What is the Longitudinal Relationship between Gait Abnormalities and Depression in a Cohort of Community-Dwelling Older People? Data From the Irish Longitudinal Study on Ageing (TILDA)

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Objective: *Does baseline gait disturbance predict incident depression in a cohort of community-dwelling older people?* **Methods:** *This is a longitudinal study, embedded within the Irish Longitudinal Study on Ageing (TILDA), examining the association between baseline depression and incident gait abnormalities, as well as between baseline gait abnormalities and incident depression at 2 year follow-up.*
Depression was defined as a score of ≥16 on the Centre for Epidemiological Studies Depression Scale (CES-D). Gait abnormality was defined as a Timed Up and Go Test (TUG) ≥12 seconds.Assessments were carried out at baseline and at 2 year follow-up.
Results: *7% (179/2,638) had baseline depression and 11% (296/2,638) had a gait abnormality at baseline.The incidence of new-onset depression and gait abnormality at Wave 2 was 4% (95/2,364) and 13% (308/2,342) respectively. Logistic regression models demonstrated that baseline gait abnormality was a significant predictor of incident depression with an Incidence Rate Ratio (IRR) of 2.00 (95% CI: 1.18 – 3.40, p =0.010, t =2.57, df =625), which was not attenuated after controlling for covariates. Baseline depression was a predictor of incident gait abnormality at Wave 2 with an IRR of 1.68 (95% CI: 1.16 – 2.43, p =0.006, t =2.75, df =625) but this association was no longer statistically significant when analysis was adjusted for clinical variables.*
Conclusions: *This study demonstrates that baseline gait disturbance, measured by TUG, predicts incident depression, defined by CES-D, in a population-representative*

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cohort of community-dwelling older people. Possible biological mechanisms for this relationship include white matter disease and executive dysfunction. (Am J Geriatr Psychiatry 2018; 26:75–86)

Key Words: Depression, gait, balance, mobility

Highlights

- There is an established cross-sectional relationship between depression and gait problems in later life but longitudinal data is less consistent.
- This study demonstrates that baseline gait problems, measured by the Timed Up and Go Test, predict incident depression at two-year follow-up in a population-representative cohort of community-dwelling older people.
- Late life depression and gait disturbance may share a common mechanistic pathway that explains this association, as although not measured in this study, both are strongly associated with white matter disease, particularly frontal lobe disease.

Although later life is generally a time of emotional well-being, depression affects 1 in 8 older people and causes significant morbidity in later life.[1,2] Depressive symptoms increase the risk of falls in older people by almost 50%.[3] Furthermore, older fallers are twice as likely to have significant depressive symptoms compared with non-fallers[4] and depression is also a strong predictor of falls in nursing home residents.[5] The association between depression and falls is complex but gait abnormalities may represent one of the underlying mechanisms.

Similarly, gait disorders also represent an often unrecognised "geriatric giant", affecting over one-third of community-dwelling people aged over 70 years.[6] They are independent predictors of adverse outcomes, such as admission to hospital,[7] cognitive decline,[8] nursing home admission,[9] and death.[6]

Gait disorders are generally classified based on the level of sensorimotor deficit involved.[10] Lower-level gait disorders are due to deficits distal to the central nervous system (e.g., osteoarthritis), whereas middle-level gait disorders are due to focal deficits caused by neurological disease, such as in Parkinson disease or stroke.[10] Higher-level gait disorders cannot be explained by demonstrable deficits in the pyramidal, extrapyramidal, sensory, or cerebellar systems and are strongly associated with cerebral white matter disease, particularly frontal lobe disease.[11]

There is an established cross-sectional relationship between late-life depression (LLD) and gait disturbance, with higher burden of depressive symptoms associated with poorer performance in specific components of gait such as velocity, stride, and swing time variability.[12,13] Studies examining the longitudinal relationship between gait and LLD are less consistent, however. The English Longitudinal Study of Ageing demonstrated a bidirectional relationship between gait speed and depressive symptoms in both sexes at 2-year follow-up, but did not control for antidepressant use.[14] The Amsterdam Longitudinal Ageing Study found that slower gait speed predicted incident depressive symptoms but this finding was significant in males alone and analysis was controlled for Centre for Epidemiological Studies Depression Scale score and height only.[15] Furthermore, longitudinal studies to date have used gait speed rather than Timed Up and Go (TUG), the most commonly utilized clinical assessment of gait.[16]

The aim of this study, therefore, is to clarify whether baseline gait problems measured with the TUG predict incident depression in community-dwelling older people. We aim to enhance the current evidence base by controlling for multiple chronic medical conditions that can contribute to gait disturbance, as well as falls burden.

METHODS

This is a longitudinal study in a cohort of community-dwelling participants aged 60 years and over, examining the relationship between gait disturbance and depression. We specifically examined the

association between baseline depression and incident gait abnormalities at 2-year follow-up, as well as baseline gait abnormalities and incident depression at 2-year follow-up.

Study Design

We analyzed data from the first and second wave of The Irish Longitudinal Study on Ageing (TILDA) collected between 2009 and 2012. TILDA is a study of a nationally representative sample of community-dwelling older adults aged 50 years and over. The TILDA study design has been outlined previously.[17]

At baseline, participants completed a computer-assisted personal interview in their own homes that included detailed questions on health, social, and economic circumstances. Each participant was then invited to a health center for a comprehensive health assessment. Participants who were unable or unwilling to attend a health center were offered a modified assessment in their own home.

The 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.

Inclusion / Exclusion Criteria

People with known or suspected dementias were ineligible at baseline for participation. Participants were included if they were aged 60 years and over at baseline, and completed the initial baseline assessment, as well as a follow-up assessment at 2 years.

Depression

The Centre for Epidemiological Studies Depression Scale (CES-D) was used to define depression. The CES-D is a 20-item scale, with response values on a 4-point Likert scale, with range 0 to 3, yielding a total possible score of 60.[18] The CES-D has been validated in an older population, and a value of 16 or more has been shown to have a sensitivity of 92% and a specificity of 87% for diagnosis of depression.[19]

The CES-D was administered at baseline and at wave 2 follow-up 2 years later. Participants with a score of 16 or more on the CES-D at baseline were considered to have baseline depression.[20] A score of 16 or more at follow-up in the baseline non-depressed cohort was used to define incident depression.

Gait

The TUG was used to assess gait.[16] This involves measuring the time taken for a participant to rise from a chair, walk 3 meters, turn around and then walk back to the chair and sit down. The TUG is a reliable screening assessment for gait disturbance at all levels, as well as a predictor of falls risk,[20] correlating well with both gait speed and the Berg Balance Scale.[21]

The TUG was administered at baseline and at the wave 2 follow-up 2 years later. Participants with a score of 12 seconds or more at baseline were considered to have gait disturbance.[22] A score of 12 or more seconds at follow-up in those with no gait abnormalities at baseline was used to define incident gait disturbance.

Other Measures

We controlled for several important covariates that may impact on the relationship between depression and gait abnormalities. Alcohol excess was measured using the CAGE scale.[23] Functional impairment was defined as having one or more impairment in instrumental activities of daily living (IADL), including shopping, housekeeping, accounting, food preparation, and telephone/transportation. Participants were asked if they had fallen in the last 12 months. Cardiac disease was defined as self-report of prior myocardial infarction, current cardiac failure, cardiac arrhythmia, hypertension, or angina. Participants were also asked if they had a history of diabetes, Parkinson disease, arthritis, or stroke. Loneliness was defined as answering either a "moderate amount of time" or "all of the time" when participants were asked "How often are you lonely?" Cognitive impairment was defined as a score of 24 or less on the Mini-Mental State Examination.[24] Additionally, medication lists were examined for antidepressant medication use.

Statistical Analysis

Data were analyzed using Stata (Stata Corp., College Station, TX).

Cross-sectional analysis was weighted. Weights were estimated by comparing the proportion of individuals in the sample across age, sex, highest level of educational attainment, marital status, and urban or rural dwelling, with the proportion of the population with the same characteristics using information from the Central Statistics Office of Ireland. Differences in baseline binary demographic and clinical variables between study groups were therefore presented as weighted prevalence estimates using proportional estimation. Continuous variables were analyzed by linear regression with study group as a predictor. Marginal mean values calculated post-estimation and data was presented by recalculating as (1 divided by the marginal mean).

Additionally, attrition weights were applied to the longitudinal analysis. These weights corrected for the difference in attrition rates over subgroups and reduced the bias caused by this difference in attrition rates. These weights are calculated based on the reciprocal probability of a wave 1 respondent taking part in wave 2. This probability was calculated using a logistic regression model. Factors that were shown to affect attrition included measures of cognitive and behavioral health, marital status, and several health measures.

Logistic regression models were used to predict binary outcomes, with incident rate ratios (IRRs); models were adjusted for relevant covariates. In order to report IRRs, a generalized linear model with Poisson distribution was used. Because it is not possible to specify robust standard errors with the survey weights used in this study, we ran the analysis with and without weights and reported both the weighted and unweighted IRRs.

Three models were tested, with the first model examining the unadjusted IRR of the variable for the outcome of interest; the second model adjusted for age, sex, and baseline depression/gait symptoms; and the third model adjusted for additional clinical factors such as coexisting chronic medical illnesses, antidepressant use, and cognitive impairment. In the third model, we controlled for clinical conditions that may cause middle and lower level gait disturbance, such as alcohol, stroke, Parkinson disease, diabetes, and arthritis. For logistic regression involving incident depression, participants with baseline depression were excluded from the analysis. Participants with baseline gait disturbance were excluded from the logistic regression models for incident gait disturbance.

Average marginal effects were calculated for relevant predictor variables post-estimation. The marginal effect is a measure of the effect that a change in an explanatory variable has on the predicted probability when other covariates are kept constant. Average marginal effects were utilized in preference to directly computing conditional predicted probabilities as several covariates were observed to impact depression/gait abnormality incidence. Average marginal effects models allow us to control for these covariates at the individual level and clarify what the average difference in probability of outcome was across individuals, whereas probability difference estimates are calculated on a casewise basis to begin with.

In order to correct for non-normality of the distribution, reciprocal transformation was applied to the TUG variables as they demonstrated a highly positive skew.

Tetrachoric correlations were used to assess collinearity among binary variables used in the regression models; variables that were highly correlated were excluded from the analyses. A tetrachoric correlation matrix demonstrated significant correlations between ADL impairment and other predictor variables. The variable defining ADL impairment was therefore excluded from the regression analyses. See Appendix A for correlation matrix.

A p value of less than or equal to 0.05 was considered statistically significant.

RESULTS

A total of 2,972 participants were eligible for inclusion in the study. Eleven percent (334 of 2,972) of this initial group did not complete 2-year follow-up and were excluded from the final study sample (see Figure 1 for flow diagram). Thus 2,638 participants were included in the full longitudinal analyses. Of this sample, 7% (179 of 2,638) had a baseline diagnosis of depression at wave 1 and 11% (296 of 2,638) had a gait abnormality at wave 1.

Cross-Sectional Analysis

Table 1 shows the baseline characteristics as weighted prevalence estimates for the study sample, based on their diagnoses at wave 1.

FIGURE 1. Flow diagram of study recruitment. CES-D: Centre for Epidemiological Studies Depression Scale; TUG: Timed Up and Go.

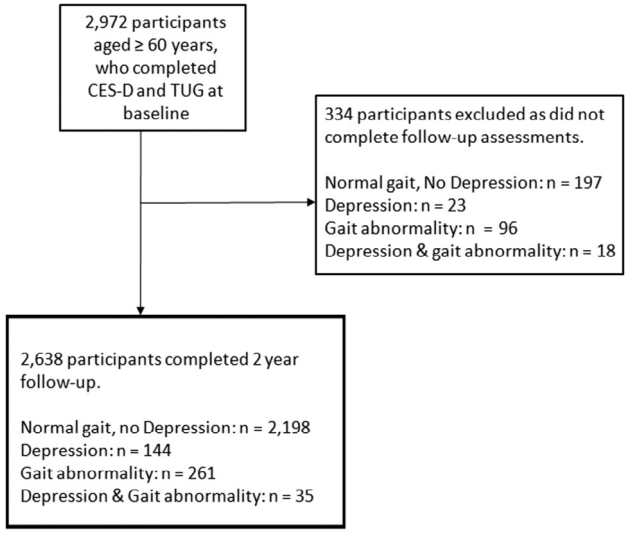
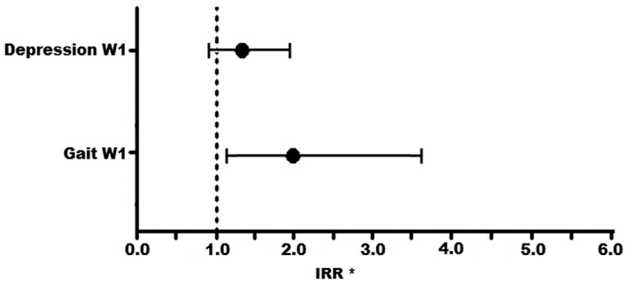


FIGURE 2. Incidence rate ratios (IRR) of baseline depression/gait abnormality as predictor of incident gait abnormality/depression, respectively. Depression W1 demonstrates the odds ratio for depression at wave 1 predicting incident gait abnormality at wave 2. Gait W1 demonstrates the odds ratio for gait abnormality at wave 1 predicting incident depression at wave 2. * IRR presented with 95% confidence interval, after controlling for age, sex, baseline mood/gait problems, alcohol, prior falls, loneliness, heart disease, stroke, diabetes, arthritis, Parkinson disease, antidepressant use, cognitive impairment.



There was a significant baseline association between depression and gait disturbance (see Table 2). Multiple logistic regression models confirmed this association with an unadjusted IRR of 1.84 (95% CI: 1.28–2.66) ($p < 0.001$; df = 625), which was not attenuated after controlling for covariates. See Appendix B.

Longitudinal Analysis

Does Gait Abnormality Predict Incident Depression?

The incidence of new-onset depression at wave 2 was 4% (95 of 2,364).

Participants with incident depression were more likely to have a baseline gait abnormality (linear regression / weighted proportion estimation: 0.23 [95% CI: 0.13–0.33] versus 0.13 [95% CI: 0.11–0.14]; df = 625).

Participants with incident depression also had a longer TUG at wave 1 compared with those with no incident depression at wave 2 (linear regression with post-estimation marginal mean values: 9.86 seconds [95% CI: 9.38–10.40] versus 9.04 seconds [95% CI: 8.94–9.14]).

Logistic regression models demonstrated that baseline gait disturbance (TUG ≥12 seconds at wave 1) was a significant predictor of incident depression at wave 2 with an IRR of 2.00 (95% CI:1.18–3.41, p = 0.010, t = 2.57, df = 625), which was not attenuated after controlling for covariates (see Table 3 and Figure 2).

Average marginal effects estimated post-analysis showed that the effects of abnormal TUG at wave 1 on incident depression at wave 2 was not statistically significant, however (0.035 [95% CI: –0.00 – 0.07], z = 1.84; p = 0.066), suggesting that TUG abnormalities alone do not have a significant effect on the likelihood of developing incident depression when other covariates are kept constant.

Analysis was repeated with participants taking antidepressants excluded. Baseline gait disturbance remained a significant predictor of incident depression after full adjustment (see Appendix C).

Does Depression Predict Incident Gait Abnormality?

The incidence of new-onset gait abnormality at wave 2 was 13% (308 of 2,342).

Participants with incident gait abnormalities were more likely to be depressed at wave 1 compared with those with no incident gait problems at wave 2 (linear

TABLE 1. Baseline Characteristics of Study Sample by Diagnosis at Wave 1

	Non-depressed, Normal gait N = 2,198	Depression N = 144	Gait Disturbance N = 261	Depression & Gait Disturbance N = 35
Age, years[a]	67.9 (67.5–68.2)	66.3 (65.4–67.3)	76.8 (75.9–77.8)	73.2 (70.6–75.8)
Female[b]	0.51 (0.50–0.53)	0.67 (0.59–0.75)	0.56 (0.51–0.62)	0.59 (0.43–0.75)
TUG, seconds[a]	8.6 (8.5–8.6)	8.8 (8.6–9.1)	14.2 (14.0–14.5)	16.1 (14.8–17.6)
≥1 IADL Impairment[b]	0.03 (0.25–0.04)	0.15 (0.09–0.21)	0.22 (0.16–0.27)	0.33 (0.18–0.49)
CAGE score ≥2[b]	0.09 (0.78–0.10)	0.16 (0.10–0.22)	0.04 (0.02–0.06)	0.11 (0.00–0.23)
Fall in last year[b]	0.20 (0.18–0.22)	0.32 (0.25–0.40)	0.26 (0.21–0.32)	0.38 (0.22–0.57)
Lonely[b,c]	0.04 (0.03–0.05)	0.38 (0.30–0.46)	0.08 (0.04–0.11)	0.39 (0.23–0.56)
Cardiac disease[b]:				
- Hypertension	0.40 (0.38–0.42)	0.53 (0.45–0.62)	0.58 (0.51–0.64)	0.63 (0.48–0.78)
- Myocardial infarct	0.05 (0.04–0.06)	0.07 (0.03–0.11)	0.09 (0.05–0.12)	0.12 (0.01–0.23)
- Cardiac failure	0.01 (0.00–0.01)	0.01 (0.00–0.02)	0.01 (0.00–0.02)	0.07 (0.00–0.16)
- Cardiac arrhythmia	0.09 (0.08–0.10)	0.12 (0.07–0.18)	0.15 (0.10–0.19)	0.20 (0.06–0.35)
Prior stroke[b]	0.01 (0.01–0.02)	0.02 (0.00–0.04)	0.04 (0.02–0.07)	0.08 (0.00–0.17)
Diabetes[b]	0.08 (0.07–0.10)	0.09 (0.04–0.14)	0.14 (0.10–0.19)	0.13 (0.02–0.25)
Arthritis[b]	0.32 (0.30–0.34)	0.50 (0.41–0.59)	0.50 (0.44–0.57)	0.66 (0.48–0.83)
Parkinson disease[b]	0.00 (0.00–0.01)	0.01 (0.00–0.02)	0.01 (0.00–0.03)	0.03 (0.00–0.08)
Antidepressant use[b]	0.05 (0.04–0.06)	0.22 (0.15–0.29)	0.10 (0.06–0.14)	0.19 (0.04–0.35)
Cognitive impairment [b,d]	0.03 (0.02–0.04)	0.06 (0.02–0.11)	0.13 (0.08–0.17)	0.11 (0.00–0.22)

Notes: Group who were non-depressed with normal gait did not meet criteria for depression or gait abnormality at wave 1. TUG: Timed Up and Go Test; IADL: instrumental activities of daily living; CES-D: Centre for Epidemiological Studies Depression Scale; MMSE: Mini-Mental State Examination.

[a]Denotes analysis by linear regression with subgroup as predictor. Marginal mean values calculated post-estimation and data presented by recalculating as 1 / (marginal mean).

[b]Denotes weighted prevalence estimates using proportional estimation, presented with 95% confidence intervals.

[c]Lonely defined as answering either a "moderate amount of time" or "all of the time" when asked "How often are you lonely?".

[d]Cognitive impairment defined as Mini-Mental State Examination score ≤24.

TABLE 2. Baseline Association Between Depression and Gait Disturbance, χ^2 Table

	Gait abnormality	Normal Gait	Total
Depression	N = 35 (19.6%)	N = 144 (80.4%)	N = 179 (100%)
Not depressed	N = 261 (10.6%)	N = 2,198 (89.4%)	N = 2,459 (100%)
Total	N = 297 (11.1%)	N = 2,345 (88.8%)	N = 2,638 (100%)

Notes: $\chi^2 = 13.384$, $p < 0.001$.

regression / weighted proportion estimation: 0.10 [0.06–0.14] versus 0.06 [0.05–0.07]; df = 613).

Baseline depression (CES-D ≥ 16 at wave 1) was a predictor of incident gait abnormality at wave 2 with an IRR of 1.68 ([95% CI: 1.16–2.43], p = 0.006, t = 2.75, df = 625) but this association was no longer statistically significant when analysis was adjusted for clinical variables (see Table 4 and Figure 2).

Addition of each of the additional model 3 covariates one by one to model 2 found that loneliness, arthritis, and cognitive impairment caused the greatest attenuation in this association. Addition of only the loneliness variable to model 2 saw a reduction in the IRR from 1.74 (1.25–2.43) to 1.55 (1.05–2.30), and addition of arthritis and cognitive impairment variables to model 2 produced an IRR of 1.64 (1.18–2.30) and 1.65 (1.18–2.32), respectively.

DISCUSSION

This study demonstrates that baseline gait disturbance, measured by TUG, predicted incident depression defined by CES-D, in a population-representative cohort of community-dwelling older people.

TABLE 3. Logistic Regression Reporting Incident Rate Ratios for Association Between Gait Abnormality at Wave 1 and Incident Depression at Wave 2

Incident Depression	IRR (weighted)	p value	t	95% CI	IRR (non-weighted) with 95% CI
Model 1:					
TUG ≥12 seconds wave 1	2.00	0.010	2.57	1.18–3.41	2.11 (1.29–3.42)
Model 2:					
TUG ≥12 seconds wave 1	2.40	0.003	2.93	1.34–4.33	2.25 (1.32–3.83)
Age:					
- Age 65–74 years	0.97	0.896	−0.13	0.60–1.56	1.14 (0.73–1.79)
- Age ≥75 years	0.39	0.022	−2.30	0.17–0.87	0.45 (0.22–0.90)
Female	1.17	0.494	0.69	0.74–1.85	1.33 (0.87–2.02)
Subsyndromal depression [a]	5.71	<0.001	7.73	3.67–8.89	5.40 (3.59–8.15)
Model 3:					
TUG ≥12 seconds wave 1	2.01	0.021	2.32	1.11–3.65	2.00 (1.18–3.39)
Age:					
- Age 65–74 years	0.87	0.562	−0.58	0.55–1.38	1.07 (0.69–1.67)
- Age ≥75 years	0.35	0.005	−2.82	0.17–0.73	0.41 (0.21–0.81)
Female	1.11	0.663	0.44	0.69–1.78	1.26 (0.81–1.96)
Subsyndromal depression [a]	5.38	<0.001	7.63	3.49–8.29	4.95 (3.24–7.57)
CAGE Score:					
- CAGE = 1	1.28	0.419	0.81	0.70–2.34	1.34 (0.71–2.51)
- CAGE = 2	1.49	0.332	0.97	0.66–3.37	1.54 (0.79–3.00)
- CAGE = 3	0.70	0.642	−0.47	0.15–3.21	1.03 (0.25–4.18)
- CAGE = 4	1.61	0.515	0.65	0.38–6.71	1.88 (0.46–7.77)
Falls in last year	0.76	0.278	−1.09	0.47–1.25	0.86 (0.54–1.35)
Lonely [b]	1.03	0.938	0.08	0.48–2.19	0.91 (0.44–1.89)
Cardiac disease [c]	1.08	0.739	0.33	0.68–1.71	1.03 (0.69–1.53)
Stroke	0.72	0.735	−0.34	0.11–4.74	0.60 (0.09–4.08)
Diabetes	1.63	0.164	1.39	0.82–3.26	1.40 (0.79–2.50)
Arthritis	2.03	0.001	3.26	1.32–3.10	1.85 (1.23–2.78)
Parkinson disease	7.02	0.052	1.95	0.99–49.97	4.43 (0.99–19.84)
Antidepressant use	2.69	<0.001	4.07	1.67–4.33	2.79 (1.72–4.52)
Cognitive impairment [d]	0.52	0.301	−1.04	0.15–1.80	0.67(0.22–2.03)

Notes: N = 2,459; design df = 625. CES-D: Centre for Epidemiological Studies Depression Scale; CI: confidence interval; IRR: incidence rate ratio; TUG: Timed Up and Go Test.

[a]Subsyndromal depression defined as CES-D score 8–15.

[b]Lonely defined as answering either a "moderate amount of time" or "all of the time" when asked "How often are you lonely?"

[c]Cardiac disease defined as self-report of prior myocardial infarction, current cardiac failure, cardiac arrhythmia, hypertension or angina.

[d]Cognitive impairment defined as Mini-Mental State Examination score ≤24.

Baseline depression predicted incident gait disturbance in unadjusted models but statistical significance was lost when adjusted for clinical covariates, particularly loneliness, arthritis, and cognitive impairment.

Our findings are supported by longitudinal studies from Finland that have shown that reduced mobility, as well as a reduction in the intensity of physical activity, increases the risk of depression.[25,26] Generally poor physical performance, including 4-meter gait speed, has also been shown to predict incident depression in later life.[27] This study adds to the current evidence base by involving a large, well-described population-based sample of older adults, using the most commonly used clinical assessment of gait and controlling for a comprehensive range of covariates.

There are several factors that may underlie this observed association. Incident depression could represent a response to the physical limitations or loss of independence conferred by mobility problems. Additionally, there may also be a neurobiological basis for this association. White matter hyperintensities (WMHs), bright foci seen in the parenchyma on brain magnetic resonance imaging sequences that represent injury to white matter tracts, have been implicated in LLD, as well as in higher-level gait disorders.[11,28] Furthermore, it appears that this association between WMHs and gait disturbance is more pronounced in the setting of LLD.[29] It is likely that much of the effect we see in this study is related to higher-level gait impairment as we controlled for the most common causes of both middle and

TABLE 4. Logistic Regression Reporting Incident Rate Ratios for Association Between Depression at Wave 1 and Incident Gait Abnormality at Wave 2

Incident Gait Abnormality	IRR (Weighted)	p	t	95% CI	IRR (non-weighted) with 95% CI
Model 1:					
Depression wave 1	1.68	0.006	2.75	1.16–2.43	1.47 (1.03–2.10)
Model 2:					
Depression wave 1	1.75	0.001	3.28	1.25–2.44	1.50 (1.07–2.11)
Age:					
- Age 65–74years	1.45	0.019	2.35	1.06–1.99	1.55 (1.15–2.09)
- Age ≥75 years	2.67	<0.001	6.02	1.94–3.68	2.78 (2.03–3.80)
Female	1.12	0.258	1.13	0.92–1.36	1.18 (0.97–1.43)
TUG at wave 1[a]:					
- TUG 2nd quartile	4.15	<0.001	4.23	2.14–8.03	4.37 (2.30–8.30)
- TUG 3rd quartile	9.40	<0.001	6.93	4.98–17.73	9.32 (5.05–17.22)
- TUG 4th quartile	14.14	<0.001	8.26	7.53–26.54	14.62 (7.91–27.05)
Model 3:					
Depression wave 1	1.35	0.115	1.58	0.93–1.98	1.19 (0.82–1.73)
Age:					
- Age 65–74 years	1.34	0.064	1.86	0.98–1.84	1.42 (1.05–1.92)
- Age ≥75 years	2.32	<0.001	4.95	1.66–3.24	2.40 (1.74–3.31)
Female	1.09	0.417	0.81	0.89–1.34	1.12 (0.92–1.38)
TUG at wave 1[a]:					
- TUG 2nd quartile	3.95	<0.001	4.08	2.04–7.64	4.15 (2.18–7.87)
- TUG 3rd quartile	8.51	<0.001	6.63	4.51–16.05	8.43 (4.56–15.58)
- TUG 4th quartile	12.62	< 0.001	7.85	6.69–23.80	12.97 (6.99–24.09)
CAGE score:					
- CAGE = 1	0.69	0.119	–1.56	0.43–1.10	0.71 (0.45–1.10)
- CAGE = 2	1.28	0.176	1.35	0.90–1.83	1.07 (0.72–1.61)
- CAGE = 3	0.62	0.310	–1.02	0.25–1.56	0.49 (0.19–1.27)
- CAGE = 4	1.09	0.851	0.19	0.46–2.58	1.22 (0.54–2.74)
Falls in last year	0.96	0.756	–0.31	0.76–1.22	1.05 (0.84–1.32)
Lonely [b]	1.26	0.211	1.25	0.88–1.83	1.25 (0.89–1.76)
Cardiac disease [c]	1.24	0.054	1.93	1.00–1.54	1.28 (1.04–1.58)
Stroke	1.34	0.226	1.21	0.83–2.17	1.39 (0.86–2.26)
Diabetes	1.10	0.548	0.60	0.80–1.53	1.04 (0.76–1.42)
Arthritis	1.27	0.023	2.28	1.03–1.57	1.25 (1.02–1.53)
Parkinson disease	1.27	0.422	0.80	0.71–2.25	1.04 (0.48–2.22)
Antidepressant use	1.21	0.323	0.99	0.83–1.77	1.23 (0.87–1.74)
Cognitive impairment [d]	1.55	0.024	2.26	1.06–2.27	1.73 (1.20–2.49)

Notes: N = 2,342; Design DF = 625. CES-D: Centre for Epidemiological Studies Depression Scale; CI: confidence interval; IRR: incidence rate ratio; TUG: Timed Up and Go Test.

[a]TUG quartiles are as follows: 1st quartile = 4.8–7.9 seconds; 2nd quartile = 7.9–8.94 seconds; 3rd quartile = 8.96–10.38 seconds; 4th quartile >10.38 seconds .

[b]Lonely defined as answering either a "moderate amount of time" or "all of the time" when asked "How often are you lonely?"

[c]Cardiac disease defined as self-report of prior myocardial infarction, current cardiac failure, cardiac arrhythmia, hypertension, or angina.

[d]Cognitive impairment defined as Mini Mental State Examination score ≤24.

lower level gait problems (arthritis, alcohol, diabetes, stroke, Parkinson disease).

Executive dysfunction, which often coexists with depression in later life,[30] may also be an important factor in this association as it has also been shown to influence performance on gait analysis such as the TUG.[31] Additionally, WMH volume is independently associated with deficits in executive functioning and studies have described a specific phenotype characterized by slow gait, impaired executive function, and depressive symptoms in an older population with significant vascular disease.[32]

The modest results for average marginal effects we have shown do not support the use of gait analysis in isolation as an objective marker of depression risk in later life. It appears that a combination of gait impairment and depression has an additive effect on the incidence of significant disability in later life, however,[33] and older people with coexisting gait problems and depression may therefore be an appropriate target for

multimodal interventions aimed at reducing functional decline. The augmentation of antidepressant therapy with physical exercise has been shown to improve remission rates in LLD.[34]

Furthermore, it must be noted that subsyndromal depressive symptoms remain the strongest predictor of incident depression in this cohort. Other significant predictors of incident depression include arthritis, another condition with significant effects on mobility.

Our study has some limitations which should be noted. Diagnosis of depression was based on the CES-D, rather than the gold standard structured psychiatric interview. Similarly, gait disturbance was also defined based on a validated tool rather than a clinical diagnosis, but the TUG is widely used in clinical settings. In the setting of a large longitudinal study such as this, however, individual clinical assessments are not feasible and both tools have been validated for use in an older population. Sufficient data on anxiety symptoms was not available to include in our analysis. The strengths of this study include the large population-based sample of community-dwelling older adults, with comprehensive health data available for analysis, including medical comorbidities, full medication lists, and gait and cognitive testing.

In conclusion, this study demonstrates that baseline gait problems are associated with a twofold increase of incident depression in a population-based sample of older adults. Further studies are required to focus on a potentially common mechanistic pathway for this association involving WMHs and executive dysfunction as potential mediators of this relationship.

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APPENDIX A: TETRACHROIC CORRELATION MATRIX FOR BINARY COVARIATES

	ADL	Falls	Lonely	Cardiac	Stoke	Diabetes	Arthritis	Parkinsons	Antidep	Cog Imp
ADL	1.00									
Falls	0.23	1.00								
Lonely	0.32		1.00							
Cardiac	0.25			1.00						
Stroke	0.31			0.35	1.00					
Diabetes				0.33		1.00				
Arthritis	0.32	0.15	0.21	0.14			1.00			
Parkinsons								1.00		
Antidep	0.27	0.21				0.16			1.00	
Cog Imp	0.34									1.00

Abbreviations: ADL = ADL Impairment; Falls = falls in last year; Lonely = loneliness; Cardiac = myocardial infarction, cardiac failure, arrhythmia or angina; Antidep = Antidepressants; Cog Imp = cognitive impairment.

APPENDIX B: LOGISTIC REGRESSION REPORTING INCIDENT RATE RATIOS (IRR) FOR CROSS-SECTIONAL ASSOCIATION BETWEEN BASELINE DEPRESSION AND GAIT ABNORMALITY AT WAVE 1

Depression Wave 1	IRR (Weighted)	p Value	t	95% CI	IRR (Non-weighted) with 95% CI
Model 1:					
TUG ≥ 12 seconds Wave 1	1.84	0.001	3.29	1.28 – 2.66	1.92 (1.36 – 2.73)
Model 2:					
TUG ≥ 12 seconds Wave 1	2.61	<0.001	4.48	1.72 – 3.99	2.73 (1.88– 3.98)
Age:					
- Age 65 – 74 years	0.81	0.192	−1.31	0.59 – 1.11	0.80 (0.59 – 1.10)
- Age ≥ 75 years	0.41	0.001	−3.23	0.24 – 0.71	0.39 (0.24 – 0.63)
Female gender	1.65	0.001	3.20	1.21 – 2.24	1.71 (1.26 – 2.31)
Model 3:					
TUG ≥ 12 seconds Wave 1	1.77	0.004	2.90	1.20 – 2.60	1.84 (1.27 – 2.67)
Age:					
- Age 65 – 74 years	0.69	0.013	−2.48	0.51 – 0.92	0.70 (0.52 – 0.95)
- Age ≥ 75 years	0.37	<0.001	−4.10	0.23 – 0.60	0.36 (0.23 – 0.57)
Female gender	1.25	0.203	1.27	0.89 – 1.75	1.27 (0.93 – 1.74)
CAGE Score:					
- CAGE = 1	1.14	0.562	0.58	0.73 – 1.78	1.14 (0.74 – 1.76)
- CAGE = 2	1.07	0.790	0.27	0.65 – 1.76	0.93 (0.55 – 1.57)
- CAGE = 3	2.11	0.002	3.12	1.32 – 3.37	2.03 (1.27 – 3.25)
- CAGE = 4	1.48	0.478	0.71	0.50 – 4.33	1.07 (0.44 – 2.60)
Falls in last year	1.38	0.031	2.16	1.03 – 1.86	1.33 (0.99 – 1.79)
Lonely [a]	6.88	<0.001	12.91	5.13 – 9.23	6.96 (5.28 – 9.17)
Cardiac Disease [b]	1.49	0.006	2.79	1.13 – 1.98	1.35 (1.04 – 1.77)
Stroke	1.55	0.192	1.31	0.80 – 3.00	1.49 (0.74 – 3.00)
Diabetes	0.89	0.612	−0.51	0.55 – 1.42	0.87 (0.55 – 1.38)
Arthritis	1.61	0.001	3.22	1.21 – 2.16	1.55 (1.17 – 2.06)
Parkinson's Disease	1.53	0.620	0.50	0.29 – 8.15	1.18 (0.19 – 7.51)
Antidepressant Use	2.38	<0.001	5.61	1.76 – 3.22	2.55 (1.89 – 3.45)
Cognitive Impairment [c]	1.41	0.308	1.02	0.73 – 2.71	1.37 (0.72 – 2.59)

Footnotes:
N = 2,638; Design DF = 625.
Abbreviations: IRR = Incident Rate Ratio; CI = Confidence Interval; TUG = Timed Up and Go Test.
[a]Lonely defined as answering either a "moderate amount of time" or "all of the time" when asked "How often are you lonely?"
[b]Cardiac disease defined as self-report of prior myocardial infarction, current cardiac failure, cardiac arrhythmia, hypertension or angina.
[c]Cognitive impairment defined as Mini Mental State Examination score ≤ 24.

APPENDIX C: LOGISTIC REGRESSION REPORTING INCIDENT RATE RATIOS (IRR) FOR ASSOCIATION BETWEEN GAIT ABNORMALITY AT WAVE 1 AND INCIDENT DEPRESSION AT WAVE 2, EXCLUDING ANTIDEPRESSANT USERS

Incident Depression	IRR (Unweighted)	p Value	z	95% CI
TUG ≥ 12 seconds Wave 1	1.98	0.041	2.04	1.03 – 3.83
Age:				
- Age 65 – 74 years	0.95	0.829	−0.22	0.58 – 1.54
- Age ≥ 75 years	0.48	0.043	−2.02	0.23 – 0.98
Female gender	1.43	0.150	1.44	0.88 – 2.32
Subsyndromal Depression [a]	5.10	<0.001	6.73	3.17 – 8.19
CAGE Score:				
- CAGE = 1	1.58	0.156	1.42	0.84 – 2.97
- CAGE = 2	1.69	0.188	1.32	0.77 – 3.70
- CAGE = 3	1.17	0.830	0.21	0.29 – 4.76
- CAGE = 4	3.17	0.077	1.77	0.88 – 11.40
Falls in last year	0.79	0.403	−0.84	0.46 – 1.37
Lonely [b]	0.68	0.405	−0.83	0.27 – 1.69
Cardiac Disease [c]	1.01	0.971	0.04	0.65 – 1.57
Stroke	6.11e-06	<0.001	−34.14	3.07 e-06 – 0.00
Diabetes	1.17	0.671	0.42	0.56 – 2.46
Arthritis	1.98	0.003	2.96	1.26 – 3.12
Parkinson's Disease	3.44	0.273	1.10	0.38 – 31.19
Antidepressant Use	Omitted			
Cognitive Impairment [d]	0.46	0.459	−0.74	0.06 – 3.63

Footnotes:
Abbreviations: IRR = Incidence Rate Ratio; TUG = Timed Up and Go Test; CES-D = Centre for Epidemiological Studies Depression Scale.
[a]Subsyndromal depression defined as CES-D score 8–15.
[b]Lonely defined as answering either a "moderate amount of time" or "all of the time" when asked "How often are you lonely?"
[c]Cardiac disease defined as self-report of prior myocardial infarction, current cardiac failure, cardiac arrhythmia, hypertension or angina.
[d]Cognitive impairment defined as Mini Mental State Examination score ≤ 24.

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