatic during measurement, which means the absence of dizziness during the test does not exclude OH as the cause of reported symptoms [1,2].

Age and sex distribution

OH prevalence increases steeply with age, driven by progressive impairment of baroreceptor sensitivity, reduced vascular compliance, and age-related autonomic neuropathy [5,15]. In those under 40, OH is uncommon except in the context of dehydration, medication effect, or autonomic disorders such as pure autonomic failure. In the eighth decade, OH is present in up to one-third of community-dwelling adults and in over half of nursing-home residents [5,16]. Sex differences are modest in older populations, but in younger cohorts POTS (the related syndrome of postural tachycardia) shows a pronounced female predominance of approximately 4:1 [17].

Table 1. OH Prevalence and Clinical Impact by Age Group.

Age Group	OH Prevalence	Falls Risk	Syncope Risk	Key Association
< 40 years	< 2% (community)	Mild	Low	Medication, dehydration, POTS
40–65 years	5–8% [5,6]	Moderate 1.4x	Moderate	Hypertension treatment, diabetes
65–75 years	12–18% [5,6]	High 1.7x [10]	High	Polypharmacy, early neurodegeneration
> 75 years	18–35% [5,16]	Very high 2.4x	Very high	Neurogenic OH, MSA, PAF, Parkinson's
Nursing home	Up to 50% [16]	Extreme	Extreme	Multimorbidity, polypharmacy, frailty

The economic burden is substantial. In Australia, falls-related hospitalisations attributable to syncope and presyncope cost an estimated AUD 560 million annually [10]. OH-related syncope is the second most common cause of emergency department syncope presentations after vasovagal syncope, and the overlap with cardiac syncope means it is frequently over-investigated with prolonged monitoring when simple orthostatic testing would be diagnostic [3,18].

Pathophysiological classification of OH by mechanism

A mechanistic classification of OH complements the temporal classification of the five orthostatic syndromes and directly informs management [1,15,22]. Volume-depleted OH occurs when total body sodium and water are reduced by diuretics, vomiting, diarrhoea, heat exposure, or inadequate oral intake — the reflex arc is intact but overwhelmed by insufficient filling pressure [1,22]. Drug-induced OH accounts for a significant proportion of OH in older adults on polypharmacy; implicated classes include antihypertensives, alpha-adrenoceptor blockers, diuretics, vasodilators, phosphodiesterase-5 inhibitors, tricyclic antidepressants, L-DOPA, and dopamine agonists [3,15,22]. Adrenal insufficiency — primary (Addison's disease) or secondary (exogenous steroid withdrawal) — impairs volume retention and vascular tone through mineralocorticoid and glucocorticoid deficiency and is a reversible cause of severe OH that must be excluded in new-onset cases [22]. Venous pooling in the absence of volume depletion is characteristic of deconditioning, prolonged bed rest, and varicose vein disease — the skeletal muscle pump is inadequate rather than the baroreflexive response [19,25].

Drug-induced OH deserves particular attention in the vestibular clinic because it is common, reversible, and frequently missed in medication reconciliation. A structured medication review asking specifically about antihypertensives (especially alpha-1 blockers used for benign prostatic hyperplasia), tricyclic antidepressants used for chronic pain or neuropathy, and L-DOPA in Parkinson's disease should be a standard component of the vestibular history in any patient with postural dizziness [3,22,42]. A drug causes table is provided in Table 5 (Section VIII) to guide systematic prescribing review.

II. Pathophysiology — Cardiovascular Reflexes and Autonomic Control

The haemodynamic challenge of standing is acute and substantial. On assumption of the upright posture, approximately 500–1000 mL of blood shifts from the thorax to the capacitance vessels of the abdomen and lower limbs within 10–15 seconds [1,19]. This abrupt reduction in central venous return causes a transient fall in cardiac filling (preload), stroke volume, and cardiac output, with a consequent brief drop in arterial BP of 20–40 mmHg [19,20]. In healthy individuals, this is corrected within three to five seconds by a coordinated autonomic reflex arc involving baroreceptor unloading, brainstem integration, and sympathetic-adrenergic effector responses [1,20].

Figure 1. Cardiovascular Autonomic Reflex Arc

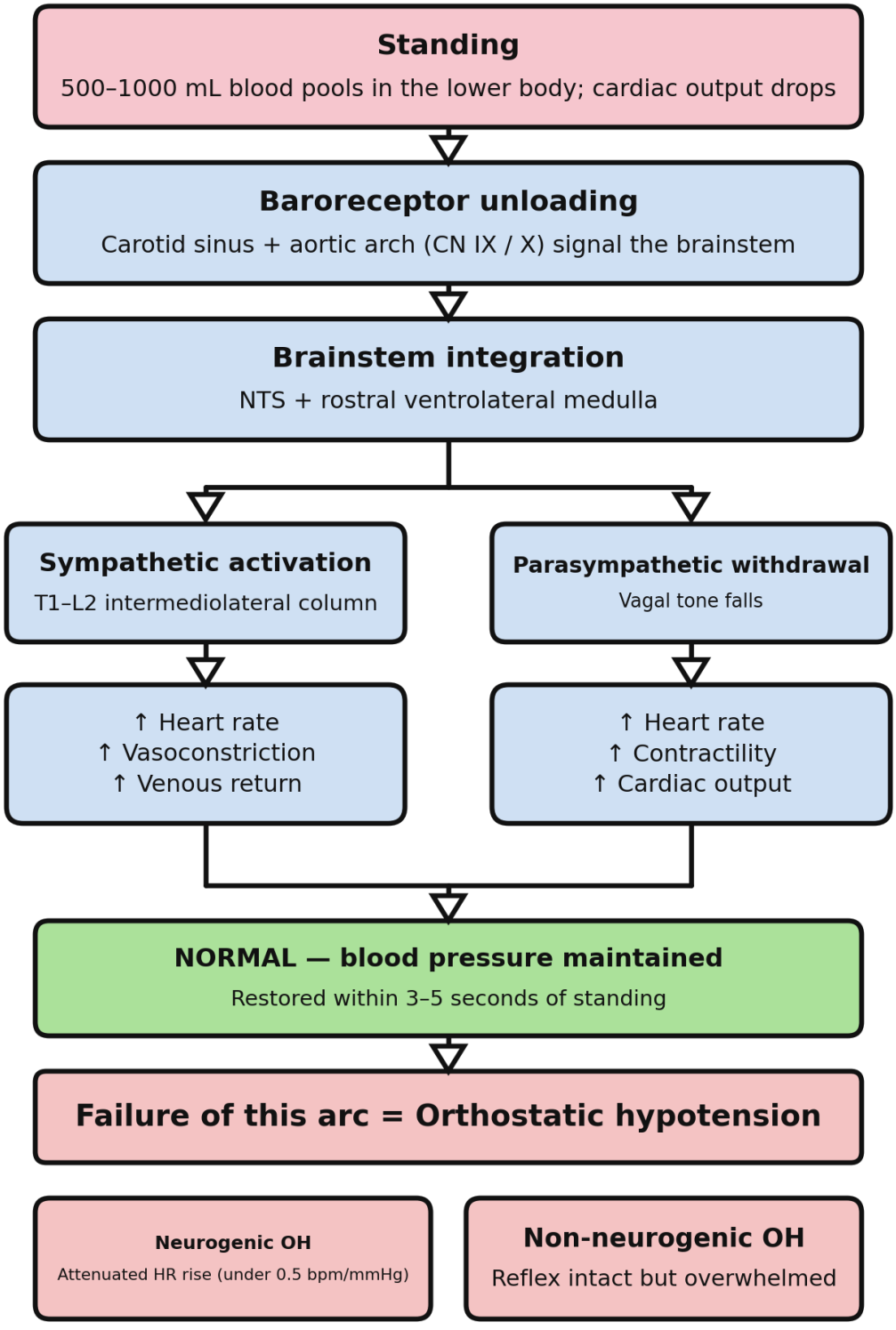


Figure 1. Cardiovascular Autonomic Reflex Arc — Normal vs. Failed Response.
Source: Adapted from Freeman et al. [1] and Low et al. [19].

The baroreceptors of the carotid sinus and aortic arch are the primary sensors [19,21]. Their afferent signals travel via the glossopharyngeal (CN IX) and vagus (CN X) nerves to the nucleus tractus solitarius (NTS) in the medulla, which relays via the rostral ventrolateral medulla (RVLM) to the spinal cord and cranial nerve nuclei [19,21]. Sympathetic efferents exit the thoracolumbar cord (T1–L2) and act on alpha-1 adrenoceptors in arteriolar smooth muscle to raise peripheral resistance, while beta-1 stimulation

increases heart rate and cardiac contractility [19]. Simultaneous vagal (parasympathetic) withdrawal removes tonic HR suppression, allowing the full chronotropic response [21]. The integrated result — increased systemic vascular resistance and cardiac output — restores BP to within 3–5 seconds of the initial haemodynamic perturbation [19,20].

Mechanisms of failure

OH arises when this reflex arc is inadequate relative to the haemodynamic load. The failure can be categorised by whether the efferent autonomic limb is structurally intact [1,22]. In non-neurogenic OH — the most common form — the reflex arc is functionally normal but overwhelmed by factors that either increase the haemodynamic challenge (volume depletion, venous pooling, post-prandial splanchnic diversion) or pharmacologically blunt the effector response (alpha-adrenergic blockade, diuretics, beta-blockade, L-DOPA, sildenafil) [1,2,22]. In neurogenic OH, the autonomic efferent pathway is structurally damaged and the compensatory HR rise is absent or markedly blunted — defined operationally as a HR rise of less than 0.5 beats per minute per mmHg of BP fall during orthostatic challenge [23,24].

□ **Clinical Insight:** The HR/BP ratio is the bedside discriminator of neurogenic vs. non-neurogenic OH. Non-neurogenic OH generates a vigorous compensatory tachycardia (often > 15 bpm); neurogenic OH does not. Document both the BP fall and the HR change at every active stand test [23,24].

Venous pooling and skeletal muscle pump

Skeletal muscle contraction in the calf and thigh provides an auxiliary pump that returns venous blood to the thorax during standing and walking [19,25]. Deconditioning, prolonged bed rest, and peripheral oedema all reduce this muscular pump effect and increase orthostatic pooling [25]. Abdominal compression garments and physical counter-manoeuvres (leg crossing, squatting, tensing thigh muscles) work by augmenting venous return via the skeletal muscle pump — the mechanistic basis for their clinical utility [25,26].

Post-prandial and post-exercise orthostatic hypotension

Post-prandial OH — a clinically relevant sub-entity in older adults and those with neurogenic disease — occurs because splanchnic vasodilatation for digestion competes with the orthostatic haemodynamic demand [7,15]. BP falls of up to 30 mmHg occurring within 15–90 minutes of a meal are well documented in Parkinson's disease and MSA [7]. Vestibular physicians should ask specifically about meal-related dizziness or falls, as this sub-type is treatable with post-meal rest, smaller portion sizes, and avoidance of alcohol at mealtimes [7,15]. Post-exercise OH is a less-recognised entity in which muscular vasodilatation persists after exercise ceases, creating orthostatic stress in the recovery period [25].

Renin-angiotensin-aldosterone system and volume regulation

The renin-angiotensin-aldosterone (RAAS) axis provides the intermediate-term haemodynamic defence against sustained volume depletion and is a critical component of the orthostatic BP maintenance system beyond the acute baroreceptor reflex [19,26]. Reduced renal perfusion pressure and sympathetically driven renin release increase angiotensin II, which elevates peripheral resistance and stimulates aldosterone-mediated renal sodium retention [26]. In OH management, fludrocortisone exploits this axis directly — acting as a supraphysiological mineralocorticoid to expand plasma volume over days to weeks [42]. Inhibition of the RAAS by ACE inhibitors, angiotensin receptor blockers, or spironolactone worsens orthostatic tolerance by impairing volume retention and vasoconstriction — a clinically important interaction in older patients managed for heart failure or chronic kidney disease who develop OH [15,26,42].

Efferent sympathetic anatomy and sites of failure

The efferent sympathetic pathway descends from the hypothalamus and RVLM through the lateral tegmental tract to the thoracolumbar intermediolateral (IML) cell column (T1–L2) [19,21]. Preganglionic myelinated B fibres synapse in the paravertebral sympathetic chain ganglia; postganglionic unmyelinated C fibres innervate resistance arterioles, capacitance veins, the heart, and adrenal medulla [19,21]. Neurogenic OH can arise from failure at any of these anatomical levels — and the site of failure provides

diagnostic clues [23,24]. Central (preganglionic) failure, as in MSA and spinal cord lesions, typically produces severe OH with absent sweating (anhidrosis) above the lesion level and preserved peripheral axon reflexes [31]. Peripheral (postganglionic) failure, as in PAF and diabetic CAN, produces absent axon reflexes on the thermoregulatory sweat test and very low supine plasma noradrenaline levels, reflecting denervation of the peripheral sympathetic terminals [32,37]. Ganglionic failure, as in autoimmune autonomic ganglionopathy (AAG), can affect both sympathetic and parasympathetic ganglia simultaneously, producing severe global autonomic failure with dry mouth, urinary retention, and intestinal dysmotility alongside OH [34].

□ **Clinical Insight:** The thermoregulatory sweat test (TST) footprint distinguishes central from peripheral neurogenic OH: central lesions produce segmental anhidrosis matching the neuroanatomical level; peripheral lesions produce length-dependent distal anhidrosis. Request TST when the site of autonomic failure will change management [37].

III. Clinical Features and the Five Orthostatic Syndromes

The five orthostatic syndromes — initial OH, classical OH, delayed OH, neurogenic OH, and POTS — share the common trigger of standing but differ in timing, magnitude, underlying mechanism, and treatment response [1,2,8]. Recognising which syndrome is present requires systematic orthostatic testing, not merely a single BP reading at one minute of standing. A truncated test protocol is the single most common reason for missing delayed OH and POTS in clinical practice [7,8].

Figure 2. The Five Orthostatic Syndromes

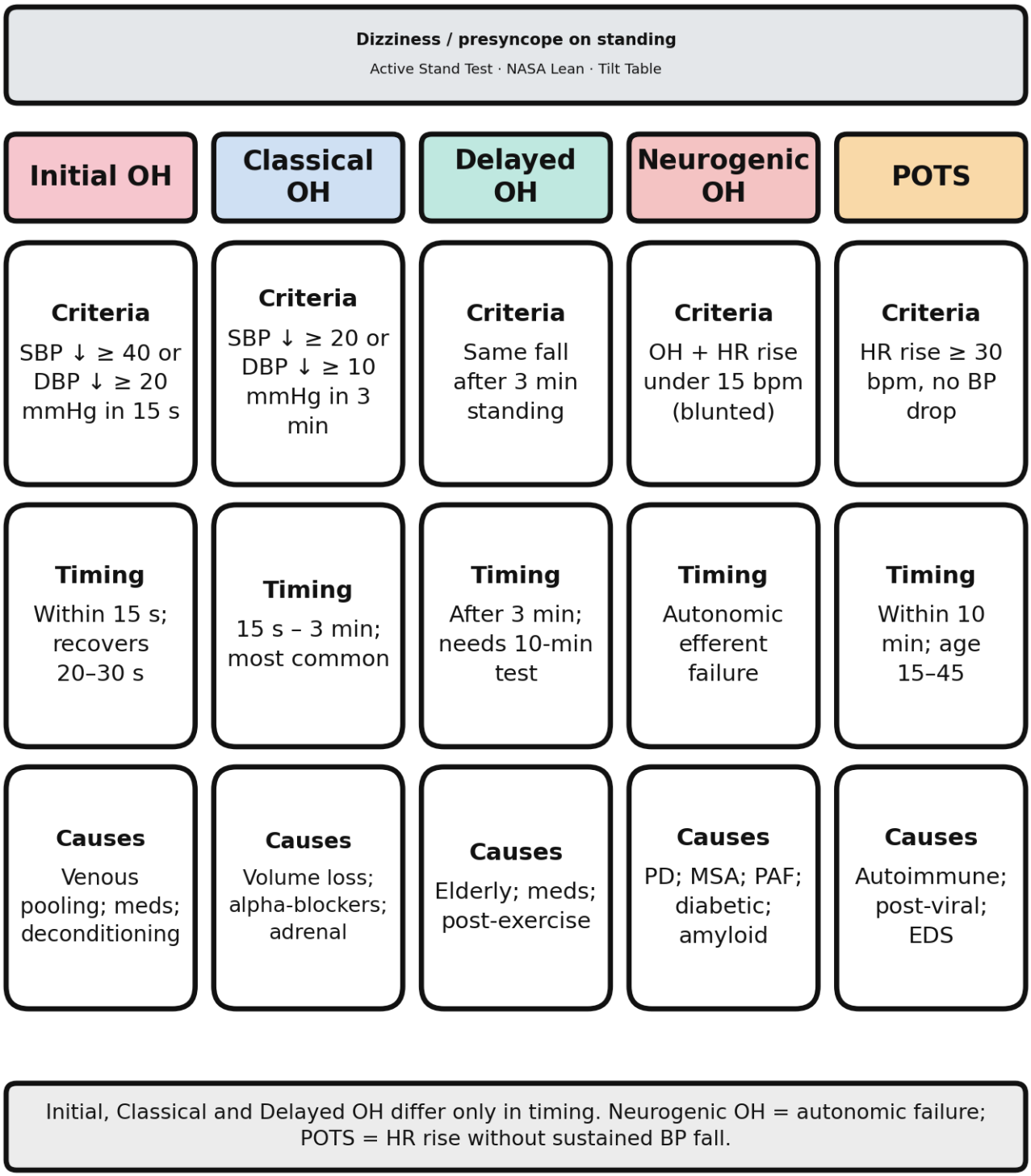


Figure 2. The Five Orthostatic Syndromes — Classification, Criteria, and Typical Causes.
Source: Adapted from Freeman et al. [1], Fedorowski [2], and Sheldon et al. [8].

Initial orthostatic hypotension

Initial OH — defined by a BP drop of at least 40 mmHg systolic or 20 mmHg diastolic within 15 seconds of standing — reflects the normal early haemodynamic perturbation that is amplitude-amplified by medication and positional factors [2,8]. Because the nadir resolves within 30 seconds and standard measurement protocols sample at 1 minute, initial OH is invisible on most clinic tests. Continuous BP

monitoring (Finometer/Portapres) is required for definitive diagnosis [8,27]. Clinically, patients report a brief blur or grey-out immediately on standing, resolving within seconds — a history that is pathognomonic for initial OH and separates it from classical presyncope [8].

Classical orthostatic hypotension

Classical OH meets the consensus definition (SBP fall >=20 or DBP fall >=10 mmHg within three minutes of standing) and is the most prevalent subtype in clinical populations [1,5]. Symptoms include dizziness, presyncope, visual blurring, and coat-hanger neck–shoulder pain reflecting cervical muscle ischaemia — a symptom that is not widely recognised but is present in up to 40% of patients [28,29]. The compensatory HR response differentiates non-neurogenic from neurogenic classical OH [23,24].

Delayed orthostatic hypotension

Delayed OH requires BP fall criteria to be met only after three minutes of sustained standing. It is prevalent in the elderly, in early autonomic neuropathies, and in post-prandial contexts [7,8]. Population studies with extended protocols (10–20 minutes standing) find delayed OH in a substantial proportion of older adults who test negative on standard three-minute protocols [7]. The NASA Lean Test (passive leaning against a wall for 10 minutes) is a practical non-laboratory alternative to tilt table testing for eliciting delayed OH [30].

Neurogenic orthostatic hypotension

Neurogenic OH is identified by the failure of compensatory HR rise — less than 0.5 bpm per mmHg of BP fall — in the context of confirmed OH [23,24]. This operational criterion identifies efferent sympathetic failure without requiring formal autonomic laboratory testing in most cases. The absence of an adequate tachycardia means the BP drop is sustained rather than brief, and symptoms are typically more severe and prolonged than in non-neurogenic classical OH [23]. Neurogenic OH is the hallmark feature of multiple system atrophy (MSA), pure autonomic failure (PAF), late Parkinson's disease, and diabetic autonomic neuropathy [24,31,32].

Postural orthostatic tachycardia syndrome (POTS)

POTS is defined by a sustained heart rate increase of at least 30 beats per minute (bpm) within ten minutes of standing (or >=40 bpm in adolescents aged 12–19 years), in the absence of sustained BP fall meeting classical OH criteria [17,33]. The haemodynamic perturbation is one of excessive HR compensation rather than inadequate autonomic response, reflecting partial sympathetic activation (excess noradrenaline release) or peripheral venous pooling due to small fibre neuropathy [17,34]. POTS predominantly affects women of reproductive age and may be triggered by prolonged deconditioning, infection (including post-COVID syndrome), autoimmune autonomic ganglionopathy (anti-AChR-g, anti-NET antibodies), or hypermobility spectrum disorder [17,34,35].

□ **Clinical Pearl:** Coat-hanger pain — aching in the neck and shoulders on prolonged standing — is a near-specific symptom of OH reflecting ischaemia of the trapezius and neck extensors. Presence of this symptom in a dizziness history increases the pre-test probability of OH substantially [28,29].

Table 2. The Five Orthostatic Syndromes — BP/HR Criteria and Distinguishing Features.

Syndrome	BP Criterion	HR Change	Onset Timing	Key Mechanism
Initial OH	SBP >=40 or DBP >=20 mmHg fall	HR rises appropriately	< 15 seconds	Normal reflex, amplified perturbation
Classical OH	SBP >=20 or DBP >=10 mmHg fall	HR rises (non-neurogenic) or blunted (neurogenic)	15 sec – 3 min	Volume, medication, or autonomic failure
Delayed OH	Same BP criteria as classical	Variable	> 3 minutes	Age, early autonomic, prandial
Neurogenic OH	Same BP criteria + blunted HR	< 0.5 bpm/mmHg BP fall	Variable (often rapid)	Efferent sympathetic failure

POTS	BP maintained (or minor drop)	HR rise >=30 bpm (>=40 in teens)	Within 10 min	Venous pooling + noradrenaline excess

IV. Diagnostic Criteria — Active Stand Test, NASA Lean Test, Tilt Table Testing

The active stand test (AST) is the cornerstone of OH diagnosis in clinical practice [1,2,36]. Its advantages over tilt table testing are accessibility (no specialised equipment), physiological realism (active standing engages the skeletal muscle pump), and brevity. The standard protocol requires: five minutes of supine rest followed by active standing; BP and HR measurement by validated automated sphygmomanometer at 30 seconds, 1 minute, 3 minutes, 5 minutes, and 10 minutes; averaging of at least two supine readings for the baseline [1,36]. Extended protocols to 10 or 20 minutes are required when delayed OH or POTS is suspected [8,30].

Figure 3. Active Stand Test — Protocol and Interpretation

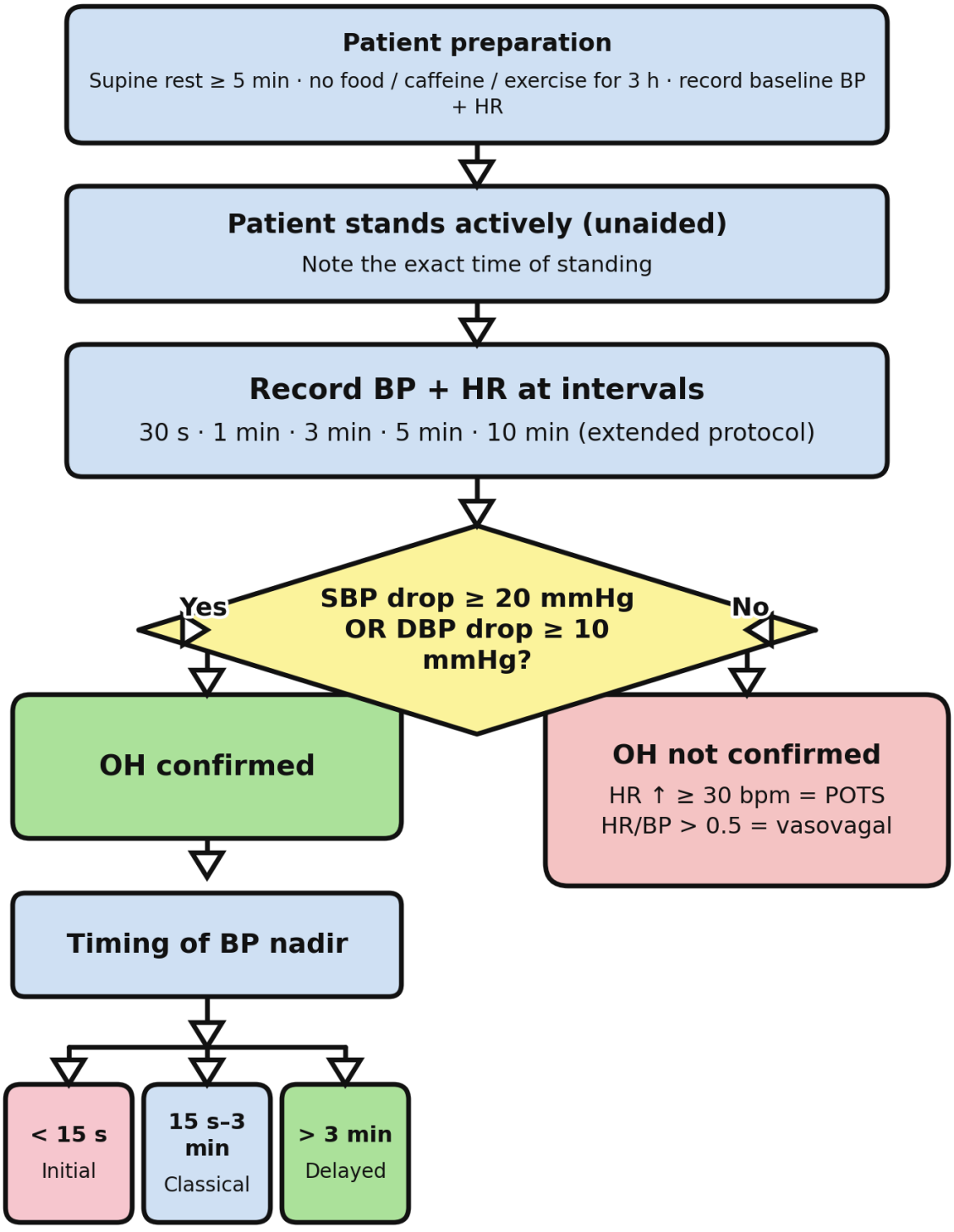


Figure 3. Active Stand Test — Protocol and Interpretation.
Source: Adapted from Freeman et al. [1] and Sheldon et al. [8].

Technical requirements

Common errors invalidate the AST result. Insufficient supine rest (less than five minutes) inflates the baseline BP, artificially reducing the measured fall. Delayed measurement after standing (recording at >

2 minutes only) misses early and initial OH. A single reading without an averaged baseline introduces measurement noise that exceeds the diagnostic threshold. For all clinical OH testing, a calibrated oscillometric device should be used on the same arm throughout the test, with the cuff at heart level during standing [1,36]. Continuous photoplethysmographic BP monitoring (Finapres, Portapres) provides beat-to-beat precision and is recommended for initial OH and POTS characterisation, though it is not required for classical or delayed OH diagnosis [27,36].

NASA Lean Test

The NASA Lean Test (NLT) offers a simple, non-laboratory alternative to tilt table testing for detecting delayed and neurogenic OH [30]. The patient stands with shoulders and buttocks resting against a wall, feet 15–30 cm from the wall, for 10–20 minutes, with BP and HR recorded at 2-minute intervals. The passive lean position removes the skeletal muscle pump contribution, increasing the haemodynamic challenge relative to active standing — potentially unmasking OH that is borderline on AST [30]. In autonomic medicine practice, the NLT has been validated against head-up tilt in neurogenic OH populations, with sensitivity of 86% and specificity of 91% at 20 minutes [30]. Its availability with standard clinic equipment makes it practical for any vestibular clinic.

Head-up tilt table testing

Tilt table testing (TTT) at 60–80 degrees provides controlled, reproducible orthostatic stress without muscular activation, making it the reference standard for complex syncope investigations [18,36]. In the assessment of OH specifically, TTT adds value when: the AST/NLT result is borderline; POTS is suspected; vasovagal syncope needs differentiation from OH; or a patient cannot stand actively [18,36]. The addition of sublingual glyceryl trinitrate or isoproterenol provocation (GTN tilt protocol) increases sensitivity for vasovagal reflex syncope at the cost of specificity [18]. For OH, pharmacological provocation is not required. In neurogenic OH populations, TTT with simultaneous plasma noradrenaline measurement (supine and 10 minutes tilt) provides biochemical confirmation of efferent sympathetic failure [24,37].

□ **Important:** Tilt table testing is contraindicated in acute aortic stenosis, haemodynamically significant coronary artery disease, and acute MI within the preceding three months. Always screen for these before referral. In OH assessment, the active stand test is safe in all patients and should be performed before considering tilt table referral [18,36].

Protocol adherence and common test errors

The diagnostic sensitivity of the AST is highly dependent on protocol adherence [1,36]. Common errors that generate false-negative results include: measuring BP more than 90 seconds after standing, which misses the maximal early BP fall; testing in the immediate post-prandial state when splanchnic pooling amplifies haemodynamic perturbation and may generate artefactual false positives; using an arm cuff on the dominant arm while the patient holds a chair for balance (positional artefact); and recording only one standing measurement rather than serial readings [1,36]. The 2018 ESC syncope guidelines specify that an adequate test requires at least three readings within three minutes of standing for classical OH diagnosis, extended to 10 minutes when POTS or delayed OH is suspected [18]. In clinical practice the commonest oversight is truncating the test at two to three minutes, missing both delayed OH and POTS — a two-minute protocol identifies only the minority of cases that peak within that window [7,8,30].

For vestibular clinics without continuous photoplethysmographic monitoring, a practical protocol upgrade is to extend all negative standard ASTs to 10 minutes of standing. This seven-minute extension per patient substantially improves yield for delayed OH and POTS without additional equipment [8,30]. The NASA Lean Test can substitute for active standing in patients with gait impairment, lower limb weakness, or labyrinthine instability where active standing generates disproportionate vestibular perturbation that confounds symptom reporting [30]. Continuous photoplethysmographic monitoring (Finapres, Portapres, or wrist-based photoplethysmography) provides beat-to-beat resolution that reveals initial OH (transient fall within 15 seconds), characterises the BP recovery curve shape, and allows reliable POTS HR quantification — all of which are invisible on standard oscillometric measurements taken at 1-minute intervals [27,36].

V. Investigations and Autonomic Profiling

The diagnostic work-up for OH has two tiers: a first-tier evaluation to identify common reversible causes, and a second-tier autonomic profiling for cases where neurogenic OH is confirmed or suspected [1,24,37]. First-tier investigations are appropriate in every patient with newly confirmed OH and include: a medication review (focused on antihypertensives, alpha-blockers, diuretics, tricyclic antidepressants, dopaminergic drugs, phosphodiesterase-5 inhibitors, and opioids); blood tests for anaemia, electrolyte abnormalities, renal function, and random glucose; a 12-lead ECG for arrhythmia and conduction disease; and lying/standing BP pair documented in the clinical record [1,3,36].

Table 3. Investigations in Confirmed OH — First-Tier and Autonomic Profiling.

Investigation	Indication	What It Provides	Tier
Medication review	All patients	Identify drug-induced OH (alpha-blockers, diuretics, TCAs, L-DOPA, PDE5i)	First
FBC, U&E, glucose	All patients	Exclude anaemia, hyponatraemia, dehydration, diabetes	First
12-lead ECG	All patients	Arrhythmia, conduction disease, bradycardia	First
24-hour ambulatory BP	All patients with confirmed OH	Supine hypertension, nocturnal dipping, diurnal pattern	First
Lying + standing plasma NE	Neurogenic OH suspected	Autonomic efferent failure (supine NE low, no rise on standing)	Second
Autonomic battery (HRV, Valsalva, QSART)	Neurogenic OH or neuropathy screen	Quantify sympathetic / parasympathetic function	Second
Skin biopsy (intraepidermal nerve fibre density)	Small fibre neuropathy suspected (POTS, diabetes)	Quantify distal small fibre loss	Second
Anti-AChR-g / anti-NET antibodies	POTS or autoimmune OH suspected	Autoimmune ganglionopathy	Second
MRI brain / spine	Neurogenic OH with neurological signs	MSA, posterior fossa lesions, spinal cord involvement	Second
Paraneoplastic panel	Subacute neurogenic OH in older adults	Anti-Hu, ANNA-1 (anti-neuronal)	Second

Supine hypertension — elevated BP in the supine position — is present in 30–50% of patients with neurogenic OH and represents an important and dangerous comorbidity [38]. The impaired baroreflexive buffering in autonomic failure allows unopposed sympathetic tone when supine, driving BP to dangerous levels (often 160–200 mmHg systolic). Treatment of supine hypertension with antihypertensives paradoxically worsens orthostatic symptoms by reducing the already-low standing BP reserve [38]. Management requires a specific protocol: head-up bed tilt of 10–30 degrees during sleep, avoiding supine rest in the daytime, and if pharmacological treatment is needed, short-acting agents at bedtime (captopril, losartan, patch nitroglycerin) [38].

Autonomic function testing battery

The full autonomic laboratory battery provides quantitative assessment of each autonomic effector pathway [37]. Heart rate variability (HRV) analysis during deep breathing (deep breathing test) evaluates cardiac vagal function — a normal E:I ratio excludes severe parasympathetic denervation [37]. The Valsalva manoeuvre — sustained expiratory effort against resistance — provides the Valsalva ratio (maximum HR/minimum HR), testing cardiac sympathetic and parasympathetic function, and the late phase II BP overshoot, which specifically tests adrenergic vasoconstriction [37,39]. Quantitative sudomotor axon reflex testing (QSART) and thermoregulatory sweat test evaluate postganglionic

sudomotor function and can localise autonomic neuropathy to preganglionic vs. postganglionic lesions [37]. The thermoregulatory sweat test (TST) is the more sensitive test for sweat-distribution abnormalities in small-fibre and length-dependent neuropathies [37].

Plasma noradrenaline — the biochemical discriminator

Measurement of plasma noradrenaline in the supine position and after 10 minutes of standing (or tilt) provides direct biochemical evidence of sympathetic efferent function [24,37]. In non-neurogenic OH, standing noradrenaline rises appropriately above 600 pg/mL, reflecting intact postganglionic noradrenaline release [37]. In peripheral neurogenic OH (PAF, diabetic CAN), supine noradrenaline is characteristically low (below 100 pg/mL) because the postganglionic terminals are denervated and cannot synthesise or release noradrenaline [32,37]. In central (preganglionic) neurogenic OH (MSA), supine noradrenaline may be near-normal (100–200 pg/mL) but fails to rise on standing because the efferent preganglionic signal is absent — this pattern differentiates MSA from PAF and has implications for droxidopa responsiveness [31,32]. Peripheral PAF responds better to droxidopa (which replaces the missing noradrenaline) than central MSA, where droxidopa is also effective but via a different mechanism (peripheral conversion supplementing absent central drive) [24,44].

Drug causes of OH — systematic review before pharmacological treatment

A structured medication deprescribing review is indicated in all patients with newly confirmed OH, particularly before pharmacological treatment is initiated [3,15,22]. The review should specifically query dose timing — midodrine taken at bedtime, antihypertensives dosed on waking, and diuretics in the morning all create predictable pharmacokinetic windows of maximal OH risk [42,43]. Reviewing the prescribing history in the context of when orthostatic symptoms began often reveals a temporal association with a medication change that is therapeutically actionable without adding another agent. The drug causes table below classifies the most clinically important OH-inducing agents by mechanism.

□ **Clinical Insight:** 24-hour ambulatory BP monitoring is underused in OH management. It identifies the common pattern of supine hypertension with orthostatic hypotension, informs the timing of medication doses, and tracks response to treatment far better than clinic BP measurements alone [38].

VI. Differential Diagnosis

The differential diagnosis of positional dizziness and presyncope on standing is broad. The vestibular physician must systematically distinguish OH from: (a) vestibular causes of positional dizziness, particularly BPPV; (b) cardiac syncope; (c) vasovagal reflex syncope; (d) PPPD (persistent postural-perceptual dizziness); and (e) cerebrovascular disease [3,4,40]. The history, orthostatic testing, and a focused vestibular examination in most cases allow confident differentiation without imaging [4].

Table 4. Differential Diagnosis of Dizziness/Presyncope on Standing.

Condition	Typical History	Orthostatic Test	Key Differentiator
Classical OH	Dizziness within 1–3 min of standing, resolves on sitting	BP fall >=20/10 mmHg	BP criterion met; HR response discriminates neurogenic vs. non-neurogenic
Vasovagal syncope	Prolonged standing / emotion / pain trigger; prodrome (warmth, nausea, blurred vision)	BP falls with HR slowing (cardioinhibitory) or mixed	Prodrome + trigger + cardioinhibitory HR response
BPPV	Brief (< 60 sec) rotatory vertigo with specific head movements (Dix-Hallpike positive)	BP normal	Nystagmus on Dix-Hallpike; no BP change
Cardiac syncope	Sudden loss of consciousness, brief / no prodrome, may occur supine	BP often normal (monitor for arrhythmia)	ECG abnormality; structural heart disease; no postural trigger pattern

PPPD	Chronic daily dizziness worse with complex environments; no brief postural trigger	BP normal	Chronic course; no BP criterion; vestibular processing disorder
Vertebrobasilar TIA	Vertigo + posterior fossa symptoms (diplopia, dysarthria, dysphagia, ataxia)	BP normal or elevated	Focal neurological signs; age/vascular risk factors; imaging
POTS	Tachycardia on standing; fatigue, palpitations, brain fog in young women	HR rise >=30 bpm; BP maintained	HR criterion without sustained BP fall
Carotid sinus syndrome	Syncope/presyncope triggered by head turning, shaving, tight collar	Normal AST; CSS on carotid massage	Carotid massage: HR/BP response

BPPV is the most important vestibular mimic because it also presents with dizziness on positional change. The distinguishing features are mechanistically clear: BPPV symptoms are triggered by specific head movements (not gravitational blood pressure changes), last less than one minute, and are accompanied by characteristic nystagmus on Dix-Hallpike or supine roll testing [40]. Orthostatic BP is normal. Conversely, OH presents with progressive dizziness or greying-out specifically on standing, without rotatory character or nystagmus, and with BP fall on AST [3,4]. The co-occurrence of BPPV and OH is not rare — older patients may have both — and both should be assessed in the same consultation [4].

PPPD deserves specific mention because its symptoms worsen with standing and complex visual environments, superficially mimicking OH. BP is normal in PPPD. The clinical distinction is in the temporal pattern: PPPD dizziness is persistent throughout the day, not confined to the postural transition, and is driven by maladaptive sensory weighting rather than haemodynamic compromise [40]. When PPPD and OH co-exist — as may occur after an index syncopal event that generates health anxiety and postural hypervigilance — both components require treatment.

Vestibular neuritis and orthostatic hypotension — the acute presentation overlap

Acute vestibular neuritis (VN) can superficially overlap with the presentation of initial or classical OH when the primary complaint is sudden dizziness or a sense of collapse. The clinical differentiation is straightforward with a structured assessment: VN generates constant spontaneous nystagmus in the acute phase (inhibited by gaze fixation), unsteadiness disproportionate to lying or sitting, and positive HINTS examination features (normal head impulse test toward the affected side would be abnormal and reassuring for peripheral disease, while normal HIT plus direction-changing nystagmus is a central alarm) [4]. OH generates no spontaneous nystagmus, no head-impulse abnormality, and symptoms confined to the postural transition [3,4]. Where genuine diagnostic uncertainty exists in the acute setting — particularly in an older patient with both vascular risk factors and medication polypharmacy — performing the HINTS battery and AST simultaneously resolves the diagnosis in a single assessment [4].

Vertebrobasilar insufficiency and posterior circulation TIA

Posterior circulation transient ischaemic attack (TIA) generates episodic vertigo that may superficially resemble OH-related presyncope when the primary complaint is brief postural dizziness [4,13]. The discriminating features are: (1) focal posterior fossa symptoms accompanying the vertigo (diplopia, dysarthria, facial numbness, unilateral limb weakness, Horner syndrome, dysphagia); (2) sudden onset without the few seconds of standing that precede OH symptoms; (3) duration often greater than one minute and less than 24 hours; (4) presence of significant vascular risk factors (hypertension, diabetes, atrial fibrillation, prior stroke) [4]. Orthostatic BP is typically elevated rather than low in this population [13]. When any focal neurological feature accompanies dizziness, neuroimaging takes priority over orthostatic testing [4].

□ **Important:** The combination of age over 70, new onset orthostatic dizziness, and neurological signs (gait ataxia, bradykinesia, rigidity, abnormal pursuit or saccades) should raise suspicion for neurogenic OH from an underlying neurodegenerative

condition. Do not attribute these cases to medication or deconditioning without a formal neurological assessment [31,32].

□ **Important:** Cardiac syncope must not be missed. Sudden loss of consciousness without prodrome, recovery in less than 30 seconds, occurrence in the supine position, or ECG abnormality (complete heart block, long QT, pre-excitation, Brugada pattern) mandates cardiology referral before OH treatment is initiated. OH can co-exist with cardiac arrhythmia [18,36].

VII. Management — Non-Pharmacological First Line

Non-pharmacological measures are the mandatory first step in OH management for all patients, regardless of aetiology [1,2,25,26]. Their combined effect on orthostatic BP in compliant patients can match or exceed the BP effect of a single pharmacological agent and carries none of the supine hypertension risk that complicates drug therapy [25,26]. Patient education is the single most important component: understanding why symptoms occur, recognising the situations that increase risk, and applying counter-manoeuvres autonomously are skills that directly reduce falls and syncopal episodes [1,25].

Figure 4. Stepwise Management Algorithm

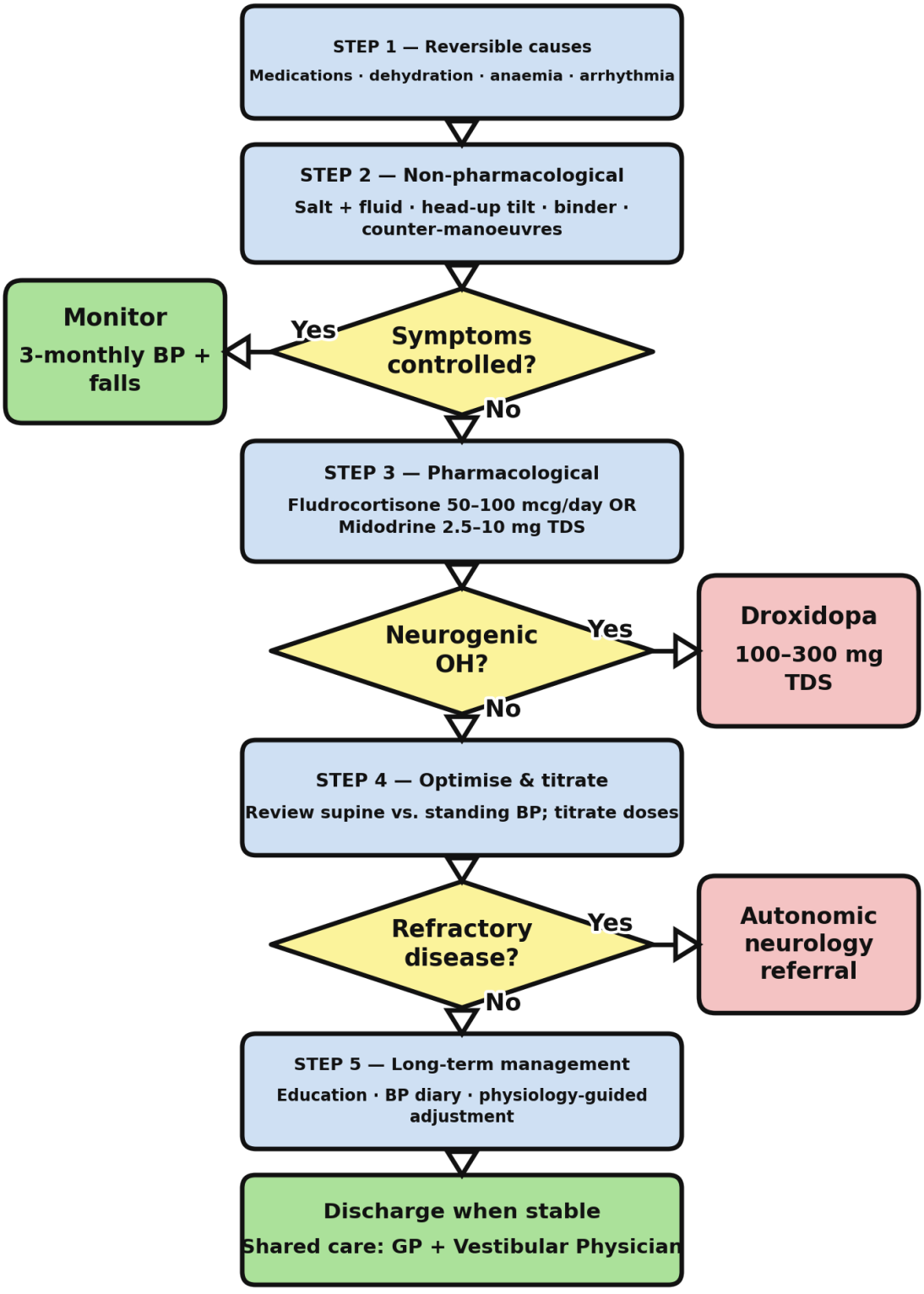


Figure 4. Orthostatic Hypotension — Stepwise Management Algorithm.
Source: Adapted from Freeman et al. [1], Gibbons et al. [24], and Kaufmann et al. [26].

Salt and fluid loading

Adequate circulating blood volume is the physiological foundation of orthostatic tolerance. Current consensus guidelines recommend daily fluid intake of 2.0–2.5 litres and dietary sodium of 6–10 grams

per day in patients without heart failure or advanced renal disease [1,26]. Acute water ingestion (500 mL bolus) produces a pressor response within 5–10 minutes (mediated by splanchnic sympathetic activation via the hepatoportal reflex), which can be strategically deployed before known triggers such as showering, morning rising, or prolonged standing [26,41]. In neurogenic OH, this pressor response may be the single most effective acute intervention.

Compression garments and abdominal binders

Compression stockings (30–40 mmHg graduated) and abdominal binders reduce the venous pooling that drives the orthostatic BP fall by physically constraining the capacitance vascular bed [25,26]. Abdominal binders (compression > 30 mmHg) are more effective than below-knee stockings in neurogenic OH because a significant proportion of pooling occurs in the splanchnic bed, which knee-high compression does not address [25,26]. In practice, adherence is limited by discomfort and heat — washable elastic abdominal binders are better tolerated than full-body garments [25].

Head-up bed tilt during sleep

Raising the head of the bed 10–20 degrees (using bed leg risers or a foam wedge) activates the renin-angiotensin-aldosterone axis by preventing recumbent nocturnal natriuresis, thereby expanding morning plasma volume [26,38]. This strategy also reduces nocturnal supine hypertension — a dual benefit in neurogenic OH. The counter-intuitive instruction to sleep head-up (rather than lying flat for rest) requires clear patient education [38].

Physical counter-manoeuvres

Counter-manoeuvres exploit the skeletal muscle pump to increase venous return and BP during the orthostatic challenge [25,26]. The most effective include: leg crossing with thigh and calf tensing; squatting (which generates the most rapid BP response but requires balance); standing with one foot elevated on a step; and slow marching on the spot [25]. These manoeuvres can raise standing systolic BP by 10–20 mmHg within 30–60 seconds — sufficient to abort many syncopal episodes if initiated at symptom onset [25]. Patients should be taught to recognise their individual prodromal symptoms and apply the manoeuvre immediately, before hypotension is severe enough to impair cognition [26].

Behavioural and lifestyle modifications

A structured set of behavioural modifications has Level B evidence for OH symptom reduction [1,26]:

- Rising slowly from bed — sit on the edge for 30 seconds before standing [1].
- Avoiding prolonged standing (>3 minutes without movement) [1,26].
- Eating smaller, more frequent meals — reduces post-prandial splanchnic pooling [7,15].
- Avoiding alcohol — which causes vasodilation and volume depletion [1].
- Avoiding hot environments (showers, baths, saunas) — heat-mediated vasodilation [26].
- Exercise rehabilitation — aerobic and resistance training improve orthostatic tolerance over weeks in POTS and non-neurogenic OH; aquatic exercise is particularly well tolerated [25,34].
- Caffeine in the morning — modest pressor effect; can be used judiciously in OH patients without contraindication [26].

Exercise rehabilitation and reconditioning

Supervised exercise rehabilitation is a first-line recommendation for POTS and deconditioning-related OH, with Level B evidence supporting its use in both conditions [17,25,34]. The Vanderbilt POTS exercise protocol — a structured 12-week programme combining rowing, recumbent cycling, and swimming (non-upright exercise initially) progressing to weight training and upright aerobic activity — produces substantial improvements in stroke volume, orthostatic heart rate, and symptom burden at three months [34]. For neurogenic OH, where the autonomic failure is structural, exercise rehabilitation cannot restore baroreflex function but improves venous return via the trained skeletal muscle pump and reduces deconditioning-related pooling [25]. In clinical practice, referral to a physiotherapist with autonomic disorder experience is preferred over generic exercise prescription — the upright posture demands of

standard rehabilitation classes can precipitate syncope in patients with uncontrolled OH before conditioning benefits accrue [25,34].

Patient self-monitoring and BP diaries

Home BP monitoring with a validated upper-arm oscillometric device is strongly recommended for all OH patients on pharmacological therapy [38,48]. The monitoring protocol should capture paired supine and standing readings at fixed times — immediately on rising (before any medication), 30 minutes after the first fludrocortisone or midodrine dose, and at the period of the patient's worst orthostatic symptoms (often mid-morning or post-meal) [38]. A 7-day BP diary at treatment initiation and at each dose titration allows direct visualisation of the supine/standing BP gap and identifies dangerous supine hypertension without requiring clinic attendance. Digital BP diaries transmitted via patient portal or photographed for the clinic record provide more actionable data than single clinic readings in this condition [48].

□ **Clinical Pearl:** Teach the 500 mL water bolus trick. Drinking 500 mL of cool water in under 5 minutes raises standing systolic BP by 15–25 mmHg for 30–45 minutes via the hepatoportal pressor reflex. It is the most effective single non-pharmacological intervention for acute orthostatic symptoms and is safe in nearly all patients [41].

VIII. Pharmacological Management

Pharmacological therapy is indicated when non-pharmacological measures fail to adequately control symptoms or prevent falls [1,2,26]. Medication selection should be guided by the clinical subtype of OH (neurogenic vs. non-neurogenic), the presence and severity of supine hypertension, comorbidities (heart failure, renal impairment), and patient factors [1,24,42]. The four agents with established evidence in OH are fludrocortisone, midodrine, droxidopa, and pyridostigmine [1,24,42].

Fludrocortisone

Fludrocortisone, a mineralocorticoid agonist, expands plasma volume by increasing renal sodium and water retention [26,42]. Starting dose is 50–100 micrograms (mcg) daily, increased to a maximum of 200–300 mcg if tolerated and required [42]. The pressor effect develops over one to two weeks as volume expansion is established. Key risks are supine hypertension (which can be severe in neurogenic OH patients), hypokalaemia (requiring potassium monitoring), and peripheral oedema [42]. Fludrocortisone is contraindicated in heart failure and significant renal impairment and should be used with caution in older patients with ischaemic heart disease [42]. It is commonly used as first-line pharmacotherapy in non-neurogenic OH and mild neurogenic OH [1,42].

Midodrine

Midodrine is a prodrug converted to desglymidodrine, a selective alpha-1 adrenoceptor agonist that increases peripheral vascular resistance [1,42,43]. It acts specifically on the standing BP without clinically significant cardiac effects, making it preferred over non-selective sympathomimetics. Dosing is 2.5–10 mg two to three times daily, taken 30 minutes before meals and periods of activity; the last dose should be at least four hours before bedtime to avoid nocturnal supine hypertension [42,43]. Midodrine is the most widely studied oral pressor agent in OH, with evidence from multiple randomised trials demonstrating a standing BP increase of 10–22 mmHg and significant reduction in syncopal episodes [43]. It is first-line or co-first-line with fludrocortisone in both neurogenic and non-neurogenic OH.

Droxidopa

Droxidopa (L-threo-DOPS) is a synthetic noradrenaline precursor — decarboxylated peripherally to noradrenaline — approved specifically for neurogenic OH in Parkinson's disease, MSA, and PAF [24,44]. Its mechanism addresses the core deficiency in neurogenic OH: inadequate noradrenaline release at peripheral vascular alpha-1 receptors. Three Phase III trials (NORTH Star A, B, C) demonstrated significant improvement in the Orthostatic Hypotension Questionnaire composite score, dizziness, and near-syncope frequency [44]. Dosing starts at 100 mg three times daily and is titrated to 600 mg three times daily [44]. Droxidopa is not licensed in Australia as of mid-2026 but is available on compassionate access for neurogenic OH cases refractory to fludrocortisone and midodrine [24].

Pyridostigmine

Pyridostigmine, an acetylcholinesterase inhibitor, enhances ganglionic transmission in the autonomic nervous system by increasing synaptic acetylcholine availability [45]. Its effect on OH is modest — a standing systolic BP increase of approximately 5–10 mmHg — but it has the critical advantage of not worsening supine hypertension, making it uniquely useful in neurogenic OH patients with significant supine hypertension where other pressor agents are unsafe [45]. Starting dose is 30–60 mg twice daily, titrated to 60–120 mg three times daily [45]. Side effects (diarrhoea, increased sweating, bradycardia) are dose-dependent. A crossover trial by Singer et al. confirmed standing BP improvement and symptom reduction without supine hypertension augmentation, supporting its use in the neurogenic OH/supine hypertension overlap [45].

Table 5. First-Line Pharmacological Agents for Orthostatic Hypotension — Dosing and Key Points.

Agent	Mechanism	Starting Dose	Max Dose	Key Caveat
Fludrocortisone	Mineralocorticoid: volume expansion	50–100 mcg/day	200–300 mcg/day	Worsens supine HT; hypokalaemia; avoid in HF
Midodrine	Alpha-1 agonist: vasoconstriction	2.5 mg TDS	10 mg TDS	Last dose >=4 h pre-bed; avoid urinary retention
Droxidopa	NE precursor: noradrenaline replacement	100 mg TDS	600 mg TDS	Neurogenic OH only; compassionate access in AUS
Pyridostigmine	AChE inhibitor: ganglionic enhancement	30–60 mg BD	120 mg TDS	Preferred when supine HT is significant
Atomoxetine	NE reuptake inhibitor (off-label)	10–18 mg/day	40 mg/day	Neurogenic OH; SSRI interaction; cardiac effects

A deprescribing-first approach — systematically ceasing or dose-reducing identified culprit agents before adding a pressor agent — frequently yields a standing BP improvement that makes pharmacological OH treatment unnecessary [3,16,22]. This is particularly relevant in older adults where polypharmacy is the dominant mechanism: a 2023 UK deprescribing trial in care home residents with OH found that structured medication review with targeted cessation of alpha-blockers and loop diuretics increased standing systolic BP by a mean 14 mmHg — equivalent to the effect of midodrine monotherapy — without adding any new drug [16].

Iatrogenic OH is among the most prevalent and reversible forms of the condition, yet it is underrecognised in both primary care and hospital settings because medication reviews are rarely framed around orthostatic haemodynamics [3,15,22]. The mechanistic categories are: (1) volume depletion — loop diuretics (frusemide, torasemide), thiazides, and osmotic agents reduce plasma volume and preload, directly impairing orthostatic BP maintenance [22]; (2) vasodilation — calcium channel blockers, ACE inhibitors, angiotensin receptor blockers, hydralazine, and nitrates reduce peripheral resistance and venous tone, blunting the vasoconstrictor response to standing [15,22]; (3) alpha-adrenergic blockade — prazosin, doxazosin, and terazosin (commonly prescribed for benign prostatic hyperplasia) competitively inhibit the vasoconstrictor effector arm of the baroreceptor reflex, a mechanism that is pharmacologically predictable and frequently missed in OH work-ups in older men [22]; (4) central sympatholytic agents — methyldopa and clonidine reduce central sympathetic outflow; (5) dopaminergic and antidopaminergic drugs — L-DOPA and dopamine agonists cause peripheral vasodilation directly, while antipsychotics and antiemetics (metoclopramide, droperidol) cause OH via alpha-blockade [42,46]; (6) tricyclic antidepressants — imipramine and amitriptyline have potent alpha-1 blocking and anticholinergic effects that impair baroreceptor-mediated HR compensation; (7) phosphodiesterase-5 inhibitors — sildenafil and tadalafil cause splanchnic and systemic vasodilation, with a particularly pronounced interaction when co-prescribed with organic nitrates [22,42].

Drug causes of orthostatic hypotension — systematic classification

□ **Clinical Insight:** The midodrine dose timing is critical. Patients who take midodrine at bedtime — a common error — develop dangerous supine hypertension overnight. Explicit written instructions specifying 'last dose by 4 pm' are necessary, not optional [42,43].

IX. Neurogenic OH and Special Populations

Neurogenic OH represents the most clinically complex and pharmacologically challenging subtype of OH [24,31,32]. Unlike non-neurogenic OH — where volume restoration and pressor agents address the primary deficiency — neurogenic OH involves a fixed structural failure of efferent sympathetic innervation to the heart and resistance vessels, requiring replacement rather than augmentation of the autonomic signal [24]. The population with neurogenic OH is also the population most at risk of rapidly progressive neurological disease (MSA, PAF), and early identification of the neurogenic subtype is a critical clinical step [31,32].

Figure 5. Neurogenic OH — Causes by Anatomical Level

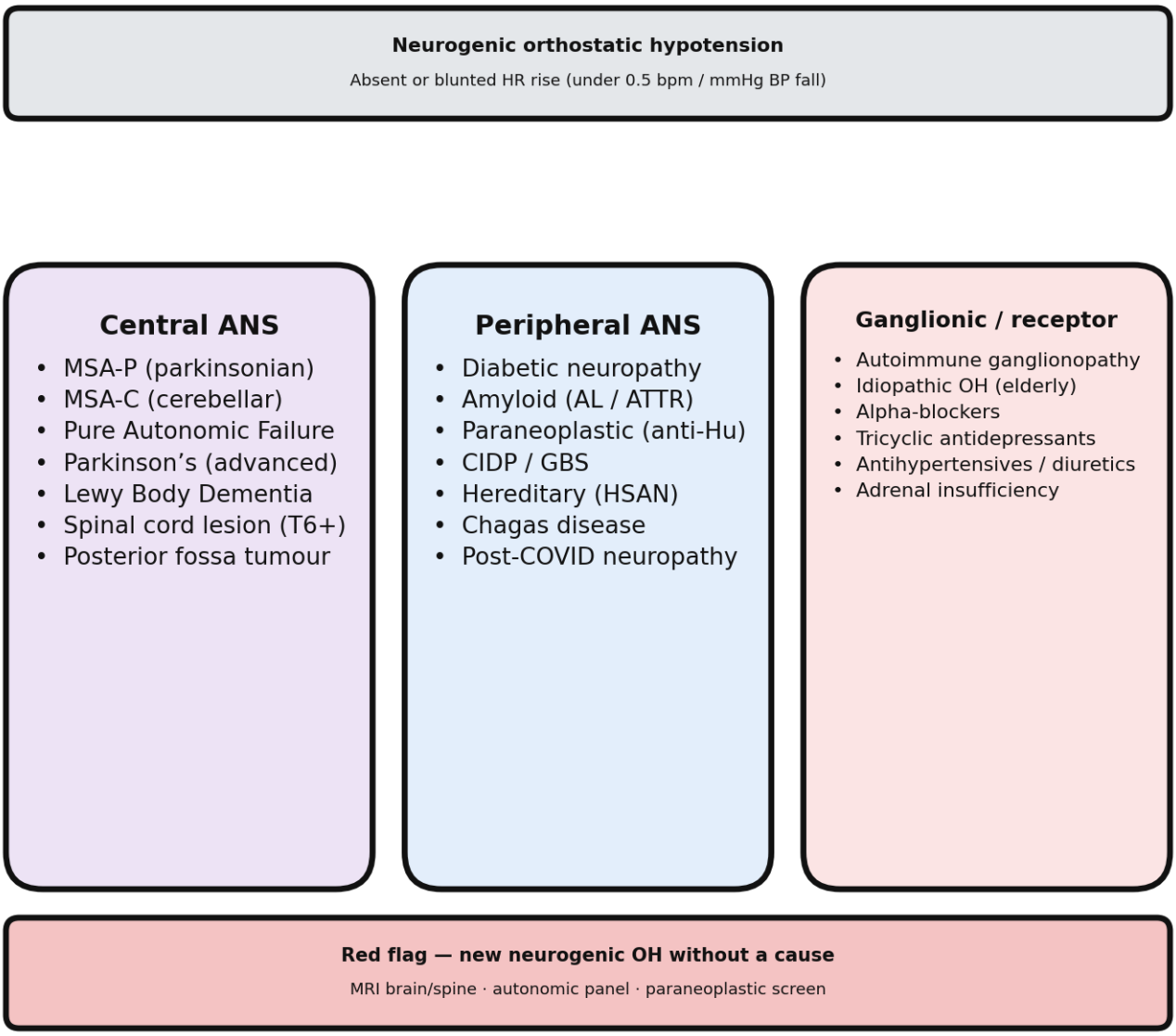


Figure 5. Neurogenic Orthostatic Hypotension — Causes by Anatomical Level.
Source: Adapted from Gibbons et al. [24] and Kaufmann et al. [26].

Multiple System Atrophy (MSA)

MSA is a rapidly progressive neurodegenerative disorder with alpha-synuclein glial cytoplasmic inclusions in the basal ganglia, cerebellum, and brainstem [31]. OH in MSA is typically severe, early in the disease course, and may predate the parkinsonian or cerebellar features that establish the diagnosis [31]. The MSA-OH is generated by preganglionic sympathetic cell loss in the thoracolumbar intermediolateral column and central autonomic failure [31]. Distinguishing MSA from Parkinson's disease with autonomic

failure requires clinical features (rapid progression, cerebellar signs, inspiratory stridor, antecollis, lack of sustained L-DOPA response, disproportionate antecollis) and functional imaging (dopamine transporter SPECT and FDG-PET showing cerebellar/striatal hypometabolism) [31].

Pure Autonomic Failure (PAF)

PAF is characterised by progressive postganglionic sympathetic failure (peripheral cell body loss) in the absence of other neurological features [32]. Onset is typically in the sixth to seventh decade. The supine noradrenaline level is very low (often below 100 pg/mL), rising minimally on standing. A proportion of PAF patients subsequently develop Parkinson's disease, MSA, or Lewy body dementia — PAF may represent the initial autonomic-predominant phase of a Lewy body spectrum disorder [32]. In PAF, droxidopa provides the most physiologically rational therapy because the deficiency is peripheral noradrenaline; midodrine and fludrocortisone are also used [24,32].

Parkinson's disease

Symptomatic OH is present in 30–50% of Parkinson's disease patients across the disease course [46]. It reflects peripheral Lewy body pathology in cardiac and splanchnic sympathetic ganglia, compounded by dopaminergic drug effects (L-DOPA, dopamine agonists) [46]. The management is complicated by competing demands: optimising motor control requires dopaminergic dosing that may worsen OH, while minimising OH may require dose reduction at the cost of motor function. Droxidopa has the most specific evidence in Parkinson's disease-associated neurogenic OH [44,46]. Timing L-DOPA doses away from periods of orthostatic challenge and using smaller, more frequent doses reduces drug-peak OH [46].

Diabetes mellitus and cardiovascular autonomic neuropathy

Cardiovascular autonomic neuropathy (CAN) develops in 25–50% of patients with longstanding Type 1 or Type 2 diabetes and is an independent predictor of cardiovascular mortality [47]. CAN-associated OH typically presents as length-dependent sympathetic denervation of mesenteric and peripheral resistance vessels. The diagnosis requires a standardised battery of cardiac autonomic reflex tests (CART) — resting HR, deep breathing HR variability (E:I ratio), Valsalva ratio, and standing HR ratio [47]. The severity of CAN at baseline strongly predicts subsequent all-cause mortality, and its presence should intensify glycaemic and cardiovascular risk management [47]. Treatment follows the same pharmacological principles as other neurogenic OH, but strict glycaemic control may slow progression [47].

Elderly patients and frailty

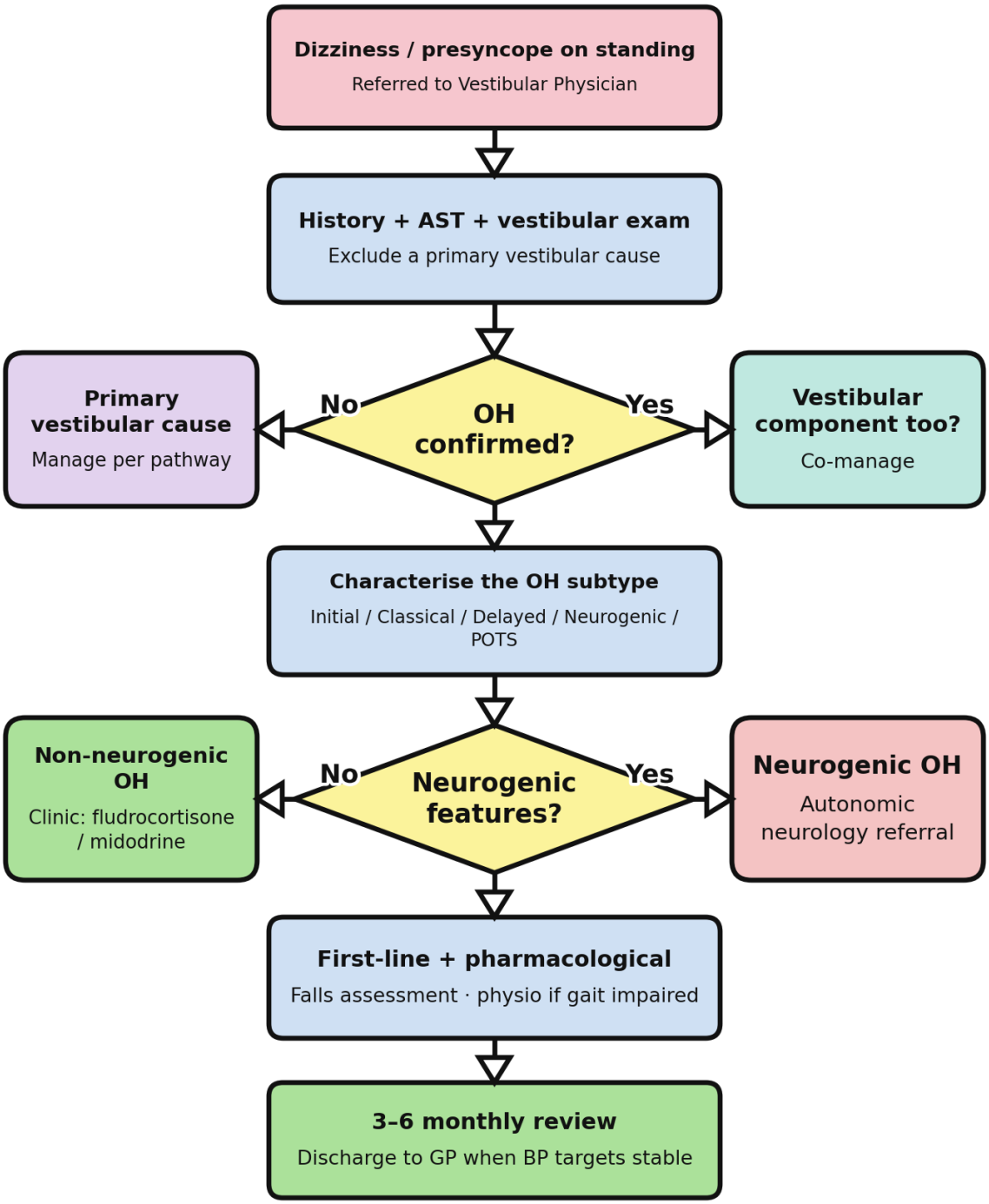
OH in older adults presents a distinctive management challenge: the pharmacological interventions that raise standing BP also risk raising supine BP to dangerous levels in a population with already-prevalent hypertension [15,16]. A 2024 meta-analysis of OH interventions in patients over 75 years found that non-pharmacological measures plus pyridostigmine had the most favourable benefit-to-risk profile, while fludrocortisone was associated with increased hospitalisation for heart failure and electrolyte disturbance [16]. Falls risk assessment and supervised exercise rehabilitation should be co-prescribed with any pharmacological intervention in this population [10,16]. Deprescribing review — identifying and ceasing medications contributing to OH — often yields a greater standing BP improvement than adding a new pressor agent [3,16].

Table 6. Special Populations in Neurogenic OH — Distinguishing Features and Management Priorities.

Population	OH Mechanism	Distinguishing Feature	Priority in Management
MSA	Preganglionic sympathetic failure (central + peripheral)	Rapid progression; cerebellar/parkinsonian signs; inspiratory stridor	Droxidopa + symptomatic; head-up sleeping; falls prevention
PAF	Postganglionic sympathetic failure; very low supine NE	Isolated autonomic failure; no somatic motor involvement	Droxidopa first-line; watch for Lewy conversion
Parkinson's disease	Peripheral cardiac/splanchnic Lewy pathology +	OH often correlated with dopaminergic dose peaks	Droxidopa; L-DOPA dose restructuring; pyridostigmine

	drug effect		
Diabetic CAN	Length-dependent sympathetic neuropathy	Absent E:I ratio; CART abnormalities; associated retinopathy/nephropathy	Glycaemic control; midodrine/fludrocortisone; CART monitoring
Elderly/frail	Mixed: medication + deconditioning + early neurodegeneration	Polypharmacy; supine HT risk; falls risk dominant	Deprescribing first; pyridostigmine preferred; physio referral
Post-COVID POTS	Small fibre neuropathy; autoimmune; deconditioning	Young women; fatigue; cognitive fog; exertion intolerance	Deconditioning rehab; low-dose beta-blockade (POTS); anti-autoimmune if Ab positive

Figure 6. Referral and Co-management Pathway



□ **Clinical Pearl:** In any patient with new neurogenic OH over the age of 50, the differential includes MSA, PAF, and Parkinson's. Rapid onset (within months), lack of somatic sensorimotor neuropathy, inspiratory stridor, antecollis, and failure to respond to L-DOPA all point toward MSA — a diagnosis requiring urgent neurological review [31].

Figure 6. Orthostatic Hypotension — Referral and Co-management Pathway.
Source: Adapted from Freeman et al. [1] and Gibbons et al. [24].

X. Guidelines, Controversies and Future Directions

Management of OH is guided by consensus documents from the European Heart Rhythm Association (EHRA/ESC syncope guidelines, 2018) [18], the American Autonomic Society (Freeman 2011, Gibbons 2017) [1,24], and condition-specific guidelines for Parkinson's disease [46] and POTS [17]. All documents converge on the primacy of non-pharmacological measures and the stepwise pharmacological algorithm described above. Areas of active debate include BP treatment targets, the management of supine hypertension, the role of droxidopa in non-Parkinsonian neurogenic OH, and the nosology of post-COVID autonomic syndromes [34,35,48].

Blood pressure treatment targets

No randomised trial has established an evidence-based standing BP target for OH management. The practical goal is a standing systolic BP above 90 mmHg combined with absence of symptoms of cerebral hypoperfusion [1,24]. In patients with pre-existing hypertension treated to guideline targets, the haemodynamic window between acceptable standing BP and dangerous supine BP may be narrow, requiring careful titration and 24-hour BP monitoring to navigate safely [38,48]. Recent modelling studies suggest that a standing BP of 100–110 mmHg systolic is associated with minimum syncopal risk in non-neurogenic OH cohorts [48].

Supine hypertension controversy

The coexistence of supine hypertension and OH creates a pharmacological dilemma that remains incompletely resolved [38,48]. Current consensus is to accept mild supine hypertension (systolic 160–179 mmHg) in neurogenic OH patients rather than treat it aggressively at the cost of worsening OH [38]. Short-acting agents at bedtime (captopril 12.5–25 mg, losartan 25 mg, or transdermal nitroglycerin 0.1 mg/h patch) provide nocturnal BP reduction with less daytime OH augmentation than standing-dose antihypertensives [38]. Head-up bed tilt alone reduces supine systolic BP by 10–15 mmHg in neurogenic OH without pharmacological risk [38].

Controversies in POTS management

The evidence base for POTS pharmacotherapy is substantially weaker than for OH. Low-dose beta-blockade (propranolol 10–20 mg), fludrocortisone, midodrine, and ivabradine have all been used with modest evidence [17,34]. The identification of autoimmune subsets (anti-AChR-g, anti-NET, anti-adrenergic receptor antibodies) has raised the possibility of immunotherapy in a minority of POTS patients, but no controlled trial data exist [34,35]. The post-COVID POTS epidemic has accelerated research in this area [35].

Future directions

Several developments are likely to change clinical practice within the next five years [32,49,50]. Alpha-synuclein biomarkers in skin biopsy and CSF are close to clinical deployment and will allow confident early diagnosis of Lewy body spectrum disease underlying neurogenic OH [49]. Continuous wearable BP monitoring (optical plethysmography rings and cuffs) will transform management by enabling real-time standing BP tracking and biofeedback — currently under evaluation in POTS and neurogenic OH [50]. Autonomic neuromodulation (transcutaneous vagal nerve stimulation, spinal cord stimulation) has early-phase evidence in neurogenic OH and represents a potential disease-modifying pathway in autonomic failure [32]. Finally, gene therapy targeting the noradrenaline synthesis pathway is preclinical but conceptually appealing for PAF, where peripheral sympathetic terminals are structurally intact but functionally depleted [32].

From the vestibular physician's perspective, the most immediately actionable advance is the integration of structured OH screening into all dizziness clinic workflows. A validated protocol combining the 500 mL water test, active stand test with 10-minute extended period, and simultaneous vestibular examination can capture OH, POTS, and vestibular causes in a single assessment visit — improving diagnostic yield and reducing unnecessary investigations [4,9].

□ **Key Point:** OH is consistently under-investigated and under-treated in dizziness clinic populations. Systematic adoption of the active stand test as part of the standard vestibular examination protocol is

the single highest-yield improvement any vestibular physician clinic can make to diagnostic accuracy for postural dizziness [4,9].

Summary

Orthostatic hypotension is a prevalent, undertreated cause of dizziness, presyncope, and falls. The vestibular physician's role spans: identifying OH as a treatable cause of postural dizziness through systematic active stand testing; distinguishing the five orthostatic syndromes by timing, HR response, and mechanism; differentiating neurogenic from non-neurogenic subtypes to guide pharmacological selection; coordinating with autonomic neurology when neurodegeneration is suspected; and implementing stepwise non-pharmacological and pharmacological management. Five practice points consolidate this review:

- **Perform the AST in every dizziness presentation —** it takes four minutes, needs no equipment, and will identify OH that would otherwise be missed [1,4].
- **Measure HR alongside BP —** the compensatory HR response is the single most important discriminator between neurogenic and non-neurogenic OH and dictates pharmacological choice [23,24].
- **Start non-pharmacological measures first —** salt loading, fluid loading, compression, counter-manoeuvres, and education have evidence and no supine hypertension risk [25,26].
- **Avoid nocturnal pressor agents —** midodrine and fludrocortisone taken in the evening generate dangerous supine hypertension. Last dose of midodrine at least four hours before bed is mandatory [42,43].
- **Flag neurogenic OH urgently —** blunted HR rise, new autonomic failure over the age of 50, cerebellar or parkinsonian signs, or inspiratory stridor mandates neurological review for MSA [31,32].

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