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Research Article

The Association Between Psychotropic Medication Use and Gait and Mobility Impairment in Community-Dwelling Older People: Data From The Irish Longitudinal Study on Ageing (TILDA)

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Abstract

Background: Little work to date has quantified the effect of psychotropic medications (antidepressants, benzodiazepines, "Z" drugs, antipsychotics, anticholinergics) on mobility and gait in later life. The aim of this study is to examine the relationship between these medications and mobility/gait parameters in a large cohort of community-dwelling older people.

Methods: Participants were included if they were aged ≥60 years at TILDA Wave 1 and underwent gait and mobility assessment (Gaitrite system), with follow-up at Wave 3 (4 years). Medication lists were examined for psychotropic medications. Regression models assessed the relationship between psychotropic medications and mobility using the following parameters: Timed Up and Go, gait speed, step length/width, and double support phase. Multilevel modeling assessed trajectories of mobility/gait variables over time by psychotropic use.

Results: Of 2620 patients, 12% were prescribed ≥1 psychotropic medication, and 3% prescribed ≥2 psychotropics. Cross-sectionally, psychotropic medication was independently associated with prolonged Timed Up and Go (β = 0.50 [95% confidence interval {CI} 0.27–0.73]; $p < .001$), slower gait speed (β = −5.65 [95% CI −7.92 to −3.38]; $p < .001$), shorter step length (β = −2.03 [95% CI −2.93 to −1.42]; $p < .001$), and increased double support phase (β = 0.47 [95% CI 0.19–0.75]; $p = .001$). Longitudinally, psychotropic use was independently associated with transition to abnormal Timed Up and Go (odds ratio 2.68 [95% CI 1.55–4.64], $p < .001$), whereas using ≥2 psychotropics was associated with transition to slower gait speed (odds ratio 2.59 [95% CI 1.01–6.68]; $p = .048$).

Conclusions: Psychotropic use was associated with significantly poorer mobility and gait performance, both cross-sectionally and longitudinally. It is imperative that psychotropic medication use is reviewed as part of a comprehensive geriatric assessment.

Keywords: Anticholinergics, Antidepressants, Antipsychotics, Benzodiazepines, Z drugs

Psychotropic medications are medications that effect mental processes, behavior, or mood and include: antidepressants, antipsychotics, benzodiazepines, drugs with anticholinergic effects, and "Z" drugs (1). Psychotropic medications are commonly prescribed for neuropsychiatric disorders in older adults, with a prevalence of use in community dwelling older adults of 19–29% (2). At least 1 in 6 adults in the United States is prescribed a psychotropic medication (3). Prior research indicates that antidepressants (4) and benzodiazepines (5) are the most frequently prescribed psychotropic medications internationally (6). Although often clinically appropriate, prescription of these medications for older adults has become increasingly prevalent, despite this cohort being most susceptible to their side effects (7).

Psychotropic medication use has consistently been shown to be a strong risk factor for future falls amongst older people, with prior data from TILDA demonstrating a 50% increase in the incidence of unexplained falls independently related to psychotropic medication use (8). Falls are the commonest cause of accidental death in this cohort (9) and the most frequent reason for injury-related presentation to the hospital (10). Many falls in later life are related to modifiable factors and may therefore be potentially preventable (11). Prescription of falls risk inducing drugs (FRIDs) is one such modifiable factor (12). The recently validated Screening Tool of Older Persons Prescriptions in older adults with high fall risk (STOPPFall) included several psychotropic classes (antipsychotics, antidepressants, Z drugs, anticholinergics, and benzodiazepines) among their list of medication groups to consider deprescribing in the setting of falls (13).

Given the profound effect falls can have on older patients in terms of physical injury, functional decline (14) and risk of

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death (15), it is vital to understand how psychotropic medications increase falls risk. Although some effects of psychotropic medications on mobility are clinically well-recognized, such as their association with drug-induced parkinsonism, little work has quantified the adverse effect psychotropics have on specific gait parameters that may predispose older people to falls.

The objective of this study therefore is to examine the effect of psychotropic medication use, both cross-sectionally and longitudinally, on functional mobility and specific spatiotemporal gait parameters in a cohort of community-dwelling older people.

Method

Study Design

This study examines the effect of psychotropic medication use on the mobility and gait of a large cohort of community-dwelling people aged ≥60 years, both cross-sectionally and longitudinally (4-year follow-up), utilizing data from The Irish Longitudinal Study on Ageing (TILDA).

The TILDA study design has been outlined previously (16). Briefly, there are 3 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 center-based health assessment or a modified home-based health assessment carried out by trained research nurses. Waves of data collection are conducted at 2-yearly intervals, and we used data from Waves 1 and 3, collected between 2009 and 2015.

Participants were included in this study if they were aged ≥60 years at Wave 1, had a medication list examined for medications of interest, and underwent the TILDA health assessment with measures of mobility and gait. Participants were excluded from participation in TILDA at Wave 1 if they had a preexisting diagnosis of dementia.

Ethics

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. All assessments were carried out by trained research nurses.

Psychotropic Medications

Medication use was recorded and cross-checked with medication labels at baseline assessment. The Anatomical Therapeutic Chemical (ATC) Classification System was used to identify specific medications. Antidepressants were identified with an ATC code of N06A. Benzodiazepines were identified with an ATC code of N05BA, N05CD, and N03AE. "Z" drugs were coded as N05CF and antipsychotics were coded as N05A.

Anticholinergic medications were included due to their known neuropsychiatric effects, along with the fact that they were included in the recently validated STOPPFall (13). Only medications classified as having 'definite' anticholinergic effects according to the Anticholinergic Cognitive Burden (ACB) scale (medications with an ACB score of ≥2) (17) were included. Medications with an ACB score of 1 were not included as they are unlikely to be deemed "culprit" medications or serve as potential targets for deprescribing (the process of identifying and discontinuing medications in which existing or potential harms outweigh potential benefits within the context of an individual patient's care goals, function, values, and preferences) (18) in the setting of gait impairment.

Anticholinergics (including medications from the following classes: urologicals, gastrologicals, parkinsonians, antihistamines, antidepressants, and antipsychotics) were identified with the following ATC codes: N06AA, N06AB05, G04BD, N05AA01, N05AA03, N05AB03, N05AB06, N05AC02, N05AH03, N05AH04, A03, N04A, R06A, M03BA03, M03BC01, N05CM05, and N05BB01.

To determine the prevalence of psychotropic medication deprescribing, prescriptions of psychotropic medication at the outset (Wave 1) and at 4-year follow-up (Wave 3) were reviewed. Patients were deemed to have had psychotropic medication deprescribed if they were on at least 1 psychotropic medication at Wave 1 and were no longer on a psychotropic medication at Wave 3.

Mobility and Gait

The Timed Up and Go Test (TUG) was used to assess mobility (19). During the TUG, the time taken for the participant to stand up from a chair, walk 10 ft/3 m at normal pace, turn, and walk back to the chair at normal pace before sitting again is measured in seconds.

The TUG was administered at baseline and at Wave 3 follow-up 4 years later. As per recently published World Falls Guidelines, participants with a TUG of ≥15 seconds were considered to have mobility impairment (11).

Spatiotemporal gait analysis was performed using the GAITRite system, a computerized mat with pressure sensors, measured at Waves 1 and 3 (20). Participants started walking 2.5 m before the mat and stopped 2 m after the mat to allow for acceleration and deceleration. They completed 2 at the usual walking pace and 2 walks while carrying out a cognitive task (reciting alternate letters of the alphabet, ie, A-C-E, etc). Data from the 2 walks in each condition were averaged; for example, the 2 "normal" walks were combined to yield one overall variable for normal walking, and the following gait variables were obtained: gait speed, step length, step width, and double support phase. We used data from the right foot for all variables.

Gait speed is defined as the distance covered by the body per unit time and is measured in cm/second. Step length is the distance between corresponding successive points of heel contact of the opposite foot. Step width is the side-to-side distance measured between the midline midpoint of one foot to the midline midpoint of the opposite foot. The double support phase is the time spent with both feet in contact with the floor, expressed as a percentage of the total gait cycle.

Other Variables

Educational attainment was by self-report (primary, secondary, or tertiary). The Cut Down, Angry, Guilty, Eye Opener (CAGE) scale was used to assess for excess alcohol intake (21). Heart disease was defined as a self-report of heart attack, angina, congestive cardiac failure, and/or arrhythmia. Chronic disease burden was assessed by self-report of the following conditions: lung disease, eye problems, cancer, osteoporosis, liver disease, arthritis, incontinence, Parkinson's disease, and diabetes. Depressive symptoms were measured with the Centre for Epidemiological Studies Depression Scale,

with a score ≥16 indicating clinically significant symptoms (22). Poor sleep was defined as responding "all the time" when asked how often a participant's sleep was restless in the last week. Cognitive impairment was defined as a score <25 on the Mini–Mental State Examination (23).

Statistical Analysis

Data were analyzed using Stata version 14.1 (StataCorp LLC, College Station, TX). Baseline characteristics of the study sample, by psychotropic medication use, were analyzed descriptively, presenting proportions with 95% confidence intervals (CI).

For cross-sectional analysis (Wave 1 data only), differences in mean values of gait and mobility parameters (TUG, gait speed, step length, step width, and double support phase) were analyzed with *t*-tests. Linear regression models, reporting β-coefficients with 95% CI, were used to assess the relationship between psychotropic medication use (taking one or more agents, taking 2 or more agents, and by specific medication classes) and gait and mobility parameters.

For longitudinal analysis (Waves 1 and 3), quartiles of mobility and gait parameters were calculated. Logistic regression models were then used to assess the relationship between psychotropic medication use at Wave 1/baseline use (taking one or more agents, taking 2 or more agents, and by specific medication classes) and gait and mobility parameters at Wave 3 (4-year follow-up). We specifically examined the likelihood of transitioning from a normal (ie, <15 seconds) to an abnormal TUG (≥15 seconds) and to the "lowest" quartile for each gait parameter (ie, the slowest gait speed quartile, the shortest step length quartile, the widest step width quartile, and the highest percentage of double support phase). For each of these transition analyses, participants with a TUG > 15 seconds at Wave 1 or in the lowest quartile in terms of gait were excluded, respectively.

Further, multilevel models with gait and mobility parameters as dependent variables nested within participants were used to compare data across specific time points by psychotropic medication use, and average marginal effects were calculated and graphed, allowing visualization of the trajectory of mobility and gait parameters from baseline to 4-year follow-up.

For analyses described earlier (cross-sectional linear regression models, longitudinal logistic regression models, and multilevel mixed effects models), 2 models were tested: the first model was unadjusted; the second model was adjusted for age, sex, educational attainment, excess alcohol intake, chronic disease burden, heart disease, depressive symptoms, poor sleep, and cognitive impairment. Variables were chosen a priori based on their likely probability of modifying the index relationship between mobility/gait and psychotropic medication use.

Data Availability Statement

TILDA provides access to datasets for research use through pseudonymized, publicly accessible dataset files and through an on-site Hot Desk Facility. The publicly accessible dataset files are hosted by the Irish Social Science Data Archive (ISSDA), based in University College Dublin, and the Interuniversity Consortium for Political and Social Research (ICPSR), based in the University of Michigan. Researchers wishing to access the data must complete a request form, available on either the ISSDA or ICPSR website.

Results

Baseline Characteristics

Of 2 620 participants, 1 in 8 were prescribed a psychotropic medication (proportion 0.12 [95% CI 0.11–0.13]), with 3% prescribed 2 or more psychotropic medications (proportion 0.03 [95% CI 0.02–0.03]).

Antidepressants were the most frequently prescribed psychotropic medications (proportion 0.06 [95% CI 0.05–0.07]), followed by benzodiazepines (proportion 0.04 [95% CI 0.03–0.05]), anticholinergics (proportion 0.04 [95% CI 0.03–0.05]), and then 'Z' drugs (proportion 0.03 [95% CI 0.02–0.04]).

Baseline characteristics of the study sample, by psychotropic medication use, are shown in Table 1. Participants prescribed psychotropic medication were more likely to be female, had higher rates of alcohol misuse and heart disease, and were more likely to have multiple medical comorbidities.

Cross-Sectional Analysis

Figure 1 shows cross-sectional differences in mobility and gait parameters by psychotropic medication use.

Participants prescribed ≥1 psychotropic medication (mean TUG 10.0 seconds [95% CI 9.7–10.3]) or ≥2 psychotropic medications (mean TUG 10.2 seconds [95% CI 9.6–10.8]) had a significantly longer TUG than those who were not prescribed psychotropic medication (mean TUG 9.0 seconds [95% CI 8.9–9.1]). Similarly, participants prescribed ≥1 psychotropic medication (gait speed 120.8 cm/s [95% CI 118.4–123.3]) and those prescribed ≥2 psychotropics (gait speed 117.2 cm/s [95% CI 112.1–122.4]) had a significantly slower gait speed compared with those not prescribed psychotropic medication (131.4 cm/s [95% CI 130.6–132.2]).

Step length was significantly shorter in participants prescribed ≥1 psychotropic medication (step length 64.2 cm [95% CI 63.2–65.2]) or ≥2 psychotropic medications (step length 62.9 cm [95% CI 60.8–65.1]), compared with participants not prescribed psychotropic medications (step length 69.1 [95% CI 68.7–69.5]). Double support phase was higher for those taking ≥1 psychotropic medication (13.6% [95% CI 13.4–13.9]) or 2 or more psychotropic medications (13.8% [95% CI 13.3–14.3]) when compared with those not taking psychotropic medication (12.8% [95% CI 12.7–12.9]). No significant differences were observed between groups for step width. Table 2 shows output from linear regression models with mobility and gait measures as dependent variables.

Taking ≥1 psychotropic medication was independently associated with prolonged TUG, slower gait speed (both normal and cognitive walks), shorter step length (both normal and cognitive walks), and a higher double support phase (both normal and cognitive walks). Similar findings, with stronger associations and larger β-coefficients, were generally observed for ≥2 psychotropic medications, apart from the double support phase, where no association was found. Benzodiazepine use was independently associated with shorter step length and a higher double support phase during the normal walk. Antidepressant use was independently associated with prolonged TUG and with slower gait speed (normal and cognitive walk), shorter step length (normal and cognitive walk), and a higher double support phase (normal walk only). Z drugs were associated with prolonged TUG and with slower gait speed (normal walk only) and shorter step length (normal walk only). Anticholinergics were associated with prolonged

Table 1. Baseline Characteristics of Study Sample by Psychotropic Medication Use

	No Psychotropics *n* = 2 314	≥1 Psychotropic *n* = 306	≥2 Psychotropics *n* = 72
Mean age, years (95% CI)	67.9 (67.6–68.1)	68.8 (68.1–69.6)	68.9 (67.4–70.3)
Female sex (prop, 95% CI)	0.52 (0.50–0.54)	0.66 (0.60–0.71)	0.67 (0.55–0.77)
Educational attainment (prop, 95% CI)			
Primary	0.28 (0.26–0.30)	0.39 (0.33–0.44)	0.36 (0.26–0.48)
Secondary	0.38 (0.36–0.40)	0.32 (0.27–0.37)	0.36 (0.26–0.48)
Tertiary	0.34 (0.32–0.36)	0.29 (0.25–0.35)	0.28 (0.18–0.39)
CAGE alcohol scale (prop, 95% CI)			
<2	0.83 (0.81–0.84)	0.77 (0.72–0.82)	0.75 (0.63–0.84)
≥2	0.09 (0.08–0.10)	0.14 (0.11–0.19)	0.17 (0.10–0.27)
Did not answer	0.08 (0.07–0.10)	0.08 (0.06–0.12)	0.08 (0.04–0.18)
Heart disease (prop, 95% CI)	0.17 (0.15–0.18)	0.27 (0.22–0.32)	0.26 (0.17–0.38)
Chronic disease number (prop, 95% CI)			
None	0.40 (0.38–0.43)	0.17 (0.13–0.22)	0.17 (0.10–0.27)
1	0.33 (0.32–0.35)	0.29 (0.24–0.34)	0.25 (0.16–0.37)
2–3	0.23 (0.22–0.25)	0.41 (0.36–0.47)	0.42 (0.31–0.54)
4+	0.03 (0.02–0.04)	0.13 (0.09–0.17)	0.17 (0.10–0.27)
Prescribed medications (prop, 95% CI)			
0	0.23 (0.21–0.24)	0.0 (0.00–0.00)	0.0 (0.00–0.00)
1–2	0.33 (0.31–0.35)	0.16 (0.12–0.20)	0.13 (0.08–0.21)
3–4	0.24 (0.22–0.26)	0.27 (0.23–0.33)	0.23 (0.16–0.32)
≥5	0.20 (0.19–0.22)	0.57 (0.51–0.62)	0.64 (0.54–0.73)
Mean (95% CI)	2.37 (2.28–2.46)	4.99 (4.67–5.30)	5.58 (5.02–6.15)
Cognitive impairment	0.04 (0.03–0.05)	0.06 (0.04–0.10)	0.03 (0.01–0.11)
Depressive symptoms	0.05 (0.04–0.06)	0.20 (0.16–0.25)	0.26 (0.17–0.38)
Poor sleep	0.05 (0.05–0.06)	0.17 (0.13–0.21)	0.18 (0.11–0.29)

Notes: CAGE = Cut Down, Angry, Guilty, Eye Opener Scale; CI = confidence interval.
Psychotropic medications include antidepressants (Anatomical Therapeutic Classification (ATC) code N06A); benzodiazepines (ATC N05BA, N05CD, and N03AE); "Z" drugs (ATC N05CF); antipsychotics (N05A); and anticholinergic medications (those classified as having "definite" anticholinergic effects according to the Anticholinergic Cognitive Burden scale).
Heart disease defined as self-report of heart attack, angina, congestive cardiac failure, and/or arrhythmia.
Chronic disease burden was assessed by self-report of the following conditions: lung disease, eye problems, cancer, osteoporosis, liver disease, arthritis, incontinence, Parkinson's disease, and diabetes.
Depressive symptoms were measured with the Centre for Epidemiological Studies Depression Scale, with a score ≥16 indicating clinically significant symptoms.
Poor sleep was defined as responding "all the time" when asked how often a participant's sleep was restless in the last week.
Cognitive impairment was defined as a score <25 on the Mini–Mental State Examination.

TUG, slower gait speed (both normal and cognitive walks), and shorter step length (both normal and cognitive walks).

Longitudinal Analysis

Just over 600 participants (606/2 620, 23% of initial sample) did not undergo repeat TUG at 4-year follow-up at Wave 3, but 870 (33% of initial sample of 2 620) did not undergo repeat gait analysis, yielding a follow-up sample of 2 014 and 1 750 for longitudinal TUG and gait analyses, respectively. Characteristics of participants who were followed to Wave 3 compared with those lost to attrition are shown in Supplementary Table 1. The group that was lost to attrition for the TUG analysis was older had lower levels of educational attainment and higher rates of cognitive impairment when compared with the full baseline sample. Those lost to attrition for the gait analysis were older and had higher rates of polypharmacy and cognitive impairment when compared with the full sample.

Almost 30% (64/226) of participants who were prescribed either antidepressants, antipsychotics, benzodiazepines, or "Z" drugs at Wave 1 and followed to Wave 3 were no longer prescribed these medications at 4-year follow-up. Over 8% (165/2 601) of those who were not prescribed an antidepressant, antipsychotic, benzodiazepine, or 'Z' drug at Wave 1 were prescribed at least one of these medications at Wave 3. Over 4% (88/1 991) of participants who had a normal TUG at Wave 1 had an abnormal TUG at Wave 3. In fully adjusted models, ≥1 psychotropic medication use was associated with transition from normal to abnormal TUG at an odds ratio (OR) of 2.68 (95% CI 1.55–4.64), $p < .001$. Further, use of ≥2 psychotropic medications was associated with a threefold higher likelihood of transition to abnormal TUG at 4-year follow-up (OR 3.14 [95% CI 1.31–7.54]; $p = .011$). Psychotropic medication classes significantly associated with transition to abnormal TUG in fully adjusted models were antidepressant medications (OR 2.01 [95% CI 1.05–4.19]; $p = .036$), anticholinergics (OR 2.94 [95% CI 1.37–6.30]; $p = .006$), and "Z" drugs (OR 3.19 [95% CI 1.35–7.58]; $p = .008$). See Figure 2.

Over 17% of participants transitioned to a gait speed less than 117.7 cm/s (ie, the 1st/slowest quartile of gait speed at

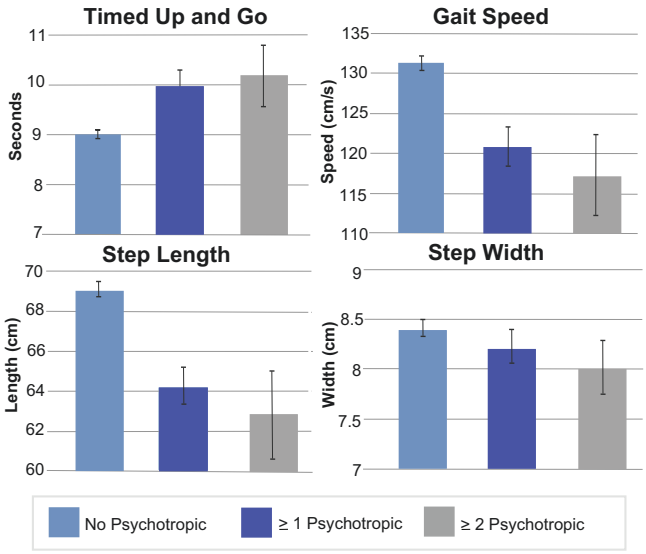

Figure 1. Mobility and gait parameters by psychotropic medication use. *Notes*: *N* = 2 620 (201 prescribed ≥1 psychotropic medication, 72 prescribed ≥2). Psychotropic medications include antidepressants (Anatomical Therapeutic Classification (ATC) code N06A); benzodiazepines (ATC N05BA, N05CD, and N03AE); "Z" drugs (ATC N05CF); antipsychotics (N05A); and anticholinergic medications (those classified as having 'definite' anticholinergic effects according to the Anticholinergic Cognitive Burden scale). The Timed Up and Go is a measure of the time taken in seconds for the participant stands up from a chair, walks 10 ft/3 m at normal pace, turn, and walk back to the chair at normal pace before sitting again. Spatiotemporal gait analysis was performed using the GAITRite system. Gait speed is defined as the distance covered by the body per unit time and is measured in cm/second. Step length is the distance in cm between corresponding successive points of heel contact of the opposite foot. Step width is the side-to-side distance in cm measured between the midline midpoint of one foot to the midline midpoint of the opposite foot. The double support phase is the time spent with both feet in contact with the floor, expressed as a percentage of the total gait cycle.

Wave 1) at Wave 3. In fully adjusted models, use of ≥1 psychotropic medication was not significantly associated with transitioning to this slowest quartile of gait speed (OR 1.60 [95% CI 0.99–2.58]; $p = .053$), but using ≥2 psychotropic medications was associated with a significant increase in the likelihood of transition to this slower gait speed (OR 2.59 [95% CI 1.01–6.68]; $p = .048$). Benzodiazepine use (OR 3.51 [95% CI 1.60–7.68]; $p = .002$) was associated with transition to slower gait speed, but antidepressants (OR 1.50 [95% CI 0.80–2.84]; $p = .210$), anticholinergics (OR 1.48 [95% CI 0.71–3.01]; $p = .294$), and "Z" Drug (OR 1.34 [95% CI 0.52–3.41]; $p = .544$) use were not. See Figure 2.

Almost 15% of participants transitioned to a step length shorter than 62.95 cm (ie, the shortest quartile of step length at Wave 1) at 4-year follow-up at Wave 3. Psychotropic medication use did not predict transition to this shortest quartile of step length at follow-up (OR 0.99 [95% CI 0.56–1.73]; $p = .970$]). Over 15% of participants transitioned from a narrower step width to a step width of >9.3 cm (ie, the widest quartile of step width at Wave 1) at Wave 3. Use of ≥1 psychotropic medication (OR 1.21 [95% CI 0.64–2.28]; $p = .557$) or ≥2 psychotropic medications (OR 0.64 [95% CI 0.23–1.77]; $p = .388$) were not associated with this transition to the widest quartile of step width at follow-up. Similarly, there was no association between psychotropic medication use and transition to the highest quartile of time spent in the double support phase at follow-up.

Figure 3 shows the trajectories in continuously measured mobility and gait parameters from baseline to follow-up using mixed effects models. In fully adjusted analyses, TUG, gait speed, and step length declined more steeply in participants prescribed psychotropic medications, although step width did not change significantly in either group.

Discussion

This study examines the association between psychotropic medication use and changes in gait and mobility in a large, population-representative sample of community-dwelling older people, both cross-sectionally and longitudinally. Cross-sectionally, we found that psychotropic use was independently associated with worse mobility and markers of poor gait performance, with slower gait speed, shorter step length, and increased double support phase. Longitudinally, psychotropic use was independently associated with an almost threefold higher likelihood of decline in mobility, as well as transitioning to the slowest quartile of gait speed if prescribed ≥2 agents.

Prior research has predominately focused on the relationship between psychotropics and falls (24–26), with relatively few studies to date examining the association between psychotropic medication use and mobility or gait in older people, though a recent meta-analysis found that the use of FRIDs with sedative properties was associated with reduced gait speed in community-dwelling older adults (27). Further, a study of 210 community-dwelling older people found that psychotropic medication use was associated with a gait speed consistent with high falls risk (28), although a study of 179 community-dwelling older people found that psychotropic medication use was associated with an increase in stride-to-stride variability, suggesting that it may disturb the higher levels of gait control, leading to gait instability (29). Additionally, the use of 2 or more psychotropic medications has been shown to impair both executive function and mobility (measured by TUG) in a cohort of community-dwelling people aged ≥55 years (30).

It is likely that several mechanisms underpin this link between psychotropic medication use and decline in gait and mobility in later life. These include oversedation and cognitive impairment, particularly executive dysfunction, related to psychotropic medication use (31), though it must be noted that the strengths of association between psychotropic use and gait across normal and cognitive walks did not necessarily support this; for example, the strength of association between the use of any psychotropic agent and gait speed was stronger on the normal walk than the cognitive walk. Other possible mechanisms include orthostatic hypotension due to psychotropic medication use (32), which can impair gait and balance, particularly across measurements such as the TUG, which involve posture change (33,34). Psychotropic medication use can also cause movement disorders such as drug-induced parkinsonism, tardive dyskinesia, and akathisia (35).

With recent improvements in the detection and treatment of mental health disorders in later life, the prevalence of psychotropic use in the community has increased to as high as 31% (6). Although this clearly has undoubted benefits, it also increases the opportunity for potentially inappropriate prescribing, with a recent study demonstrating that almost half

Table 2. Fully Adjusted Linear Regression Models With Mobility and Gait Parameters as Dependent Variables

	TUG	Gait Speed		Step Length		Step Width		DSP	
		Normal	Cognitive	Normal	Cognitive	Normal	Cognitive	Normal	Cognitive
≥1 Psych	β = 0.50 (0.27, 0.73) *p* < .001	β = −5.65 (−7.92, −3.38) *p* < .001	β = −4.86 (−7.82, −1.90) *p* = .001	β = −2.03 (−2.93, −1.42) *p* < .001	β = −2.09 (−3.19, −0.98) *p* < .001	β = 0.07 (−0.18, 0.32) *p* = .574	β = −0.16 (−0.51, 0.19) *p* = .367	β = 0.47 (0.19, 0.75) *p* = .001	β = 0.40 (0.05, 0.75) *p* = .024
≥2 Psych	β = 0.69 (0.24, 1.13) *p* = .002	β = −8.68 (−13.02, −4.35) *p* < .001	β = −9.30 (−14.95, −3.64) *p* = .001	β = −3.07 (−4.78, −1.37) *p* < .001	β = −3.37 (−5.47, −1.26) *p* = .002	β = −0.13 (−0.62, 0.35) *p* = .585	β = −0.35 (−1.03, 0.32) *p* = .306	β = 0.51 (−0.03, 1.05) *p* = .062	β = 0.11 (−0.55, 0.77) *p* = .745
Benzo	β = 0.13 (−0.26, 0.51) *p* = .516	β = −3.22 (−6.93, 0.49) *p* = .089	β = −1.31 (−6.17, 3.55) *p* = .598	β = −1.61 (−3.00, −0.22) *p* = .023	β = −1.53 (−3.26, 0.21) *p* = .085	β = 0.22 (−0.19, 0.64) *p* = .287	β = −0.14 (−0.72, 0.45) *p* = .648	β = 0.66 (0.20, 1.12) *p* = .005	β = 0.53 (−0.03, 1.11) *p* = .064
Antidep	β = 0.46 (0.15, 0.77) *p* = .004	β = −7.01 (−10.03, −3.99) *p* < .001	β = −7.71 (−11.67, −3.75) *p* < .001	β = −2.67 (−3.80, −1.54) *p* < .001	β = −2.84 (−4.25, −1.42) *p* < .001	β = −0.08 (−0.42, 0.26) *p* = .653	β = −0.23 (−0.70, 0.25) *p* = .353	β = 0.45 (0.07, 0.83) *p* = .019	β = 0.37 (−0.09, 0.84) *p* = .117
"Z" Drugs	β = 0.58 (0.15, 1.00) *p* = .008	β = −6.09 (−10.18, −1.99) *P* = .004	β = −4.13 (−9.49, 1.24) *p* = .132	β = −2.05 (−3.59, −0.52) *p* = .009	β = −1.69 (−3.61, 0.23) *p* = .084	β = −0.19 (−0.64, 0.27) *p* = .422	β = −0.21 (−0.85, 0.43) *p* = .524	β = 0.38 (−0.13, 0.90) *p* = .139	β = 0.47 (−0.37, 0.89) *p* = .420
Antichol	β = 0.71 (0.33, 1.09) *p* < .001	β = −6.01 (−9.71, −2.31) *p* = .001	β = −7.02 (−11.86, −2.18) *p* = .005	β = −2.20 (−3.43, −0.65) *p* = .004	β = −2.80 (−4.53, −1.07) *p* = .002	β = 0.05 (−0.36, 0.47) *p* = .804	β = −0.21 (−0.79, 0.37) *p* = .478	β = 0.21 (−0.25, 0.67) *p* = .373	β = 0.22 (−0.35, 0.79) *p* = .443

Notes: *N* = 2 620. Antichol = Anticholinergic medication; Antidep = Antidepressant; Benzo = Benzodiazepine; Cog = Cognitive walk; DSP = Double support phase; Psych = psychotropic medication; TUG = Timed Up and Go.

Psychotropic medications include antidepressants (Anatomical Therapeutic Classification (ATC) code N06A); benzodiazepines (ATC N05BA, N05CD, and N03AE); "Z" drugs (ATC N05CF); antipsychotics (N05A); and anticholinergic medications (those classified as having "definite" anticholinergic effects according to the Anticholinergic Cognitive Burden scale).

The Timed Up and Go is a measure of the time taken in seconds for the participant stands up from a chair, walks 10 ft/3 m at normal pace, turn, and walk back to the chair at normal pace before sitting again.

Spatiotemporal gait analysis was performed using the GAITRite system. Gait speed is defined as the distance covered by the body per unit time and is measured in cm/second. Step length is the distance in cm between corresponding successive points of heel contact of the opposite foot. Step width is the side-to-side distance in cm measured between the midline midpoint of one foot to the midline midpoint of the opposite foot. Double support phase is the time spent with both feet in contact with the floor, expressed as a percentage of the total gait cycle. Cognitive Walk performed but carrying out a cognitive task (reciting alternate letters of the alphabet, ie, A-C-E, etc).

Analysis adjusted for age, sex, educational attainment, excess alcohol intake, chronic disease burden, heart disease, depressive symptoms, poor sleep, and cognitive impairment.

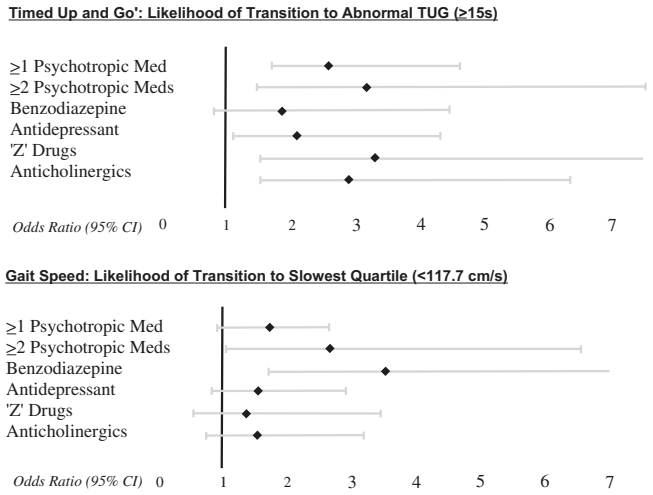

Figure 2. Association between psychotropic medication use and subsequent decline in mobility and gait. *Notes:* $N = 2\,620$. TUG = Timed Up and Go. Psychotropic medications include antidepressants (Anatomical Therapeutic Classification (ATC) code N06A); benzodiazepines (ATC N05BA, N05CD, and N03AE); "Z" drugs (ATC N05CF); antipsychotics (N05A); and anticholinergic medications (those classified as having 'definite' anticholinergic effects according to the Anticholinergic Cognitive Burden scale). The Timed Up and Go is a measure of the time taken in seconds for the participant stands up from a chair, walks 10 ft/3 m at normal pace, turn, and walk back to the chair at normal pace before sitting again. Spatiotemporal gait analysis was performed using the GAITRite system. Gait speed is defined as the distance covered by the body per unit time and is measured in cm/second. Analysis shown is logistic regression, reporting odds ratios with 95% confidence intervals, with abnormal TUG and slowest quartile of gait speed as dependent variables. TUG/Gait Speed measured at Wave 1 and Wave 3 (4-year follow-up). Analysis adjusted for age, sex, educational attainment, excess alcohol intake, chronic disease burden, heart disease, depressive symptoms, poor sleep, and cognitive impairment.

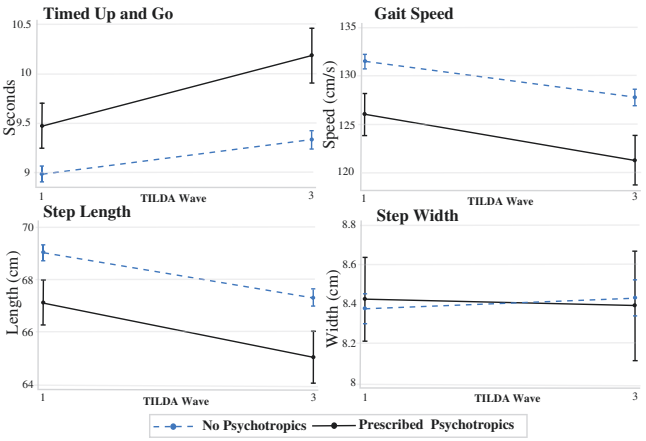

Figure 3. Trajectories of mobility and gait parameters by psychotropic medication use. *Notes:* $N = 2\,620$ Psychotropic medications include antidepressants (Anatomical Therapeutic Classification (ATC) code N06A); benzodiazepines (ATC N05BA, N05CD, and N03AE); "Z" drugs (ATC N05CF); antipsychotics (N05A); and anticholinergic medications (those classified as having 'definite' anticholinergic effects according to the Anticholinergic Cognitive Burden scale). The Timed Up and Go is a measure of the time taken in seconds for the participant stands up from a chair, walks 10 ft/3 m at normal pace, turn, and walk back to the chair at normal pace before sitting again. Spatiotemporal gait analysis was performed using the GAITRite system. Gait speed is defined as the distance covered by the body per unit time and is measured in cm/second. Step length is the distance in cm between corresponding successive points of heel contact of the opposite foot. Step width is the side-to-side distance in cm measured between the midline midpoint of one foot to the midline midpoint of the opposite foot. The double support phase is the time spent with both feet in contact with the floor, expressed as a percentage of the total gait cycle. TUG/Gait Parameters measured at Wave 1 and Wave 3 (4-year follow-up). Analysis is mixed-effects multilevel modeling, adjusted for age, sex, educational attainment, excess alcohol intake, chronic disease burden, heart disease, depressive symptoms, poor sleep, and cognitive impairment.

of noninstitutionalized older adults who recently commenced on an antidepressant, anxiolytic, or antipsychotic agent did not meet criteria for a mental health disorder (36). Further, there is a lack of consensus regarding the duration of treatment required with psychotropic medications, and many older people may therefore inappropriately stay on long-term maintenance therapy, increasing the risk of mobility and gait issues, as well as other adverse events related to psychotropic use (37).

Deprescribing psychotropics is challenging, however, with concern regarding withdrawal, lack of access to alternative therapeutic options, and difficulty engaging patients and carers in the deprescribing process serving as important barriers (38,39). However, over 90% of older patients attending a psychiatry service reported that they would be happy to stop a psychotropic medication if their prescriber advised it (40). In the acute setting, physicians may be reluctant to deprescribe psychotropic medications post falls, as treating resulting injuries, concomitant medical issues, and investigating the mechanism of the fall takes precedence. Furthermore, guidelines recommend that some classes of psychotropic medications are best weaned cautiously under the supervision of a patient's treating psychiatrist (41). Indeed, the evidence base for improvements in gait and mobility after withdrawal of psychotropic medications is limited, with a small, single study demonstrating improved TUG along with 10-minute walk test times (42).

There are some important limitations of this study that should be noted. Although medication lists were examined to verify prescribed medications, we do not have information on medication doses or adherence with prescribed medications, both of which may modify the association between psychotropics and adverse effects. This study focuses on prescription medications, but the lack of data on over-the-counter medications has negligible effect on the overall analysis as psychotropic medications are not available over the counter in Ireland. Whilst we have adjusted for a wide range of covariates in this study, the complex and often multifactorial nature of gait and balance amongst older people is such that there remains a possibility of residual confounding that we have not adjusted for.

We report the prevalence of psychotropic medication deprescribing, but our longitudinal analyses do not separate the subset who had psychotropic medication stopped by Wave 3. These participants were included in the longitudinal analyses as we did not have information regarding the timing of psychotropic medication cessation, which may have occurred at any point up to the date of data collection for Wave 3. Previous studies have shown that symptoms can persist months post cessation of psychotropic medications in conditions such as drug-induced parkinsonism (43). Participants may therefore have suffered from psychotropic-induced gait impairment even after the offending medication had been

deprescribed. The uncertainty regarding the timing of psychotropic cessation and the possibility of persisting side effects necessitated the inclusion of all patients prescribed psychotropics at Wave 1 in the longitudinal analyses. Future studies are, however, warranted to explore how duration of exposure to psychotropic medications effects these gait parameters and whether deprescribing these psychotropic medications leads to an objective improvement in gait parameters.

To allow for the longitudinal analysis, we utilized data from Waves 1–3 of TILDA, collected from 2009–2015. Although the longitudinal design resulted in an unavoidable time lag, limited progress has been made in psychotropic pharmacotherapy in the intervening period (44), ensuring that our data is relevant to current prescribers. Strengths of the study include the large, well-described population-representative sample of older people involved, the robust longitudinal follow-up, and the use of objective measures of both mobility and gait.

In conclusion, this study shows that psychotropic medication use is significantly associated, both cross-sectionally and longitudinally, with a decline in mobility and gait, characterized by a prolonged TUG, slower gait speed, and shorter step length. Psychotropic medications are often necessary, effective treatments in later life, and deprescribing psychotropic medication can be complex, but given the significant effect mobility and gait impairment can have on functional status and well-being, it is imperative that their ongoing use is reviewed as part of a comprehensive geriatric assessment. Further studies delineating changes seen in mobility, gait parameters, and falls after deprescribing psychotropic medications are required to support these findings.

Supplementary Material

Supplementary data are available at *The Journals of Gerontology, Series A: Biological Sciences and Medical Sciences* online.

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None.

Conflict of Interest

None.

Author Contributions

The study was designed by R.B. with support from D.O'D., R.A.K., and F.M. Investigations and formal analyses were performed by D.O'D., R.B, F.M., and A.L. The original draft was written by D.O'D. and was subsequently reviewed and edited by all authors.

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