Age and Ageing 2023; **52:** 1–10
https://doi.org/10.1093/ageing/afad005

RESEARCH PAPER

The 'Bermuda Triangle' of orthostatic hypotension, cognitive impairment and reduced mobility: prospective associations with falls and fractures in The Irish Longitudinal Study on Ageing

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Abstract

Background: Orthostatic hypotension (OH), cognitive impairment (Cog) and mobility impairment (MI) frequently co-occur in older adults who fall. This study examines clustering of these three geriatric syndromes and ascertains their relationship with future falls/fractures in a large cohort of community-dwelling people ≥ 65 years during 8-year follow-up.
Methods: OH was defined as an orthostatic drop ≥ 20 mmHg in systolic blood pressure (from seated to standing) and/or reporting orthostatic unsteadiness. CI was defined as Mini Mental State Examination ≤ 24 and/or self-reporting memory as fair/poor. MI was defined as Timed Up and Go ≥12 s. Logistic regression models, including three-way interactions, assessed the longitudinal association with future falls (explained and unexplained) and fractures.
Results: Almost 10% (88/2,108) of participants had all three Bermuda syndromes. One-fifth of participants had an unexplained fall during follow-up, whereas 1/10 had a fracture. There was a graded relationship with incident unexplained falls and fracture as the number of Bermuda syndromes accumulated. In fully adjusted models, the cluster of OH, CI and MI was most strongly associated with unexplained falls (odds ratios (OR) 4.33 (2.59–7.24); $P < 0.001$) and incident fracture (OR 2.51 (1.26–4.98); $P = 0.045$). Other clusters significantly associated with unexplained falls included OH; CI and MI; MI and OH; CI and OH. No other clusters were associated with fracture.
Discussion: The 'Bermuda Triangle' of OH, CI and MI was independently associated with future unexplained falls and fractures amongst community-dwelling older people. This simple risk identification scheme may represent an ideal target for multifaceted falls prevention strategies in community-dwelling older adults.

Keywords: orthostatic hypotension, falls, cognitive impairment, mobility, fracture, older people

Key Points

- The combination of orthostatic hypotension, cognitive impairment and mobility impairment has been labelled the Bermuda Triangle of Falls.
- Having all three syndromes was independently associated with a >4-fold risk of future unexplained falls.
- There was also double the likelihood of future fracture in those with the Bermuda Triangle of Falls.

- The risk of falls attributable to these syndromes appears to be additive, with one syndrome amplifying the effect of another.
- This simple risk identification scheme may represent an ideal target for multifaceted falls prevention strategies in later life.

Background

Falls represent the commonest cause of accidental death in older people [1] and the most frequent reason for presentation to hospital. Falls, particularly falls causing injury, increase the likelihood of nursing home admission [2], prolonged hospital length of stay [3], cognitive decline [4], fear of falling [5] and early mortality [6].

However, many falls in later life are related to modifiable factors and are therefore potentially preventable. Defining which older people are at higher risk of falls, and identifying the factors, or combinations of factors, that heighten this risk are therefore important to inform preventative strategies [7]. Three frequently cited causes of falls in later life are orthostatic hypotension (OH) [8], problems with mobility, gait and balance [9] and cognitive impairment [10].

One in five community-dwelling older people have OH [11], defined as a drop in systolic blood pressure (SBP) ≥20 mmHg and/or diastolic blood pressure (DBP) ≥10 mmHg within 3 min of standing [8]. In later life, OH is characterised by delayed BP recovery after standing [12], causing cerebral hypoperfusion and increasing the risk of falls [13] and fractures [14].

Similarly, the prevalence of mobility and gait abnormalities in community-dwelling older people is 35% [15], and older people identified with an unsteady gait have a >50% independent higher likelihood of falls during the following 21 months [16]. There is a 7% increase in the risk of falls for every 10 cm/s slowing of gait speed in later life [17].

Cognitive impairment is associated with double the risk of serious injury from falls in older people [18]. When followed over an average of 2.5 years, 1/3 of people with dementia had a fall requiring hospitalisation [19] and falls are more frequent in those with co-existing gait and balance deficits [20].

Clinically, it has been hypothesised that the co-existence or clustering of these three geriatric syndromes in an older individual may increase the risk of falls and fractures beyond what is seen with each of the syndromes in isolation. A synergy between the factors can be explained by OH destabilising the underlying mobility impairment (MI), and cognitive impairment reducing prudential anticipation of the increased gait instability as well as impaired ability to appropriately react to the instability. This hypothesis was termed the 'Bermuda Triangle' of falls, representing physiological instability across three integrated systems, but this had yet to be demonstrated in a well-designed study [21, 22, 23]. The aim of this study was therefore to examine clustering of these three common geriatric syndromes—OH, cognitive and MI—and examine the longitudinal relationship between clusters of these syndromes and incident falls and fractures during an 8-year follow-up period.

Methods

Study design

This study utilised data from The Irish Longitudinal Study on Ageing (TILDA), a large population-based nationally representative sample of community-dwelling older adults aged ≥50 years. Waves of data collection were conducted at 2-yearly intervals. In this study, we used data from Waves 1 to 5, collected between 2009 and 2018.

The TILDA study design has been outlined previously [24]. The study was designed to investigate how the health, social and economic circumstances of the older Irish population interact in the determination of 'healthy' ageing. Briefly, there are three components to data collection: a computer-assisted personal interview carried out by social interviewers in the participants' own home; a self-completion questionnaire completed and returned by the participant; and a comprehensive centre-based health assessment or a modified home-based health assessment carried out by trained research nurses.

Participants were included in this study if they were aged ≥ 65 years at Wave 1 and underwent assessments of postural blood pressure, memory and mobility outlined below, and completed at least 2 years follow-up within the study. Subsequent waves were conducted at 2-yearly intervals. Assessments were carried out by trained research nurses. Longitudinal analysis examines the association of Bermuda Triangle variables at Wave 1 with future falls (at any of Waves 2–5). Any changes in Bermuda Triangle variables from Waves 2 to 5 were not included in the study.

Participants were excluded from participation in TILDA at Wave 1 if they had a pre-existing diagnosis of dementia.

The Bermuda Triangle

Participants were assessed for each of the three geriatric syndromes comprising the 'Bermuda Triangle' of falls at Wave 1: OH, cognitive impairment and MI. See Supplementary Figure 1.

OH was defined as a drop of ≥20 mmHg in SBP when measured after standing from a seated position and/or reporting unsteadiness when getting up from a chair. An abnormal orthostatic fall in DBP without an abnormal fall in SBP is rare amongst patients with syncope and orthostatic intolerance. And ∼95% of patients with classical OH can be identified by systolic criterion alone [25]. BP was measured using an Omron digital cuff.

Cognitive impairment was defined as a Mini Mental State Examination (MMSE) Score ≤ 24 and/or self-reporting memory as fair or poor [26].

MI was defined as a Timed Up and Go Score ≥ 12 s [27]. The TUG is a quick, standardised assessment of mobility [27].

Falls and fractures

At Waves 2–5, participants were asked 'Have you had any falls since the last interview?' This was used to derive the 'Falls' variable.

If they answered yes to this, participants were then asked, 'Were any of these falls non-accidental, i.e., with no apparent or obvious reason?' This was used to inform the 'Unexplained Falls' variable. Explained falls were therefore accidental falls, because of slips or trips.

We distinguished falls types as explained and unexplained as this mirrors clinical practice, where unexplained falls are managed similarly to unexplained syncope in terms of diagnostic evaluation [28] and are more likely to be recurrent, injurious and associated with cardiovascular disease and cognitive impairment [29, 30, 31].

Participants were also asked about a history of fracture since the last interview (hip, wrist, vertebral and other fractures) at Waves 2–5 and this was used to derive the 'Fractures' variable.

Other measures

Highest level of educational attainment (a surrogate marker of social deprivation) was collected by self-report (primary, secondary and tertiary). Heart disease, which is associated with all three components of the Bermuda Triangle [32, 33, 34], was also defined as a self-reported history of heart attack, angina, congestive cardiac failure and/or arrhythmia. The Cut Down, Angry, Guilty, Eye Opener (CAGE) scale was used to assess for excess alcohol intake [35]. Polypharmacy was defined as regularly taking greater than or equal to 5 medications and medication lists were examined to confirm this. It was not possible to assess compliance with medications. Chronic disease burden was assessed by self-report of the following conditions: cancer, liver disease, kidney disease, thyroid disease, arthritis and lung disease.

Statistical analysis

Data were analysed using Stata version 14.1 (Statacorp, Texas).

Clustering of geriatric syndromes was reported descriptively with differences between groups analysed with chi-square tests.

Baseline characteristics of the study sample by number of geriatric syndromes were presented descriptively using proportions and mean values with 95% confidence intervals.

Logistic regression models, reporting odds ratios (OR) and 95% confidence intervals (CI), with falls (explained and unexplained) and fractures during follow-up as dependent variables, were used to assess the longitudinal association between the Bermuda Triangle clusters and the longitudinal outcomes of interest. All participants were included in regression models with analysis adjusted for follow-up time. Two models were used: Model 1 was adjusted only for follow-up time, whereas Model 2 was adjusted for age (in groups 65–69 years (reference group), 70–74 years and ≥ 75 years), sex, educational attainment, alcohol excess, heart disease, polypharmacy and chronic disease burden (in groups of $n = 0$ (reference group), $n = 1$ and $n \geq 2$). These covariates were chosen a priori based on their likelihood of modifying the association between variables of interest and falls.

Geriatric syndromes were analysed within these regression models in two ways. First, participants were divided into four groups based on the number of geriatric syndromes present, with participants with no geriatric syndromes serving as the reference value in the models. Second, a three-way interaction was used to examine the independent association of different clusters of these geriatric syndromes, compared with the reference of no OH, normal cognition and normal mobility, yielding seven comparison groups.

Ethics

Each wave of the TILDA study was approved by the Faculty of Health Sciences Research Ethics Committee at Trinity College Dublin and all participants gave informed written consent. All experimental procedures adhered to the Declaration of Helsinki.

Results

Just over half (1,115/2,108, 53%) of participants had neither OH, cognitive impairment nor MI.

Of the participants with cognitive impairment (546/2,108, 26% of study sample), 1/3 (169/546) had co-existing MI ($X^2 = 77.973$; $P < 0.001$) and 1/3 (173/546) had co-existing OH ($X^2 = 26.885$; $P < 0.001$). Almost half of participants with cognitive impairment (254/546) had either OH or MI.

Almost one-quarter of participants had OH (497/2,108, 24% of study sample). Almost 35% of participants with OH had co-existing cognitive impairment (173/497) and over 1/3 (183/497, 37%) had co-existing MI. Almost half of participants with OH (229/497, 46%) had either cognitive impairment or MI.

One-fifth (387/2108) of participants had MI ; almost half (183/387, 47%) had co-existing OH and 44% had co-existing cognitive impairment (169/387). Over 2/3 of participants with MI (264/387, 68%) had co-existing OH or cognitive impairment. See Figure 1.

Of those with at least one geriatric syndrome of the Bermuda Triangle (993/2,108, 47%), over 2/3 (644/993) had any one of the three geriatric syndromes, one-quarter had any two features (261/993) and almost 10% (88/993) had all three geriatric syndromes.

The baseline characteristics of the study sample by number of Bermuda syndromes are shown in Table 1.

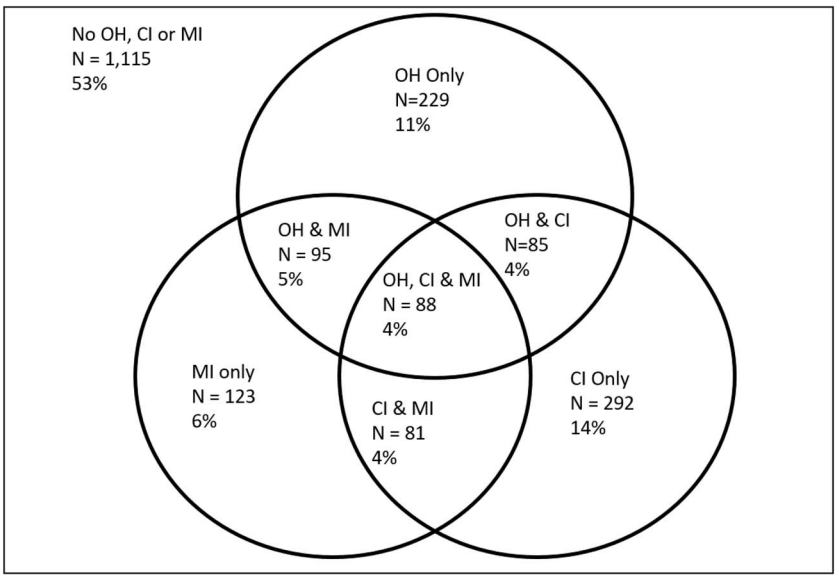

Figure 1. Clustering of OH, Cognitive Impairment and MI. *Notes*: CI, cognitive impairment. OH was defined as a drop of ≥20 mmHg in SBP when measured after standing from a seated position and/or reporting unsteadiness when getting up from a chair. Blood pressure was measured using an Omron digital cuff. Cognitive impairment was defined as an MMSE Score ≤ 24 and/or self-reporting memory as fair or poor. MI was defined as a Timed Up and Go Score ≥ 12 s.

Participants who did not have OH, cognitive impairment or MI were younger with higher levels of educational attainment and lower proportions of heart disease, polypharmacy and chronic disease burden than those with one or more Bermuda Triangle components. Of participants with polypharmacy, 85% were prescribed anti-hypertensives, 15% were prescribed antidepressants and 10% were prescribed anticholinergic medications.

When compared with participants with no Bermuda Triangle geriatric syndromes, those with all three were on average almost 7 years older, twice as likely to have left school at primary level and had significantly higher proportions of heart disease, polypharmacy and chronic disease.

Longitudinal analysis: explained falls

Almost half (944/2,108, 45%) of the study sample had an explained fall during follow-up (mean follow-up 6.6 years (95% CI 6.5–6.7)). There was no significant association between number of Bermuda syndromes and explained falls. Similarly, specific clusters of OH, cognitive impairment and MI were not associated with explained falls. See Supplementary Table 1.

Longitudinal analysis: unexplained falls

Over 1/5 (470/2108) of the study sample had an unexplained fall during follow-up. In fully adjusted models, having all three geriatric syndromes of the Bermuda Triangle of Falls was associated with a >4-fold increased likelihood of unexplained falls (OR 4.36 (2.61–7.28); $P < 0.001$)). Furthermore, the cluster of OH, cognitive impairment and MI was the one with the closest independent association with unexplained falls when compared with other clusters. See Table 2 and Figure 2.

Longitudinal analysis: fracture

Almost 9% (182/2108) of the study sample had a fracture during follow-up. The combination of all three geriatric syndromes was independently associated with more than double the likelihood of incident fracture during follow-up (OR 2.51 (1.27–4.96); $P = 0.008$). The triple combination of OH, cognitive impairment and MI was again the most closely associated with incident fracture in fully adjusted models. See Table 3 and Figure 2.

Discussion

The combination of OH, cognitive impairment and MI has been labelled the Bermuda Triangle of Falls [21, 22]. This study examines clustering of these three common geriatric syndromes, as well as the likelihood of falls related to these clusters, in a large, population-representative sample of community-dwelling older people. OH, cognitive impairment and MI tended to cluster together closely. For example, over 2/3 of participants with gait problems had co-existing OH and/or cognitive impairment.

Furthermore, specific clusters were independently associated with falls and fracture during the 8-year follow-up. In fully adjusted models, the combination of all three syndromes was associated with a >4-fold likelihood of unexplained falls and a two-fold higher likelihood of fracture when compared with participants who did not have any of the syndromes of the Bermuda Triangle. There was also a

Table 1. Baseline characteristics by number of geriatric syndromes comprising the 'Bermuda triangle' of OH, cognitive impairment and MI

	0 Ger syndromes *n* = 1,115	1 Ger syndrome *n* = 644	2 Ger syndromes *n* = 261	3 Ger syndromes *n* = 88
Age category:				
65–69 years	0.47 (0.44–0.50)	0.36 (0.33–0.40)	0.21 (0.17–0.27)	0.10 (0.05–0.19)
70–74 years	0.30 (0.27–0.33)	0.29 (0.26–0.33)	0.23 (0.18–0.29)	0.23 (0.15–0.33)
≥ 75 years	0.29 (0.20–0.25)	0.35 (0.31–0.38)	0.56 (0.49–0.62)	0.67 (0.56–0.76)
Mean age, years (95% CI)	70.95 (70.65–71.24)	72.61 (72.15–73.06)	76.01 (75.17–76.85)	77.88 (76.42–79.33)
Female sex	0.51 (0.49–0.54)	0.51 (0.47–0.55)	0.57 (0.51–0.63)	0.48 (0.37–0.58)
Educational attainment:				
Primary	0.29 (0.26–0.31)	0.43 (0.39–0.47)	0.51 (0.45–0.57)	0.60 (0.49–0.70)
Secondary	0.37 (0.34–0.40)	0.34 (0.30–0.37)	0.32 (0.26–0.38)	0.28 (0.20–0.39)
Tertiary	0.34 (0.32–0.37)	0.24 (0.21–0.27)	0.17 (0.13–0.22)	0.11 (0.06–0.20)
CAGE alcohol score:				
<2	0.86 (0.84–0.88)	0.83 (0.80–0.86)	0.80 (0.74–0.84)	0.74 (0.64–0.82)
≥2	0.07 (0.06–0.09)	0.08 (0.06–0.11)	0.05 (0.03–0.09)	0.08 (0.04–0.16)
Did not answer	0.07 (0.06–0.09)	0.08 (0.06–0.11)	0.15 (0.11–0.20)	0.18 (0.11–0.28)
Heart Disease[a]	0.18 (0.16–0.21)	0.25 (0.22–0.29)	0.32 (0.26–0.38)	0.30 (0.21–0.40)
Polypharmacy[b]	0.24 (0.22–0.27)	0.36 (0.32–0.40)	0.50 (0.44–0.56)	0.69 (0.59–0.78)
Chronic Disease number[c]				
None	0.55 (0.52–0.58)	0.45 (0.41–0.49)	0.31 (0.26–0.37)	0.33 (0.24–0.44)
1	0.38 (0.35–0.41)	0.44 (0.40–0.48)	0.53 (0.47–0.59)	0.49 (0.38–0.59)
≥2	0.07 (0.05–0.08)	0.11 (0.09–0.14)	0.15 (0.11–0.20)	0.18 (0.11–0.28)
Mean follow-up, years (95% CI)	7.00 (6.89–7.12)	6.58 (6.41–6.74)	5.75 (5.46–6.05)	4.91 (4.39–5.43)

Notes: CI, confidence interval; Ger Syndromes, geriatric syndromes. The Bermuda Triangle of Falls comprises OH, cognitive impairment and MI. OH was defined as a drop of ≥20 mmHg in SBP when measured after standing from a seated position and/or reporting unsteadiness when getting up from a chair. Blood pressure was measured using an Omron digital cuff. Cognitive impairment was defined as an MMSE Score ≤ 24 and/or self-reporting memory as fair or poor. MI was defined as a Timed Up and Go Score ≥ 12 s. [a]Heart disease was defined as a self-reported history of heart attack, angina, congestive cardiac failure and/or arrhythmia; [b]polypharmacy was defined as taking greater than or equal to five medications and medication lists were examined to confirm this; [c]chronic disease burden was assessed by self-report of the following conditions: cancer, liver disease, kidney disease, thyroid disease, arthritis and lung disease.

graded relationship, with a stronger association seen as the number of geriatric syndromes accumulated. Similarly, when examined in three-way interaction models, the cluster of OH, cognitive impairment and MI was most strongly associated with both unexplained falls and fractures, compared with other clusters.

There was no association observed between clusters of Bermuda syndromes and explained falls. Explained falls were defined as falls because of slips or trips, and often occur in the absence of underlying falls risk factors, particularly if not recurrent. This is reflected by the fact almost half of the study sample had an explained fall during follow-up. Unexplained falls are more likely to be recurrent, injurious and associated with comorbidities [29, 30, 31].

Prior studies have demonstrated linkages between these three geriatric syndromes. Previous studies using TILDA data have demonstrated that delayed orthostatic BP recovery was associated with slower gait speed [35], as well as a decline in cognitive performance [36]. While the association between mobility and cognitive impairment is also well-described [37, 38], to our knowledge, this is the first study to examine clustering of all three interconnected syndromes, particularly in a large, population-representative sample of older people, as well as examine the relationship with incident falls and fracture.

Unpacking the biological mechanisms that underpin the links between these three geriatric syndromes is complex. Shared mechanistic pathways, including mid-life hypertension [39, 40], heart disease [41, 42] and structural brain changes, including white matter disease [43, 44], may partially explain the associations we report. It is also possible that there is a more direct link between these syndromes; for example, via the cerebral perfusion deficits seen in OH affecting balance and cognition [45], and/or the effect of deficits in executive function and motor planning on maintenance of steady gait [46]. While progressive neurodegeneration could also represent a common mechanistic pathway, participants with dementia were excluded at Wave 1 when assessments were completed, and prevalence of Parkinson's Disease within the study was very low.

The findings in this study support what is often seen clinically in older people who have fallen; that these common geriatric syndromes often cause falls; that the risk of falls attributable to these syndromes appears to be additive, with one syndrome amplifying the effect of another and that the likelihood of falls therefore increases sequentially with accumulation of deficits, dictating the need for multifaceted preventative interventions to reduce falls risk in frail, older people [47]. Indeed, frailty defined as accumulation of deficits has been shown to be independently associated with falls in older people [48]. In addition, they help inform a more focused clinical attention on these three factors in the context of older people presenting to emergency departments with falls, directing assessment towards these three relevant and remediable factors, and helping to avoid

Table 2. Logistic regression models, with unexplained falls as dependent variable, including three-way interaction of OH, cognitive impairment and MI

Model 1: 'Bermuda Triangle', adjusted for follow-up time only			
	OR (95% CI)	***z***	***P***
Bermuda Triangle:			
Ref: 0 Ger Syndromes	Ref	Ref	Ref
1 Ger Syndrome	1.68 (1.31–2.14)	4.14	<0.001
2 Ger Syndromes	3.93 (2.88–5.37)	8.62	<0.001
All 3 Ger Syndromes	5.83 (3.60–9.45)	7.15	<0.001
Model 2: 'Bermuda Triangle', Fully Adjusted			
	OR (95% CI)	***z***	***P***
Bermuda Triangle:			
Ref: 0 Ger Syndromes	Ref	Ref	Ref
1 Ger Syndrome	1.53 (1.19–1.97)	3.29	0.001
2 Ger Syndromes	3.15 (2.26–4.39)	6.77	<0.001
All 3 Ger Syndromes	4.36 (2.61–7.28)	5.63	<0.001
Model 3: 3-Way Interaction, Adjusted for follow-up time only			
	OR (95% CI)	***z***	***P***
MI # Cog impairment # OH			
Ref: normal mobility # normal cognition # No OH	Ref	Ref	Ref
MI with normal cognition, No OH	1.65 (1.03–2.65)	2.09	0.037
OH with normal mobility, normal cognition	2.04 (1.46–2.84)	4.17	<0.001
Cog impairment with normal mobility, No OH	1.44 (1.04–1.99)	2.18	0.029
MI and Cog Impairment with no OH	3.76 (2.29–6.16)	5.25	<0.001
MI and OH with normal cognition	4.68 (2.94–7.45)	6.51	<0.001
Cognitive impairment and OH with normal mobility	3.42 (2.12–5.53)	5.01	<0.001
MI, cognitive impairment and OH	5.86 (3.62–9.51)	7.17	<0.001
Model 4: 3-Way Interaction, Fully Adjusted			
	OR (95% CI)	***z***	***P***
MI # Cog impairment # OH			
Ref: normal mobility # normal cognition # No OH	Ref	Ref	Ref
MI with normal cognition, No OH	1.35 (0.83–2.20)	1.21	0.225
OH with normal mobility, normal cognition	1.82 (1.29–2.56)	3.41	0.001
Cog impairment with normal mobility, No OH	1.38 (0.99–1.93)	1.89	0.059
MI and Cog impairment with no OH	2.92 (1.73–4.92)	4.03	<0.001
MI and OH with normal cognition	3.44 (2.10–5.63)	4.91	<0.001
Cognitive impairment and OH with normal mobility	3.03 (1.85–4.97)	4.40	<0.001
MI, cognitive impairment and OH	4.33 (2.59–7.24)	5.59	<0.001

Notes: $n = 2{,}108$. The Bermuda Triangle of Falls comprises OH, cognitive impairment and MI. OH was defined as a drop of $\geq$20 mmHg in SBP when measured after standing from a seated position and/or reporting unsteadiness when getting up from a chair. Blood pressure was measured using an Omron digital cuff. Cognitive impairment was defined as an MMSE Score ≤ 24 and/or self-reporting memory as fair or poor. MI was defined as a Timed Up and Go Score ≥ 12 s. Unexplained Falls defined as falls not because of slips or trips, with no clear reason for the fall. Abbreviations: Ger Syndromes, Geriatric Syndromes; CI, confidence interval; Cog, cognition. Models 1 and 3 adjusted for follow-up time only. Models 2 and 4 adjusted for age, sex, educational attainment, alcohol excess, heart disease, polypharmacy and chronic disease burden.

unnecessary investigations that both have costs and increase length of stay [49].

These findings have important implications for clinical practice and research. The risk of falls associated with the Bermuda Triangle may be modifiable, but likely requires a multifaceted approach. OH is often related to culprit medications, such as anti-hypertensives [50] or antidepressants [51], which could be rationalised. General medication optimisation, including pharmacist-led interventions, has been shown to reduce falls risk amongst frail, older people [52]. Similarly, gait re-education and adaptability training has been shown to reduce falls in older people [53]. While the effect of falls prevention interventions in older people with cognitive impairment and dementia remains unclear [54], there is a need for robust studies examining tailored interventions [55]. The high potential for easy identification and falls/fractures prevention in the primary care setting is underscored by the fact that the assessments required to ascertain the presence of Bermuda syndromes as described in our study takes less than 10 min.

There are some limitations of this study that should be noted. Data on falls, as well as chronic disease information and fracture history, were based on self-report and may therefore be subject to recall bias. While we included

Table 3. Logistic regression models, with fracture as dependent variable, including three-way interaction of OH, cognitive impairment and MI

Model 1: 'Bermuda Triangle', adjusted for follow-up time only			
	OR (95% CI)	***z***	***P***
Bermuda Triangle:			
Ref: 0 Ger Syndromes	Ref	Ref	Ref
1 Ger Syndrome	1.18 (0.83–1.68)	0.92	0.360
2 Ger Syndromes	1.57 (0.98–2.50)	1.89	0.058
All 3 Ger Syndromes	2.89 (1.53–5.49)	3.26	0.001
Model 2: 'Bermuda Triangle', Fully Adjusted			
	OR (95% CI)	***z***	***P***
Bermuda Triangle:			
Ref: 0 Ger Syndromes	Ref	Ref	Ref
1 Ger Syndrome	1.09 (0.76–7.68)	0.48	0.630
2 Ger Syndromes	1.19 (0.72–10.75)	0.69	0.493
All 3 Ger Syndromes	2.51 (1.27–4.96)	2.64	0.008
Model 3: 3-Way Interaction, Adjusted for follow-up time only			
	OR (95% CI)	***z***	***P***
MI # Cog impairment # OH			
Ref: normal mobility # normal cognition # No OH	Ref	Ref	Ref
MI with normal cognition, No OH	1.97 (1.10–3.53)	2.29	0.022
OH with normal mobility, normal cognition	0.93 (0.53–1.62)	−0.27	0.789
Cog impairment with normal mobility, No OH	1.09 (0.68–1.75)	0.36	0.719
MI and Cog impairment with no OH	2.82 (1.51–5.30)	3.23	0.001
MI and OH with normal cognition	0.47 (0.14–1.52)	−1.27	0.206
Cognitive impairment and OH with normal mobility	1.74 (0.86–3.51)	1.55	0.122
MI, cognitive impairment and OH	2.91 (1.73–7.68)	3.27	0.001
Model 4: 3-Way Interaction, Fully Adjusted			
	OR (95% CI)	***z***	***P***
MI # Cog impairment # OH			
Ref: normal mobility # normal cognition # No OH	Ref	Ref	Ref
MI with normal cognition, No OH	1.57 (0.85–2.89)	1.45	0.147
OH with normal mobility, normal cognition	0.84 (0.48–1.49)	−0.59	0.557
Cog impairment with normal mobility, No OH	1.10 (0.67–1.79)	0.38	0.704
MI and Cog impairment with no OH	2.02 (1.02–4.00)	2.01	0.045
MI and OH with normal cognition	0.36 (0.11–1.21)	−1.65	0.099
Cognitive impairment and OH with normal mobility	1.44 (0.70–2.95)	0.99	0.324
MI, cognitive impairment and OH	2.51 (1.26–4.98)	2.63	0.045

Notes: $n = 2{,}108$ The Bermuda Triangle of Falls comprises OH, cognitive impairment and MI. OH was defined as a drop of ≥20 mmHg in SBP when measured after standing from a seated position and/or reporting unsteadiness when getting up from a chair. Blood pressure was measured using an Omron digital cuff. Cognitive impairment was defined as an MMSE Score ≤ 24 and/or self-reporting memory as fair or poor. MI was defined as a Timed Up and Go Score ≥ 12 s. Fracture defined as self-report of incident hip, wrist, vertebral or other fracture during follow-up. Abbreviations: Ger Syndromes, Geriatric Syndromes; CI, Confidence Interval; Cog, Cognition. Models 1 and 3 adjusted for follow-up time only. Models 2 and 4 adjusted for age, sex, educational attainment, alcohol excess, heart disease, polypharmacy and chronic disease burden.

polypharmacy as a covariate, this was based solely on prescribed medications as it was not possible to assess compliance within the study. Diagnoses of OH, cognitive impairment and MI were not based on gold standard diagnostic assessments; for example, the diagnosis of OH was based on sitting and standing BP measurements and on self-report of postural unsteadiness, rather than on continuous BP monitoring during an active stand [56]. This also represents a strength of the study; however, as we have shown that an accessible, rapid assessment that can be performed without specialised equipment in most settings can reliably stratify older people at risk of incident unexplained falls and fractures. Further strengths of the study include the large, well-described population-representative sample of older people, with robust follow-up.

In conclusion, this study demonstrated that the 'Bermuda Triangle' of Falls, i.e. the co-existence of OH, cognitive impairment and MI , is independently associated with a significantly increased risk of future unexplained falls and fracture amongst community-dwelling older people, more so than each of the geriatric syndromes in isolation. A rapid assessment delineating the components of the Bermuda Triangle of Falls can therefore be used to identify older people at risk of falls. This simple risk identification scheme may represent an ideal target for multifaceted falls prevention strategies in community-dwelling older adults, as well as

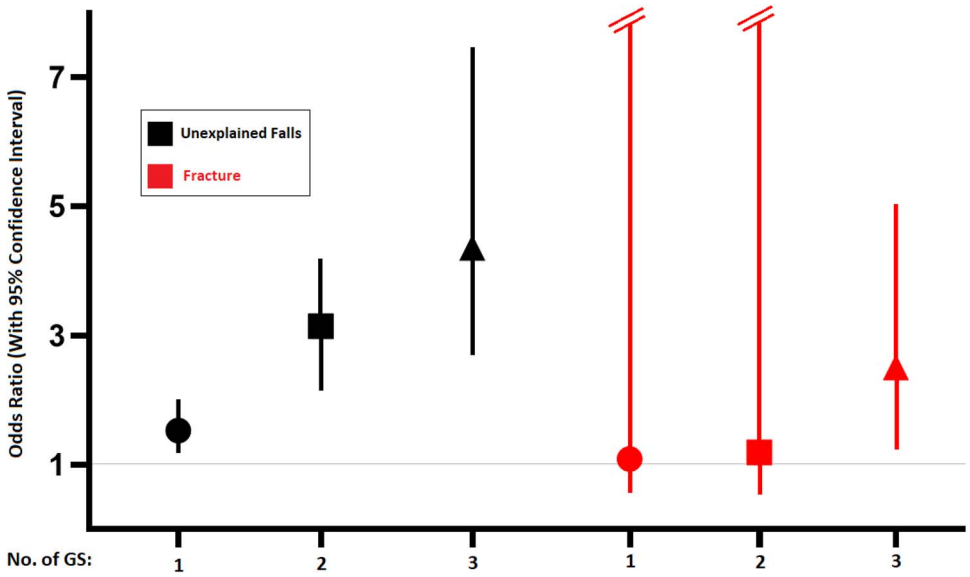

Figure 2. OR with 95% confidence intervals with unexplained falls and fracture as dependent variables by number of geriatric syndromes. *Notes*: the Bermuda Triangle of Falls comprises OH, cognitive impairment and MI. OH was defined as a drop of ≥20 mmHg in SBP when measured after standing from a seated position and/or reporting unsteadiness when getting up from a chair. Blood pressure was measured using an Omron digital cuff. Cognitive impairment was defined as an MMSE Score ≤ 24 and/or self-reporting memory as fair or poor. MI was defined as a Timed Up and Go Score ≥ 12 s. Unexplained Falls defined as falls not because of slips or trips, with no clear reason for the fall. Fracture defined as self-report of incident hip, wrist, vertebral or other fracture during follow-up. Abbreviation: No. of GS, number of geriatric syndromes. OR from logistic regression models with unexplained falls and fractures as dependent variables. Analysis adjusted for follow-up time, age, sex, educational attainment, alcohol excess, heart disease, polypharmacy and chronic disease burden.

more efficient triage, assessment and management in acute settings.

Declaration of Conflicts of Interest: None.

Declaration of Sources of Funding: None.

Data Availability Statement: Researchers interested in using regular waves of TILDA data may access the data for free from the following sites: Irish Social Science Data Archive (ISSDA) at University College Dublin (http://www.ucd.ie/issda/data/tilda/); Interuniversity Consortium for Political and Social Research (ICPSR) at the University of Michigan (http://www.icpsr.umich.edu/icpsrweb/NACDA/studies/34315). Replication of the results reported in this article requires access to the full TILDA dataset. Researchers seeking access to the full TILDA dataset may apply to access the data (tilda.tcd.ie).

References

1. Hartholt KA, Lee R, Burns ER, van Beeck EF. Mortality from falls among US adults aged 75 years or older, 2000-2016. JAMA 2019; 321: 2131–3.
2. Aditya BS, Sharma JC, Allen SC, Vassallo M. Predictors of a nursing home placement from a non-acute geriatric hospital. Clin Rehabil 2003; 17: 108–13.
3. Dunne TJ, Gaboury I, Ashe MC. Falls in hospital increase length of stay regardless of degree of harm. J Eval Clin Pract 2014; 20: 396–400.
4. Trevisan C, Ripamonti E, Grande G *et al.* The association between injurious falls and older adults' cognitive function: the role of depressive mood and physical performance. J Gerontol A Biol Sci Med Sci 2021; 76: 1699–706.
5. Lavedán A, Viladrosa M, Jürschik P *et al.* Fear of falling in community-dwelling older adults: a cause of falls, a consequence, or both? PLoS One 2018; 13: e0194967. https://doi.org/10.1371/journal.pone.0194967.
6. Donald IP, Bulpitt CJ. The prognosis of falls in elderly people living at home. Age Ageing 1999; 28: 121–5.
7. Dellinger A. Older adult falls: effective approaches to prevention. Curr Trauma Rep 2017; 3: 118–23.
8. Freeman R, Abuzinadah AR, Gibbons C, Jones P, Miglis MG, Sinn DI. Orthostatic hypotension: JACC state-of-the-art review. J Am Coll Cardiol 2018; 72: 1294–309.
9. Brown CJ, Flood KL. Mobility limitation in the older patient: a clinical review. JAMA 2013; 310: 1168–77.
10. Shaw FE. Falls in cognitive impairment and dementia. Clin Geriatr Med 2002; 18: 159–73.
11. Saedon NI, Pin Tan M, Frith J. The prevalence of orthostatic hypotension: a systematic review and meta-analysis. J Gerontol A Biol Sci Med Sci 2020; 75: 117–22.
12. Dani M, Dirksen A, Taraborrelli P *et al.* Orthostatic hypotension in older people: considerations, diagnosis and management. Clin Med 2021; 21: e275–82.

13. Finucane C, O'Connell MD, Donoghue O, Richardson K, Savva GM, Kenny RA. Impaired orthostatic blood pressure recovery is associated with unexplained and injurious falls. J Am Geriatr Soc 2017; 65: 474–82.
14. Doyle K, Lavan A, Kenny RA, Briggs R. Delayed blood pressure recovery after standing independently predicts fracture in community-dwelling older people. J Am Med Dir Assoc 2021; 22: 1235–41.e1.
15. Verghese J, LeValley A, Hall CB, Katz MJ, Ambrose AF, Lipton RB. Epidemiology of gait disorders in community-residing older adults. J Am Geriatr Soc 2006; 54: 255–61.
16. Verghese J, Ambrose AF, Lipton RB, Wang C. Neurological gait abnormalities and risk of falls in older adults. J Neurol 2010; 257: 392–8.
17. Verghese J, Holtzer R, Lipton RB, Wang C. Quantitative gait markers and incident fall risk in older adults. J Gerontol A Biol Sci Med Sci 2009; 64: 896–901.
18. Muir SW, Gopaul K, Montero Odasso MM. The role of cognitive impairment in fall risk among older adults: a systematic review and meta-analysis. Age Ageing 2012; 41: 299–308.
19. Sharma S, Mueller C, Stewart R *et al.* Predictors of falls and fractures leading to hospitalization in people with dementia: a representative cohort study. J Am Med Dir Assoc 2018; 19: 607–12.
20. Chantanachai T, Sturnieks DL, Lord SR, Payne N, Webster L, Taylor ME. Risk factors for falls in older people with cognitive impairment living in the community: systematic review and meta-analysis. Ageing Res Rev 2021; 71: 101452. https://doi.org/10.1016/j.arr.2021.101452.
21. O'Neill D. A piece of my mind. To live (and die) as an original. JAMA 2012; 308: 679–80.
22. Romero-Ortuno R, Martinez-Velilla N, Sutton R *et al.* Network physiology in aging and frailty: the grand challenge of physiological reserve in older adults. Front Netw Physiol 2021; 1. https://doi.org/10.3389/fnetp.2021.712430.
23. Briggs R, O'Neill D. Vascular gait dyspraxia. Clin Med 2014; 14: 200–2.
24. Donoghue OA, McGarrigle CA, Foley M, Fagan A, Meaney J, Kenny RA. Cohort profile update: The Irish Longitudinal Study on Ageing (TILDA). Int J Epidemiol 2018; 47: 1398–l.
25. Fedorowski A, Hamrefors V, Sutton R *et al.* Do we need to evaluate diastolic blood pressure in patients with suspected orthostatic hypotension? Clin Auton Res 2017; 27: 167–73.
26. Folstein MF, Folstein SE, McHugh PR. 'Mini-mental state'. A practical method for grading the cognitive state of patients for the clinician. J Psychiatr Res 1975; 12: 189–98.
27. Bischoff HA, Stähelin HB, Monsch AU *et al.* Identifying a cut-off point for normal mobility: a comparison of the timed 'up and go' test in community-dwelling and institutionalised elderly women. Age Ageing 2003; 32: 315–20.
28. Brignole M, Moya A, de Lange FJ *et al.* 2018 ESC guidelines for the diagnosis and management of syncope. Eur Heart J 2018; 39: 1883–948.
29. Bhangu J, King-Kallimanis BL, Donoghue OA, Carroll L, Kenny RA. Falls, non-accidental falls and syncope in community-dwelling adults aged 50 years and older: implications for cardiovascular assessment. PLoS One 2017; 12: e0180997. https://doi.org/10.1371/journal.pone.0180997.
30. Kenny RA, Richardson DA, Steen N, Bexton RS, Shaw FE, Bond J. Carotid sinus syndrome: a modifiable risk factor for nonaccidental falls in older adults (SAFE PACE). J Am Coll Cardiol 2001; 38: 1491–6.
31. Frewen J, King-Kallimanis B, Boyle G, Kenny RA. Recent syncope and unexplained falls are associated with poor cognitive performance. Age Ageing 2015; 44: 282–6.
32. Verwoert GC, Mattace-Raso FU, Hofman A *et al.* Orthostatic hypotension and risk of cardiovascular disease in elderly people: the Rotterdam study. J Am Geriatr Soc 2008; 56: 1816–20.
33. Briggs R, Donoghue OA, Carey D, O'Connell MDL, Newman L, Kenny RA. What is the relationship between orthostatic blood pressure and spatiotemporal gait in later life? J Am Geriatr Soc 2020; 68: 1286–92.
34. Rusanen M, Kivipelto M, Levälahti E *et al.* Heart diseases and long-term risk of dementia and Alzheimer's disease: a population-based CAIDE study. J Alzheimers Dis 2014; 42: 183–91.
35. Bush B, Shaw S, Cleary P, Delbanco TL, Aronson MD. Screening for alcohol abuse using the CAGE questionnaire. Am J Med 1987; 82: 231–5.
36. McNicholas T, Tobin K, Carey D, O'Callaghan S, Kenny RA. Is baseline orthostatic hypotension associated with a decline in global cognitive performance at 4-year follow-up? Data from TILDA (The Irish Longitudinal Study on Ageing). J Am Heart Assoc 2018; 7: e008976. https://doi.org/10.1161/JAHA.118.008976.
37. Darweesh SKL, Licher S, Wolters FJ, Koudstaal PJ, Ikram MK, Ikram MA. Quantitative gait, cognitive decline, and incident dementia: the Rotterdam study. Alzheimers Dement 2019; 15: 1264–73.
38. Jayakody O, Breslin M, Ayers E *et al.* Relative trajectories of gait and cognitive decline in aging. J Gerontol A Biol Sci Med Sci 2021; 77: 1230–8.
39. Walker KA, Sharrett AR, Wu A *et al.* Association of midlife to late-life blood pressure patterns with incident dementia. JAMA 2019; 322: 535–45.
40. Mahinrad S, Kurian S, Garner CR *et al.* Cumulative blood pressure exposure during young adulthood and mobility and cognitive function in midlife. Circulation 2020; 141: 712–24.
41. Angelousi A, Girerd N, Benetos A *et al.* Association between orthostatic hypotension and cardiovascular risk, cerebrovascular risk, cognitive decline and falls as well as overall mortality: a systematic review and meta-analysis. J Hypertens 2014; 32: 1562–71.
42. Jansen S, Bhangu J, de Rooij S, Daams J, Kenny RA, van der Velde N. The Association of Cardiovascular Disorders and Falls: a systematic review. J Am Med Dir Assoc 2016; 17: 193–9.
43. Buckley A, Carey D, Meaney JM, Kenny R, Harbison J. Is there an association between orthostatic hypotension and cerebral white matter hyperintensities in older people? The Irish Longitudinal Study on Ageing. JRSM Cardiovasc Dis 2020; 9: 204800402095462. https://doi.org/10.1177/2048004020954628.
44. de Laat KF, Tuladhar AM, van Norden AG, Norris DG, Zwiers MP, de Leeuw FE. Loss of white matter integrity is associated with gait disorders in cerebral small vessel disease. Brain 2011; 134: 73–83.
45. Frewen J, Savva GM, Boyle G, Finucane C, Kenny RA. Cognitive performance in orthostatic hypotension: findings from a nationally representative sample. J Am Geriatr Soc 2014; 62: 117–22.

46. Montero-Odasso M, Hachinski V. Preludes to brain failure: executive dysfunction and gait disturbances. Neurol Sci 2014; 35: 601–4.
47. Stubbs B, Brefka S, Denkinger MD. What works to prevent falls in community-dwelling older adults? Umbrella review of meta-analyses of randomized controlled trials. Phys Ther 2015; 95: 1095–110.
48. Liu Z, Wang Q, Zhi T *et al.* Frailty index and its relation to falls and overnight hospitalizations in elderly Chinese people: a population-based study. J Nutr Health Aging 2016; 20: 561–6.
49. Jusmanova K, Rice C, Bourke R *et al.* Impact of a specialist service in the emergency department on admission, length of stay and readmission of patients presenting with falls, syncope and dizziness. QJM 2021; 114: 32–8.
50. Bhanu C, Nimmons D, Petersen I *et al.* Drug-induced orthostatic hypotension: a systematic review and meta-analysis of randomised controlled trials. PLoS Med 2021; 18: e1003821. https://doi.org/10.1371/journal.pmed.1003821.
51. Briggs R, Carey D, McNicholas T *et al.* The association between antidepressant use and orthostatic hypotension in older people: a matched cohort study. J Am Soc Hypertens 2018; 12: 597, e1–604.e1.
52. Gross K, King AN, Steadman E. Impact of a pharmacy-led fall prevention program for institutionalized older people. Sr Care Pharm 2021; 36: 217–22.
53. Nørgaard JE, Jorgensen MG, Ryg J *et al.* Effects of gait adaptability training on falls and fall-related fractures in older adults: a systematic review and meta-analysis. Age Ageing 2021; 50: 1914–24.
54. Racey M, Markle-Reid M, Fitzpatrick-Lewis D *et al.* Fall prevention in community-dwelling adults with mild to moderate cognitive impairment: a systematic review and meta-analysis. BMC Geriatr 2021; 21: 689. https://doi.org/10.1186/s12877-021-02641-9.
55. Harwood RH, van der Wardt V, Goldberg SE *et al.* A development study and randomised feasibility trial of a tailored intervention to improve activity and reduce falls in older adults with mild cognitive impairment and mild dementia. Pilot Feasibility Stud 2018; 4: 49. https://doi.org/10.1186/s40814-018-0239-y.
56. Cooke J, Carew S, O'Connor M, Costelloe A, Sheehy T, Lyons D. Sitting and standing blood pressure measurements are not accurate for the diagnosis of orthostatic hypotension. QJM 2009; 102: 335–9.

Received 3 August 2022; editorial decision 11 November 2022