

Association of anticholinergic burden with adverse effects in older people with intellectual disabilities: an observational cross-sectional study

Máire O'Dwyer, Ian D. Maidment, Kathleen Bennett, Jure Peklar, Niamh Mulryan, Philip McCallion, Mary McCarron and Martin C. Henman

Background

No studies to date have investigated cumulative anticholinergic exposure and its effects in adults with intellectual disabilities.

Aims

To determine the cumulative exposure to anticholinergics and the factors associated with high exposure.

Method

A modified Anticholinergic Cognitive Burden (ACB) scale score was calculated for a representative cohort of 736 people over 40 years old with intellectual disabilities, and associations with demographic and clinical factors assessed.

Results

Age over 65 years was associated with higher exposure (ACB 1–4 odds ratio (OR)=3.28, 95% CI 1.49–7.28, ACB 5+ OR=3.08, 95% CI 1.20–7.63), as was a mental health

condition (ACB 1–4 OR=9.79, 95% CI 5.63–17.02, ACB 5+ OR=23.74, 95% CI 12.29–45.83). Daytime drowsiness was associated with higher ACB ($P<0.001$) and chronic constipation reported more frequently (26.6% ACB 5+ v. 7.5% ACB 0, $P<0.001$).

Conclusions

Older people with intellectual disabilities and with mental health conditions were exposed to high anticholinergic burden. This was associated with daytime dozing and constipation.

Declaration of interest

None.

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Many medicines used to treat conditions prevalent in older people possess anticholinergic activity and they may produce central and peripheral side-effects – sedation, confusion, dry mouth, adverse dental outcomes and constipation.¹ The risk of adverse outcomes including admission to hospital and falls increases with increasing anticholinergic exposure.^{1,2} Frail, older people are particularly vulnerable to anticholinergic adverse effects because of the high probability of exposure to treat multiple conditions, and increased age-related sensitivity to anticholinergic-related cognitive adverse effects.³ Furthermore, medical problems prevalent in older people such as constipation, sleep difficulties and dementia may be worsened by use of anticholinergics.⁴ Consequently, anticholinergic medications are considered potentially inappropriate in older populations, particularly those with dementia who have limited cognitive reserve.^{3,5} A systematic review examining associations between drugs with anticholinergic effects and adverse outcomes in older adults carried out by Ruxton and colleagues concluded that exposure to individual medicines with anticholinergic effects or increased overall anticholinergic exposure may increase risk of falls, cognitive impairment and all-cause mortality.⁶ In those over 65 years of age one recent study has shown associations with dementia and cognitive impairment.⁷

People with intellectual disabilities continue to have a shorter life expectancy compared with the general population, are at increased risk of mortality from preventable or treatable illnesses,⁸ and experience health inequities, including barriers to accessing primary care.⁹ They experience up to 2.5 times the health problems¹⁰ and higher incidence of morbidities such as dental disease, eye disease, epilepsy and dementia.^{11,12} Dual diagnosis is common, with one study reporting 41% of adults with intellectual disabilities with mental illness,¹³ which increases the likelihood of polypharmacy. Higher use of antipsychotics and other

psychotropics prescribed to manage mental health conditions and challenging behaviours is a concern^{14–16} and may confer additional risk as organic brain dysfunction may lead to idiosyncratic responses to drugs.¹⁷ Drug-induced anticholinergic activity is thought to be additive; the overall burden of anticholinergic drugs determining the risk of adverse effects.¹⁸ People with intellectual disabilities may be at additional risk of experiencing the 'prescribing cascade' as for example, the high prevalence of antipsychotic use may lead to the prescribing of anticholinergics for movement disorders (extrapyramidal symptoms; anatomical therapeutic chemical (ATC) N04A), a practice no longer recommended in older people.^{5,6} Anticholinergic effects may be misattributed to a consequence of the normal ageing process and drugs with anticholinergic properties may be a cause of unrecognised adverse drug reactions.¹⁹

People with intellectual disabilities receive a variety of different medicines with anticholinergic activity, and scales that capture cumulative burden are needed to stratify risk. The Anticholinergic Cognitive Burden (ACB) scale is one such scale that computes a total score of drugs to determine individual anticholinergic burden.¹ The ACB scale identifies the burden of anticholinergic negative effects on cognition of medications (prescribed and over the counter); drugs with no anticholinergic effects score 0, drugs with possible anticholinergic effects score 1, drugs with definite cognitive anticholinergic effects score 2 or 3.¹ In one study an ACB score of 5 or more was associated with an Mini-Mental State Examination (MMSE) score of one point lower compared with an ACB score of 0.²⁰ It also found the largest effect on cognitive decline was observed in people with mild dementia (MMSE 26–30). The ACB scale has been demonstrated to have predictive validity, with higher ACB scores associated with adverse clinical outcomes.²¹ Given evidence in the general older population of

the risks associated with anticholinergic exposure and of frailty, cognitive decline and adverse effects, we hypothesised that adverse effects would be associated with exposure to a high anticholinergic load in older people with intellectual disabilities. Our objectives were: (a) to determine each individual's cumulative exposure to anticholinergic medications by using the ACB scale; (b) to describe the pattern of anticholinergic medication use in relation to demographic and clinical characteristics and the most frequently reported therapeutic classes contributing to the anticholinergic burden; (c) to examine factors associated with higher anticholinergic burden exposure; and (d) to explore the relationship between ACB scale scores and indicators of central and peripheral anticholinergic adverse effects.

Method

Study design

Medication data for this study was drawn from Wave 1 (2009/2010) of the Intellectual Disability Supplement to the Irish Longitudinal Study on Ageing (IDS-TILDA), which contains a nationally representative sample of 753 people with an intellectual disability, aged between 41 and 90 years (online Fig. DS1)²² IDS-TILDA is a longitudinal study of older adults with intellectual disabilities and has been described in detail elsewhere.^{22,23} Age 40 years and over was selected to reflect the lower longevity of people with intellectual disabilities and their earlier onset of chronic disease, for example dementia.^{24,25} This would also ensure that there would be sufficient participants for future waves of data collection and provide opportunities to offer insights into ageing for those who may age prematurely. Everyone included in the study was registered on the Irish National Intellectual Disability Database, and therefore had an intellectual disability. The person's level of intellectual disabilities was checked and confirmed from case notes at the time of the face-to-face interview. The STROBE (The Strengthening the Reporting of Observational Studies in Epidemiology) reporting guidelines for cross-sectional studies was used.²⁶ Ethical approval for the study was received from the Faculty of Health Sciences Trinity College Dublin and 138 intellectual disability service providers, and all participants and/or proxies, as appropriate, provided informed consent to partake in the study.

Medication exposure measures

Participants/proxies were asked 'Can you tell me what medications (including prescribed and over-the-counter, herbal medicines) you take on a regular basis – like every day or every week?' in the pre-interview questionnaire.²² The pre-interview questionnaire was sent to participants and/or proxies 1 week in advance of the face-to-face interview to give them time to check patient records or charts to record the medicines they were taking. This information was then cross-checked by interviewers at the time of interview, by asking whether the list they had provided in the pre-interview questionnaire included all of their medicines, and where necessary checking patient files if they had permission. Medicines were recorded by brand or generic name, including prescription and non-prescription and over the counter, and all data were anonymised. Medications were coded using the World Health Organization (WHO) ATC classification system.²⁷ Two pharmacists (M.O'D., J.P.) independently reviewed and confirmed medication entries.

Measuring exposure to anticholinergic medications

The dependent variable was participants' score for anticholinergic burden calculated using the updated 2012 ACB scale.²⁸ In

addition, the ACB list was assessed and modified to include drugs with anticholinergic properties taken by participants, available in Ireland, but not included in the ACB scale.²⁰ Two pharmacists (M.O'D., I.M. – who developed the original scale) independently consulted standard reference sources, the product characteristics (SmPC) information and the other validated anticholinergic rating scales, to assign a score to other drugs with anticholinergic properties available in Ireland but not included in the ACB list; this was based on the approach used to develop the original scale. The 22 medicines not included in the original ACB list with respective scoring are listed in online Table DS1. Medications with anticholinergic properties that were not available in Ireland and/or not present in the data-set were excluded (42 medications).

We categorised exposure to anticholinergics in three ways: (a) the total ACB score of each individual, created by summing the score of each possible (ACB 1) or definite (ACB 2 or 3) anticholinergic; (b) a binary variable – those exposed to any anticholinergic medicine (ACB score ≥ 1) and no anticholinergic exposure (ACB 0); and (c) a categorical variable – no exposure to anticholinergic medications (ACB 0), ACB score of 1–4, and ACB score of ≥ 5 , as in previous studies.²⁰

Covariates

Covariates included gender, age (a categorical variable: 40–49 years, 50–64 years, 65+ years), level of intellectual disability, place of residence (independent, community group home or residential setting). Residential settings were defined as living arrangements where ten or more people share a single living unit or where the living arrangements are campus based. Community group homes are in a community setting with staff support for small groups (<10) of people with intellectual disabilities. Other covariates included any dementia (doctor's diagnosis of dementia, organic brain dysfunction, senility or serious memory impairment), polypharmacy (no polypharmacy 0–4 medicines; polypharmacy ≥ 5 medicines). Participants/proxies reported if the participant had ever received a doctor's diagnosis of 12 chronic health conditions.²³ Dementia, lung disease, stroke, cancer and liver disease had insufficient numbers (<5% prevalence) and were excluded from further multivariate analysis.

The relationship between anticholinergic exposure and indicators of anticholinergic adverse effects was examined; if the participant had reported fall(s) in the previous year, daytime dozing, constipation or physician-diagnosed chronic constipation and laxative use. Participants were also divided into those who were dentate or edentulous.²⁹

Statistical analyses

Descriptive statistics (percentages, medians (as the data were not normally distributed) and 95% confidence intervals) described the characteristics of the eligible study population.

We used univariate analysis to examine the associations between the dependant (anticholinergic exposure (ACB ≥ 1) *v.* no exposure) and clinical and demographic variables. Here, for categorical variables chi-squared (χ^2) tests for independence were used to test for a significant association between the three ACB groupings. For continuous variables, a one-way analysis of variance (ANOVA) was used to test for a significant difference. Multinomial logistic regression identified factors associated with an ACB of 1–4 and an ACB of 5+, with those with no anticholinergic exposure (ACB 0) as the reference category. All demographic variables were included in the model (age, gender and level of intellectual disabilities). Those with an unverified level of intellectual disabilities ($n = 54$) were excluded from regression

analyses. Those who lived independently or in community group homes were combined as a single group, as the numbers in the independent setting with anticholinergic exposure were small ($n=11$). Variables with a $P<0.10$ in univariate analysis were included in our multivariable model (this P -value was selected to ensure that important or influential factors were not omitted).³⁰ All variables were entered into the model simultaneously. The model is adjusted for polypharmacy status (polypharmacy *v.* no polypharmacy), with results presented as adjusted odds ratios (ORs) with corresponding 95% confidence intervals.

Sample size calculation for the logistic regression was based on the guideline of Peduzzi *et al* (for a minimum number of cases (N) needed for the study; $N=10 k/p$, where p is the smallest of the proportions of negative or positive cases in the population, k the number of covariates (independent variables)).³¹ For the regression model there were ten covariates and the proportion of negative cases (ACB 0) was 0.284, therefore a minimum sample size (N) of 352 was needed. There were data from 658 individuals available for regression analyses, so sample size was sufficient. The ACB scale score and anticholinergic adverse effects were explored at univariate level. To control for problems of Type I error associated with multiple comparisons a Bonferroni correction was applied,³² testing six associations, with a desired α of 0.05, resulting in $\alpha=0.05/6=0.008$. Statistical analyses were carried out using the Statistical Package for Social Sciences, Version 20.

Results

Of 753 participants, 736 (98%) provided medication use data. Baseline characteristics of our sample are presented in Table 1. The mean age of participants was 54.1 years (s.d.=8.8, range 41–90 years), with almost half (45.7%) aged between 50 and 64 years. Almost half (46%) of the sample with recorded level of intellectual disabilities ($n=682$) reported moderate intellectual disabilities. Overall, participants reported a mean of 5.7

(s.d.=4.4) medicines, with 53.7% exposed to polypharmacy (5+ medicines). In the total sample of 736, no exposure was reported by 214 (29.1%, ACB 0) whereas 308 (41.8%) had a score of ACB 1–4 and 214 (29.1%) ACB score 5+ (online Table DS2). Of those reporting medications with ACB =1 score (522) 71% (370) received medicines with an ACB score of 2 or 3, and of those ($n=370$), 43% (159) reported concurrent use of two or more ACB 2 or 3 drugs. The median total ACB score was 4.0 (s.d.=3.0) (range 1–16; $n=522$). There was a significant association between ACB score and reporting mental health conditions ($n=706$) ($P<0.001$); 46.6% had ACB 5+, and a further 47.2% had a score of 1–4 ($P<0.001$).

Similarly, level of intellectual disabilities was associated with anticholinergic exposure; 36.5% of those with severe/profound intellectual disabilities had an ACB score of 5+, compared with just 19.9% of those with mild intellectual disabilities ($n=682$, $P<0.001$, online Table DS2). In total, 72 different anticholinergic medicines were reported in 1266 instances (online Table DS3); most were ACB 1 medications (52.1%) with 36.3% ACB 3 drugs.

Antipsychotics comprised 35.4% of the total cumulative ACB score, followed by anticholinergics (16%) (ATC N04A, for example biperiden) (Fig. DS2). Of those taking antipsychotics (319), 26% ($n=82$) received two or more concurrently. Medications with ACB score 2 were reported by 26.6% of those with exposure, with carbamazepine being the most frequent ($n=127$). ACB score 3 medicines were reported by 59.1% ($n=309$), with olanzapine the most frequent ($n=101$). Antipsychotics accounted for 46% of ACB 3 medicines, N04A anticholinergics (27.6%) and antidepressants (9.4%). Of those who reported N04A anticholinergics ($n=122$), 91.7% reported concurrent use of antipsychotics with anticholinergic properties and of those receiving antipsychotics (319), 35.2% also received N04A anticholinergic agents, and of those with antipsychotic polytherapy ($n=82$), over half (58.5%, $n=48$) received a N04A anticholinergic.

Table 1 Anticholinergic exposure binary table

	n (%)			P ^a
	Total population (n = 736)	Anticholinergic use (n = 522)	No anticholinergic use (n = 214)	
Gender				
Male	330 (44.8)	225 (68.2)	105 (31.8)	0.08
Female	406 (55.2)	297 (73.2)	109 (26.8)	
Age, years				
40–49	266 (36.1)	171 (64.3)	95 (35.7)	<0.001
50–64	336 (45.7)	234 (69.6)	102 (30.4)	
65+	134 (18.2)	117 (87.3)	17 (12.7)	
Level of intellectual disabilities ^b				
Mild	163 (23.9)	107 (65.6)	56 (34.4)	<0.001
Moderate	316 (42.9)	207 (65.5)	109 (34.5)	
Severe/profound	203 (27.6)	173 (85.2)	30 (14.8)	
Residential setting				
Independent	122 (16.6)	47 (38.5)	75 (61.5)	<0.001
Community group home	265 (36.0)	183 (69.1)	82 (30.9)	
Residential	349 (47.4)	292 (83.7)	57 (16.3)	
Polypharmacy status				
No polypharmacy	341 (46.3)	160 (46.9)	181 (53.1)	<0.001
Polypharmacy	395 (53.7)	362 (91.6)	33 (8.4)	
Number of comorbidities				
0	51 (6.9)	27 (52.9)	24 (47.1)	<0.001
1	157 (21.3)	84 (53.5)	73 (46.5)	
2	192 (26.1)	137 (71.4)	55 (28.6)	
3+	336 (45.7)	279 (83.0)	57 (17.0)	

a. $P<0.05$ is significant.

b. For level of intellectual disabilities $n=682$, as the level was not verified in 54 individuals.

Those aged over 65 years were more likely to report an ACB score of 1–4 (OR=3.28, 95% CI 1.49–7.28) and ACB of 5+ (OR=3.08, 95% CI 1.20–7.63), after controlling for other factors (Table 2). Having a mental health condition was associated with having a score of ACB 1–4 (OR=9.79, 95% CI 5.63–17.02) and ACB 5+ (OR=23.74, 95% CI 12.29–45.83). Levels of intellectual disabilities, gender or place of residence were not significant with

either level of anticholinergic exposure, nor were the other clinical conditions.

Daytime drowsiness was significantly associated with a higher ACB score at univariate level ($P < 0.001$), with 46.3% of those with an ACB score of 5+ reporting a moderate/high likelihood of daytime drowsiness, compared with 23.4% of those with no anticholinergic exposure (Table 3). A greater proportion of those

Table 2 Multivariate analysis of factors associated with Anticholinergic Cognitive Burden (ACB) scale scores of 1–4 and 5+ ($n = 658$)^a

Characteristic	ACB score 1–4		ACB score 5+	
	OR (95% CI)	P	OR (95% CI)	P
<i>Characteristic</i>				
Gender				
Male	1 (reference)		1 (reference)	
Female	1.34 (0.84–2.15)	0.22	0.74 (0.41–1.31)	0.31
Age, years				
40–49	1 (reference)		1 (reference)	
50–64	1.13 (0.69–1.85)	0.64	0.97 (0.52–1.79)	0.91
65+	3.28 (1.49–7.25)	0.003	3.08 (1.2–7.63)	0.02
Level of intellectual disabilities ^b				
Mild	1 (reference)		1 (reference)	
Moderate	0.78 (0.45–1.37)	0.39	0.66 (0.33–1.36)	0.26
Severe/profound	1.44 (0.67–3.09)	0.35	0.83 (0.33–2.07)	0.68
Residence				
Independent/community group home	1 (reference)		1 (reference)	
Residential	0.92 (0.53–1.58)	0.75	1.56 (0.82–2.97)	0.18
<i>Conditions</i>				
Mental health ^c				
No	1 (reference)		1 (reference)	
Yes	9.79 (5.63–17.02)	< 0.001	23.74 (12.29–45.83)	< 0.001
Neurological				
No	1 (reference)		1 (reference)	
Yes	1.30 (0.76–2.20)	0.34	0.73 (0.39–1.37)	0.33
Gastrointestinal				
No	1 (reference)		1 (reference)	
Yes	1.21 (0.66–2.22)	0.54	1.27 (0.64–2.53)	0.52
Eye				
No	1 (reference)		1 (reference)	
Yes	0.81 (0.50–1.32)	0.41	0.68 (0.37–1.24)	0.21
Hypertension				
No	1 (reference)		1 (reference)	
Yes	0.66 (0.32–1.35)	0.25	0.74 (0.32–1.70)	0.48

a. Reference category: ACB 0. $P < 0.05$ is significant, all significant factors in bold Cox and Snell $R^2 = 0.46$, Nagelkerke $R^2 = 0.52$. Data are adjusted odds ratio (OR). Model is adjusted for polypharmacy status.
b. 54 no verified level of intellectual disabilities.
c. 30 missing data/do not know.

Table 3 Anticholinergic Cognitive Burden (ACB) scale scores and adverse effects

Characteristic	n (%)				P ^a
	Total population ($n = 736$)	No anticholinergic exposure ($n = 214$)	ACB score 1–4 ($n = 308$)	ACB score 5+ ($n = 214$)	
<i>Central anticholinergic adverse effects</i>					
Likelihood of daytime dozing					
High/moderate likelihood	267 (36.3)	50 (23.4)	118 (38.3)	99 (46.3)	< 0.001
Slight/would never doze	469 (63.7)	164 (76.6)	190 (61.7)	115 (53.7)	
Have fallen in previous year ^b	200 (27.4)	43 (20.3)	95 (31.0)	62 (29.1)	0.02
<i>Peripheral adverse effects</i>					
'Is constipation a problem for you?' ^c					
Doctor's diagnosis of chronic constipation	128 (17.4)	16 (7.5)	55 (17.9)	57 (26.6)	< 0.001
Any laxative use	276 (37.5)	41 (19.2)	119 (38.6)	116 (54.2)	< 0.001
1 Laxative	146 (19.8)	31 (14.5)	61 (19.8)	54 (25.2)	
2+ Laxatives	130 (17.7)	10 (4.7)	58 (18.8)	62 (29.0)	
Dentate status ^d					
Dentate	547 (74.5)	169 (80.5)	228 (74.0)	150 (69.4)	0.03
Edentulous	187 (25.5)	41 (18.5)	80 (26.0)	66 (30.6)	

a. From χ^2 -test (and applying Bonferroni correction), $P < 0.008$ for significance.
b. Five missing data.
c. Eleven missing data.
d. Two missing data.

with higher anticholinergic burden reported a doctor's diagnosis of chronic constipation; 26.6% of those with an ACB score of 5+ compared with 7.5% of those with no anticholinergic exposure ($P < 0.001$). Furthermore, 29.0% of those with an ACB 5+ used two or more concurrent laxatives, compared with 4.7% of those with no exposure ($P < 0.001$).

Discussion

Principal findings

As the first study in a representative population of older adults with intellectual disabilities, our findings reveal high levels of cumulative anticholinergic exposure, with 30% exposed to an ACB score of 5+. Multivariable regression analysis showed that those over 65 years and those with mental health conditions were much more likely to have high anticholinergic exposure. Antipsychotics, N04A anticholinergics, anti-epileptics and antidepressants were the most frequent classes contributing to the ACB. Antipsychotics accounted for over one-third of the cumulative burden, with a notably high prevalence of typical antipsychotics and with one in four of these individuals taking two or more antipsychotics. Our findings revealed that higher anticholinergic burden was associated with greater likelihood of reporting daytime dozing, constipation and use of multiple laxatives.

Comparison with other studies

There are no equivalent studies with other cohorts with participants with intellectual disabilities. Compared with studies that used the ACB scale with cohorts of older adults without intellectual disabilities, the degree of the anticholinergic burden found in our study was much greater and the types of anticholinergic drugs were different (online Table DS4).^{20,33,34}

Factors associated with anticholinergic burden and adverse effects

Our analysis showed no association between higher scores and gender, but age over 65 years was a significant factor both for exposure to a score of 1–4 and exposure to an ACB score of five or more (Table 2). After adjusting for relevant confounders, we did not find an association between the level of intellectual disabilities and anticholinergic burden; however, it was notable that 85% of those with severe or profound intellectual disabilities were exposed to anticholinergic medications, and over one-third to an ACB score of 5+. The confidence intervals across all the categories were quite wide indicating the scale of variation remaining after adjusting for confounding factors, including polypharmacy. Other studies have only examined psychotropic polypharmacy^{35,36} or polypharmacy³⁷ and have reported varying associations with age, gender and level of intellectual disabilities, but in contrast to the general elderly population, where women are identified as being more likely to be exposed to psychotropic polypharmacy.³⁸ It may be that many of the conditions that are treated with anticholinergic medicines occur earlier in the lives of people with intellectual disabilities than in those without intellectual disabilities so that the use of these medicines has become similar in men and women and is increasing to a lesser extent in these older age groups.

Almost half of those with a mental health condition and four in ten of those over 65 were exposed to an ACB of 5+. The wide confidence intervals of the association of mental health conditions may reflect variability in reporting of mental health conditions; however, 12 of the 16 highest contributors to the ACB score were

drugs for mental health. We found that 35% of those with anti-psychotics had concurrent exposure to N04A anticholinergics, which was higher than previously reported in a UK study (14%),³⁹ yet Parkinson's disease was reported by only 1% in this cohort. The risks associated with using these medicines in combination in patients who are vulnerable and cognitively impaired are substantial.⁴⁰ Our findings revealed that over one-fifth of those reporting antipsychotic use reported chlorpromazine and 14% reported haloperidol, both agents that carry significant anticholinergic, noradrenergic and antihistamine adverse effects.⁴¹ These older agents are associated with more extrapyramidal side-effects⁴¹ and people with intellectual disabilities may be more susceptible to these side-effects compared with the general population.^{17,41} Risperidone was also the second most commonly used antipsychotic, an agent also associated with extrapyramidal side-effects.⁴¹ Although our findings are limited by the fact that we did not have information in relation to side-effects of medications, it is probable that these anticholinergic agents are being to some extent used to treat, or in prophylaxis of, extrapyramidal symptoms associated with antipsychotic agents. There is recent evidence of increased incident dementia associated with higher anticholinergic burden and length of exposure in those over 65 years.⁷

Our univariate findings must be interpreted conservatively; while a higher anticholinergic burden was associated with a risk of daytime dozing, falls in the previous year were not significantly associated, in contrast to studies in the general older population.^{6,42} Constipation is common in older people, and increases with age.⁴³ People with intellectual disabilities are at risk of constipation from several factors,⁴⁴ and we found an association between increasing anticholinergic burden and constipation and laxative use, and furthermore, almost 30% of those with an ACB score of 5+ had laxative polytherapy, compared with <5% of those with no anticholinergic exposure. Multiple laxative use poses risks of electrolyte disturbance and dehydration that may exacerbate constipation.⁴³ The relationship between anticholinergic medications and xerostomia and tooth loss has been previously established⁴⁵ but although a higher proportion of the participants with an ACB score of 5+ were edentulous (30.6%), this was not significant.

Impact of findings on practice

Since anticholinergic activity may affect both central and peripheral systems, several factors make managing the anticholinergic burden complex in people with intellectual disabilities. Multimorbidity combined with complex mental health conditions and epilepsy increases the number and different classes of drugs with anticholinergic activity prescribed for people with intellectual disabilities and the cumulative burden. The sensitivity of people with intellectual disabilities to the effects of these drugs may be greater, and may increase with age, but is unquantifiable because of lack of evidence. Consequently, the prevalence of anticholinergic side-effects may be greater in this population, especially as the oldest age group were exposed to the greatest burden. Patient assessment is challenging, which may lead to diagnostic overshadowing¹⁴ and initiation of inappropriate drugs. Physical problems, such as constipation, may present as challenging behaviours,⁴¹ which could trigger a prescribing cascade with a significant anticholinergic burden, as the association of antipsychotic, anticholinergic and laxative use in this study suggests.

A high proportion of people with intellectual disabilities are prescribed drugs with anticholinergic effects from an early age, and are likely to be exposed for many years.¹⁷ Length of exposure may increase as life expectancy of people with intellectual disabilities

grows, potentially increasing the risks of chronic use of psychotropics.⁴⁶ These factors imply that the extent and burden of anticholinergic side-effects in people with intellectual disabilities are greater than in the general older population, and could have an impact on their quality of life. Therefore, assessment of this burden, particularly among the oldest and those with mental health conditions and multiple morbidities, and who receive psychotropic polypharmacy is essential.

The risks of cumulative anticholinergic burden could be reduced through regular, multidisciplinary medication review. Scales such as the ACB scale, allied to review of patient symptoms, currently remain useful aids to guide clinical decision-making.⁴⁷ Little is known about the influence of ageing on people with intellectual disabilities and their response to medicines, which reinforces the need for review and education of healthcare professionals. Integrated and coordinated care is receiving increased attention in the older population,⁴⁸ and needs to be further developed when providing care to people with intellectual disabilities. In older people and those with cognitive impairment, anticholinergic-induced cognitive impairment is more likely to occur at therapeutic doses potentially increasing risks of medication errors⁴⁹ for people with intellectual disabilities managing their own medicines. Continuing deinstitutionalisation creates challenges for primary care professionals who may not have the necessary expertise or experience to provide care for people with intellectual disabilities, nor may they be able to meet the needs of their carers.⁵⁰ Guidelines are needed to support professionals, people with intellectual disabilities and carers to optimise anticholinergic medicines use. However, since people with intellectual disabilities are often excluded from randomised controlled trials,⁵¹ additional data may also need to be generated by national audits and longitudinal studies.¹⁴

Strengths and limitations

Our study has four important strengths. First, use of a large, randomly selected population-representative sample offered sufficient power for multivariate analysis, with findings generalisable to the population with intellectual disabilities in Ireland. Second, the great majority of respondents recorded detailed medication data, including over-the-counter medicines (98%). Third, participants and/or proxy respondents underwent a detailed assessment of health characteristics, providing data on potential confounders for the regression model. The use of the Bonferroni correction addressed the problem of multiplicity. Fourth, we used the ACB scale, which has been widely used, making the assessment of anticholinergic burden robust and relevant to clinical practice.^{3,20} We added to its content validity by reviewing other anticholinergic medicines available in Ireland with an independent expert.

There are also limitations. There was no independent confirmation of medicines or conditions, but cross-checking of medicines in the pre-interview questionnaire at the time of interview improved accuracy. Information was also not recorded about disease severity. Data on dose and frequency of medicines were not always available and adverse effects may be dose dependent,⁴⁷ however, the ACB scale does not take dose into account. Although a higher dose of an anticholinergic agent would be expected to cause more central effects, the relationship may not be linear.⁵² The ACB scale has not been validated against measures of *in vitro* anticholinergic activity. However, assays are difficult to interpret, not readily available in practice and due to variations in blood-brain barrier permeability may not reflect levels in the central nervous system. It is currently accepted, that allied to a careful review of the patient's symptoms and medicines, scales

and lists such as the ACB scale remain the best aid to guide clinical decision-making.⁴⁷ The ACB scale does not take into account influences of patient variability in drug response associated with older age, frailty, multimorbidity, cognitive reserve and individual pharmacokinetic factors.

As an observational study, we could only describe associations between anticholinergic burden and clinical and demographic factors. In our multivariate analysis, potential bias was reduced by adjusting for known confounders; however, residual confounding may remain. Although potential adverse effects associated with anticholinergic exposure were examined at univariate level, other factors such as functional status, or baseline cognitive status that could influence the prescription of anticholinergics were not measured in this study, and this analysis was descriptive and not adjusted for confounders.

In conclusion, the use of medications with anticholinergic activity is commonplace among older adults with intellectual disabilities, with psychotropic agents accounting for much of the burden. For the first time in people with intellectual disabilities a high anticholinergic burden has been shown to be associated with daytime dozing, constipation and multiple laxative use. The possible impact that anticholinergics may have on cognitive and executive function should be evaluated and more attention should be paid to the assessment of peripheral anticholinergic effects, such as constipation. People with intellectual disabilities are among the most vulnerable members of society and regular, multidisciplinary review of medications to decrease the use of anticholinergic medicines is likely to reduce morbidity and improve quality of life in this population.

Máire O'Dwyer, PhD, School of Pharmacy and Pharmaceutical Sciences and IDS-TILDA School of Nursing and Midwifery, Trinity College Dublin, Dublin, Ireland; **Ian D. Maidment**, PhD, School of Life and Health Sciences, Aston University, Birmingham, UK; **Kathleen Bennett**, PhD, Department of Pharmacology and Therapeutics, Trinity Centre for Health Sciences, St James Hospital, Dublin, Ireland; **Jure Peklar**, MPharm, School of Pharmacy, University of Ljubljana, Ljubljana, Slovenia; **Niamh Mulryan**, MB MRCPsych, IDS-TILDA School of Nursing and Midwifery, Trinity College Dublin, Dublin, Ireland; **Philip McCallion**, PhD, Centre for Aging and Excellence in Community Wellness, University At Albany, New York, USA; **Mary McCarron**, PhD, Trinity College Dublin, Ireland; **Martin C. Henman**, PhD, School of Pharmacy and Pharmaceutical Sciences, Trinity College Dublin, Ireland

Correspondence: Máire O'Dwyer, IDS-TILDA, School of Pharmacy and Pharmaceutical Sciences, Panoz Institute, Trinity College, Dublin 2, Ireland. Email: modwyer@tcd.ie

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