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Ten-Year Outcomes of Anticholinergic Use Among Older Adults With Intellectual Disability: Findings From the Intellectual Disability Supplement to the Irish Longitudinal Study on Ageing (IDS-TILDA)

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ABSTRACT

Background: People with intellectual disability are frequently exposed to medication with anticholinergic activity. In the general population, the long-term exposure to anticholinergics has been associated with declines in both physical and cognitive function. This study aimed to examine anticholinergic exposure longitudinally in a cohort of older adults with intellectual disability (aged 40 years or over).

Method: The study examined individuals with intellectual disability aged 40 and over, who participated at two time points (Waves 1 and 4), 10 years apart, in the Intellectual Disability Supplement to the Irish Longitudinal Study on Ageing (IDS-TILDA). The Anticholinergic Cognitive Burden (ACB) scale was used to quantify anticholinergic exposure. Logistic regression analysis was employed to examine the adverse outcomes reported at time point 2 in relation to ACB scores at time point 1. Models were adjusted for age, gender, level of intellectual disability, residence, epilepsy and polypharmacy.

Results: The study included 487 participants who provided medication data at both time points. Anticholinergic exposure remained consistent over the studied period, with approximately 30% having no exposure, 40% having mild exposure (ACB = 1–4) and 30% having high exposure (ACB = 5+). Antipsychotic medications contributed the most to the total score at both time points (Wave 1 = 35%, Wave 4 = 37%), with other anticholinergics, antiepileptics and antidepressant medications contributing 10%–16% each. Mild and high ACB scores at time point 1 were significantly associated with a higher risk of falls (odds ratio [OR] = 1.86, 95% CI: 1.03–3.38) and mental health conditions (ACB 1–4; OR = 6.60, 95% CI: 3.69–11.77; ACB 5+, OR = 17.38, 95% CI: 8.97–33.61) and lower OR for reporting dementia/Alzheimer's disease (ACB 1–4; OR = 0.39, 95% CI: 0.15–0.97; ACB 5+; OR = 0.21, 95% CI: 0.07–0.64).

Conclusion: Older adults with intellectual disability are exposed to high anticholinergic burden at the two time points, 10 years apart. Being exposed to anticholinergics at Wave 1 is significantly associated with a higher risk of falls and reporting mental health conditions at Wave 4. A review of antipsychotic prescribing practice is urgently needed to reduce the anticholinergic exposure and its adverse outcomes among older adults with intellectual disability.

1 | Introduction

People with intellectual disability have greater multimorbidity, starting at an earlier age, with poorer health outcomes compared with the general population (Cooper et al. 2015; Glover et al. 2017; Kinnear et al. 2018). This early morbidity and mortality are potentially preventable because up to 37% of all deaths among people with intellectual disability were classified as amenable to health care intervention (Hosking et al. 2016). Diseases of the circulatory system, including ischaemic heart diseases, hypertensive diseases and cerebrovascular diseases, were the leading classified cause of death among adults with intellectual disabilities in England, accounting for 14.0% of all deaths in 2022 (Leder 2022).

People with intellectual disability are considered among 'the most medicated groups in society' and they are exposed to excessive polypharmacy (≥ 10 medication), with a rate six times higher than the general population (Peklar et al. 2017; O'Dwyer et al. 2018). The term 'inappropriate polypharmacy' is defined as the prescribing of multiple medications inappropriately or when the intended benefit of the medication is not realized (Tsang et al. 2024). Additionally, they are exposed to high anticholinergic burden compared with the general population (Ward et al. 2021; O'Dwyer et al. 2016; O'Connell et al. 2018). Anticholinergic Burden has been studied previously at a cross-sectional level in older adults with intellectual disability in Ireland and high exposure was associated with adverse effects including constipation, daytime dozing and higher dependency level (O'Dwyer et al. 2016; O'Connell et al. 2018). However, a recent scoping review did not identify any studies that examined the adverse effects associated with the long-term exposure to high anticholinergic burden among older adults with intellectual disability (Al Shuhaimi et al. 2022). In the older population long-term use of anticholinergics has been associated with a decline in physical function (Wouters et al. 2020; Han et al. 2008; Brombo et al. 2018), cognitive function (Cai et al. 2013; Jamsen et al. 2017; Wouters et al. 2020; Han et al. 2008; Brombo et al. 2018) and a higher risk of dementia (Gray et al. 2015).

This cohort study aims to examine anticholinergic exposure longitudinally in a cohort of older adults with intellectual disability (aged 40 years or over). The study objectives were the following: (i) examine the anticholinergic exposure of people who took part in Wave 1 (2009/2010) and remained for 10 years in the study at Wave 4 (2019/2020), (ii) identify the most frequently reported medicines and therapeutic classes of medicines contributing to anticholinergic exposure at the two time points and (iii) investigate the 10-year outcomes of anticholinergic exposure.

2 | Methods

2.1 | Study Design

The Intellectual Disability Supplement to the Irish Longitudinal Study on Ageing (IDS-TILDA) is a nationally representative longitudinal study of older adults with intellectual disability aged 40 or over in Ireland. IDS-TILDA has collected five waves of data between 2009 and 2023. Intervals between the waves were 2–3 years: Wave 1 (2009/2010), Wave 2 (2013/2014), Wave 3 (2016/2017), Wave 4 (2019/2020) and Wave 5 (2022/2023).

An easy-to-read information booklet was provided at each wave, and self-consent was obtained from those who were able to do so (McCarron et al. 2011). For those who lacked the capacity to consent themselves, a consent declaration was in place from the Health Research Consent Declaration Committee (HRCDC), meaning the consent of an individual was not required to obtain or use their personal data. This is legally allowed in Ireland. However, in addition to this, IDS-TILDA obtained assent from a proxy (a family member or a guardian who knew the participant well) before proceeding with data collection. Consent was reaffirmed at the interviews and appointments for health measurements (i.e., at each stage of data collection) in all waves. Further details on study design and sampling criteria have been described previously (McCarron et al. 2011).

2.2 | Ethics Statement

Ethical approval was granted, and details were removed for anonymization.

2.3 | Study Cohort

Data used is Wave 1 (2009/2010) and Wave 4 (2019/2020). Wave 1 is considered the baseline, and Wave 4 the follow-up time point, 10 years apart. The sample study flowchart is illustrated in Figure 1.

2.4 | Medication Data Collection

Medication data were provided by participants or their proxies as part of the Pre-interview Questionnaire (PIQ) (McCarron et al. 2011). This was reviewed and confirmed at the face-to-face computer-assisted personal interview (CAPI) at each wave. Medication information gathered included details of medication regularly taken or, if needed, prescribed or over the counter. All medicines were classified based on the Anatomical Therapeutic Chemical (ATC) code system (WHO) (WHO Collaborating Centre for Drug Statistics Methodology 2025).

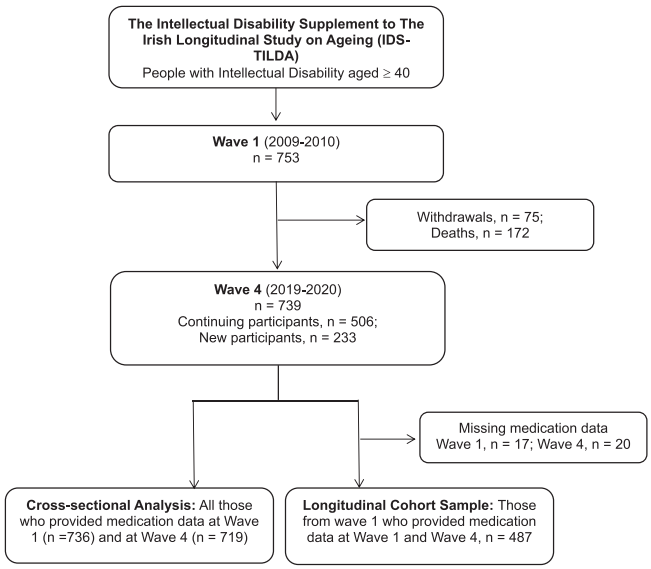

FIGURE 1 | Flowchart of the study sample.

2.5 | Anticholinergic Burden Quantification

Anticholinergic burden was quantified using the Anticholinergic Cognitive Burden (ACB) scale, developed previously with input from academics and experts (O'Dwyer et al. 2016; O'Connell et al. 2020). The scale had been used in previous waves in IDS-TILDA. For this study, the list of anticholinergic medications and their ACB scores was reviewed and updated by the research team, including an academic who was involved in the development of the original scale (IM) (Appendix S1). In the ACB scale, medications are assigned scores of 0–3 based on their affinity to muscarinic receptors, their ability to cross the blood–brain barrier, and cause delirium and cognitive decline. An ACB score of zero indicates no anticholinergic activity; possible anticholinergics are scored with ACB = 1. Those with definite anticholinergic activity are assigned a score of 2 or 3.

Cumulative anticholinergic burden was calculated by summing the total ACB scores of all medications reported. Participants were classified into three groups: (i) ACB score of 0 indicating no anticholinergic exposure, (ii) ACB 1–4 considered as mild anticholinergic exposure and (iii) ACB 5+ for high anticholinergic exposure. This categorization had been used previously within IDS-TILDA (O'Dwyer et al. 2016) because ACB score of 5+ is significantly associated with a decline in Mini-Mental State Examination (MMSE) score at 2 years (Fox et al. 2011).

ACB scales were calculated for each participant at Waves 1 and 4 to examine change in the ACB exposure at two different time points 10 years apart, confirming that participants continued to be exposed to anticholinergics over the examined period. The outcomes from the full Wave 4 cohort were compared with previous results obtained from the full cohort in Wave 1 (O'Dwyer 2015).

2.6 | Measured and Reported Physical and Cognitive Outcomes

Outcomes: constipation, falls, Barthel Index, edentulous, mental health conditions, and dementia or Alzheimer's disease in both waves. The Barthel Index is a scoring measure with a range from 0 to 20 for activities of daily living, including feeding, transfer, using stairs, dressing, grooming, bathing, toileting, bladder continence and bowel continence. Mental health conditions include hallucinations, anxiety, depression, emotional problems, schizophrenia, psychosis, mood swings, manic depression or post-traumatic stress disorder. Details of the questions used to gather data in Wave 4 are provided in Appendix S2.

2.7 | Covariates

Demographic covariates: age categories (40–49; 50–64; 65+ years), sex (male; female), type of residence (family/independent; community group home; residential care). A community group home provides a communal environment with dedicated staff supporting individuals with intellectual disability in a small group setting. Residential care settings are supported, service-provided residences in campus-based living arrangements or where > 10 people share a single living unit.

Health-related covariates: level of intellectual disability (mild, moderate, severe/profound), ability to walk 100 yards (no/some difficulty; a lot of difficulty/cannot do at all), epilepsy (yes/no), multimorbidity (the presence of two or more chronic conditions), chronic constipation (yes/no), falls (yes/no), mental health condition (yes/no), dementia/Alzheimer's disease (yes/no), Barthel Index (mild dependence/total independence or moderate/severe/total dependence) and dentate or edentulous, in addition to medication-related variables: multiple laxatives use (none/1 laxative/2+ laxatives), multiple antipsychotic use (yes/no) and non-ACB medication polypharmacy (yes/no). Polypharmacy was defined as the concurrent use of five or more medications. Polypharmacy included prescribed and over-the-counter (OTC) medications and excluded supplements and herbal medicines. Non-ACB medication polypharmacy variable was created by exclusion of anticholinergic medication taken by participants because the anticholinergic medication was counted and quantified as part of the anticholinergic burden score.

2.8 | Statistical Analysis

Median and interquartile ranges were reported for discrete data as the data was not normally distributed. Descriptive analysis is presented as the proportion of the total sample (n, %). McNemar's test was used to test differences in proportions between the longitudinal cohort sample (Waves 1 and 4) for dichotomous variables, while the McNemar–Bowker test was used for variables with three or more categories. A Holm–Bonferroni correction was used to control type 1 error (false positive results), and statistical significance was set as 0.025 (0.05/2 comparison), and for variables with three sub-categories and p-value of 0.017 for variables with three comparisons (0.05/3).

Multivariate logistic regression was used to examine the longitudinal association between ACB scores at Wave 1 (predictor or independent variable) and the physical and cognitive outcomes reported at Wave 4 (outcomes or dependent variable) in the longitudinal cohort sample. Each outcome was examined in separate models, and all models were adjusted for demographic covariates: age, sex, type of residence and level of intellectual disability. The models were also adjusted for epilepsy because of its high prevalence and frequent use of anti-epileptic medication, which has a major impact on the level of anticholinergic exposure and the associated outcomes such as falls and constipation. In addition, the models were adjusted for polypharmacy status, excluding anticholinergic medication. Odds ratios (ORs), 95% confidence interval (CI) for the likelihood of adverse outcomes in those with higher ACB categories compared with ACB burden of 0 and *p*-values were reported for all models. *p*-values <0.05 were statistically significant. Data analysis was performed using IBM SPSS Version 28.0.

2.9 | Demographic Characteristics

Demographic characteristics of the longitudinal cohort sample and the change in participants' health status at the two time points are illustrated in Table 1. As the same cohort was observed at two time points, people had aged over the 10 years and therefore no one was aged 40–49 years by the time of Wave 4. The proportion of people living in a community group home increased by 9% with a reduction in participants living in a residential care setting and with family or independently of 6.2% and 2.8%, respectively. Sex and level of intellectual disability are time-independent factors.

Participants reported a significant increase in constipation, laxative use and being edentulous while ageing.

For medication use, $n=450$ (92.4%) had an anticholinergic exposure at the two time points, and more details are provided in Appendix S3.

3 | Results

3.1 | Comparison on Contribution of Medication Therapeutic Classes to Total ACB Score of the Whole Cohort in Waves 1 and 4

Analysis of the contribution of medication therapeutic classes to total ACB scores was conducted based on participants who had provided medication data and had anticholinergic exposure (ACB score = 1+).

Antipsychotic medication made the greatest contribution to the total score at the two time points (Wave 1 = 35%, Wave 4 = 37%), with other anticholinergics, antiepileptic and antidepressant medications contributing 10%–16% each (Figure 2).

The prevalence of anticholinergic medication use fell from 16% to 12% between the two time points. Additionally, there was a slight reduction in the usage of anxiolytics by 1.3%.

The top four most reported medicines were in the same order at both time points (Table 2). Carbamazepine (ACB = 2) was most frequently reported, with 22.2%–24.3% by those with anticholinergic exposure at the two time points, followed by risperidone (21%), olanzapine (17.4%–19.3%) and biperiden (11.0%–16.2%). Procyclidine, citalopram and paroxetine have been replaced by cetirizine, mirtazapine and hyoscine (scopolamine score 3). The use of diazepam, chlorpromazine and haloperidol had reduced by almost 7%, 6% and 2%, respectively. The use of escitalopram, quetiapine and furosemide had increased by around 2%–3%.

3.2 | Longitudinal Analysis of Outcomes Associated With ACB

Multivariate logistic regression analysis examined the longitudinal association between the ACB scores at Wave 1 and reported health-related outcomes at Wave 4 ($n=487$) (Table 3). Each outcome was examined in a separate model, and all models were adjusted for age, sex, level of intellectual disability, residence and epilepsy at Wave 4 to address the participants' status at that time and adjusted for Wave 1 polypharmacy (excluding medication with anticholinergic activity) to avoid over-adjustment, given the high correlation between the ACB score and polypharmacy when anticholinergic medications were included (Spearman's rho 0.524).

There was a significant association between ACB exposure at Wave 1 and reporting falls, mental health conditions, and dementia or Alzheimer's disease at Wave 4, adjusting for all other factors in the model. Detailed results of the models and covariates included are presented in Appendix S4.

3.2.1 | Falls

Participants with an ACB score of 5 or more at Wave 1 were almost twice as likely to report falls at Wave 4 (OR = 1.86, 95% CI of 1.03–3.38, *p*-value 0.04) compared with those with an ACB of 0, adjusting for all other factors in the model.

3.2.2 | Mental Health Condition

Participants with mild and high ACB scores at Wave 1 were six times and 17 times more likely to report a mental health condition at Wave 4, respectively, compared with those with ACB 0 (ACB 1–4; OR = 6.60, 95% CI 3.69–11.77, *p*-value <0.001; ACB 5+, OR = 17.38, 95% CI 8.97–33.61, *p*-value <0.001), adjusting for all other factors in the model. Additionally, participants with epilepsy were less likely to report a mental health condition (OR = 0.57, 95% CI 0.35–0.93), adjusting for all other factors in the model (Table 3 and Appendix S4).

3.2.3 | Dementia, Alzheimer's Disease or Taking Anti-Dementia Medicines (N06D)

Mild and high ACB at the baseline (Wave 1) were less likely to report dementia or Alzheimer's disease or taking anti-dementia medication at the follow-up time point (Wave 4) (ACB 1–4; OR = 0.39, 95% CI 0.15–0.97, *p*-value 0.042; ACB 5+; OR = 0.21, 95% CI 0.07–0.64, *p*-value 0.006) compared

TABLE 1 | Demographic characteristics of the longitudinal cohort sample at Waves 1 and 4 ($n = 487$).

	Wave 1, *N* (%), ($n = 487$)	Wave 4, *N* (%), ($n = 487$)	Differences in proportions (*p*-value)
Age (years)			
40–49	212 (43.5)	—	—
50–64	222 (45.6)	313 (64.3)	**< 0.001**
65+	53 (10.9)	174 (35.7)	
Sex			
Male	213 (43.7)	213 (43.7)	NA
Female	274 (56.3)	274 (56.3)	
Residence			
Independent/family	74 (15.2)	60 (12.4)	**< 0.001**
Community group home	185 (38.0)	227 (47.0)	
Residential care	228 (46.8)	196 (40.6)	
Missing	$n = 0$	$n = 4$	
Level of intellectual disability			
Mild	108 (24.1)	108 (24.1)	NA
Moderate	207 (46.1)	207 (46.1)	
Severe/profound	134 (29.8)	134 (29.8)	
Missing	$n = 38$	$n = 38$	
Walking 100 yards			
No/some difficulty	422 (86.8)	338 (73.2)	**< 0.001**
A lot of difficulty/cannot do at all	64 (13.2)	124 (26.8)	
Missing	$n = 1$	$n = 25$	
Epilepsy			
No	331 (68.4)	323 (66.3)	0.09
Yes	153 (31.6)	164 (33.7)	
Missing	$n = 3$	$n = 0$	
Chronic constipation			
No	405 (83.2)	248 (51.3)	**< 0.001**
Yes	82 (16.8)	235 (48.7)	
Missing	$n = 0$	$n = 4$	
Falls			
No	349 (72.1)	332 (68.9)	0.239
Yes	135 (27.9)	150 (31.1)	
Missing	$n = 3$	$n = 5$	
Mental health condition			
No	227 (48.4)	231 (47.4)	0.586
Yes	242 (51.6)	256 (52.6)	
Missing	$n = 18$	$n = 0$	

(Continues)

TABLE 1 | (Continued)

	Wave 1, *N* (%), (*n* = 487)	Wave 4, *N* (%), (*n* = 487)	Differences in proportions (*p*-value)
Dementia and Alzheimer's disease			
No	470 (96.5)	456 (93.6)	0.038
Yes	17 (3.5)	31 (6.4)	
Missing	*n* = 0	*n* = 0	
Barthel Index			
Mild dependence/total independence	155 (31.8)	87 (18.6)	**< 0.001**
Moderate/severe/total dependence	321 (65.9)	380 (81.4)	
Missing	*n* = 11	*n* = 20	
Dentate/edentulous			
Dentate	387 (79.8)	354 (72.8)	**< 0.001**
Edentulous	98 (20.2)	132 (27.2)	
Missing	*n* = 2	*n* = 1	
Multiple laxative use			
Non	316 (64.9)	248 (50.9)	**< 0.001**
1 laxative	91 (18.7)	139 (28.5)	
2+ laxatives	80 (16.4)	100 (20.5)	
Multiple antipsychotic use			
Non	265 (54.4)	273 (56.1)	0.112
1 antipsychotic	163 (33.5)	168 (34.5)	
2+ antipsychotics	59 (12.1)	46 (9.4)	
Non-ACB medication polypharmacy			
No	318 (65.3)	224 (46.0)	**< 0.001**
Yes	169 (34.7)	263 (54.0)	
ACB exposure			
No exposure (ACB = 0)	146 (30.0)	139 (28.5)	0.115
Moderate exposure (total ACB score = 1–4)	193 (39.6)	219 (45.0)	
High exposure (total ACB score = 5+)	148 (30.4)	129 (26.5)	

Note: *p*-value derived from McNemar's and McNemar–Bowker test. Holm–Bonferroni correction applied, and all significant *p*-values are in bold.

with those with an ACB score of 0, controlling for all factors included in the model.

There was no association between ACB exposure and Barthel Index, constipation, laxative use and edentulous (see Appendix S4).

4 | Discussion

To the best of our knowledge, this study is the first longitudinal cohort study examining anticholinergic exposure in older adults with intellectual disability at two time points 10 years apart. Most participants were exposed to anticholinergics at both time points (450 out of 487). Only 37 participants stopped being exposed at some time between the two waves (Table 1 and Appendix S3).

There was a reduction by 3.5% in the number of participants who were exposed to a high ACB score. This reduction could be due to a change in prescribing guidance related to combining anticholinergics with antipsychotics to avoid possible extrapyramidal side effects, as this study identified a reduction of 4.3% in anticholinergic medication prescribing, although there was an increase of 1.5% in antipsychotic prescribing between the two waves. Specifically, procyclidine (which is an anticholinergic agent) scored 9th on the most frequently prescribed medicines, with 7% at Wave 1, but it was not reported within the list at Wave 4 (Table 2). Furthermore, the frequency

of prescribing biperiden (also an anticholinergic agent) was reduced by 5.3%. While the top four anticholinergic medicines remained the same at both time points (carbamazepine, risperidone, olanzapine and biperiden), there was a notable decrease in some older antipsychotics; e.g., chlorpromazine use reduced from 13.4% to 7.6% in Wave 4.

Wave 2 of this study found that one-third of participants who were taking antipsychotics for behaviours that challenge were taking anticholinergic medication such as biperiden (O'Dwyer et al. 2019). In these cases, the anticholinergic agent was most likely prescribed to manage extrapyramidal side effects due to the long-term use of antipsychotics (O'Dwyer et al. 2016).

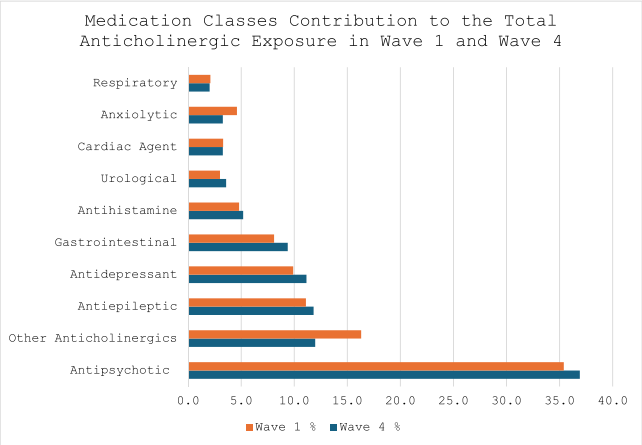

FIGURE 2 | Medication classes contributing to the total anticholinergic score in Wave 1 ($n = 523$) and Wave 4 ($n = 499$) in percentage (%).

Therefore, individuals might be exposed to anticholinergics to manage antipsychotic adverse effects, which were likely prescribed to manage behaviours that challenge at a certain time and never reviewed or assessed for appropriateness of continued use. Research is needed to explore the indication of anticholinergic medication in this population, as anticholinergics are used effectively to control the symptoms of Parkinson's disease in some cases.

In this study, the prevalence of polypharmacy of non-anticholinergic medication increased from 34.7% to 54.0%, potentially due to ageing-related health conditions (IDS-TILDA 2017). The results of this study confirmed that there was a significant increase in the prevalence of constipation, laxative use, dependency level in activities of daily living, edentulousness, and dementia/Alzheimer's disease or usage of anti-dementia agents. That could explain the increase in the use of non-anticholinergic medications, as agents are commonly prescribed to control ageing-related health conditions such as laxatives, cataract treatment, anti-osteoporotic medicines and anti-dementia medicines.

This study found that antipsychotic medication was the class of medication that contributed most to the total ACB scores in the studied cohort, and the most frequently reported antipsychotics included olanzapine, chlorpromazine, quetiapine and risperidone. Although the use of antipsychotics remained high, there was a reduction in reporting of typical antipsychotics, for instance, haloperidol (1.8%) and chlorpromazine (5.3%). The overuse of antipsychotics among people with intellectual disability is an established finding (Advokat et al. 2000) and it has been reported that antipsychotic use and polypharmacy have a negative impact on gait in people with intellectual disability (Maas et al. 2020). Furthermore,

TABLE 2 | Frequently reported medicines with anticholinergic activity at Wave 1 ($n = 523$) and Wave 4 ($n = 499$).

No.	Wave 1 ($n = 523$)	ACB score	*n* (%)	Wave 4 ($n = 499$)	ACB score	*n* (%)
1	Carbamazepine	2	127 (24.3%)	Carbamazepine	2	111 (22.2%)
2	Risperidone	1	112 (21.4%)	Risperidone	1	106 (21.2%)
3	Olanzapine	3	101 (19.3%)	Olanzapine	3	87 (17.4%)
4	Biperiden	3	85 (16.2%)	Biperiden	3	55 (11.0%)
5	Diazepam	1	82 (15.7%)	Escitalopram	1	48 (9.6%)
6	Chlorpromazine	3	70 (13.4%)	Loperamide	1	45 (9.0%)
7	Loperamide	1	56 (10.7%)	Diazepam	1	44 (8.8%)
8	Haloperidol	1	44 (8.4%)	Quetiapine	3	41 (8.2%)
9	Procyclidine	3	37 (7.1%)	Chlorpromazine	3	38 (7.6%)
10	Escitalopram	1	35 (6.7%)	Haloperidol	1	33 (6.6%)
11	Ipratropium	1	31 (5.9%)	Cetirizine	1	33 (6.6%)
12	Quetiapine	3	27 (5.1%)	Furosemide	1	33 (6.6%)
13	Citalopram	1	25 (4.8%)	Ipratropium	1	28 (5.6%)
14	Paroxetine	3	25 (4.8%)	Mirtazapine	1	25 (5.0%)
15	Furosemide	1	23 (4.3%)	Scopolamine	3	24 (4.8%)

TABLE 3 | Multivariate logistic regression model of health-related outcomes reported at Wave 4, associated with ACB scores (1–4) (5+) at Wave 1.

	Anticholinergic exposure at the baseline (Wave 1) ($n=487$)	
	ACB = 1–4 ($n=193$)	ACB = 5+ ($n=148$)
Outcomes reported at the follow-up (Wave 4)	**OD, 99% CI, *p*-value**	**OD, 99% CI, *p*-value**
Falls	1.51 (0.86, 2.64), 0.15	**1.86 (1.03, 3.38), 0.04**
Mental health conditions	**6.60 (3.69, 11.77), <0.001**	**17.38 (8.97, 33.61), <0.001**
Dementia or Alzheimer's disease OR N06D	**0.39 (0.15, 0.97), 0.042**	**0.21 (0.07, 0.64), 0.006**
Barthel Index	0.95 (0.48, 1.86), 0.88	0.87 (0.37, 2.01), 0.74
Constipation	1.09 (0.65, 1.85), 0.73	1.05 (0.60, 1.85), 0.86
Laxative use	1.18 (0.68, 2.02), 0.55	1.42 (0.79, 2.53), 0.24
Edentulous	0.81 (0.44, 1.48), 0.49	1.24 (0.67, 2.30), 0.49

Note: Reference category: ACB = 0 ($n=146$). Significant *p*-value is <0.05, and all significant values are in bold. The model was adjusted for Wave 4 age, sex, level of intellectual disability, residence, epilepsy and Wave 1 polypharmacy status excluding anticholinergic medications.

two studies conducted in Sweden and the United Kingdom reported that older adults with intellectual disability might be prescribed antipsychotics without a psychiatric diagnosis (Axmon et al. 2019; Sheehan et al. 2015). However, due to less evidence on the safety and efficacy of using antipsychotics for controlling behaviours that challenge, the National Institute for Health and Care Excellence (NICE) guidelines state that antipsychotics should only be used to control behaviours that challenge if psychological and other interventions were not effective within an agreed timeframe (NICE 2015).

Both anticholinergics and psychotropics cause constipation as an adverse effect. A previous study found that constipation can cause pain and distress in people with intellectual disabilities who are unable to communicate their symptoms (Christensen et al. 2009; Robertson et al. 2018). This is often misattributed to challenging behaviour and treated accordingly (O'Dwyer et al. 2019). Behavioural disorders and pain have been found to be more prevalent in older people with intellectual disability compared with younger age (Rousseau et al. 2019). Additionally, the presence of pain has been associated with an increased incidence of behaviours that challenge (Walsh et al. 2011). Furthermore, there is growing evidence of an association between pain and self-injurious behaviour in people with intellectual disability (Carr and Owen-Deschryver 2007; Huisman et al. 2018; Oliver and Richards 2010). However, a previous study conducted in IDS-TILDA did not find an association between constipation or pain and challenging behaviours. The study suggested the need for further investigation in this area (O'Dwyer et al. 2019).

A previous cross-sectional study conducted based on Wave 1 data did not find a cross-sectional association between high ACB scores and falls, but it was significantly associated with daytime drowsiness (O'Dwyer et al. 2016). This longitudinal analysis established a significant association between high ACB score at Wave 1 and reporting falls at Wave 4, having adjusted for all other factors. This reflects findings of eight studies reporting association between ACB and risk of falls among older adults in the general population, as reported by a systematic review (Stewart et al. 2021).

There was a significant association between reporting non-anticholinergic polypharmacy at baseline (Wave 1) and having constipation, laxative use and higher dependency levels at Wave 4 (Appendix S4). Consequently, further care is required for those on polypharmacy. It is necessary to complete frequent medication reviews, including anticholinergic medications, and to develop a review tool tailored based on the characteristics of this population. A newly developed tool (Optimizing Pharmaco-Therapy and Improving Medication for Ageing with Intellectual Disability, OPTIMA-ID) is currently being investigated for its utility in this population (O'Connell et al. 2024).

High ACB scores at Wave 1 were significantly associated with lower OR to report dementia/Alzheimer's disease or the use of anti-dementia medication at Wave 4. In contrast to the results of a systematic review conducted by Zheng et al. among the general population, which also identified a dose-dependent relationship between ACB exposure and risk of dementia (Zheng et al. 2021). However, in the current study, only a small sample size ($n=29$) reported dementia/Alzheimer's disease or taking anti-dementia agents (N06D), and only half of these individuals reported ACB exposure. Furthermore, the wide CI (95% CI: [0.15, 0.97], [0.07, 0.64]) indicates limited certainty on the effect, and further investigation is needed. Additionally, the diagnosis of dementia in people with intellectual disability is difficult due to the existing cognitive impairment associated with the intellectual disability conditions and limited access to screening services (IDS-TILDA 2023).

The incidence of dementia is higher in people with intellectual disability compared with the general older population, particularly among people with Down syndrome. Due to triplication of chromosome 21 in Down syndrome, they develop the neuropathology of Alzheimer's disease by age 40 (IDS-TILDA 2017). In this longitudinal cohort, 74 out of 487 participants were reported to have Down syndrome, and 19 of them had a diagnosis of dementia, Alzheimer's disease or were taking anti-dementia medication. According to the Wave 5 report in IDS-TILDA, 42.7% of those with Down syndrome who had no recorded diagnosis of dementia had never undergone a dementia assessment, which may contribute to the underreporting of dementia in this

population (IDS-TILDA 2023). Since 2020 (after Wave 4), dementia screening has increased following the establishment of the National Intellectual Disability Memory Service, which provides memory screening and assessment for all individuals with intellectual disabilities in Ireland (IDS-TILDA 2023).

Therefore, a larger sample size would be needed to investigate the relationship between the ACB and dementia/Alzheimer's disease in older adults with intellectual disability. Further investigation is needed to observe the prevalence of ACB exposure among participants with Down syndrome and those with intellectual disability from other aetiologies. High ACB scores could explain the high prevalence of dementia among participants with Down syndrome, and further care should be taken among this vulnerable group.

4.1 | Impact on Practice

The study highlights the need to evaluate the prescribing guidance of antipsychotics, particularly antipsychotics with definite anticholinergic activity (ACB score 3, such as olanzapine, chlorpromazine, quetiapine) for older adults with intellectual disability. In addition, frequent medication review is essential for older adults with intellectual disability, the majority of whom experience polypharmacy to investigate the possibility of deprescribing anticholinergic and non-anticholinergic medications.

4.2 | Strengths and Limitations

This is the first longitudinal study to examine the association between anticholinergic use and reported outcomes after 10 years among older adults with intellectual disability. The study examined the cohort with a sufficient follow-up period between the two time points (Waves 1 and 4), allowing for the examination of adverse effects having been exposed to ACB 10 years previously. Additionally, the study used a large, randomly selected population-representative sample size that participated at the two time points to generalize the findings of the study to older adults with intellectual disability in Ireland. Well-trained field researchers in IDS-TILDA resulted in 97% of the participants providing medication data at both time points. The accuracy of medication data was confirmed through a review of medication data provided by the patient/proxy by the field researchers at the CAPI. Furthermore, at Wave 4, the participant was asked to confirm or dispute health conditions reported previously, which improved the accuracy of the gathered data. Another strength is that the ACB score has been used to quantify anticholinergic burden, ensuring findings are robust and applicable to clinical practice. The list of anticholinergic medications was reviewed and updated prior to the study to ensure its validity. The study determined the ACB scores at both waves to examine the exposure over the studied two time points. IDS-TILDA gathered large datasets at each wave, ensuring this study could measure associations of factors and outcomes with ACB scores.

As a limitation, the study explored the measured and reported adverse effects at Wave 4; however, further possible adverse effects should be examined in future research, such as frailty, cognitive impairment and daytime dozing. Further analysis is needed to include medication taken at Waves 2 and 3, which are 3 years apart. Complex longitudinal models, such as generalized estimating equations, could be used to capture the population's average responses over time. Alternatively, generalized linear mixed models could model individual responses over time using random effects, allowing inclusion of all participants, even those who did not complete all waves.

In conclusion, older adults with intellectual disability are exposed to high anticholinergic burden, often for long periods of time. Antipsychotic medications are the class most frequently contributing to the high anticholinergic burden among this population, followed by anticholinergic medications. Mild and high ACB scores at Wave 1 were significantly associated with a higher risk of falls and the presence of a mental health condition in older adults with intellectual disability after 10 years. Antipsychotic and anticholinergic medication reviews are highly needed for this vulnerable population to reduce the risk of avoidable anticholinergic adverse effects and to enhance quality of life.

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Ethics Statement

Ethical approval was granted from the Faculty of Health Sciences Research Ethics Committee in Trinity College Dublin and from 138 Intellectual Disability Service Providers in Ireland (McCarron et al. 2011).

Conflicts of Interest

The authors declare no conflicts of interest.

Data Availability Statement

The data that support the findings of this study are available on request from the corresponding author. The data are not publicly available due to privacy or ethical restrictions.

References

Advokat, C. D., E. A. Mayville, and J. L. Matson. 2000. "Side Effect Profiles of Atypical Antipsychotics, Typical Antipsychotics, or No Psychotropic Medications in Persons With Mental Retardation." *Research in Developmental Disabilities* 21: 75–84.

Al Shuhaimi, L., M. Henman, P. Mccallion, M. McCarron, and M. O'Dwyer. 2022. "The Adverse Effects of Long-Term Exposure to Anticholinergics Among People With Intellectual Disabilities: A Scoping Review." *HRB Open Research* 5: 63.

Axmon, A., P. Björne, M. Nygren, and G. Ahlström. 2019. "Demographic and Diagnostic Profiles of Older People With Intellectual Disability and Antipsychotic Drug Use." *BMC Psychiatry* 19, no. 1: 143. https://link.springer.com/article/10.1007/s00127-019-01695-w.

Brombo, G., L. Bianchi, E. Maietti, et al. 2018. "Association of Anticholinergic Drug Burden With Cognitive and Functional Decline Over Time in Older Inpatients: Results From the CRIME Project." *Drugs Aging* 35: 917–924.

Cai, X., N. Campbell, B. Khan, C. Callahan, and M. Boustani. 2013. "Long-Term Anticholinergic Use and the Aging Brain." *Alzheimer's & Dementia* 9: 377–385.

Carr, E. G., and J. S. Owen-Deschryver. 2007. "Physical Illness, Pain, and Problem Behavior in Minimally Verbal People With Developmental Disabilities." *Journal of Autism and Developmental Disorders* 37, no. 3: 413–424. https://link.springer.com/article/10.1007/s10803-006-0176-0.

Christensen, T. J., J. E. Ringdahl, J. J. Bosch, T. S. Falcomata, J. R. Luke, and M. S. Andelman. 2009. "Constipation Associated With Self-Injurious and Aggressive Behavior Exhibited by a Child Diagnosed With Autism." *Education and Treatment of Children* 32, no. 1: 89–103. https://www.jstor.org/stable/42900009.

Cooper, S. A., G. Mclean, B. Guthrie, et al. 2015. "Multiple Physical and Mental Health Comorbidity in Adults With Intellectual Disabilities: Population-Based Cross-Sectional Analysis." *BMC Family Practice* 16: 110.

Fox, C., K. Richardson, I. D. Maidment, et al. 2011. "Anticholinergic Medication Use and Cognitive Impairment in the Older Population: The Medical Research Council Cognitive Function and Ageing Study." *Journal of the American Geriatrics Society* 59: 1477–1483.

Glover, G., R. Williams, P. Heslop, J. Oyinlola, and J. Grey. 2017. "Mortality in People With Intellectual Disabilities in England." *Journal of Intellectual Disability Research* 61: 62–74.

Gray, S. L., M. L. Anderson, S. Dublin, et al. 2015. "Cumulative Use of Strong Anticholinergics and Incident Dementia: A Prospective Cohort Study." *JAMA Internal Medicine* 175: 401–407.

Han, L., J. V. Agostini, and H. G. Allore. 2008. "Cumulative Anticholinergic Exposure Is Associated With Poor Memory and Executive Function in Older Men." *Journal of the American Geriatrics Society* 56: 2203–2210.

Hosking, F. J., I. M. Carey, S. M. Shah, et al. 2016. "Mortality Among Adults With Intellectual Disability in England: Comparisons With the General Population." *American Journal of Public Health* 106: 1483–1490.

Huisman, S., P. Mulder, J. Kuijk, et al. 2018. "Self-Injurious Behavior." *Neuroscience & Biobehavioral Reviews* 84: 483–491. https://www.sciencedirect.com/science/article/abs/pii/S0149763416303372.

IDS-TILDA. 2017. *Health, Wellbeing and Social Inclusion: Ageing With an Intellectual Disability in Ireland*. Trinity College Dublin.

IDS-TILDA. 2023. *Longitudinal Dynamics in the Ageing of People With an Intellectual Disability*. Trinity College Dublin.

Jamsen, K. M., D. Gnjidic, S. N. Hilmer, et al. 2017. "Drug Burden Index and Change in Cognition Over Time in Community-Dwelling Older Men: The CHAMP Study." *Annals of Medicine* 49: 157–164.

Kinnear, D., J. Morrison, L. Allan, A. Henderson, E. Smiley, and S. A. Cooper. 2018. "Prevalence of Physical Conditions and Multimorbidity in a Cohort of Adults With Intellectual Disabilities With and Without Down Syndrome: Cross-Sectional Study." *BMJ Open* 8: e018292.

Leder. 2022. "Annual Report 2022. London: King's College London." https://www.kcl.ac.uk/ioppn/assets/fans-dept/leder-2022-v2.0.pdf.

Maas, S., D. A. M. Festen, T. I. M. Hilgenkamp, and A. Oppewal. 2020. "The Association Between Medication Use and Gait in Adults With Intellectual Disabilities." *Journal of Intellectual Disability Research* 64, no. 10: 745–753. https://doi.org/10.1111/jir.12773.

McCarron, M., J. Swinburne, E. Burke, E. Mcglinchey, N. Mulryan, and V. Andrews. 2011. *Growing Older With an Intellectual Disability in Ireland 2011: First Results From the Intellectual Disability Supplement to the Irish Longitudinal Study on Ageing*. School of Nursing, Trinity College.

NICE. 2015. "Challenging Behaviour and Learning Disabilities: Prevention and Interventions for People With Learning Disabilities Whose Behaviour Challenges (NG11)".

O'Connell, J., É. Burke, N. Mulryan, et al. 2018. "Drug Burden Index to Define the Burden of Medicines in Older Adults With Intellectual Disabilities: An Observational Cross-Sectional Study." *British Journal of Clinical Pharmacology* 84: 553–567.

O'Connell, J., A. Gorman, É. Burke, et al. 2024. "OPTIMA-ID: Development and Validation of a Medicine Optimization Tool for Older Adults With Intellectual Disability." *Expert Review of Clinical Pharmacology* 17, no. 9: 837–851. https://doi.org/10.1080/17512433.2024.2390913.

O'Connell, J., M. C. Henman, N. Mcmahon, et al. 2020. "Medication Burden and Frailty in Older Adults With Intellectual Disability: An Observational Cross-Sectional Study." *Pharmacoepidemiology and Drug Safety* 29: 482–492.

O'Dwyer, C., P. Mccallion, M. Henman, et al. 2019. "Prevalence and Patterns of Antipsychotic Use and Their Associations With Mental Health and Problem Behaviours Among Older Adults With Intellectual Disabilities." *Journal of Applied Research in Intellectual Disabilities* 32: 981–993.

O'Dwyer, M. 2015. "Prevalence, Patterns and Factors Associated With Multiple Medicines Use in an Ageing Population With Intellectual Disability in Ireland." Doctor of Philosophy, University of Dublin, Trinity College.

O'Dwyer, M., I. D. Maidment, K. Bennett, et al. 2016. "Association of Anticholinergic Burden With Adverse Effects in Older People With Intellectual Disabilities: An Observational Cross-Sectional Study." *British Journal of Psychiatry* 209: 504–510.

O'Dwyer, M., P. Mccallion, M. McCarron, and M. Henman. 2018. "Medication Use and Potentially Inappropriate Prescribing in Older Adults With Intellectual Disabilities: A Neglected Area of Research." *Therapeutic Advances in Drug Safety* 9: 535–557.

Oliver, C., and C. Richards. 2010. "Self-Injurious Behaviour in People With Intellectual Disability." *Current Opinion in Psychiatry* 23, no. 5: 412–416. https://journals.lww.com/co-psychiatry/abstract/2010/09000/self_injurious_behaviour_in_people_with.4.aspx.

WHO Collaborating Centre for Drug Statistics Methodology. 2025. "WHO Collaborating Centre for Drug Statistics Methodology [Online]." Norwegian Institute of Public Health. https://www.whocc.no.

Peklar, J., M. Kos, M. O'Dwyer, et al. 2017. "Medication and Supplement Use in Older People With and Without Intellectual Disability: An Observational, Cross-Sectional Study." *PLoS ONE* 12: e0184390.

Robertson, J., S. Baines, E. Emerson, and C. Hatton. 2018. "Constipation Management in People With Intellectual Disability: A Systematic Review." *Journal of Applied Research in Intellectual Disabilities* 31, no. 5: 709–724. https://doi.org/10.1111/jar.12426.

Rousseau, M.-C., T. Billette De Villemeur, S. Khaldi-Cherif, et al. 2019. "Polyhandicap and Aging." *Disability and Health Journal* 12, no. 3: 375–380. https://www.sciencedirect.com/science/article/pii/S1936657419300342.

Sheehan, R., A. Hassiotis, K. Walters, D. Osborn, A. Strydom, and L. Horsfall. 2015. "Mental Illness, Challenging Behaviour, and Psychotropic Drug Prescribing in People With Intellectual Disability: UK Population Based Cohort Study." *BMJ (Clinical Research Ed.)* 351: h4326. https://www.bmj.com/content/351/bmj.h4326.

Stewart, C., M. Taylor-Rowan, R. L. Soiza, T. J. Quinn, Y. K. Loke, and P. K. Myint. 2021. "Anticholinergic Burden Measures and Older People's Falls Risk: A Systematic Prognostic Review." *Therapeutic Advances in Drug Safety* 12: 20420986211016645.

Tsang, J. Y., M. Sperrin, T. Blakeman, R. A. Payne, and D. Ashcroft. 2024. "Defining, Identifying and Addressing Problematic Polypharmacy Within Multimorbidity in Primary Care: A Scoping Review." *BMJ Open* 14, no. 5: e081698. https://doi.org/10.1136/bmjopen-2023-081698.

Walsh, M., T. G. Morrison, and B. E. McGuire. 2011. "Chronic Pain in Adults With an Intellectual Disability: Prevalence, Impact, and Health Service Use Based on Caregiver Report." *Research in Developmental Disabilities* 32, no. 2: 681–688. https://doi.org/10.1016/j.ridd.2010.11.029.

Ward, L. M., B. Stanley, N. Greenlaw, et al. 2021. "Risk of Anticholinergic Burden in Adults With Intellectual Disabilities: A Scottish Retrospective Cohort Study of $n = 17\ 220$." *Journal of Intellectual Disability Research* 65: 813–830.

Wouters, H., S. N. Hilmer, D. Gnjidic, et al. 2020. "Long-Term Exposure to Anticholinergic and Sedative Medications and Cognitive and Physical Function in Later Life." *Journals of Gerontology. Series A, Biological Sciences and Medical Sciences* 75: 357–365.

Zheng, Y.-B., L. Shi, X.-M. Zhu, et al. 2021. "Anticholinergic Drugs and the Risk of Dementia: A Systematic Review and Meta-Analysis." *Neuroscience & Biobehavioral Reviews* 127: 296–306.

Supporting Information

Additional supporting information can be found online in the Supporting Information section.