

## Do the cardiovascular drugs have an impact on recurrent falling in nursing home residents?

### Czy leki kardiologiczne mają wpływ na powtarzanie się upadków u mieszkańców w domach pomocy społecznej?

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#### Abstract

**Introduction.** The aim of the study was to establish association of cardiovascular drugs with recurrent falling among residents of nursing homes (NHs). **Material and methods.** The study was conducted in 7 NHs for 822 residents in city of Krakow. A prospective calendar-recorded registration of all falls using "a fall registration chart" since July 2005 to December 2006 was performed by nursing staff in NHs. Data concerning age, gender and medication taken in the day preceding the fall were collected. Poisson regression model was then applied to find drugs enhancing the rate of recurrent falling. **Results.** 289 falls were registered in 162 NH residents. The rate of falling (IR) was less than one per year in case of 77 fallers; at least one but less than two falls in 50 fallers and two or more falls in 35 fallers. According to both univariate and multivariate analysis angiotensin-converting enzyme inhibitors (ACEI), calcium channel blockers, beta-blocking agents, organic nitrates, cardiac glycosides and diuretics had no significant influence on recurrent falling in NH residents. The rate of falling decreased with the use of potassium chloride (crude Incident Rate Ratio= cIRR = 0.75;  $p < 0.03$ ), but it did not differ significantly when taking into account age, gender and the use of other drugs. Contrary to that, a number of central nervous system drugs significantly increased the rate of falling (IRR=1.175; CI 1.094 – 1.262;  $p < 0.001$ ). **Conclusion.** Cardiovascular drugs had no influence on recurrent falling in NH residents. (Gerontol Pol 2016, 24, 219-226)

**Key words:** recurrent falls, cardiovascular drugs, nursing home, older people

#### Streszczenie

**Cel.** Celem badania było ustalenie związku pomiędzy stosowaniem leków działających na układ sercowo-naczyniowy i powtarzaniem się upadków u mieszkańców domów pomocy społecznej (DPS). **Materiał i metody.** Badanie przeprowadzono w 7 DPS w Krakowie, w których przebywało 822 mieszkańców. W okresie od lipca 2005 do grudnia 2006 personel pielęgniarski rejestrował wszystkie kolejne upadki na „karcie rejestracji upadku” odnotowując wiek, płeć i leki przyjęte w dniu poprzedzającym upadek. Następnie przeprowadzono analizę z zastosowaniem modelu regresji Poisson'a w celu ustalenia leków, które mogą zwiększać częstość powtarzania się upadków. **Wyniki.** Zarejestrowano 289 upadków u 162 mieszkańców DPS. Częstość upadków (IR) niższą niż jeden na rok odnotowano u 77 mieszkańców; co najmniej jeden upadek, lecz mniej niż dwa w roku odnotowano u 50 upadkowiczów, a dwa lub więcej upadków w ciągu roku zaobserwowano u 35 mieszkańców DPS. Analiza regresji zarówno jednej i wielu zmiennych wykazała, że inhibitory konwertazy angiotensyny (ACEI), blokery kanału wapniowego, beta-blokery, azotany organiczne, glikozydy nasercowe i leki moczopędne nie miały istotnego wpływu na częstość upadania mieszkańców DPS. Częstość upadania była mniejsza u osób przyjmujących chlorek potasu (crude Incident Rate Ratio= cIRR=0.75;  $p < 0.03$ ), jednak po standaryzacji względem wieku i płci oraz innych leków, również ten efekt utracił istotność statystyczną. W przeciwieństwie do leków kardiologicznych, leki stosowane w chorobach ośrodkowego układu nerwowego statystycznie istotnie zwiększały częstość upadania. (IRR = 1.175; CI 1.094 – 1.262;  $p < 0.001$ ). **Wnioski.** Leki stosowane w chorobach sercowo-naczyniowych nie miały wpływu na powtarzanie się upadków u mieszkańców DPS. (Gerontol Pol 2016, 24, 219-226)

**Słowa kluczowe:** powtarzające się upadki, leki kardiologiczne, dom pomocy społecznej, osoby starsze

## Abbreviations

Ch-NHs – nursing homes for older and chronically ill people

cIRR – crude Incident Rate Ratio

CNS drugs – central nervous system drugs

CV drugs – cardiovascular drugs

IRR – incidence rate ratio

LTC – long term care

NH – nursing home

P-NH – nursing home for psychiatric ill people

## Introduction

Falls are the most common reason for injuries suffered by older people [1]. Many different factors may be responsible for them. One possible reversible cause is inappropriate treatment in terms of high number of drugs, their interactions or side effects. Many researches provided evidence for the influence of psychotropic drugs on fall incidence in older people. The results concerning other drugs were less conclusive. An extensive research has been conducted to find out if medicines used in cardiovascular diseases had any effect on falls occurrence.

The meta-analysis of twenty nine studies performed by Leipzig et al. showed that among cardiovascular medicines only the use of digoxin, type IA antiarrhythmics and diuretics was associated – yet weakly – with falls in older adults [2]. Later meta-analysis of studies concerning influence of antihypertensives, beta-blocking agents and diuretics on fall incidence indicated a weak, however significant, influence only of antihypertensive drugs on any fall incidence, but it did not confirm that effect in nursing home (NH) residents [3]. According to other systematic review by Hartikainen et al., the use of: beta-blocker agents and peripheral vasodilators increased risk for recurrent falls; nitrates increased risk for any falls; and antihypertensives – for fall-related injuries [4-6]. However cardiovascular drugs were not associated with falls in nine other studies [7].

NH residents are definitely at high risk of recurrent falling and fall related injury due to their disability, comorbidity and polypharmacy. They use high numbers of drugs and cardiovascular medicines are the most frequent on the list of their treatments. Study of the nature of the relation between those drugs and the rate of falling is valuable for physicians, since it may help practitioners to select appropriate drugs for patients being at a high risk of falling to protect them against serious injuries like hip fracture.

Majority of research on influence of medicines on falls has been conducted in community dwelling older

people, whose health status and physical condition differed very much from NH population. Few studies concerned recurrent falls suffered by NH residents. Most of those studies provided evidence for CNS drugs influence on the rate of falling. The results concerning impact of other drugs did not lead to a clear conclusion. Thus the aim of our study was to assess the association of specific drugs prescribed for cardiovascular diseases with recurrent falling in residents of NHs. The study was conducted within the European Network for Safety among the Elderly (funded by the EC in European Public Health Programme 2003-2008).

## Material and methods

The following definition of a fall was applied in the study: “an unexpected event in which participants come to rest on the ground, floor, or lower level”. It is concordant with the one proposed by ProFaNe group, which is currently admitted as a standard for fall definition [8]. Thus falls resulting from a loss of consciousness, sudden onset of paralysis as in a stroke, or an epileptic seizure were also included in the analysis. All falls meeting above criteria were registered since July 2005 to December 2006 in 3 NHs and since January 2006 to December 2006 in other 4 NHs, without any exclusions. We excluded from analysis only intentional falls, resulting from getting pushed or hit by somebody.

Recurrent falls are usually defined as two or more falls in a one year period [8]. In our study group the observation period of fallers started at the beginning of the project and usually ended with the end of it. However, in some cases it differed due to a later resident's accommodation to the NH (19 persons), resident's death (37) or leaving the NH (4) before the end of the study. Therefore we calculated rate of falling for each NH resident by dividing number of falls sustained by her/him during time of observation and multiplied by 365.25 days (adjustment to year period). Thus we received three classes of rate of falling: less than one, at least one and less than two, and two or more falls per year.

The falls registration form was developed based on a previous review of the guidelines of fall prevention among older adults [9]. It included date of birth, gender, information on the time, place and causes of falls, their consequences, risk factors and drugs taken in the day of fall occurrence. Nurses and nurse assistants in 7 NHs in Kraków underwent an one hour training according to the same protocol, by the same researcher. They were then obliged to register all falls in the institution and collect information about them (filling the form) no later than one hour after each fall.

The Anatomical Therapeutic Chemical (ATC) Classification was applied to classify drugs considered in statistical analysis. The medicines used in cardiovascular diseases were divided into the following classes: cardiac glycosides (Digitalis glycosides), organic nitrates and other vasodilators used in cardiac diseases (like molsidomine), diuretics, beta-blocking agents, calcium channel blockers and angiotensin-converting enzyme inhibitors (ACEI). Potassium chloride (A12BA) was added to that group as mineral supplement frequently prescribed in addition to diuretics used in cardiovascular diseases. Additionally, *acetylsalicylic acid (in a preventive dose of 75 mg/per day)* was also involved in regression analysis. Number of cardiovascular drugs was a sum of numbers of all of the above-mentioned medicines, except for *acetylsalicylic acid*. Number of CNS drugs was a sum of: antiepileptics, anti-Parkinson medicines, antipsychotics, anxiolytics, hypnotics, antidepressants, anti-dementia drugs (anticholinesterases), psychostimulants and nootropics improving cognitive functioning. Any other than the above-specified medicines were grouped in a variable called 'other than cardiovascular and CNS drugs'.

### Statistical analysis

The characteristics of fallers and falls was presented using means and standard deviations or frequencies and percentages where appropriate. Kruskal-Wallis or t-test tests (for continuous variables) and Chi-square test (for categorized) were applied to indicate the differences between the subgroups of fallers or falls. Afterwards simple and multivariable Poisson regression analysis was performed to specify associations between certain classes of drugs used in cardiovascular diseases and rate of falling, expressed as incidence rate ratio (IRR) (for more detailed description of the method see [10]).

Basing on comparison of falls by type of NH we found that falls in NH for psychiatric patients (P-NH) were related to the use of significantly higher number of CNS drugs and lower number of cardiovascular drugs. Therefore beside certain classes of medicines applied in cardiovascular diseases, number of CNS drugs was introduced as a variable into multivariate regression model. A number of medicines other than cardiovascular and CNS drugs was also included in the model to consider potential influences of all drugs on the rate of falling. Yet, a number of cardiovascular drugs was excluded from the analysis to avoid multiplication of effect of the medicines, which have been already involved into regression model. SPSS v. 16 was used for statistical analysis.

### Results

A total of 302 falls were registered during the time of observation among 166 fallers in 7 NHs (for 822 residents). Due to lacking data concerning drugs, eventually 289 falls were analyzed in 162 residents.

Some differences between falls in nursing homes for older and chronically ill persons (Ch-NH) and for psychiatric patients (P-NH) were found. The falls registered in Ch-NH were more frequently observed in females and persons at older age than falls reported in P-NH. Significantly more falls associated with the use of drugs typically prescribed in cardiovascular diseases (with exception of nitrates and cardiac glycosides) were sustained by Ch-NH residents. Consequently falls recorded in Ch-NH were related to higher average number of cardiovascular drugs. On the other hand, falls in P-NH residents were associated with higher number of CNS drugs and higher total number of medicines taken by residents who sustained falls. The analysis of number of other than cardiovascular and CNS medicines showed no statistically significant difference between falls observed in two types of NHs (Table I).

However, the use of antidiabetics including insuline (14.5% vs. 4.9%;  $\chi^2 = 4.0$ ;  $p < 0.05$ ) and medicines applied in thyroid diseases (7.9% vs. 0%;  $\chi^2 = 5.1$ ;  $p < 0.05$ ) was more often associated with falls in Ch-NH than in P-NH. The use of mirodrine (13.1% vs. 0.9%;  $\chi^2 = 21.6$ ;  $p < 0.001$ ) and theophiline (27.9% vs. 8.3%;  $\chi^2 = 16.8$ ;  $p < 0.001$ ) was more frequent in falls registered in P-NH residents. Despite those differences, pharmacological treatment applied in cardiovascular and other somatic diseases did not influence the rate of falling (table III).

Some gender differences should be noted. Falls associated with the use of theophiline were more frequent among men than women (25.7% vs. 7.9%;  $\chi^2 = 15.9$ ;  $p < 0.001$ ). On the other hand, falls associated with the use of diuretics, nitrates (or/and molsidomine) and potassium chloride were more frequent among women (30.2% vs. 13.5%;  $\chi^2 = 8.0$ ;  $p < 0.005$ ; 33.5% vs. 5.4%;  $\chi^2 = 22.4$ ;  $p < 0.001$ ; and 30.7% vs. 18.9%;  $\chi^2 = 3.8$ ;  $p = 0.051$ , respectively). The percentage of falls associated with the use of ACEI, calcium channel blockers, cardiac glycosides, beta-blocking agents did not differ depending on gender. Falls were definitely more frequent in women. Nevertheless, gender did not influence the rate of falling (table III).

The comparison of baseline characteristics of fallers depending on their rate of falling is presented in table II. The average age of fallers did not differ significantly between groups divided according to falling rate. Most

Table I. The characteristics of falls by type of NH (n = 289)

	NH for older and chronically ill people	NH for psychiatric ill	Total	P value
<b>Number of falls [% (n)]</b>	78.9% (228)	21.1% (61)	100.0% (289)	
<b>Age [mean (± SD)]</b>	<b>78.4 (11.1)</b>	61.9 (12.7)	74.9 (13.3)	p < 0.001
<b>Females [% (n)]</b>	<b>77.2% (176)</b>	63.9% (39)	74.4% (215)	p < 0.05
<b>Total number of drugs [mean (± SD)]</b>	4.8 (± 2.7)	<b>6.7 (± 2.8)</b>	5.2 (± 2.8)	p < 0.001
<b>Number of cardiovascular drugs [mean (± SD)]</b>	<b>1.8 (± 1.6)</b>	1.0 (± 1.3)	1.7 (± 1.6)	p < 0.001
<b>Number of CNS drugs [mean (± SD)]</b>	1.2 (± 1.3)	<b>3.8 (± 1.9)</b>	1.7 (± 1.8)	p < 0.001
<b>Number of other than cardiovascular and CNS drugs [mean (± SD)]</b>	1.8 (± 1.6)	1.9 (± 1.8)	1.8 (± 1.6)	NS
<b>ACE inhibitors [% (n)]</b>	<b>33.3% (76)</b>	<b>19.7% (12)</b>	30.4% (88)	p < 0.05
<b>Calcium channel blockers [% (n)]</b>	<b>8.8% (20)</b>	<b>0% (0)</b>	6.9% (20)	p < 0.02
<b>Beta-blocking agents [% (n)]</b>	<b>24.6% (56)</b>	<b>4.9% (3)</b>	<b>20.4% (59)</b>	p < 0.001
<b>Nitrates and other vasodilators used in cardiac diseases [% (n)]</b>	27.2% (62)	23.0% (14)	26.3% (76)	NS
<b>Cardiac glycosides [% (n)]</b>	<b>21.9% (50)</b>	<b>16.4% (10)</b>	<b>20.8% (60)</b>	NS
<b>Diuretics [% (n)]</b>	<b>30.3% (69)</b>	<b>9.8% (6)</b>	<b>26.0% (75)</b>	p < 0.001
<b>Potassium chloride [% (n)]</b>	<b>30.3% (69)</b>	<b>18.0% (11)</b>	<b>27.7% (80)</b>	p = 0.058
<b>Acetylsalicylic acid [% (n)]</b>	<b>27.6% (63)</b>	31.1% (19)	28.4% (82)	NS

P-values refer to  $\chi^2$  test in case of comparisons of categorized variables; to t-test in comparisons of continuous variables.

Table II. Comparison of baseline characteristics of fallers depending on their rate of falling (n = 162)

Characteristics	Fallers N = 162			Total
	IR < 1	1 ≤ IR < 2	IR ≥ 2	
Rate of falling (IR=Fall Incidence Rate per year)	IR < 1	1 ≤ IR < 2	IR ≥ 2	Total
<b>Number of fallers [% (n)]</b>	47.5% (77)	30.9% (50)	21.6% (35)	100.0% (162)
<b>Age (years) [mean (±SD)]</b>	73.8 (± 12.3)	77.3 (± 13.3)	74.6 (± 13.9)	75.1 (± 12.9)
<b>Female gender [% (n)]</b>	79.2% (61)	78.0% (39)	65.7% (23)	75.9% (123)
<b>Total number of drugs [mean (±SD)]</b>	4.6 (± 3.3)	4.9 (± 2.7)	5.4 (± 2.7)	4.9 (± 3.0)
<b>Number of cardiovascular drugs [mean (±SD)]</b>	1,6 (± 1.7)	1,8 (± 1.6)	1,7 (± 1.6)	1,8 (± 1,4)
<b>Number of CNS drugs [mean (±SD)]</b>	1.2 (± 1.4)	1.3 (± 1.4)	1.9 (± 1.9)	1.4 (± 1.5)
<b>Number of other than cardiovascular and CNS drugs [mean (±SD)]</b>	1,8 (± 1.7)	1,8 (± 1.5)	1,7 (± 1.5)	1,8 (± 1,6)
<b>ACE inhibitors [% (n)]</b>	26.0% (20)	24.0% (12)	37.1% (13)	27.8% (45)
<b>Calcium channel blockers [% (n)]</b>	10.4% (8)	6.0% (3)	5.7% (2)	8.0% (13)
<b>Beta-blocking agents [% (n)]</b>	16.9% (13)	26.0% (13)	11.4% (4)	18.5% (30)
<b>Nitrates and other vasodilators used in cardiac diseases [% (n)]</b>	28.6% (22)	26.0% (13)	17.1% (6)	25.3% (41)
<b>Cardiac glycosides [% (n)]</b>	13.0% (10)	18.0% (9)	20.0% (7)	16.0% (26)
<b>Diuretics [% (n)]</b>	23.4% (18)	32.0% (16)	31.4% (11)	27.8% (45)
<b>Potassium chloride [% (n)]</b>	33.8% (26)	34.0% (17)	20.0% (7)	30.9% (50)
<b>Acetylsalicylic acid [% (n)]</b>	28.6% (22)	28.0% (14)	28.6% (10)	28.4% (46)

There were no significant differences between fallers divided by rate of falling at p < 0.05.

fallers in the studied groups were females. Most of them resided in Ch-NH. We did not find significant association between the rate of falling and the frequency of use of specific drugs prescribed in cardiovascular diseases. Neither the total number of drugs, nor the number of cardiovascular drugs were associated with the rate of falling.

Simple and multivariate Poisson regression models were applied to analyze the influence on the rate of falling of the following variables: age, gender, total number

of drugs taken, number of cardiovascular drugs, number of CNS drugs (the in depth analysis of influence of particular CNS medicines on the rate of falling was a subject of another article), the use of ACEI, calcium channel blockers, beta-blocking agents, nitrates and other vasodilators used in cardiac diseases, cardiac glycosides, diuretics, potassium chloride, *acetylsalicylic acid* and a number of other than cardiovascular and CNS drugs [10].



**Table III. Risk estimates of recurrent falls in univariate and multivariate models of Poisson regression analyses (n = 289)**

Determinants of the falling rate	Univariate models			Multivariate model		
	Crude IRR	95% CI	P value	IRR	95% CI	P value
Intercept	–	–	–	<b>0.002</b>	<b>0.001 – 0.005</b>	<b>&lt; 0.000</b>
Age	0.998	0.989 – 1.007	= 0.663	1.006	0.995 – 1.016	= 0.282
Females	0.783	0.604 – 1.014	= 0.064	0.773	0.580 – 1.029	= 0.077
Total number of drugs	1.016	0.987 – 1.056	= 0.404	–	–	–
Number of cardiovascular drugs	0.960	0.895 – 1.029	= 0.251	–	–	–
Number of CNS drugs	<b>1.161</b>	<b>1.086 – 1.242</b>	<b>&lt;0.001</b>	<b>1.175</b>	<b>1.094 – 1.262</b>	<b>&lt; 0.000</b>
Number of other than cardiovascular and CNS drugs	0.956	0.889 – 1.028	= 0.229	0.974	0.897 – 1.057	= 0.527
ACE inhibitors	1.075	0.841 – 1.373	= 0.565	1.155	0.879 – 1.518	= 0.300
Calcium channel blockers	0.798	0.512 – 1.244	= 0.319	0.839	0.533 – 1.321	= 0.448
Beta-blocking agents	0.844	0.627 – 1.136	= 0.263	0.996	0.723 – 1.373	= 0.981
Nitrates and other vasodilators used in cardiac diseases	0.810	0.623 – 1.052	= 0.114	0.925	0.694 – 1.232	= 0.592
Cardiac glycosides	1.290	0.978 – 1.701	= 0.071	1.228	0.915 – 1.649	= 0.171
Diuretics	0.909	0.704 – 1.173	= 0.461	1.082	0.790 – 1.482	= 0.623
Potassium chloride	<b>0.752</b>	<b>0.582 – 0.972</b>	<b>&lt; 0.03</b>	0.786	0.575 – 1.074	= 0.130
<i>Acetylsalicylic acid</i>	0.952	0.738 – 1.227	= 0.702	0.974	0.731 – 1.297	= 0.855

Univariate models include separate variables. Multivariate model - includes all variables adjusted (age, gender, number of CNS drugs, number of other than CNS and cardiovascular drugs, taking particular cardiovascular drugs). Abbreviations: IRR – Incident Rate Ratio; 95% CI – confidence interval.

As indicated in table III, among all variables analyzed separately in the univariate models only the use of potassium chloride (cIRR = 0.75;  $p < 0.03$ ) and higher number of CNS drugs (cIRR = 1.16;  $p < 0.001$ ) had significant influence on the rate of falling expressed with crude Incident Rate Ratio (cIRR). However, a multivariate model adjusted to age, gender, number of CNS drugs, a number of other than cardiovascular and CNS drugs and the use of particular cardiovascular medicines, showed that only higher number of CNS drugs significantly increased the rate of falling (IRR = 1.175;  $p < 0.001$ ). The role of medicines usually prescribed in cardiovascular diseases was out of influence on the falling rate.

## Discussion

Falls constitute 12.7% adverse effects of drugs prescribed for NH residents [11]. Most of them are preventable and could be avoided by eliminating errors made by physicians at stage of medicines ordering and monitoring [12]. Nevertheless, falls are usually not reported as potential side effects of drugs in the informative materials for patients and health professionals, since they are not a specific symptom or sign that might be solely related to certain drug action. In our opinion recommendation to register falls by pharmaceutical companies dur-

ing clinical trials and report them among adverse effects in the Summary of Product Characteristics (SPC) and Patient Information Leaflets (PIL) might be helpful for physicians to avoid prescribing drugs that due to interactions may enhance risk of falling.

Basing on pathophysiology models of drugs action, we might expect that some cardiovascular medicines promote falls. For example, through lowering blood pressure (antihypertensive drugs, diuretics, vasodilators), inducing arrhythmia (cardiac glycosides) or causing atrioventricular blockade (verapamil), they may cause syncope or collapse that result with sliding or fall [13]. Orthostatic hypotension is another side effect that may occur as a consequence of the use of cardiovascular drugs [14]. However, the relation between orthostatic hypotension and antihypertensive therapy has not been proven in geriatric patients [15]. Most observational studies did not provide strong evidence for potential influence of cardiovascular drugs on recurrent falling among older people. Research conducted in community-dwelling older people resulted in inconsistent and sometimes contradictory outcomes. For example, Stalenhoeff et al. found that diuretics weakly increased risk of any fall and recurrent falling, but Lim et al. proved that loop diuretics had no influence on it in older women enrolled in Study of Osteoporotic Fractures [16,17]. According to

the above mentioned study antihypertensive and other cardiac agents did not affect repeated falling [16]. Contrary to that Luukinen et al., based on a study of 1016 home-dwelling elderly studied different classes of cardiovascular drugs. They found a weak influence of the use of cardiac glycosides on increased recurrent falling [18]. However, these results have not been confirmed in a study conducted in NHs according to the same design as the one in home-dwelling older people [19]. Lipsitz et al. while studying influence of different drug classes (cardiovascular, psychotropic and analgesic medicines) on recurrent falling found as only antidepressants imposed a greater risk of falls in frail institutionalized populations with underlying gait instability [20]. Similarly, most other studies conducted in NHs speak against influence of cardiovascular drugs on recurrent falling among NH residents [19-22].

In our study, falls registered in Ch-NH residents were associated with the use of cardiovascular drugs more frequently than in P-NH. Nevertheless none of those drugs did influence the rate of falling. On the contrary, a higher number of CNS drugs significantly increased recurrent falling, what has been reported also in other studies [23,24]. The interpretation of those findings should be done with caution, considering if the drug or disease treated with that drug causes a fall. For example, falls in patients taking IA antiarrhythmic agents could be attributable to arrhythmia, not to the antiarrhythmic drug [2]. This interpretation problem has been mentioned also by Hartikainen et al. and Woolcott et al. and defined as confounding by indication, which may occur when the medication class assessed is a marker for a clinical diagnosis that in itself changes the risk of experiencing a fall and also requires treatment with the medication being assessed [3,7].

Some conditions like orthostatic hypotension, urinary incontinence or behavioral symptoms, including wandering and agitation, were reported in several studies as independent risk factors for recurrent falling [22,25,26]. Based on a study of a large group of women attending general practices, Lawlor et al. found that coronary heart disease, any circulation system disease, thyroid disease, chronic obstructive pulmonary disease, depression and arthritis increased the risk of recurrent falls [27]. They reported that chronic diseases, multiple pathology and a high number of diseases, rather than polypharmacy, were the most important predictors of frequent falling. Thus cardiovascular drugs and medicines used in other somatic chronic diseases had no influence either on recurrent nor any fall incidence [27]. Moreover, Lee et al. suggested that association between medications and recurrent falls appeared to be due to the underlying dis-

eases and non-drug factors rather than to the medications themselves [28]. The issue of overlapping syndromes and multi-etiology of syncope (that is the one of possible causes of falls) has been considered by Gopinathannair et al., who indicated complexity of reasons and diagnostic difficulties in two-thirds of syncope particularly in older patients [29].

Unfortunately, we could not perform Poisson regression analysis to adjust our study results to diseases, since we decided not to consider information about diseases from the routine patient history of disease due to meaningful differences in ways of reporting health conditions there depending on NH organization. However, we designed our study to assure a “good” medication and falls ascertainment, which means that the use of specific drugs was reported at the time of the fall (no longer than one hour after fall) and fall incidence was documented prospectively on the structured fall registration form [30]. It resulted in a high accuracy of the collected data, as opposed to many studies reporting falls based on retrospective recollection of incidents that happened during the previous year or several months. We used Poisson regression analysis, which is not frequent, although the most appropriate for prediction of the incidence of accidents like fall or injury.

Previous reports concerning the role of drugs for the recurrent falling led to inconsistent conclusions. Our study delivered information on the potential lack of influence of cardiovascular drugs on the rate of falling. In our opinion none or weak associations observed between the use of those drugs and the rate of falling may be a result of the complexity of reasons of falls, like coincidence of diseases, interaction of drugs and coexisting environmental factors, co-playing the role of a complex risk factor for recurrent falls. Identifying fall risk factors seems to be more difficult in NH residents due to that complexity and a multifactorial background of the risk of fall.

## Conclusions

Cardiovascular drugs have no influence on recurrent falling in NH residents. More research should be done to explain the role of certain drugs and diseases in causing falls in NH residents. Probably complex risk models including diseases, drugs and possibly other factors should be applied to explain the role of cardiovascular drugs in causing falls. Studies leading us to a better understanding of pathophysiological mechanisms of direct causes of falls might be helpful to develop more effective fall prevention programs.

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The authors guarantee that privacy of the NH residents has been strictly respected. The data was collected by NH staff and provided to researchers with no personal details to analyse it anonymously, according to local Ethics Committee requirements.

**Conflict of interest**

None

**References**

1. Brongel L, Hładki W, Grodzicki T, Friedlein J, Nazimek R, Lorkowski J, et al. obrażenia ciała u ludzi w podeszłym wieku. *Pol Prz Chir.* 2007;79:189-201.
2. 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;47:40-50.
3. Woolcott JC, Richardson KJ, Wiens MO, Patel B, Marin J, Khan KM, et al. Meta-analysis of the impact of 9 medication classes on falls in elderly persons. *Arch Intern Med.* 2009;169:1952-60.
4. Bergland A, Wyller TB. Risk factors for serious fall related injury in elderly women living at home. *Inj Prev.* 2004;10:308-13.
5. Rozenfeld S, Camacho LA, Veras P. Medication as a risk factor for falls in older women in Brazil. *Rev Panam Salud Publica.* 2003;13:369-75.
6. Graafmans WC, Ooms ME, Hofstee HM, Bezemer PD, Bouter LM, Lips P. Falls in the elderly: a prospective study of risk factors and risk profiles. *Am J Epidemiol.* 1996;143:1129-36.
7. Hartikainen S, Lonroos E, Louhivuori K. Medication as a risk factor for falls: critical systematic review. *J Gerontol A Biol Sci Med Sci.* 2007;62:1172-81.
8. Hauer K, Lamb SE, Jorstad EC, Todd C, Becker C, PROFANE-Group. Systematic review of definitions and methods of measuring falls in randomised controlled fall prevention trials. *Age Ageing.* 2006;35:5-10.
9. Guideline for the prevention of falls in older persons. American Geriatrics Society, British Geriatrics Society, and American Academy of Orthopaedic Surgeons Panel on Falls Prevention. *J Am Geriatr Soc* 2001;49:664-72.
10. Szczerbińska K, Topór-Mądry R. Association between central nervous system drugs and recurrent falling based on prospective falls registration in nursing homes. *Eur Geriatr Med.* 2012;3:82-86.
11. Field TS, Gurwitz JH, Avorn J, McCormick D, Jain S, Eckler M, et al. Risk factors for adverse drug events among nursing home residents. *Arch Intern Med* 2001;161:1629-34.
12. Gurwitz JH, Field TS, Judge J, Rochon P, Harrold LR, Cadoret C, et al. The incidence of adverse drug events in two large academic long-term care facilities. *Am J Med.* 2005;118:251-8.
13. Jacob S, Bharadwaj AS, Ganguly J, Kottam A. Verapamil toxicity causing anterograde atrioventricular blockade with preserved retrograde conduction: An electrophysiological paradox. *Cardiol J.* 2010;17:636-7.
14. Tykocki T, Guzek K, Nauman P. Orthostatic hypotension and supine hypertension in primary autonomic failure. Pathophysiology, diagnosis and treatment. *Kardiologia Pol.* 2010;68:1057-63.
15. Coutaz M, Iglesias K, Morisod J. Is there a risk of orthostatic hypotension associated with antihypertensive therapy in geriatric inpatients? *Eur Geriatr Med.* 2012;3: in press.
16. Stalenhoef PA, Diederiks JP, Knottnerus JA, de Witte LP, Crebolder HF. The construction of a patient record-based risk model for recurrent falls among elderly people living in the community. *Fam Pract.* 2000;17:490-6.
17. Lim LS, Fink HA, Blackwell T, Taylor BC, Ensrud KE. Loop diuretic use and rates of hip bone loss and risk of falls and fractures in older women. *J Am Geriatr Soc.* 2009;57:855-62.
18. Luukinen H, Koski K, Laippala P, Kivela SL. Predictors for recurrent falls among the home-dwelling elderly. *Scand J Prim Health Care.* 1995;13:294-9.

19. Luukinen H, Koski K, Laippala P, Kivela SL. Risk factors for recurrent falls in the elderly in long-term institutional care. *Public Health*. 1995;109:57-65.
20. Lipsitz LA, Jonsson PV, Kelley MM, Koestner JS. Causes and correlates of recurrent falls in ambulatory frail elderly. *J Gerontol*. 1991;46:M114-22.
21. Kallin K, Lundin-Olsson L, Jensen J, Nyberg L, Gustafson Y. Predisposing and precipitating factors for falls among older people in residential care. *Public Health*. 2002;116:263-71.
22. Hasegawa J, Kuzuya M, Iguchi A. Urinary incontinence and behavioral symptoms are independent risk factors for recurrent and injurious falls, respectively, among residents in long-term care facilities. *Arch Gerontol Geriatr*. 2010;50:77-81.
23. Thapa PB, Gideon P, Fought RL, Ray WA. Psychotropic drugs and risk of recurrent falls in ambulatory nursing home residents. *Am J Epidemiol*. 1995;142:202-11.
24. Hanlon JT, Boudreau RM, Roumani YF, Newman AB, Ruby CM, Wright RM, et al. Number and dosage of central nervous system medications on recurrent falls in community elders: the Health, Aging and Body Composition study. *J Gerontol A Biol Sci Med Sci*. 2009;64:492-8.
25. Ooi WL, Hossain M, Lipsitz LA. The association between orthostatic hypotension and recurrent falls in nursing home residents. *Am J Med*. 2000;108:106-11.
26. van Nieuwenhuizen RC, van Dijk N, van Breda FG, Scheffer AC, Korevaar JC, van der Cammen TJ, et al. Assessing the prevalence of modifiable risk factors in older patients visiting an ED due to a fall using the CAREFALL Triage Instrument. *Am J Emerg Med*. 2010;28:994-1001.
27. Lawlor DA, Patel R, Ebrahim S. Association between falls in elderly women and chronic diseases and drug use: cross sectional study. *BMJ*. 2003;327:712-7.
28. Lee JS, Kwok T, Leung PC, Woo J. Medical illnesses are more important than medications as risk factors of falls in older community dwellers? A cross-sectional study. *Age Ageing*. 2006;35:246-51.
29. Gopinathannair R, Mazur A, Olshansky B. Syncope in congestive heart failure. *Cardiol J*. 2008;15:303-12.
30. 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;47:30-9.