

SYSTEMATIC REVIEW

Prevalence of initial orthostatic hypotension in older adults: a systematic review and meta-analysis

JENNIFER TRAN^{1,†}, SARAH L. HILLEBRAND^{2,†}, CAREL G.M. MESKERS³, REBECCA K. ISELI¹, ANDREA B. MAIER^{1,2,4}

¹Department of Medicine and Aged Care, @AgeMelbourne, The University of Melbourne, The Royal Melbourne Hospital, Parkville, Victoria 3050, Australia

²Department of Human Movement Sciences, @AgeAmsterdam, Amsterdam Movement Sciences, Vrije Universiteit Amsterdam, Amsterdam, The Netherlands

³Department of Rehabilitation Medicine, Amsterdam UMC, Vrije Universiteit, Amsterdam Movement Sciences, Amsterdam, The Netherlands

⁴Healthy Longevity Program, Yong Loo Lin School of Medicine, National University of Singapore, Singapore; Centre for Healthy Longevity, @AgeSingapore, National University Health System, Singapore

Address correspondence to Andrea B. Maier, Department of Human Movement Sciences, @AgeAmsterdam, Vrije Universiteit, Van der Boeorchstraat 9, Amsterdam, The Netherlands. Tel: (+31) 6 1514 4751. Email: a.b.maier@vu.nl

[†] Authors contributed equally.

Abstract

Background: Initial orthostatic hypotension (OH) is a clinical syndrome of exaggerated transient orthostasis associated with higher risks of falls, frailty and syncope in older adults.

Objective: To provide a prevalence estimate of initial OH in adults aged 65 years or older.

Methods: Literature search of MEDLINE (from 1946), Embase (from 1947) and Cochrane Central Register of Controlled Trials was performed until 6 December 2019, using the terms ‘initial orthostatic hypotension’, ‘postural hypotension’ and ‘older adults’. Articles were included if published in English and participants were 65 years or older. Random effects models were used for pooled analysis.

Results: Of 5,136 articles screened, 13 articles (10 cross-sectional; 3 longitudinal) reporting data of 5,465 individuals (54.5% female) from the general ($n = 4,157$), geriatric outpatient ($n = 1,136$), institutionalised ($n = 55$) and mixed ($n = 117$) population were included. Blood pressure was measured continuously and intermittently in 11 and 2 studies, respectively. Pooled prevalence of continuously measured initial OH was 29.0% (95% CI: 22.1–36.9%, $I^2 = 94.6\%$); 27.8% in the general population (95% CI: 17.9–40.5%, $I^2 = 96.1\%$), 35.2% in geriatric outpatients (95% CI: 24.2–48.1%, $I^2 = 95.3\%$), 10.0% in institutionalised individuals (95% CI: 2.4–33.1%, $I^2 = 0\%$) and 21.4% in the mixed population (95% CI: 7.0–49.6, $I^2 = 0\%$). Pooled prevalence of intermittently measured initial OH was 5.6% (95% CI: 1.5–18.9%, $I^2 = 81.1\%$); 1.0% in the general population (95% CI: 0.0–23.9%, $I^2 = 0\%$) and 7.7% in geriatric outpatients (95% CI: 1.8–27.0%, $I^2 = 86.7\%$).

Conclusion: The prevalence of initial OH is high in older adults, especially in geriatric outpatients. Proper assessment of initial OH requires continuous blood pressure measurements.

Keywords: aged, blood pressure, frail older people, hypotension, orthostatic intolerance, posture

Key Points

- Initial orthostatic hypotension (OH) is associated with higher risks of falls, frailty and syncope in older adults.
- Initial OH affects 27.8% (95% CI: 17.9–40.5%) of older general populations.
- Initial OH affects 35.2% (95% CI: 24.2–48.1%) of geriatric outpatients.
- Continuous blood pressure monitoring is recommended to diagnose initial OH.

Introduction

Initial orthostatic hypotension (OH) is a clinical syndrome of exaggerated transient orthostasis and is defined as a decrease of ≥ 40 mmHg in systolic blood pressure (SBP) and/or ≥ 20 mmHg in diastolic blood pressure (DBP) within 15 seconds of active standing [1,2]. It differs distinctly from classical OH, defined as a decrease of ≥ 20 mmHg in SBP and ≥ 10 mmHg in DBP within 3 minutes of standing or to at least 60° upright tilting [1]. Initial OH may be accompanied by orthostatic intolerance symptoms of light-headedness, dizziness, unsteadiness or visual disturbance [1,2], which has been attributed to impaired cerebral perfusion [3]. Older adults with initial OH have higher risks of falls, frailty and syncope [2,4–7], regardless of the presence of symptoms [5,8]. Age-related changes such as low skeletal muscle strength and cardiorespiratory fitness may further impair restoration of systemic blood pressure and aggravate negative outcomes of initial OH [4,9,10].

The negative implications associated with initial OH highlight the need to identify this variant of OH, particularly in older adults who may already be susceptible to presyncopal episodes and falls [10]. Unlike classical OH which can be detected intermittently, the rapid blood pressure changes that occur in initial OH are less likely to be detected with a sphygmomanometer [10,11]. Therefore, continuous blood pressure monitoring is recommended to capture the transient changes in blood pressure upon immediate active standing or passive tilting [1,12]. Limited availability of beat-to-beat blood pressure monitoring devices in clinical settings may cause initial OH to be underdiagnosed.

The aim of this systematic review and meta-analysis is to provide pooled estimates of the prevalence of initial OH in adults aged 65 years or older by both intermittent and continuous blood pressure monitoring.

Methods

Data search and sources

The review protocol was registered with the PROSPERO International prospective register of systematic reviews (CRD42020170696) and developed in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines [13]. MEDLINE (from 1946), EMBASE (from 1974) and Cochrane Central Register of Controlled Trials were systematically searched for articles published until 6 December 2019, in assistance of research librarian Lindy Cochrane of the University of Melbourne. The search strategy included the following keywords: ‘initial orthostatic hypotension’, ‘postural hypotension’ and ‘older adults’. The complete search strategy is presented in [Supplementary Table S1](#), Supplementary data are available in *Age and Ageing* online.

Article selection

All identified articles were managed with EndNote (Version: X9 Clarivate Analytics, Philadelphia, USA). After the removal of duplicates, articles were exported into Covidence and assessed by screening titles and abstracts for potential eligibility by two independent reviewers (J.T. and S.L.H.). Subsequent full texts of eligible articles were screened by the same reviewers. Disagreements between the reviewers were resolved by a third reviewer (R.K.I.). Articles were eligible if they met the following inclusion criteria: cohorts with a mean or median age of 65 years or older, diagnosis of initial OH that encompassed a decrease of ≥ 40 mmHg in SBP and/or ≥ 20 mmHg in DBP up to 1 minute after postural change and written in English. Studies that experimentally induced initial OH with medication were excluded. Conference abstracts, case reports (less than five participants), reviews, editorials and letters to the editor were excluded. Reference lists from the included full-text articles were searched to identify potential additional articles.

Data extraction

The following variables were extracted independently by two reviewers (J.T., S.L.H.): first author, year of publication, population, study design, study setting, number of participants, % of valid blood pressure measurements, % female, mean or median age, initial OH definition, resting period (min), standing period (min), type of postural change (active stand, passive stand, active supine-to-sit or passive supine-to-sit), blood pressure measurement (continuous or intermittent) and types of devices used to measure initial OH. Active stand was defined as activation of lower limb muscles upon standing up, whereas passive stand or supine-to-sit was defined as immobility or inactivation of lower limb muscles during the transition from supine to standing or sitting. The prevalence of initial OH was extracted for the total population and, if given, for subpopulations. If initial OH prevalence was reported at more than one time point, the first point in time with the highest reported number of participants was included.

Study quality

The quality and risk of bias of individual articles were assessed by two independent reviewers (J.T., S.L.H.) using the nine-point Newcastle–Ottawa Scale (NOS) [14] adapted for cross-sectional studies. Articles with an NOS score between 0–3, 4–6 and 7–9 points were defined as low, moderate and high quality, respectively [14]. The specified NOS is provided in [Supplementary Table S2](#), Supplementary data are available in *Age and Ageing* online.

Meta-analysis

Analyses were stratified by method of blood pressure measurement (continuously and intermittently), initial OH definition (with symptoms and without symptoms) and study

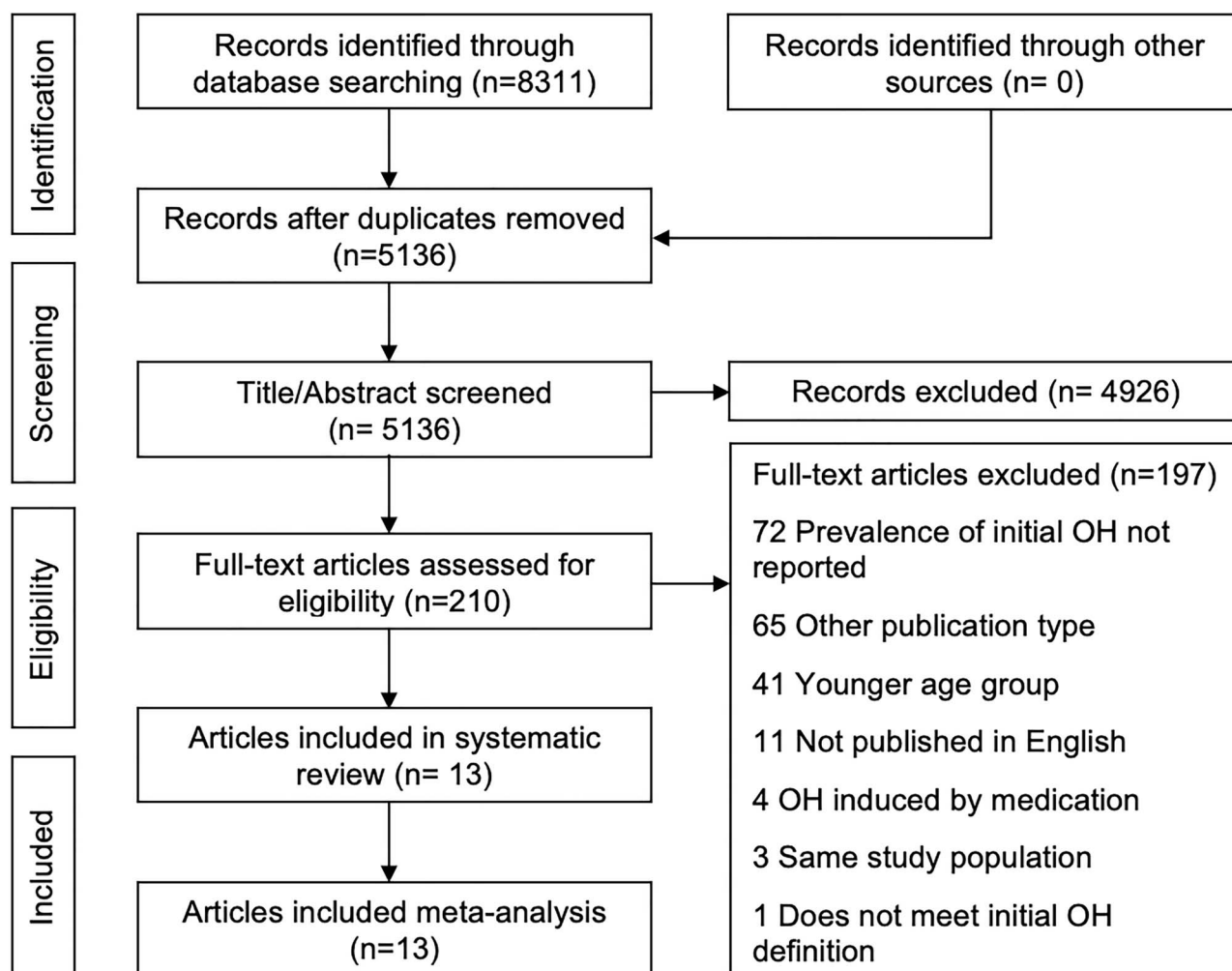


Figure 1. PRISMA Flowchart—article screening and selection.

population (categorised as general population, geriatric outpatients, institutionalised or mixed population). Additional analyses were performed excluding studies using passive postural changes to test for initial OH. The pooled prevalence of initial OH was presented as a percentage and 95% confidence interval (CI). A random effects model was used to account for heterogeneity. Heterogeneity was assessed using the I^2 -test (<25% low; 25–75% moderate and >75% high) [15]. P -values less than 0.05 were considered statistically significant. All analyses were performed using Comprehensive Meta-Analysis (version 3.3; Biostat Inc., Englewood, NJ).

Results

Article selection

Figure 1 shows the PRISMA flow diagram. The search yielded 8,311 articles. After duplicate removal, 5,136 titles and abstracts were screened of which 210 were selected for full text screening. Thirteen articles were included in the systematic review and meta-analysis.

Study and participant characteristics

Table 1 and Supplementary Table S3, Supplementary data are available in *Age and Ageing* online, list the study characteristics. A total of 5,465 participants (54.5% females ranging between 43.0 and 71.7%) with a mean age ranging between 67.8 ± 6.1 and 84.2 ± 0.9 years, representing the general population ($n = 4,157$) [16–18], geriatric outpatients ($n = 1,136$) [4,10,19–24], institutionalised population ($n = 55$) [7] and mixed population ($n = 117$) [5], were included. Ten studies were cross-sectional ($n = 4,914$) [4,5,10,16,18–22,24] and three studies were longitudinal ($n = 551$) [7,17,23].

Diagnosis

Initial OH was defined as a decrease of ≥ 40 mmHg in SBP and/or ≥ 20 mmHg in DBP within 15 seconds of standing [4,5,10,16–18,20–24], within 30 seconds of sitting [7] and within the first minute of standing [19]. The diagnosis of initial OH included the presence of symptoms in three articles [4,16,20] and the recovery of blood pressure within 30–60 seconds in one article [10]. Blood pressure was measured

Table 1. Study characteristics, stratified by population

First author, year (reference)	Study design	Population	N	Valid measures, N (%)	Female, Na (%)	Age, years mean (SD)	Period R/S (min)	Postural change	Devices used
Geriatric outpatients									
Bengtsson-Lindberg, 2015 [19]	C	AD, Advasc, DLB	154	154 (100)	95 (61.7)	76 (6.3)	10/10	AS	Digital sphyg.
		Control	50	48 (96)	33 (66)	76 (7)	10/10	AS	Digital sphyg.
Breeuwsma, 2017 [20]	C	CVD, DM, HTN	127	104 (81.9)	45 (43)	68.8 (8.5)	5/4	AS,ASS	Finometer Pro
De Bruine, 2017 [21]	C	Mobility, cogn, morbid	24	24 (100)	14 (58.3)	79.3 (7.7)	5/3	AS	Nexfin
De Bruine, 2019 [22]	C	Mobility	62	58 (93.5)	33 (56.9)	80.6 (7.0)	5/3	PS	Finometer Pro
Hayakawa, 2015 [23]	L	MCI	141	130 (93)	76 (54)	74 (6.8)	10/3	AS	Finometer
		Control	75	69 (92)	32 (43)	69 (7.1)	10/3	AS	Finometer
McJunkin, 2015 [10]	C	General	115	115 (100)	57 (49.5)	71.1	5–10/3	AS	Manual sphyg.
Mol, 2018 [24]	C	Mobility, cogn, mixed	109	109 (100)	60 (55)	81.7 (7.0)	5/3	AS	Nexfin
Romero-Ortuno, 2011 [4]	C	General	608	442 (72.7)	317 (71.7)	72.1 (7.1)	10/3	AS	Finometer Pro
General population									
Finucane, 2014 [16]	C	Community	2,647	2,409 (91)	1,266 (52.6)	67.8 (6.1)	10/2	AS	Finometer
McDonald, 2017 [17]	L	Community	353	297 (84.1)	40 (50.6)	73 (6.8)	10/3	AS	Portapres; Finapres
Saedon, 2019 [18]	C	Community	1,245	1,245 (100)	693 (55.7)	67.9 (6.9)	5/3	AS	Taskforce; CNSys
Institutionalised									
Shaw, 2019 [7]	L	Long-term care	55	55 (100)	65 (56)*	84.2 (0.9)*	15/15	PSS	Finometer Pro
Mixed population									
Saedon, 2016 [5]	C	Fallers AED, primary care, geriatrics, hospital	155	117 (75.5)	107 (69.0)	75 (7)	10/3	AS	Portapres; Finapres
		Control	112	89 (79.5)	77 (68.7)	72 (6)	10/3	AS	Portapres; Finapres

C, Cross-sectional; L, Longitudinal; AD, Alzheimer's disease; ADVASC, AD and vascular components; DLB, Dementia with Lewy bodies; MCI, Mild Cognitive Impairment; Cogn, Cognition; Morbid, Morbidity; CVD, Cardiovascular Disease; DM, Diabetes Mellitus; HTN, Hypertension; OH, Orthostatic Hypotension; AED, Accident and Emergency Department; R, Resting; S, Standing/Sitting; AS, Active Stand; ASS, Active Supine-to-Sit; PS, Passive Stand; PSS, Passive Supine-to-Sit; Sphyg., Sphygmomanometer; CNSys, CNSystems. *Sample size for these characteristics, $n = 116$.

continuously using Finometer Pro [4,5,7,16,17,20,22,23], Nexfin [21,24] and Task Force CNSystems [18] or intermittently using either a digital sphygmomanometer [19] or manual sphygmomanometer [10]. The resting period prior to postural change varied between 5 [10,18,20–22,24], 10 [4,5,16,17,19,23] and 15 minutes [7]. Standing or sitting period varied between 2 [16], 3 [4,5,10,17,18,21–24], 4 [20], 10 [19] and 15 minutes [7]. The postural change included active stand [4,5,10,16–21,23,24], passive-transition-to-stand [22], active supine-to-sit [20] or passive supine-to-sit [7]. In one article using a passive-transition-to-stand, participants were asked to stand unsupported after reaching a standing position [22]. In one article, both active stand and active supine-to-sit were tested in all participants [20], in which active stand showed a significant larger SBP drop between 0 and 40 seconds after postural change [20] and was included in the meta-analysis. Valid blood pressure measurements were reported to be 100% in five articles [7,10,18,21,24]; the lowest reported percentage of valid measurements was 77.2% [4].

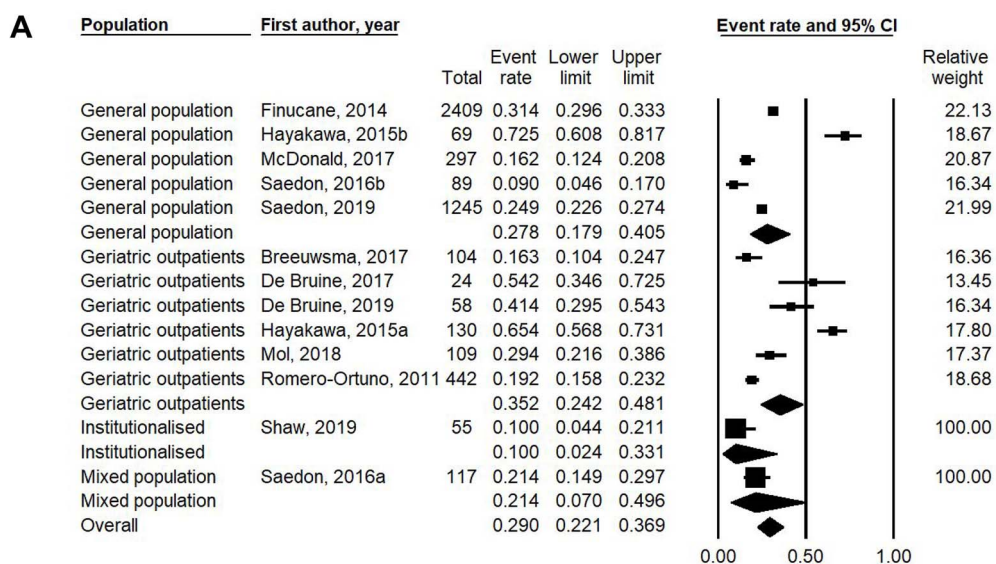
Quality assessment

Ten articles, including general populations [16–18], geriatric outpatients [4,20–24] and a mixed population [5], were of high quality (NOS score ≥ 7). The remaining three

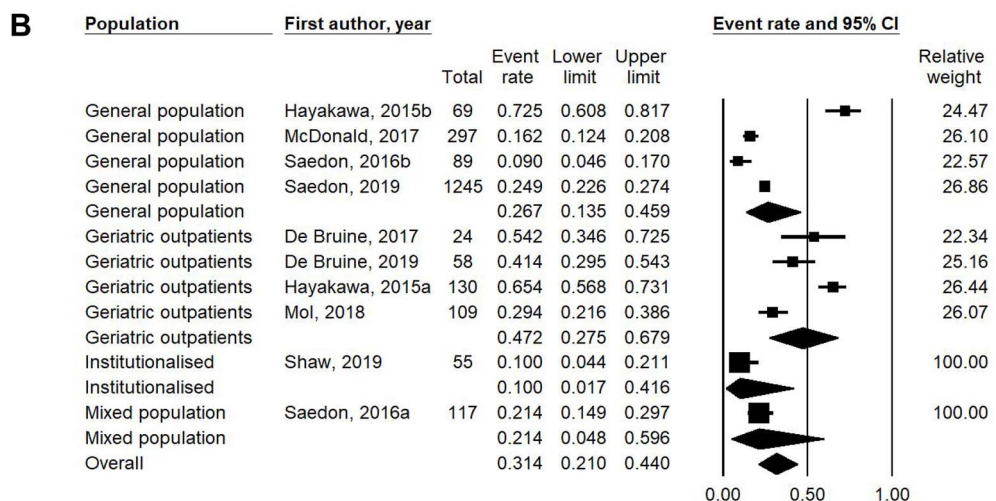
articles were of moderate quality (NOS score 4–6) [7,10,19] (Table 3).

Meta-analysis: prevalence of initial OH

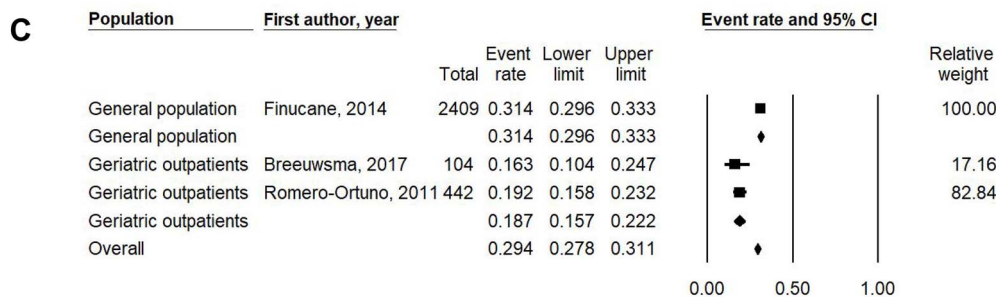
Initial OH prevalence ranged between 0.0 and 72.5% (Table 2). Pooled prevalence of continuously measured initial OH was 29.0% (95% CI: 22.1–36.9%, $I^2 = 94.6\%$); 27.8% (95% CI: 17.9–40.5%, $I^2 = 96.1\%$) in the general population; 35.2% (95% CI: 24.2–48.1%, $I^2 = 95.3\%$) in geriatric outpatients; 10.0% (95% CI: 2.4–33.1%, $I^2 = 0\%$) in institutionalised individuals and 21.4% (95% CI: 7.0–49.6, $I^2 = 0\%$) in mixed populations (Figure 2a). Excluding studies using passive postural change resulted in a slightly higher pooled prevalence of continuously measured initial OH of 29.8% (95% CI: 22.3–38.6%, $I^2 = 95.2\%$) (Supplemental Figure S1a, Supplementary data are available in *Age and Ageing* online). When studies were stratified by initial OH definition, pooled prevalence of continuously measured initial OH was 31.4% (95% CI: 21.0–44.0%, $I^2 = 95.2\%$) without symptoms and 29.4% (95% CI: 27.8–31.1%, $I^2 = 94.2\%$) with symptoms in the definition. Prevalence of continuously measured initial OH without symptoms was 26.7% (95% CI: 13.5–45.9%, $I^2 = 96.3\%$) in the general population, 47.2% (95% CI: 27.5–67.9%, $I^2 = 90.3\%$) in geriatric outpatients, 10.0% (95% CI: 1.7–41.6%, $I^2 = 0\%$) in institutionalised



CI: confidence interval. $I^2 = 94.6\%$

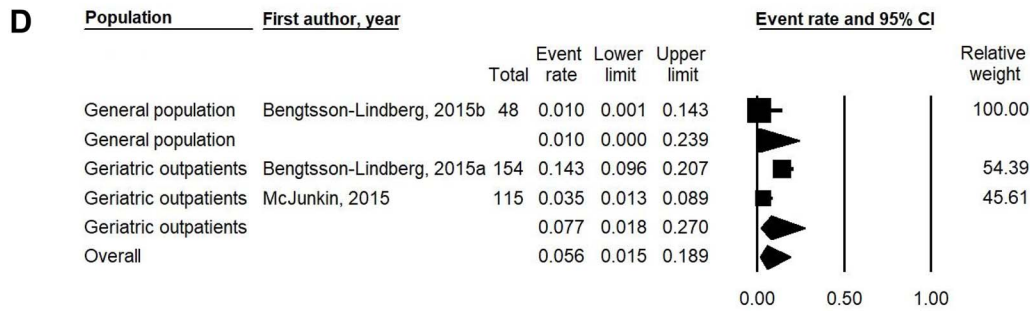


CI: confidence interval. $I^2 = 95.2\%$



CI: confidence interval. $I^2 = 94.2\%$

Figure 2. (a) Pooled initial orthostatic hypotension prevalence using continuous blood pressure monitoring, stratified by population. (b) Pooled initial orthostatic hypotension prevalence using continuous blood pressure monitoring and initial orthostatic hypotension definition without inclusion of symptoms, stratified by population. (c) Pooled initial orthostatic hypotension prevalence using continuous blood pressure monitoring and initial orthostatic hypotension definition with inclusion of symptoms, stratified by population. (d) Pooled initial orthostatic hypotension prevalence using intermittent blood pressure monitoring.



CI: confidence interval. $I^2 = 81.1\%$

Figure 2. Continued

Table 2. Definition and prevalence of initial OH, stratified by populations

First author, year (reference)	BP measurement	Initial OH definition	Initial OH prevalence (%)	Initial OH prevalence in subgroups (%)
Geriatric outpatients				
Bengtsson-Lindberg, 2015a [19]	Int.	IOH-60	14.3	AD (4) ADvasc (6) DLB (34)
Breeuwisma, 2017 [20]	Cont.	IOH-15 + S	16.3	AS (16.3) ASS (5.8)
De Bruine, 2017 [21]	Cont.	IOH-15	54.2	
De Bruine, 2019 [22]	Cont.	IOH-15	41.1	
Hayakawa, 2015a [23]	Cont.	IOH-15	65.4	MCI (65.4)
McJunkin, 2015 [10]	Int.	IOH-15 + R30	3.5	
Mol, 2018 [24]	Cont.	IOH-15	29.4	
Romero-Ortuno, 2011 [4]	Cont.	IOH-15 + S	19.2	
General population				
Bengtsson-Lindberg, 2015b [19]	Int.	IOH-60	0.0	Control (0)
Finucane, 2014 [16]	Cont.	IOH-15 + S	31.4	
Hayakawa, 2015b [23]	Cont.	IOH-15	72.5	Control (72.5)
McDonald, 2017 [17]	Cont.	IOH-15	16.2	
Saedon, 2016b [5]	Cont.	IOH-15	9.0	Non-fallers (9.0)
Saedon, 2019 [18]	Cont.	IOH-15	24.9	
Institutionalised				
Shaw, 2019 [7]	Cont.	IOH-30	10	Frail (15) Non-frail (4)
Mixed population				
Saedon, 2016a [5]	Cont.	IOH-15	21.4	Fallers (21.4)

BP, Blood Pressure; Int., Intermittent; Cont., Continuous beat-to-beat analyses; IOH, Initial Orthostatic Hypotension; IOH-15, SBP or DBP drop within 15 seconds; IOH-15 + S, plus, symptoms; IOH-15 + R30, correcting within 30–60 seconds; IOH-30, SBP or DBP drop within 30 seconds; IOH-60, SBP or DBP within 60 seconds; AD, Alzheimer's disease; ADVASC, AD and vascular components; DLB, Dementia with Lewy bodies; MCI, Mild Cognitive Impairment; AS, Active Stand; ASS, Active Supine-to-Sit.

individuals and 21.4% (95% CI: 4.8–59.6%, $I^2 = 0\%$) in mixed populations (Figure 2b). Excluding studies using passive postural change resulted in a slightly higher pooled prevalence of continuously measured initial OH without symptoms in the definition of 33.5% (95% CI: 21.1–48.7%, $I^2 = 96.0\%$) (Supplemental Figure S1b, Supplementary data are available in *Age and Ageing* online). Prevalence of continuously measured initial OH with symptoms was 31.4% (95% CI: 29.6–33.3%, $I^2 = 0\%$) in the general population and 18.7% (95% CI: 15.7–22.2%, $I^2 = 0\%$) in geriatric outpatients (Figure 2c). Pooled prevalence of intermittently measured initial OH was 5.6% (95%

CI: 1.5–18.9%, $I^2 = 81.1\%$). Prevalence of intermittently measured initial OH was 1.0% (95% CI: 0.0–23.9%, $I^2 = 0\%$) in the general population and 7.7% in geriatric outpatients (95% CI: 1.8–27.0%, $I^2 = 86.7\%$) (Figure 2d).

Discussion

This systematic review and meta-analysis demonstrate a high prevalence of initial OH in older adults aged 65 years or older. Over a quarter of older adults from the general population and over a third of geriatric outpatients are

Table 3. Risk of bias quality assessment using the NOS

First author, year	Selection Representativeness of exposed cohort	Sample size	Selection of non-exposed cohort	Ascertainment of exposure: continuous BP	Comparability Adjustment for potential confounders	Assessment of outcome	Outcome Statistical test	Score	Quality
Bengtsson-Lindberg, 2015 [19]	*	*	*	–	*	–	*	5	Moderate
Breeuwisma, 2017 [20]	*	*	*	*	–	**	*	7	High
De Bruine, 2017 [21]	*	*	*	*	–	**	*	7	High
De Bruine, 2019 [22]	*	*	*	*	*	**	*	8	High
Finucane, 2014 [16]	*	*	*	*	–	**	*	7	High
Hayakawa, 2015 [23]	*	*	*	*	**	**	*	9	High
McDonald, 2017 [17]	*	*	*	*	*	**	*	8	High
McJunkin, 2015 [10]	*	*	*	–	–	**	*	6	Moderate
Mol, 2018 [24]	*	*	*	*	*	**	*	8	High
Romero-Ortuno, 2011 [4]	*	*	*	*	–	**	*	7	High
Saedon, 2016 [5]	*	*	*	*	**	**	*	9	High
Saedon, 2019 [18]	*	*	*	*	**	**	*	9	High
Shaw, 2019 [7]	*	*	*	*	–	*	*	6	Moderate

Maximum total score of 9 points. 0–3, low quality; 4–6, moderate quality; 7–9, high quality.

affected by initial OH. The pooled prevalence of initial OH in older adults is higher when blood pressure is measured continuously compared with intermittently.

There were considerable variations in the diagnosis of initial OH. Currently, the consensus statement on the definition of initial OH [1] does not clearly specify whether the presence of symptoms, in addition to the hemodynamic criteria, is required to diagnose initial OH. Inclusion of symptoms in the initial OH definition excludes asymptomatic older adults who exhibit a large initial blood pressure drop. However, asymptomatic older adults with a substantial initial blood pressure drop may still be at risk of negative consequences of initial OH such as falls or syncope [5,8]. Thus, the inclusion of symptoms in the definition of initial OH seems implausible and results in a lower prevalence as demonstrated in our findings. Participants with dementia with Lewy bodies [19] and diabetes mellitus [25] are at higher risk of initial OH due to autonomic dysfunction and therewith delayed compensatory response to postural change. Damaged elastin fibres and increased arterial stiffness caused by diabetes mellitus can lead to decreased vascular resistance [25] and impaired baroreceptor function [26]. Given that initial OH is associated with increased risks of falls [18], frailty [7] and syncope [2] in older adults, it is clinically important to assess initial OH to target interventions to minimise these poor clinical outcomes.

Active stand is commonly used because it allows clinicians to assess the cardiovascular responses to standing [1,12]. However, frail older adults may find it difficult to complete an active stand test [27], so passive sitting is a safe alternative [7]. Given that institutionalised older adults are more likely to be frail, with increased morbidity and mortality compared with the general population [28], they may require a longer transition time during postural change. The slow transition time during the passive seated orthostatic stress may explain the low prevalence in the institutionalised population [7]. Slow transition times allow for adaptation and counter

manoeuvring such as activation of muscles for effective use of the skeletal muscle pump, thereby counteracting the relative blood pressure drop in the first 15 seconds [21]. Another effective intervention to counteract the effects of initial OH include lower body muscle tensing immediately after standing [29] as it decreases venous pooling in the lower limbs and helps to sustain cardiac output [11]. Salt supplementation [30] and medication reviews may also be considered.

Orthostatic blood pressure should be measured continuously to capture the immediate blood pressure changes that occur upon standing [12]. The rapid blood pressure changes that occur in initial OH cannot be detected using a conventional sphygmomanometer because there is insufficient time to inflate the cuff upon standing [12]. This results in an underestimation of the initial OH prevalence, which is in line with the presented results. Additionally, continuous blood pressure monitoring facilitates the analysis of blood pressure recovery [31]. Currently, the consensus statement on the definition of initial OH does not specify the duration of the blood pressure drop in initial OH [1]. The recent availability of a structured protocol using continuous blood pressure devices for the active stand test will help clinicians to improve the standardisation of beat-to-beat blood pressure measurements in clinical practice and research studies [31], thereby optimising the detection of initial OH.

Strengths and limitations

This is the first systematic review to estimate the prevalence of initial OH in older adults aged 65 years or older. Selection bias was avoided by including all populations and definitions of initial OH that met the hemodynamic criteria of a decrease of ≥ 40 mmHg in SBP and ≥ 20 mmHg in DBP up to 1 minute after postural change. Articles that were not published in English were excluded and hence may be open to reporting bias. The high heterogeneity in the pooled

analyses can be attributed to variations in study populations, measurement protocols and initial OH definitions.

Conclusion

Initial OH is highly prevalent in older adults aged 65 years or older, particularly when measured continuously, highlighting the need to screen and diagnose initial OH. Future research should investigate whether the inclusion of symptoms in the definition of initial OH is clinically relevant. Furthermore, there is a need to establish a consensus on the diagnosis of initial OH using continuous blood pressure devices to consistently identify participants with initial OH.

Supplementary Data: Supplementary data mentioned in the text are available to subscribers in *Age and Ageing* online.

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Declaration of Conflicts of Interest: None.

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