

**ORIGINAL ARTICLE**

# Using pharmacy dispensing data to predict falls in older individuals

Marle Gemmeke<sup>1</sup>  | Ellen S. Koster<sup>1</sup>  | Romin Pajouheshnia<sup>1</sup>  |  
Martine Kruijtbosch<sup>1,2</sup>  | Katja Taxis<sup>3</sup> | Marcel L. Bouvy<sup>1</sup> 

<sup>1</sup>Division of Pharmacoepidemiology and Clinical Pharmacology, Utrecht Institute for Pharmaceutical Sciences (UIPS), Faculty of Science, Utrecht University, Utrecht, The Netherlands

<sup>2</sup>SIR Institute for Pharmacy Practice and Policy, Theda Mansholtstraat 5B, Leiden, JE, 2331, The Netherlands

<sup>3</sup>Department of Pharmacotherapy, Pharmacoepidemiology and Pharmacoconomics (PTEE), Faculty of Science and Engineering, Groningen Research Institute of Pharmacy, University of Groningen, Groningen, The Netherlands

**Correspondence**

E.S. (Ellen) Koster, PhD, Division of Pharmacoepidemiology and Clinical Pharmacology, Utrecht Institute for Pharmaceutical Sciences, Faculty of Science, Utrecht University, PO Box 80082, 3508 TB, Utrecht, The Netherlands.  
Email: e.koster@uu.nl

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**Aims:** Associations between individual medication use and falling in older individuals are well-documented. However, a comprehensive risk score that takes into account overall medication use and that can be used in daily pharmacy practice is lacking. We, therefore, aimed to determine whether pharmacy dispensing records can be used to predict falls.

**Methods:** A retrospective cohort study was conducted using pharmacy dispensing data and self-reported falls among 3454 Dutch individuals aged  $\geq 65$  years. Two different methods were used to classify medication exposure for each person: the drug burden index (DBI) for cumulative anticholinergic and sedative medication exposure as well as exposure to fall risk-increasing drugs (FRIDs). Multinomial regression analyses, adjusted for age and sex, were conducted to investigate the association between medication exposure and falling classified as nonfalling, single falling and recurrent falling. The predictive performances of the DBI and FRIDs exposure were estimated by the polytomous discrimination index (PDI).

**Results:** There were 521 single fallers (15%) and 485 recurrent fallers (14%). We found significant associations between a DBI  $\geq 1$  and single falling (adjusted odds ratio: 1.30 [95% confidence interval {CI}: 1.02–1.66]) and recurrent falling (adjusted odds ratio: 1.60 [95%CI: 1.25–2.04]). The PDI of the DBI model was 0.41 (95%CI: 0.39–0.42) and the PDI of the FRIDs model was 0.45 (95%CI: 0.43–0.47), indicating poor discrimination between fallers and nonfallers.

**Conclusion:** The study shows significant associations between medication use and falling. However, the medication-based models were insufficient and other factors should be included to develop a risk score for pharmacy practice.

**KEYWORDS**

dispensing records, drug burden index, elderly, fall risk-increasing drugs, falling, risk prediction

The authors confirm that the Principal Investigator for this paper is Marcel Bouvy and that he had direct clinical responsibility for participants.

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## 1 | INTRODUCTION

In the Netherlands, about 1/3 of community-dwelling individuals aged 65 years and older experience at least 1 fall each year.<sup>1</sup> Falling leads to physical injury, increased healthcare consumption and impairment in social and physical activities.<sup>2</sup> Since the general population is aging, falling is a growing societal problem in many countries. Older individuals more often have multimorbidity and consequently use more medication (e.g. polypharmacy).<sup>3</sup> Although the underlying causes for falling are often multifactorial, medication use and polypharmacy increase the risk for falls in older adults.<sup>4</sup> Fall prevention should therefore be a major concern for healthcare providers, including pharmacists who are responsible for safe medication use. Deprescribing fall-related medications is considered an effective intervention for fall prevention.<sup>5-8</sup>

So-called fall risk-increasing drugs (FRIDs) have been widely associated with falls.<sup>9-11</sup> FRIDs belong to different pharmacological classes and increase fall risk by different mechanisms. For example, the anticholinergic and general depressant effects of psychotropic medications affect postural balance, cognition and cause sedation, which increase fall risk.<sup>12,13</sup> Cardiovascular medication, which lower blood pressure or decrease heart rate, often increase the risk of orthostatic hypotension.<sup>13,14</sup> Antidiabetic medication, antihistamines and nonsteroidal anti-inflammatory drugs belong to the group of other FRIDs.<sup>11</sup> Many studies have investigated the association between medication use and fall risk,<sup>9-11</sup> but less is known about associations between combination of FRIDs and risk of falling. An exception is the use of the drug burden index (DBI), a measure of total anticholinergic and sedative load, taking the dose into account.<sup>15,16</sup> Although different instruments for measuring anticholinergic load exist, the DBI previously showed the strongest association with fall risk.<sup>17</sup>

Pharmacists increasingly perform clinical medication reviews to optimize pharmacotherapy, especially in older people on polypharmacy.<sup>18,19</sup> Preventing medication-related falls is an important goal of clinical medication reviews<sup>20</sup> and an effective method to deprescribe FRIDs.<sup>5</sup> In order to efficiently identify individuals at increased risk of falling, a screening tool is helpful. In the pharmacy setting it would be useful to predict fall risk by a medication-based measure. Current measures are often based on more time-consuming interviews with subjects.<sup>21</sup>

In this study, we aimed to determine whether medication exposure data from dispensing records can be used to predict falls in older individuals using FRIDs.

## 2 | METHODS

### 2.1 | Study design

We used data from a retrospective cohort study of self-reported fall information and information about medication use from persons' pharmacy records. We studied the association between medication

### What is already known about this subject

- Certain medications, known as fall risk-increasing drugs, are associated with an increased fall risk.
- The use of these fall risk-increasing drugs is common in individuals 65 years and older.
- The drug burden index measures total anticholinergic and sedative load and has been associated with falls.

### What this study adds

- The predictive value of dispensing data-based models is insufficient for use in clinical pharmacy practice.
- Pharmacists should preferably screen for fall risk by asking individuals about their fall history.

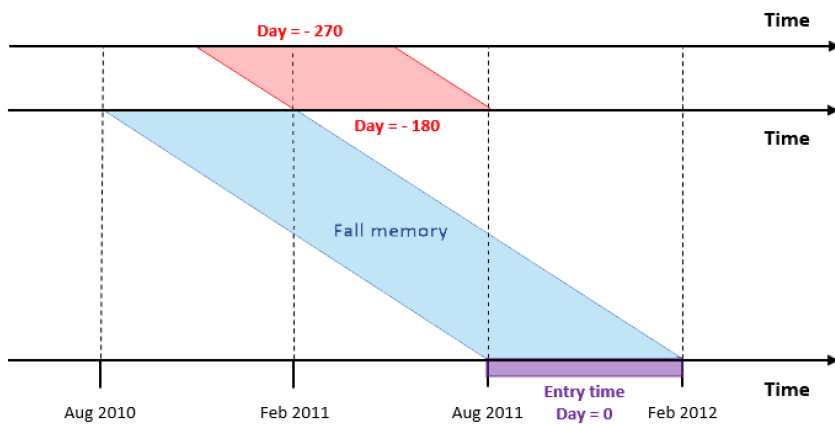
exposure and falls. In addition, we determined the discrimination ability of medication exposure to predict falls.

### 2.2 | Setting

Data were nationwide collected with the help of pharmacists who were affiliated with a national pharmacy franchise in the Netherlands. Individuals were invited to join the study between August 2011 and February 2012 (Figure 1). The index date was the date the invitation letter was sent. This study was not subject to formal ethical approval as participants were not subject to procedures or were required to follow rules of behaviour. Participation in the study was voluntary. All participants were carefully informed through a patient information letter and gave written informed consent before start of the study. The consent included explicit permission to use persons' medication dispensing records. Both medication dispensing data and questionnaire data were pseudonymized.

### 2.3 | Data sources

Individuals were all aged  $\geq 65$  years, using  $\geq 5$  different medicine of which at least 2 were FRIDs. Medication that was classified as FRIDs are listed in Appendix A: Table 1. Because the included individuals were also offered a medication review and follow-up, a preselection was performed by the pharmacist or general practitioner to determine whether individuals were eligible for invitation. Individuals reported their fall history in a short questionnaire, which was sent along with the invitation letter. The questionnaire, collected by their community pharmacist, consisted of only 2 questions: "Did you experience a fall in the previous year?" and "If yes: did you experience 2 or more falls in the previous year?"



**FIGURE 1** Study design. The index date (day = 0) was the sending date of the invitation letter. The medication use at time day = -180 was determined by analysing the dispensed medications during the preceding 90 days

Data on medication use up to 4 years before invitation of all participating individuals were collected from the pharmacy information systems. All pharmacies had automated dispensing records, including information on sex, date of birth and dispensed medication. In the Netherlands, the majority of individuals obtain all medication from the same pharmacy and thus pharmacy records represent a complete medication history for an individual.<sup>22</sup> The pharmacy records contained information about dispensing data, including the names of the dispensed medications, medication doses, dose instructions, processing dates of prescriptions and dispensed amounts. The medicines in the pharmacy records were classified by Anatomical Therapeutic Chemical groups, according to the World Health Organization classification system.<sup>23</sup>

## 2.4 | Outcome definitions

The outcome was self-reported falls in the year before the invitation letter was sent, in terms of 3 categories: nonfalling, single falling and recurrent falling.

## 2.5 | Exposure definitions

Medication exposure was classified in 2 ways: the DBI for cumulative anticholinergic and sedative medication exposure (method 1) and by determining the use of individual FRID groups for each subject (method 2). For both methods, medication use was determined at 180 days before the index date (time  $[t] = -180$  d). As individuals reported having fallen in the 365 days before index date, we that estimated medication exposure at  $t = -180$  days was most likely to represent the actual medication use during the time of outcome. All prescriptions in the preceding 90 days before time point -180 days were used to estimate medication exposure at the time of outcome ( $t = -180$  d). When  $>1$  prescription of the same medication was given in the time period, the last prescription was used to assess medication exposure. Thus, medication exposure was determined from the dispensing data of  $t = -270$  to -180 days (Figure 1).

For method 1, exposure was defined as the cumulative DBI.<sup>15</sup> It was calculated the same way as by Meer *et al.* using the following formula:

$$DBI = \sum \frac{D}{D + \delta}$$

where  $D$  = prescribed daily dose and  $\delta$  = the minimum recommended daily dose according to Dutch pharmacotherapeutic reference sources.<sup>24–26</sup> All prescription medications dispensed by the pharmacy with mild or strong anticholinergic and/or sedative (side) effects during the study period were included in the DBI calculation. For medications without exact known prescribed daily dose the daily dose was estimated. For the dose instruction *known use* the dose was estimated as once daily and the mean estimated *as needed* use depended on the prescribed maximum dose. *Over the counter* dispensed medications were not captured within the pharmacy dispensing records and were therefore not included. The DBI per medication varied between 0 and 1, depending on the daily dose. The subjects were divided into 3 DBI categories: (1)  $DBI = 0$ , (2)  $DBI = > 0$  and  $< 1$ , and (3)  $DBI \geq 1$ . This was based on previous studies, where this highest threshold category was considered as a high anticholinergic/sedative load.<sup>24,27,28</sup>

For method 2, all potential FRIDs (available in Table 1 of appendix A) dispensed by the pharmacy in the period ( $t = -270$  to -180 days) were included. Again, when more than when prescription of the same medication was given in the time period, the last prescription was used to assess medication exposure.

## 2.6 | Data analysis

First, descriptive statistics (proportions and medians) were calculated for the 3 outcome groups (nonfallers, single fallers and recurrent fallers). Chi-square and Kruskal–Wallis tests were used to assess statistically significant differences between the outcome groups. A significance level of  $P < .05$  was considered statistically significant. Second, multinomial logistic regression analyses were conducted to investigate the associations of both medication exposure methods.

Based on previous studies, age and sex were included as covariates to control for confounding.<sup>2</sup>

For method 1, the DBI was calculated per person and the individuals were divided as per the 3 DBI threshold categories. The prediction model included these 3 DBI levels, age and sex. In addition, multinomial logistic regression analysis was performed with DBI as a continuous variable, modelled with restricted cubic splines to model a nonlinear association, adjusted for age and sex. For method 2, adjusted odds ratios (aORs) for single and recurrent falling compared to nonfalling were calculated for the FRIDs using unadjusted multinomial regression analyses. When there were <10 users of a FRID, it was not added to the model. The prediction model included all other FRIDs, age and sex. The aORs and 95% confidence intervals (CIs) of all variables in the FRIDs model were estimated.

The ability of the FRIDs model (method 1) and DBI model (method 2) to predict fall risk were assessed by measures of model discrimination and calibration.<sup>29</sup> Model discrimination was assessed by calculating the polytomous discrimination index (PDI) for multivariate models, analogous to the area under the receiver operating characteristic curve (AUC) for binary logistic regression.<sup>30</sup> A PDI of 1 means perfect discrimination between the 3 outcomes and a PDI of 0.33 (comparable to an AUC of 0.5), indicates that the model does not discriminate between outcomes.<sup>31</sup> The PDI and 95% CIs were calculated by a bootstrap internal validation procedure.<sup>32</sup> We compared the PDI of the FRIDs model to the PDI of the DBI model to decide which model can better discriminate between categories of falling. We also analysed the discriminative ability of a combined model, which included both DBI and FRIDs as predictors. Model calibration

(i.e. the agreement between predicted risks made by the model and observed outcomes in the data) was assessed by plotting calibration curves, where a curve at 45° from the origin indicates perfect calibration.<sup>29</sup>

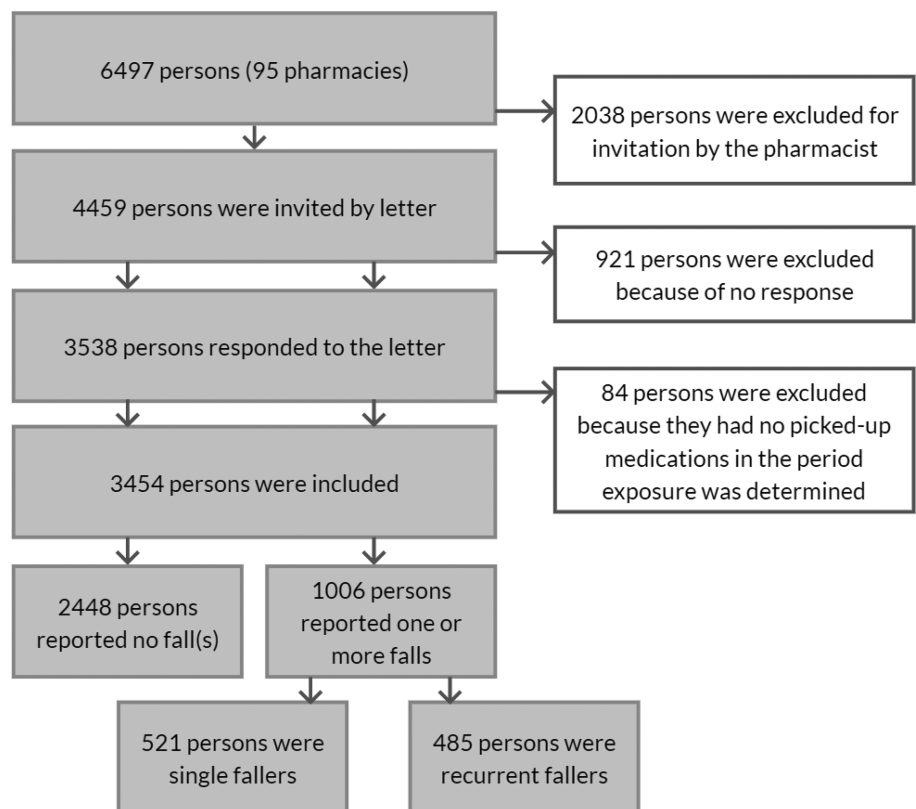
All data were analysed using R version 3.6.1 (R Foundation for Statistical Computing, Vienna, Austria).

## 2.7 | Sensitivity analyses

Because the exact time of the outcome was unknown, we conducted sensitivity analyses at  $t = -365$  days and  $t = 0$  days. By all means, time  $t = -365$  days represented medication exposure before the outcome (fall). Time  $t = 0$  represented medication exposure after the outcome (fall) and was added to illustrate the consistency of our findings. For both time points all prescriptions in the preceding 90 days were counted in the same way as described for  $t = -180$  days.

## 3 | RESULTS

As shown in Figure 2, a total of 6497 individuals from 95 pharmacies met the inclusion criteria. Pharmacists excluded 2038 individuals for invitation, because either the pharmacist or general practitioner determined these individuals were not eligible for the research project. Therefore, a total of 4459 individuals were invited by letter. Of the 3538 individuals who responded to the letter, 84 were excluded because they did not have medication dispensed during the



**FIGURE 2** Flowchart of the individuals who were invited to join and included in the study

time exposure was determined ( $t = -270$  days to  $t = -180$  days), resulting in a total of 3454 subjects for analysis.

### 3.1 | Characteristics

In Table 1 the population characteristics are summarized. Among the 3,454 included individuals there were 2,448 nonfallers (71%), 521 single fallers (29%) and 485 recurrent fallers (14%). Single fallers and recurrent fallers were relatively more often female and older compared to nonfallers ( $P < .001$ ).

### 3.2 | Multinomial logistic regression

For method 1, the aOR for  $DBI \geq 1$  was 1.30 [95% CI: 1.02–1.66] and 1.60 [95% CI: 1.25–2.04] respectively for single falling and recurrent falling. The aOR for  $DBI = > 0$  and  $< 1$  was 1.00 [95% CI: 0.79–1.25] and 1.00 [95% CI: 0.78–1.27] respectively for single falling and recurrent falling. For method 2, The FRIDs that were included in the model along with age and sex, are shown in Table 2. The following FRIDs showed significant association with recurrent falling in the multinomial model: selective serotonin reuptake inhibitors (aOR: 2.49 [95% CI: 1.69–3.65]), antiepileptics (aOR: 2.16 [95% CI: 1.37–3.40]), codeine (aOR: 1.67 [95% CI: 1.04–2.66]), urinary spasmodics (aOR: 1.78 [95% CI: 1.07–2.98]) and antivertigo drugs (aOR: 1.70 [95% CI: 1.01–2.85]). The aORs for the other predictors can be found in Table 2. The crude ORs for FRIDs can be found in Appendix A.

### 3.3 | Internal validation and predictive performance

The DBI model had a PDI of 0.41 (95% CI: 0.39–0.42) and the FRIDs model had a PDI of 0.45 (95% CI: 0.43–0.47). A model with age and sex only had a PDI of 0.39 (95% CI: 0.38–0.41). This indicates that neither model could discriminate well between nonfallers, single fallers and recurrent fallers. Modelling of DBI as a continuous variable

did not improve the PDI (0.41 [95% CI: 0.40–0.43]). Adding DBI to the model with FRIDs did not improve model discrimination (PDI [95% CI]: 0.45 [0.43–0.47]). Model calibration was good for all models, but the model with FRIDs as a predictor slightly underestimated fall risk in higher-risk individuals.

### 3.4 | Sensitivity analyses

At  $t = -365$  days, the DBI model had a PDI of 0.40 (95% CI: 0.39–0.42) and the FRIDs model had a PDI of 0.45 (95% CI: 0.43–0.46), compared to a PDI of 0.39 (95% CI: 0.37–0.41) for the model with age and sex only. At  $t = 0$  days, the DBI model had a PDI of 0.41 (95% CI: 0.39–0.42) and the FRIDs model had a PDI of 0.45 (95% CI: 0.43–0.47), compared to a PDI of 0.39 (95% CI: 0.38–0.41) for the model with age and sex only. The results of the sensitivity analyses are available in Appendixes B and C.

## 4 | DISCUSSION

This study shows that although medication exposure defined by both use of FRIDs and the DBI are associated with an increased risk of falling, the discriminative ability of the predictive models incorporating these factors is poor and therefore seems to be of no use as a standalone screening tool.

Although studies have investigated associations between medication use and falls,<sup>9–11</sup> the predictive performance of an individual's complete medication regimen on falls has not been well investigated. Furthermore, many currently used fall risk assessment tools, including a diversity of fall risk factors, appear to have low predictive validity. Although the range of factors included in the fall risk assessment tools is large, accuracy is mostly unsatisfactory.<sup>33,34</sup> Tools with a small number of predictors are suboptimal for predicting falls. A previous study showed low predictive performance for medication exposure on falls.<sup>35</sup> Eventually, Tiedemann *et al.* developed a fall risk assessment tool with reasonable predictive power (a total AUC of 0.72) for

**TABLE 1** Characteristics of study population

	Nonfallers $n = 2448$	Single fallers $n = 521$	Recurrent fallers $n = 485$	<i>P</i> -value	Total $n = 3454$
Female sex ( $n, \%$ )*	1376 (56.2%)	336 (64.5%)	301 (62.1%)	<.001	2013 (58.2%)
Age (y), median [Q1–Q3]**	75 [70–81]	78 [72–84]	79 [72–84]	<.001	76 [71–82]
Number of dispensed medications, median [Q1–Q3]**	7 [5–9]	7 [5–10]	7 [6–10]	<.001	7 [5–9]
Number of dispensed FRIDs, median [Q1–Q3]**	3 [3–5]	4 [3–5]	4 [3–5]	.037	4 [3–5]
Number of dispensed DBI medications, median [Q1–Q3]**	1 [0–2]	1 [0–2]	1 [0–2]	<.001	1 [0–2]
DBI, median [Q1–Q3]**	0.5 [0–1]	0.64 [0–1.21]	0.67 [0–1.33]	$P < 0.001$	0.51 [0–1.17]

Q1 = first quartile; Q3 = third quartile; DBI = drug burden index; FRID = fall risk-increasing drug

\*differences analysed using  $\chi^2$  test;

\*\*differences analysed using Kruskal–Wallis test.

**TABLE 2** A comparison of the predictive performance of the 3 models to predict falls and the odds ratios of all included predictors

Predictors	Model 1: Age + sex	
	aOR [95% CI] for single falling	aOR [95% CI] for recurrent falling
Age (per y)	1.04 [1.03–1.06]	1.05 [1.04–1.07]
Female sex	1.30 [1.07–1.59]	1.14 [0.93–1.40]
Predictors	Model 2: Age + sex + DBI	
	aOR [95% CI] for single falling	aOR [95% CI] for recurrent falling
Age (per y)	1.04 [1.03–1.06]	1.05 [1.04–1.07]
Female sex	1.30 [1.06–1.58]	1.13 [0.92–1.39]
0 < DBI < 1	1.00 [0.79–1.25]	1.00 [0.78–1.27]
DBI ≥ 1	1.30 [1.02–1.66]	1.60 [1.25–2.04]
Predictors	Model 3: Age + sex + FRIDs	
	aOR [95% CI] for single falling	aOR [95% CI] for recurrent falling
Age (per y)	1.04 [1.03–1.06]	1.05 [1.04–1.07]
Female sex	1.26 [1.01–1.56]	1.05 [0.84–1.31]
SSRI	1.58 [1.04–2.41]	2.49 [1.69–3.65]
TCA	1.21 [0.72–2.02]	1.37 [0.82–2.31]
Antiepileptics	1.27 [0.76–2.14]	2.16 [1.37–3.40]
Loop-diuretics	1.25 [0.94–1.64]	1.11 [0.83–1.49]
Benzodiazepines	0.92 [0.73–1.67]	0.84 [0.65–1.08]
Digoxin	1.03 [0.66–1.61]	0.98 [0.60–1.60]
Nitrates + ivabradine	0.86 [0.63–1.89]	1.25 [0.93–1.69]
Thiazides	0.89 [0.71–1.12]	0.95 [0.76–1.20]
Aldosteron antagonists	1.73 [1.14–2.64]	0.95 [0.55–1.63]
Beta-blocking agents	1.15 [0.95–1.42]	1.09 [0.88–1.34]
Calcium channel blockers	0.91 [0.74–1.14]	0.89 [0.71–1.11]
RAAS-inhibitors	0.94 [0.77–1.16]	0.95 [0.77–1.18]
Insulin	0.57 [0.30–1.09]	1.27 [0.78–2.08]
Sulfonylurea derivatives	1.06 [0.78–1.44]	1.14 [0.84–1.55]
Alpha blockers	1.05 [0.73–1.52]	0.69 [0.46–1.04]
Strong opiates	0.86 [0.47–1.60]	1.14 [0.64–2.04]
Codeine	1.97 [1.28–3.01]	1.67 [1.04–2.66]
Tramadol	2.06 [1.34–3.18]	1.42 [0.86–2.33]
Antihistamines	1.06 [0.68–1.64]	1.08 [0.68–1.70]
Statins	0.77 [0.62–0.94]	0.95 [0.77–1.18]
NSAIDs	1.08 [0.76–1.52]	1.26 [0.89–1.77]
Urinary spasmotics	1.50 [0.89–2.55]	1.78 [1.07–2.98]
Antivertigo drugs	0.87 [0.47–1.63]	1.70 [1.01–2.85]
Dipyridamole	0.99 [0.64–1.55]	1.39 [0.94–2.06]

aOR = adjusted odds ratio; DBI = drug burden index; SSRI = selective serotonin reuptake inhibitor; TCA = tricyclic antidepressant; RAAS-inhibitors = renin-angiotensin-aldosterone system inhibitors; NSAID = nonsteroidal anti-inflammatory drug; CI = confidence interval

primary care, but this tool included several other potential predictors in addition to medication (e.g. visual function, tactile sensitivity, mobility tests and fall history).<sup>35</sup> This suggests that augmenting medication-based models with nonmedication-based factors should improve the discriminative ability. This would, however, be a very labour-intensive exercise, which is not feasible in daily clinical care.

Most previous studies investigating the association between medication use and falls compared individuals who had at least 1 fall to persons who did not fall.<sup>36</sup> In this study, the strongest associations between medication and falling were seen in individuals who had recurrent falls. For those with a DBI ≥ 1, the odds of a single fall were 30% greater while the odds of recurrent falls were 60% greater. This

is in line with the notion that single falling could be a coincidence and that recurrent fallers are particularly at risk.<sup>37</sup>

## 4.1 | Strengths

A strength of this study is that we investigated both single fallers and recurrent fallers. Guidelines recommend an extensive multifactorial fall risk assessment for individuals who report recurrent falls in the past year. However, for individuals who report a single fall only a quick screening on gait and balance is recommended to determine whether a multifactorial fall risk assessment is necessary.<sup>38</sup> Recurrent falls more often lead to loss of independence and fear of falling.<sup>36</sup> Therefore, recurrent falling seems a better predictor for a subsequent fall than experiencing 1 fall.

Another strength of this study is it classified medication exposure in different ways to examine its predictive performance on falls. The advantage of a predictive model based on FRIDs is that it covers all known medications that have been associated with falls in the literature. The use of DBI to predict fall risk is advantageous in that it takes into account dosing effects. Additionally, the DBI combines effects of different medicines related to falls and can easily be expressed in a single number. By contrast, a disadvantage for using the DBI is that all medication with anticholinergic and sedative characteristics are considered as equivalent.<sup>39</sup> The DBI as a measurement might be improved if the strength of the anticholinergic and sedative load were to be taken into account. Due to their varying pharmacological actions, not all FRIDs contribute to the DBI. While cardiovascular FRIDs may also cause falling (e.g. through orthostasis or bradycardia), they often do not have anticholinergic or sedative properties and, therefore, do not contribute to the DBI.

Self-reported falls were used to determine the outcome. A strength of the questionnaire was its shortness. Moreover, individuals did not need to remember exactly when the fall happened. However, a weakness of self-report was that individuals might forget the experience of a fall and when the experience of a fall had low impact, individuals might report not to have fallen.

## 4.2 | Limitations

The major limitation of our data was that the exact time of the fall was unknown. We considered that the medication use at 180 days before the index date was most representative for the medication use at time of fall. Moreover, sensitivity analyses were conducted for the medication use at 365 days before index date and for the medication use at index date. Both times showed similar results. Sensitivity analyses only showed minor discrepancies regarding significances of associations between individual FRIDs and falls. However, the trend of the associations were similar over all sensitivity analyses. Most medication could be considered as chronic and did not change appreciably over the year preceding the self-reported fall(s). In this study we also included medications that were prescribed with use as

needed. We reasoned that *as needed* medications could trigger a fall, because a sudden increase in the drug burden might actually be associated with a higher risk compared to chronic exposure. However, we do not know whether individuals were exposed to *as needed* medication at the time of falling. Therefore, there could have been an over-estimation of medication exposure. Another limitation of the study is the generalizability of the models. The individuals in this study were selected on basis of both polypharmacy and the use of at least 1 cardiovascular or centrally acting FRID. In 2014 the prevalence of polypharmacy in Dutch individuals older than 65 years was 25–30%.<sup>40</sup> The mean medication use of the subjects in this study, thus, may be higher compared to real world data. Due to the high mean medication use, the included individuals could have been more fragile. Still, the fall incidence of approximately 1/3 was similar to the fall incidence that is usually reported in the general population.<sup>1</sup>

Another limitation of our data was that they were collected between August 2011 and February 2012. However, prescribing patterns of most FRIDs did not change appreciably. Only the use of strong opiates and, to a lesser extent, gabapentinoids has increased in the past 5–10 years.<sup>41</sup> We expect that small shifts that have occurred in a subject's medication use are unlikely to affect sums of exposure in the general population, as measured by the DBI. Furthermore, we do not think there is evidence that specific FRIDs have evidently strong associations with falls and that these could be used as a standalone predictor by itself.

Finally, this study was not controlled for confounders other than age and sex. Comorbidities might have affected our results.<sup>38</sup> However, we decided not to include these confounders in our models. Firstly, because we corrected for the use of other medication in the FRIDs model, comedication may be considered a proxy for some comorbidities. More importantly, the aim of the study was to investigate whether pharmacy dispensing data could be used to predict falls and information on comorbidity is usually not available in pharmacy information systems.

## 4.3 | Implications

For community pharmacists, to efficiently identify individuals who are at increased risk of falling, a sensitive medication-based screening tool with a limited number of additional predictors would be ideal. History of falls is a strong fall risk predictor.<sup>42</sup> Measurements of physical performance and mobility, such as the short physical performance battery or gait speed, are also strong fall risk predictors.<sup>42</sup> The disadvantage of mobility tests is that these are very time-consuming and cannot easily be implemented in pharmacies. On the basis of the combination of an age  $\geq 65$  years, exposure to FRIDs and fall history the pharmacist should be able to select individuals with increased fall risk and using medications that potentially cause this increased risk. Evaluating the medication use in these individuals should be a priority for them. Ideally, the information on FRIDs should be integrated in the pharmacy information system as has been done for the DBI.<sup>43</sup> As a start, pharmacists should ask older individuals frequently about fall

history and record their responses. We recommend integrating a fall alert in the pharmacy information system for individuals who have experienced a fall before. When new FRIDs are prescribed, the pharmacist is then alerted to discuss the problem and alternatives with the person and prescriber.

## 5 | CONCLUSION

This study shows significant associations between DBI and falling, and the use of FRIDs and falling. We attempted to build a dispensing data-based fall prediction model. The predictive value of such a model seems insufficient for use in clinical pharmacy practice. The addition of non-medication-based factors presumably improves the model. In the meantime, we suggest community pharmacists to screen for use of FRIDs among older individuals in combination with asking about their fall history. Incorporating a fall warning signal in the pharmacy information system for individuals who have experienced a fall before could also help to prevent inappropriate medication use in these subjects.

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## COMPETING INTERESTS

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## CONTRIBUTORS

M.G. analysed the data and wrote the draft of the manuscript. E.K. and M.B. supervised all analyses and supported interpretation of the results. K.T. supported with the DBI analyses, supervised, and supported interpretation of the results. R.P. helped developing the statistical model and computing predictive performances. M.K. collected the data. All authors participated in writing the manuscript and approved the final manuscript.

## 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.

## ORCID

Marle Gemmeke  <https://orcid.org/0000-0003-4689-2430>

Ellen S. Koster  <https://orcid.org/0000-0001-5973-7953>

Romin Pajouheshnia  <https://orcid.org/0000-0002-4208-3583>

Martine Kruijtbosch  <https://orcid.org/0000-0002-4725-5292>

Marcel L. Bouvy  <https://orcid.org/0000-0002-4596-0684>

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## SUPPORTING INFORMATION

Additional supporting information may be found online in the Supporting Information section at the end of this article.

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