

Drug Burden and its Association with Falls Among Older Adults in New Zealand: A National Population Cross-Sectional Study

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Abstract

Background Adverse outcomes associated with advanced diseases are often exacerbated by polypharmacy.

Objectives The current study investigated an association between exposure to anticholinergic and sedative medicines and falls in community-dwelling older people, after controlling for potential confounders.

Methods We conducted a retrospective cross-sectional study of a continuously recruited national cohort of

community-dwelling New Zealanders aged 65 years and over. Participants had an International Resident Assessment Instrument–Home Care (interRAI-HC) assessment between 1 September 2012 and 31 January 2016. InterRAI-HC is a comprehensive, multi-domain, standardised assessment. This study captured 18 variables, including fall frequency, from the interRAI. These data were deterministically matched with the Drug Burden Index (DBI) for each participant, derived from an anonymised national dispensed pharmaceuticals database. DBI groupings were statistically ascertained, and ordinal regression models employed.

Results Overall, there were 71,856 participants, with a mean age of 82.7 years (range 65–106); 43,802 (61.0%) were female, and 63,578 (88.5%) were New Zealand European. In unadjusted and adjusted analyses, DBI groupings were related to falls ($p < 0.001$). A DBI score > 3 was associated with a 41% increase in falls compared with a DBI score of 0 ($p < 0.001$). There was a ‘dose-response’ relationship between DBI levels and falls risk.

Conclusions DBI was found to be independently and positively associated with a greater risk of falls in this cohort after adjustment for 18 known confounders. We suggest that the DBI could be a valuable tool for clinicians to use alongside electronic prescribing to help reduce falls in older people.

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Key Points

A study of 71,856 older adults found the Drug Burden Index (DBI) to be independently and positively associated with falls after data were adjusted for 18 possible confounding factors.

The DBI could be a valuable tool for clinicians to use alongside electronic prescribing to help reduce falls in older people.

1 Introduction

Aging is associated with greater disease prevalence and with it the likelihood of greater medication use [1]. Although medications are prescribed on the premise of improving health outcomes, any medication usage is not without risk and there are often side effects, particularly for older people who have reduced renal and hepatic clearance, multiple comorbidities, and geriatric syndromes [2, 3].

Previous studies have demonstrated that medications with sedative and anticholinergic properties are likely to increase the risk of falls among older people [4–7]. Both sedative and anticholinergic medications are used extensively in older people and for a wide range of conditions, including allergies, urinary incontinence, insomnia, anxiety, chronic obstructive pulmonary disease (COPD), depression, and gastrointestinal disorders [8]. The Drug Burden Index (DBI) estimates the cumulative anticholinergic and sedative load of over 400 different medications, and uses the principles of dose response and maximal effect [9]. It can be used worldwide and is not medication or therapeutic class-specific, but allows for the summation of side effects over multiple classes of medications. It can also be used for assessing the functional impact of exposure to these particular groups of drugs in a variety of clinical settings [8, 9].

Previous studies have demonstrated that high DBI scores can be associated with functional impairment in older people [9–11], and a high DBI score may predict falls, frailty, hospitalisation, primary care doctor visits, and mortality [12]. However, the poor outcomes of people taking more anticholinergic and sedative medications could reflect their more advanced diseases and increased levels of frailty.

We considered this issue and examined the association between the DBI and falls in community-dwelling older people by combining anonymised medication data with potential confounders obtained from cross-matched data from New Zealand's national standardised older persons health assessment (International Resident Assessment Instrument–Home Care [interRAI-HC]).

The aim of the current study was to determine if an increased anticholinergic and sedative load, as defined by the DBI, is associated with an increased risk of falls in community-dwelling older people after adjustment for 18 possible confounding factors.

2 Methods

2.1 Study Design

We undertook a retrospective cross-sectional study of a continuously recruited national cohort.

2.2 Participants

New Zealand currently has a total population of 4.8 million, of whom approximately 15% are aged 65 years or greater and over two-thirds live in the major urban areas (Statistics New Zealand; <http://www.stats.govt.nz>). Schluter et al. [13] demonstrated that the interRAI population is generally representative of the different ethnic groups in New Zealand, but with Māori and Pacific people being overrepresented. The younger age groups are underrepresented and the older age groups overrepresented, signifying that older people have more health problems and higher needs. The sex ratio is like that of the New Zealand older population, with close to 60% being female.

Participants were home-based adults aged 65 years and over who had an interRAI-HC assessment between 1 September 2012 and 31 January 2016, and who consented to their data being used for planning and research purposes. The interRAI-HC instrument is used for all community care assessments of older people needing publicly funded long-term community or residential care services in New Zealand [13]). The interRAI-HC is used within all 20 district health boards of the New Zealand public health system. InterRAI-HC information is stored electronically and is National Health Index (NHI) number-linked to other databases using encryption for data security. The NHI number is a unique identifier that is assigned to every person who uses health and disability support services in New Zealand. Participants with invalid encrypted NHI numbers or who were aged <65 years were excluded. Where an individual had more than one interRAI-HC assessment during the study period, only the first assessment was used. New Zealand's interRAI database was validated by Schluter et al. [13].

2.3 Instrument and Primary Measures

The interRAI-HC 9.1 instrument (© interRAI Corporation, Washington, DC, 1994–2009), modified with permission for New Zealand, is used under licence to the New Zealand Ministry of Health (www.interrai.co.nz). It comprises 236 questions, which form 27 standardized instruments, and yields internationally valid and reliable scales [13, 14]. Self-reported falls history within the last 90 days is elicited from a single question; namely, participants are asked if they have experienced a fall, with the following response options: (0) no fall in last 90 days; (1) no fall in last 30 days, but fell 31–90 days ago; (2) one fall in last 30 days; and (3) two or more falls in last 30 days.

DBI exposure was calculated for medicines with anticholinergic and sedative properties dispensed from 1 September 2011 through 31 October 2015. The New Zealand Ministry of Health maintains a national archive of

prescription use. The NHIs are encrypted in all datasets, but there is only one encrypted version of each NHI, which is never changed. Consequently, we were able to cross-match the prescription data with interRAI data. The pharmaceutical information database (Pharms) includes records of all prescription claims made by community pharmacists funded by PHARMAC (The Pharmaceutical Management Agency), including the medicine name, medicine strength, quantity dispensed, daily supply, and prescription date [8, 15, 16]. (PHARMAC decides which medicines and pharmaceuticals are to be subsidised for use in the community and public hospitals.) We extracted the dose for all anticholinergic and/or sedative exposures for the 90-day time period prior to the interRAI assessment date. The drug burden attributable to each anticholinergic or sedative medicine was calculated using the following equation:

$$\text{Drug Burden Index} = D/(D + \delta),$$

where D is the daily dose taken by the individual and δ is the minimum efficacious dose. Daily dose was derived by dividing the ‘quantity dispensed’ by the ‘days’ supply’, and both these variables are recorded in the Pharms dataset. For example, to derive the daily dose for citalopram, the ‘quantity supplied’ and the ‘days’ supply’ were both 28, therefore the ‘daily dose’ was 1. For the purpose of our calculations, we utilised the 90-day period prior to the interRAI-HC assessment for the derivation of the DBI.

2.4 Demographic and Potentially Confounding Measures

Age, sex, ethnicity, cognitive performance, alcohol consumption, smoking status, hearing status, vision status, fatigue, mobility, coronary heart disease (CHD), COPD, congestive heart failure (CHF), depression, body mass index (BMI), self-reported health, dizziness and unsteady gait were considered as potential confounding factors [17–19] and were subsequently utilised. All these measures arose from the interRAI-HC assessment (variable specification details appear in electronic supplementary Appendix S1).

2.5 Procedure

A detailed account of the interRAI-HC assessment instrument and procedure within New Zealand has been described previously ([13]). In brief, the standardised interRAI-HC instrument is used to conduct all community care assessments on older people needing publicly funded long-term community or residential care services. Individuals are referred by a health practitioner to have their needs assessed by one of over 1800 trained interRAI assessors. Assessors visit clients in their own home to produce

individualized care plans according to a standardized protocol. Data provided by clients are validated against their clinical records. Individuals are explicitly asked if they consent to their de-identified interRAI-HC information being used for planning and research purposes. All data are directly entered into the electronic interRAI-HC database, maintained by New Zealand’s Technical Advisory Services (TAS; <http://centraltas.co.nz>). With approval, consented data are released by TAS, through the New Zealand Ministry of Health.

2.6 Statistical Analysis

Reporting of analyses was informed by the STrengthening the Reporting of OBServational studies in Epidemiology (STROBE) guidelines (www.strobe-statement.org). The interRAI-HC and National Minimum Data Set (NMDS) databases were deterministically matched by participants’ encrypted NHI numbers. Several interRAI-HC variables were reclassified, as detailed in electronic supplementary Table S1, with contiguous categories combined when cell sizes were relatively small. Descriptive statistics of all variables of interest were then reported, and two-way cross-tabulations were statistically assessed using Pearson’s Chi-square test. While DBI is a continuous measure, it was decided a priori to categorise it into four groupings based on its empirical distribution informed by thresholds used previously [20]. Categorisation of DBI was primarily adopted to avoid the otherwise strong linear assumption associated with its continuous specification within regression models, but also to aid clinical utility and interpretability. Various DBI threshold combinations were systematically investigated in complete case multivariable ordinal regression models, and compared using the Bayesian Information Criterion (BIC) [21]. The BIC can be employed to choose between non-nested models, balancing model complexity with goodness-of-fit to data, with the preferred model having the lowest estimated BIC. Given the preponderance of zeros present in DBI distributions associated with general populations, a DBI score of 0 was taken as the first (reference) category. Thresholds T_1 and T_2 defined the remaining three categories, where $T_1 < T_2$. The categories $0 < \text{DBI} \leq T_1$, $T_1 < \text{DBI} \leq T_2$, and $T_2 < \text{DBI}$ were allowed to span the $0.5 \leq T_1 \leq 2$ and $0.75 \leq T_2 \leq 5$ ranges, respectively, with increments of 0.25. Once the model with T_1 and T_2 values yielding the lowest BIC was identified, an unadjusted ordinal regression model was undertaken to estimate odds ratios (ORs) and associated 95% confidence intervals (CIs), and to determine if further collapsing of contiguous categories was required. This was followed by a main effects multivariable model, using the same suite of demographic and potentially confounding variables employed for the threshold specification. Interactions

between DBI \times age groups, DBI \times sex, and DBI \times cognitive performance were introduced to this main effects model, and subsequently assessed. Rather than using bivariable analyses to screen these risk factors, in the spirit of Sun and colleagues [22], all candidate variables were included in the multivariable models regardless of their statistical significance. However, Wald's type III Chi-square statistic was used to determine the significance of the DBI variable and interactions within the regression models. All analyses and graphics were performed using Stata SE version 14.1 (StataCorp LLC, College Station, TX, USA), with $\alpha = 0.05$ defining statistical significance.

2.7 Ethics

This study was approved by the New Zealand Ministry of Health's Health and Disability Ethics Committees (14/STH/140).

3 Results

Overall, 71,859 individuals consented to their data being used in the study. The mean age of this eligible sample was 82.7 years (range 65–106), 43,802 (61.0%) were female, and 63,578 (88.5%) were New Zealand European (see Table 1).

3.1 Falls

Information on falls was available from 71,856 participants (99.99%), with 42,563 (59.2%) having no fall within the 90 days prior to the interRAI-HC assessment; 8218 (11.4%) reporting no fall in the last 30 days, but fell 31–90 days prior to the assessment; 12,406 (17.3%) reporting one fall 30 days prior to the assessment; and 8669 (12.1%) participants reporting two or more falls in the 30 days prior to their interRAI-HC assessment. The distribution of falls varied by age groups, sex, and ethnicity (all Pearson's Chi-square $p < 0.001$) (also included in Table 1). The likelihood of self-reported falls appeared to increase with increasing age and in males, but appeared to be less common among Māori and Pacific people.

3.2 Drug Burden Index (DBI)

Overall, 27,505 participants (38.3%) had an estimated DBI equalling 0 within the 90 days preceding the interRAI-HC assessment (i.e. people not taking any medications or taking medications but without anticholinergic or sedative properties). The overall distribution was highly skewed (see Fig. 1), with a median DBI score of 0.94, 25th percentile score of 0, and 75th percentile score of 1.85. The

systematic search over various DBI threshold values from the complete case multivariable ordinal regression models ($n = 71,825$, 99.95%) yielded the lowest BIC statistic when $T_1 = 1$ and $T_2 = 3$ (electronic supplementary Table S2). As such, the DBI was subsequently categorised by DBI = 0, $0 < \text{DBI} \leq 1$, $1 < \text{DBI} \leq 3$, and $3 < \text{DBI}$ groupings.

The distribution of falls by DBI groupings appears in Fig. 2 and Table 2. The likelihood of falls was greater, in a dose-response fashion, with increasing DBI load.

3.3 Unadjusted Analyses

In the unadjusted ordinal logistic regression model, DBI groupings were related to falls ($p < 0.001$), with increasing DBI levels associated with increased odds of falls (see Table 2). Post hoc tests revealed a significant increase in estimated ORs between the DBI = 0 and $0 < \text{DBI} \leq 1$ categories ($p < 0.001$), the $0 < \text{DBI} \leq 1$ and $1 < \text{DBI} \leq 3$ categories ($p < 0.001$), and the $1 < \text{DBI} \leq 3$ and $3 < \text{DBI}$ categories ($p < 0.001$). Thus, these four DBI groupings were retained for the pursuant multivariable analyses.

3.4 Adjusted Analyses: Main Effects Model

Table 2 also includes the results from the full complete case multivariable ordinal logistic regression model ($n = 71,825$; 99.95%). In this adjusted model, DBI grouping remained related to falls ($p < 0.001$). The dose-response relationship between estimated ORs observed in the unadjusted analysis remained, with each increase in DBI level being different to the previous level ($p < 0.001$). Relatively modest confounding was observed, with adjusted ORs being between 5.9 and 15.6% lower than their unadjusted equivalents. Electronic supplementary Table S3 also provides the empirical distribution of the considered demographic and potentially confounding variables by falls outcome, together with ORs and 95% CI derived from the bivariable and multivariable models.

3.5 Adjusted Analyses: Effect Modifications

Exploring for a differential influence of sex and age on the relationship between DBI grouping and falls likelihood, the multivariable model was repeated with the addition of the DBI grouping \times sex and DBI grouping \times age interaction terms. However, no evidence of DBI grouping effect modification was seen by sex ($p = 0.40$) or age grouping ($p = 0.65$). Similarly, when investigating if the effect observed between DBI and falls may be differentially affected by cognitive impairment, no significant relationship was observed ($p = 0.051$).

Table 1 Distribution of demographic and potentially confounding variables by falls outcome

Variable	No fall in last 90 days		No fall in last 30 days, but fell 31–90 days ago		One fall in last 30 days		Two or more falls in last 30 days	
	<i>n</i>	%	<i>n</i>	%	<i>n</i>	%	<i>n</i>	%
Age (years)								
65–74	7908	63.7	1169	9.4	1788	14.4	1549	12.5
75–84	18,046	61.1	3327	11.3	4761	16.1	3405	11.5
85–94	15,454	56.1	3416	12.4	5270	19.1	3390	12.3
95 +	1155	48.7	306	12.9	587	24.7	325	13.7
Sex ^a								
Female	26,595	60.7	5174	11.8	7445	17.0	4586	10.5
Male	15,964	56.9	3044	10.9	4961	17.7	4083	14.6
Ethnicity								
European	37,152	58.4	7412	11.7	11,210	17.6	7801	12.3
Māori	2527	64.8	374	9.6	563	14.4	433	11.1
Pacific	1578	70.9	183	8.2	302	13.6	162	7.3
Other	1306	60.5	249	11.5	331	15.3	273	12.6
Cognitive impairment								
None or minimal	24,063	63.8	4268	11.3	5842	15.5	3548	9.4
Mild	12,247	54.8	2720	12.2	4144	18.5	3230	14.5
Moderate	3949	51.3	852	11.1	1608	20.9	1290	16.8
Severe +	2303	56.3	377	9.2	812	19.8	601	14.7
Alcohol consumption (drinks in a single sitting in the last 14 days)								
None	33,855	58.7	6574	11.4	10,150	17.6	7082	12.3
1 +	8708	61.3	1644	11.6	2255	15.9	1587	11.2
Smoking status								
Non-smoker	40,256	59.2	7790	11.5	11,781	17.3	8118	11.9
Smoker	2307	59.0	428	10.9	624	16.0	551	14.1
Hearing impairment								
None	23,084	62.5	3957	10.7	5936	16.1	3930	10.6
Minimal	12,071	57.4	2562	12.2	3719	17.7	2671	12.7
Moderate +	7395	53.2	1697	12.2	2747	19.8	2065	14.9
Vision impairment								
None	31,190	61.1	5796	11.4	8356	16.4	5681	11.1
Minimal	7634	54.4	1594	11.4	2749	19.6	2050	14.6
Moderate+	3725	54.9	826	12.2	1297	19.1	934	13.8
Fatigue								
None	13,546	66.3	2058	10.1	3036	14.9	1793	8.8
Minimal	14,108	59.9	2898	12.3	4072	17.3	2473	10.5
Moderate	9619	53.8	2193	12.3	3441	19.2	2639	14.7
Severe+	5290	53.0	1069	10.7	1856	18.6	1764	17.7
Mobility (distance walked)								
1+ km	3724	75.7	399	8.1	530	10.8	265	5.4
100 + m	7837	65.7	1361	11.4	1702	14.3	1026	8.6
50–99 m	6944	59.2	1446	12.3	1996	17.0	1353	11.5
5–49 m	16,309	55.7	3566	12.2	5467	18.7	3948	13.5
<5 m	4611	53.6	951	11.1	1660	19.3	1377	16.0
Did not walk	3138	58.3	495	9.2	1051	19.5	700	13.0
CHD								
No	29,117	59.5	5682	11.6	8328	17.0	5844	11.9

Table 1 continued

Variable	No fall in last 90 days		No fall in last 30 days, but fell 31–90 days ago		One fall in last 30 days		Two or more falls in last 30 days	
	<i>n</i>	%	<i>n</i>	%	<i>n</i>	%	<i>n</i>	%
Yes	13,446	58.8	2536	11.1	4078	17.8	2825	12.3
COPD								
No	32,257	58.4	7023	11.6	10,596	17.6	7447	12.3
Yes	7306	63.3	1195	10.4	1810	15.7	1222	10.6
CHF								
No	35,309	59.6	6717	11.3	10,165	17.2	7069	11.9
Yes	7254	57.6	1501	11.9	2241	17.8	1600	12.7
Depression								
No	37,692	59.9	7103	11.3	10,813	17.2	7351	11.7
Yes	4871	54.7	1115	12.5	1593	17.9	1318	14.8
BMI								
Underweight	2138	56.1	493	12.9	682	17.9	497	13.0
Normal	10,526	58.2	2214	12.2	3139	17.3	2214	12.2
Overweight	8000	60.5	1535	11.6	2152	16.3	1532	11.6
Obese	5640	63.2	1018	11.4	1371	15.4	896	10.0
Unknown	16,259	58.5	2958	10.6	5062	18.2	3530	12.7
Self-rated health								
Excellent	1482	68.7	219	10.1	285	13.2	172	8.0
Good	18,068	62.8	3316	11.5	4652	16.2	2739	9.5
Fair	14,530	57.3	3035	12.0	4578	18.0	3220	12.7
Poor	4808	55.2	930	10.7	1496	17.2	1472	16.9
No response	3675	53.6	718	10.5	1394	20.3	1066	15.6
Dizziness								
No	32,251	61.8	5706	10.9	8733	16.7	5471	10.5
Yes, not in last 3 days	4762	55.5	1188	13.9	1537	17.9	1089	12.7
1 of last 3 days	1686	53.2	378	11.9	624	19.7	483	15.2
2 of last 3 days	899	50.8	199	11.2	342	19.3	329	18.6
Daily over last 3 days	2965	48.0	747	12.1	1170	18.9	1297	21.0
Unsteady gait								
No	21,448	72.2	2777	9.3	3875	13.0	1602	5.4
Yes, not in last 3 days	2590	58.5	596	13.5	803	18.1	440	9.9
1 of last 3 days	1601	56.3	344	12.1	575	20.2	325	11.4
2 of last 3 days	1019	53.4	234	12.3	381	20.0	274	14.4
Daily over last 3 days	15,905	48.2	4267	12.9	6772	20.5	6028	18.3

CHD coronary heart disease, *CHF* congestive heart failure, *COPD* chronic obstructive pulmonary disease, *BMI* body mass index

^aFour observations missing (two listed as indeterminate)

4 Discussion

4.1 Key Findings in Context

This study found increased anticholinergic and sedative load was positively associated with a greater likelihood of falls in a subsection of vulnerable community-dwelling older people of New Zealand. These results concur with published reports that show an association between falls

and the DBI in older populations [\[\[20, 23\]\]](#). Importantly, after accounting for 18 potential confounders, including walking speed, activities of daily living (ADL) function, and comorbidities, the relationship between falls and DBI was confirmed. Falls were likely to have affected the participants' confidence and quality of life, their fracture rates, and their numbers entering aged residential care.

Previous work has related the DBI to falls in older people. An increased risk of falls has been reported in

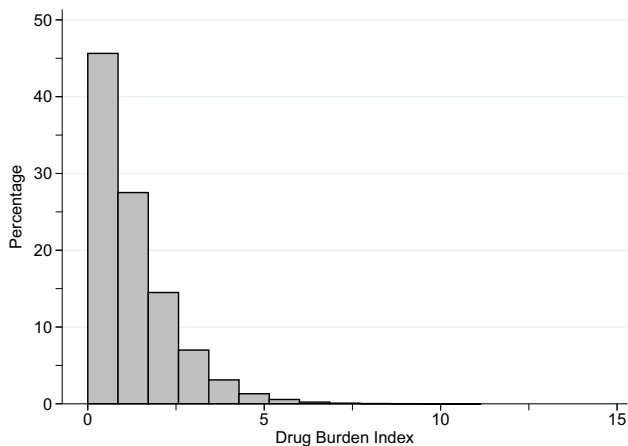


Fig. 1 Drug Burden Index 90 days pre-assessment for all eligible participants (*n* = 71,859)

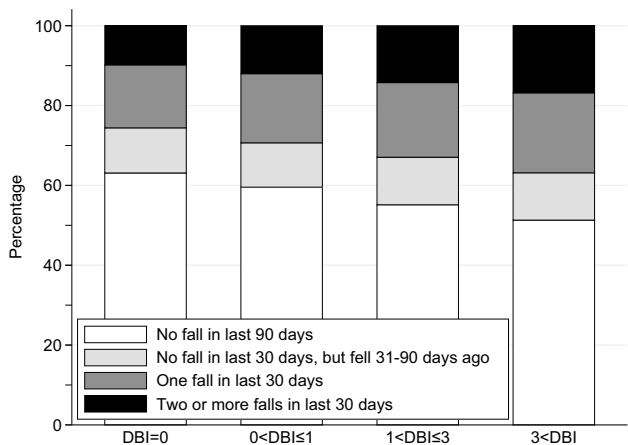


Fig. 2 Participant falls within the last 90 days by Drug Burden Index within the preceding 90 days before the International Resident Assessment Instrument–Home Care assessment

association with specific medication groups, including sedatives, narcotics and psychotropic medicines [5, 24–27]. This previous work did not consider the cumulative anticholinergic and sedative load of the large number of medications that are included in the DBI, nor the influence of potential confounders [9]. A 12-month Australian study examined the association between the DBI and falls in 602 older people living in long-term care [20]. Falls were identified from nursing notes and incident forms, and adjusted analysis suggested that the DBI was significantly and independently associated with falls (incidence rate ratio [IRR] 1.61, 95% CI 1.17–2.23) for DBI < 1; and 1.90, 95% CI 1.30–2.78 for DBI > 1, when compared with those with a DBI of 0). That study did not account for the broad range of confounders included in our study and had a smaller participant group than our national study. Nishtala et al. (*n* = 537,387) investigated the DBI and its association with falls, primary care physician visits, and mortality in older people [23]. In that study, falls data were cross-matched with Chronic Disease Scores, which are based on the number of prescribed medications [28]. DBI medications were found to be associated with falls-related hospitalisations (IRR 1.56, 95% CI 1.47–1.65), greater numbers of physician visits (IRR 1.13, 95% CI 1.12–1.13) and an increased risk of mortality (IRR 1.29, 95% CI 1.59–1.73). Our study differed from that of Nishtala et al. [23] in that we utilised interRAI-HC assessment data from older people being considered for residential care, which suggests that our cohort was generally more frail. We also accounted for 12 potential confounders associated with functional decline, and captured all falls—not just those associated with hospital admission. All falls can be considered clinically significant in that they are likely to reflect an

Table 2 Distribution of DBI groupings by falls outcome, together with ORs and 95% CIs for the unadjusted and adjusted (using complete cases *n* = 71,825; 99.95%) ordinal logistic regression models

Total	<i>n</i>	No fall in last 90 days		No fall in last 30 days, but fell 31–90 days ago		One fall in last 30 days		Two or more falls in last 30 days		Unadjusted		Adjusted ^a	
		<i>n</i>	%	<i>n</i>	%	<i>n</i>	%	<i>n</i>	%	OR	95% CI	OR	95% CI
DBI = 0	27,505	17,359	63.1	3108	11.3	4339	15.8	2698	9.8	1	Reference	1	Reference
0 < DBI ≤ 1	21,180	12,613	59.6	2353	11.1	3669	17.3	2544	12.0	1.18	1.14–1.22	1.11	1.07–1.15
1 < DBI ≤ 3	18,297	10,089	55.1	2179	11.9	3421	18.7	2607	14.2	1.41	1.36–1.47	1.27	1.22–1.32
3 < DBI	4877	2502	51.3	578	11.9	977	20.0	820	16.8	1.67	1.58–1.77	1.41	1.32–1.50

DBI Drug Burden Index, OR odds ratio, CI confidence interval

^aAdjusted for age group, sex, ethnicity, cognitive performance, alcohol consumption, smoking status, hearing status, vision status, fatigue, mobility, coronary heart disease, chronic obstructive pulmonary disease, congestive heart failure, depression, body mass index, self-rated health, dizziness, and unsteady gait

individual's general frailty and declining function, and are an indicator of the likelihood of further potentially more serious falls [29, 30].

Other work also investigated the effects of the DBI on functional performance without specifically focussing on falls [12]. One study highlighted an association between the DBI and the physical function of older men ($n = 1705$), including slower walking speed ($p < 0.05$) and balance difficulty ($p < 0.01$) [10]. Another study found an association between DBI and lower objective physical function over a 5-year period in community-dwelling older people [12]. The findings from these investigations strongly support the positive association found in our study, and the potential for the DBI to be used as a risk assessment tool by clinicians to guide deprescribing.

4.2 Strengths and Weaknesses

The major strengths of this study were the use of the interRAI-HC, a large contemporary national electronic database deterministically linked with a national unique identifier, and a thorough biostatistical analysis. InterRAI is an evidenced-based assessment tool that is used internationally and which allowed us to consider data on falls at a national level. The interRAI-HC data also gave us the opportunity to take into consideration a suite of potential clinical, functional, and demographic confounders [31]. However, we acknowledge that the data on falls are self-reported and that there may be a degree of misreporting, particularly if an individual experienced cognitive impairment or poor memory. In cases where an individual is known to have cognitive impairment, assessments are usually completed in the company of a spouse or other family member, and primary care records and other clinical records are checked to verify the information provided.

There was no way of ascertaining if all dispensed medications had been consumed. Furthermore, data were not available for non-prescription medications and 'as required' medications, including some antihistamines and mild opioids, which could have influenced the relationship with falls. In addition, the study is cross-sectional, and while we are interested in the relationship between DBI and falls, it is possible there is reverse causality and our design could not distinguish between these relationships.

Finally, the DBI is a reliable and valuable tool and is one of the few that takes into account the medication dose [32]. However, it does not account for differing pharmacokinetic and pharmacodynamic profiles between different individuals and medications [33]. Furthermore, there are other non-DBI-related side effects of medications other than anticholinergics and sedatives captured by the DBI that were not assessed and could impact on falls.

5 Conclusions

Falls are associated with poor outcomes for older people [34], and our study found the DBI was independently associated with an increased risk of falls in this vulnerable subsection of the community-dwelling older population. The DBI could be an invaluable risk assessment tool for clinicians considering prescribing or deprescribing medications for older people. With the increasing application of electronic prescribing, DBI values could potentially be automatically calculated on the drug chart, and therefore become more readily available to clinicians.

Compliance and Ethical Standards

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Conflict of interest Hamish Jamieson, Prasad Nishtala, Richard Scrase, Joanne Deely, Rebecca Abey-Nisbet, Martin Connolly, Sarah Hilmer, Darrell Abernethy and Philip Schluter declare that they have no conflicts of interest relevant to the content of this article.

References

- Goulding MR. Inappropriate medication prescribing for elderly ambulatory care patients. *Arch Intern Med.* 2004;164:305–12.
- Linjakumpu T, Hartikainen S, Klaukka T, Veijola J, Kivelä S-L, Isoaho R. Use of medications and polypharmacy are increasing among the elderly. *J Clin Epidemiol.* 2002;55:809–17.
- Mangoni AA, Jackson SH. Age-related changes in pharmacokinetics and pharmacodynamics: basic principles and practical applications. *Br J Clin Pharmacol.* 2004;57(1):6–14.
- Rothberg MB, Herzig SJ, Pekow PS, Avrunin J, Lagu T, Lindenauer PK. Association between sedating medications and delirium in older inpatients. *J Am Geriatr Soc.* 2013;61:923–30.
- Rolita L, Spegman A, Tang X, Cronstein BN. Greater number of narcotic analgesic prescriptions for osteoarthritis is associated with falls and fractures in elderly adults. *J Am Geriatr Soc.* 2013;61:335–40.
- Ray WA, Thapa PB, Gideon P. Benzodiazepines and the risk of falls in nursing home residents. *J Am Geriatr Soc.* 2000;48:682–5.
- Hubbard R, Farrington P, Smith C, Smeeth L, Tattersfield A. Exposure to tricyclic and selective serotonin reuptake inhibitor antidepressants and the risk of hip fracture. *Am J Epidemiol.* 2003;158:77–84.
- Nishtala MPS, Hilmer SN, McLachlan AJ, Hannan PJ, Chen TF. Impact of residential medication management reviews on drug burden index in aged-care homes. *Drugs Aging.* 2009;26:677–86.
- Hilmer SN, Mager DE, Simonsick EM, et al. A drug burden index to define the functional burden of medications in older people. *Arch Intern Med.* 2007;167:781–7.
- Gnjidic D, Cumming RG, Le Couteur DG, et al. Drug burden index and physical function in older Australian men. *Br J Clin Pharmacol.* 2009;68:97–105.
- Lowry E, Woodman RJ, Soiza RL, Hilmer SN, Mangoni AA. Drug burden index, physical function, and adverse outcomes in older hospitalized patients. *J Clin Pharmacol.* 2012;52:1584–91.

12. Hilmer SN, Mager DE, Simonsick EM, et al. Drug burden index score and functional decline in older people. *Am J Med.* 2009;122(1142–1149):e1142.
13. Schluter PJ, Ahuriri-Driscoll A, Anderson TJ, et al. Comprehensive clinical assessment of home-based older persons within New Zealand: an epidemiological profile of a national cross-section. *Aust N Z J Public Health.* 2016;40:349–55.
14. Hirdes JP, Ljunggren G, Morris JN, et al. Reliability of the interRAI suite of assessment instruments: a 12-country study of an integrated health information system. *BMC Health Serv Res.* 2008;8:277.
15. Nishtala P, Nduke H, Chyou TY, Salahudeen M, Narayan S. An overview of pharmacoepidemiology in New Zealand: medical databases, registries and research achievements. *N Z Med J.* 2017;130:52–61.
16. Nishtala PS, Jamieson HJ. New Zealand interRAI: a resource for examining health outcomes in geriatric pharmacoepidemiology. *J Am Geriatr Soc.* 2017;65:876–7.
17. Gnjidic D, Cumming RG, Le Couteur DG, Handelsman DJ, Naganathan V, Abernethy DR, et al. Drug Burden Index and physical function in older Australian men. *Br J Clin Pharmacol.* 2009;68:97–105.
18. Hilmer SN, Mager DE, Simonsick EM, Ling SM, Windham BG, Harris TB, Shorr RI, Bauer DC, Abernethy DR, ABC Health Study. Drug burden index score and functional decline in older people. *Am J Med.* 2009;122(12):1142–9.
19. Rolita L, Spegman A, Tang X, Cronstein BN. Greater number of narcotic analgesic prescriptions for osteoarthritis is associated with falls and fractures in elderly adults. *J Am Geriatr Soc.* 2013;61:335–40.
20. Wilson NM, Hilmer SN, March LM, et al. Associations between drug burden index and falls in older people in residential aged care. *J Am Geriatr Soc.* 2011;59:875–80.
21. Schwarz G. Estimating the dimension of a model. *Ann Stat.* 1978;6:461–4.
22. Sun GW, Shook TL, Kay GL. Inappropriate use of bivariable analysis to screen risk factors for use in multivariable analysis. *J Clin Epidemiol.* 1996;49(8):907–16.
23. Nishtala PS, Narayan SW, Wang T, Hilmer SN. Associations of drug burden index with falls, general practitioner visits, and mortality in older people. *Pharmacoepidemiol Drug Saf.* 2014;23(7):753–8.
24. Leipzig RM, Cumming RG, Tinetti ME. Drugs and falls in older people: a systematic review and meta-analysis: II. Cardiac and analgesic drugs. *J Am Geriatr Soc.* 1999;47(1):40–50.
25. Leipzig RM, Cumming RG, Tinetti ME. Drugs and falls in older people: a systematic review and meta-analysis: I. Psychotropic drugs. *J Am Geriatr Soc.* 1999;47(1):30–9.
26. Allain H, Bentue-Ferrer D, Polard E, Akwa Y, Patat A. Postural instability and consequent falls and hip fractures associated with use of hypnotics in the elderly. *Drugs Aging.* 2005;22(9):749–65.
27. Schneeweiss S, Wang PS. Association between SSRI use and hip fractures and the effect of residual confounding bias in claims database studies. *J Clin Psychopharmacol.* 2004;24(6):632–8.
28. Von Korff M, Wagner EH, Saunders K. A chronic disease score from automated pharmacy data. *J Clin Epidemiol.* 1992;45(2):197–203.
29. Francis RM. Falls and fractures. *Age Ageing.* 2001;30:25–8.
30. Woolf AD, Åkesson K. Preventing fractures in elderly people. *BMJ.* 2003;327:89–95.
31. interRAI.HC. interRAI Home Care. 2016. <http://interrai.org/home-care.html>. Accessed 9 May 2016.
32. Kouladjian L, Gnjidic D, Chen TF, Mangoni AA, Hilmer SN. Drug burden index in older adults: theoretical and practical issues. *Clin Interv Aging.* 2014;9:1503.
33. Gnjidic D, Couteur DGL, Abernethy DR, Hilmer SN. Drug burden index and Beers criteria: impact on functional outcomes in older people living in self-care retirement Villages. *J Clin Pharmacol.* 2012;52:258–65.
34. Skelton D, Todd C. What are the main risk factors for falls amongst older people and what are the most effective interventions to prevent these falls? WHO Regional Office for Europe; 2004. http://www.euro.who.int/__data/assets/pdf_file/0018/74700/E82552.pdf. Accessed 20 May 2016.