Effectiveness of Medication Withdrawal in Older Fallers: Results from the Improving Medication Prescribing to reduce Risk Of FALLs (IMPROveFALL) Trial

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ABSTRACT

Objectives: To investigate the effect of withdrawal of Fall-Risk-Increasing-Drugs (FRIDs) versus 'care as usual' on reducing falls in community-dwelling older fallers.

Design: Randomized multicenter trial.

Participants: 612 older adults who visited an Emergency Department (ED) because of a fall.

Interventions: Systematic FRIDs assessment combined with FRIDs-withdrawal or modification, when safely possible.

Main Outcomes and Measures: Primary outcome was time to the first self-reported fall. Secondary outcomes were time to the second self-reported fall and to falls requiring a general practitioner (GP)-consultation or ED visit. Intention-to-treat (primary) and a per-protocol (secondary) analysis were conducted. The hazard ratios for time-to-fall were calculated using a Cox-regression model. Differences in cumulative incidence of falls were analysed using Poisson regression.

Results: During 12 months follow-up, 91 (34%) control and 115 (37%) intervention participants experienced a fall; 35% of all attempted interventions failed, either due to non-compliance or recurrence of the initial indication for prescribing or additional medication for newly diagnosed disorders; compared to baseline, the overall percentage of users of ≥3 FRIDs at 12 months did not change in either the intervention or the control group. Our intervention approach did not have a significant effect on time to first fall (hazard ratio [HR] 1.17; 95% confidence interval [CI] 0.89-1.54), time to second fall (1.19; 0.78-1.82), time to first fall-related GP-consultation (0.66; 0.42-1.06), or time to first fall-related ED-visit (0.85; 0.43-1.68).

Conclusions and Relevance: In this population of complex multimorbid patients visiting an ED because of a fall our single intervention approach of FRIDs-withdrawal was not effective

in reducing falls. Non-compliance was a significant factor; this may have affected the outcomes negatively, but also mirrors clinical practice.

Keywords: RCT, FRID, withdrawal, falls

INTRODUCTION

Falls affect a large proportion of persons aged 65 years and older [1], and are associated with high morbidity and mortality rates [2-4], disability, loss of quality of life, and institutionalization [5-8]. Furthermore, fall-related injuries place a substantial burden on healthcare systems due to the large number of visits to Emergency Departments (ED), hospital admissions, and admissions to long-term care and rehabilitation facilities [6,9-12]. In order to reduce the prevalence of falls, risk factors have been identified and documented [13-15], and a substantial number of falls-prevention trials has been published [1,16,17].

The use of certain drugs, i.e. the so-called fall-risk increasing drugs (FRIDs) [18-21], which are mainly psychotropic and cardiovascular drugs, has been associated with increased risk of falls and related injuries [18,19,21,22]. Although FRIDs withdrawal is frequently incorporated in multifactorial intervention programs and trials, evidence regarding overall FRID withdrawal as a single intervention is scarce [17,20,23-25].

In the present study, we investigated the effect of a structured medication assessment including withdrawal of FRIDs versus 'care as usual' on reducing falls in community-dwelling older men and women, who visited the ED after experiencing a fall [26].

METHODS

Study population

The IMPROveFALL study is a randomized, multicenter trial, assessing the effect of a structured medication assessment including withdrawal of FRIDs versus 'care as usual' as a method for falls reduction [26]. Patients meeting the following inclusion criteria were eligible for enrolment: aged 65 years or older, visited the ED of a participating hospital because of a fall, use of one or more fall-risk increasing drugs [18,19,21,26] (Table 1), Mini-Mental State Examination (MMSE) score of at least 21 out of 30 points [27,28], ability to walk 6 meters independently without assistive devices, and community dwelling. Participating hospitals included two academic and four regional hospitals in the Netherlands. Enrolment started in October 2008 and was completed in October 2011. The follow-up period was 12 months. The study was performed in accordance with the Declaration of Helsinki and all participants gave written informed consent. The local Medical Research Ethics Committees in all participating hospitals approved the study protocol.

Covariates

All persons visiting the ED because of a fall received care as usual for their injuries. Following the ED visit, patients were contacted by telephone. Subsequently, eligible and interested potential study participants received an appointment for the research outpatient clinic (OPC). The visits to the research OPC took place within two months after the fall-related ED visit. If the patient met all eligibility criteria, the patient was asked to sign the Informed Consent Form. During the visit to the research OPC, a fall-related assessment was performed by the research physician. This included a falls history (a single faller was defined as someone who had fallen once in the 12 months preceding inclusion, a recurrent faller was

defined as someone who had fallen twice or more in the 12 months preceding inclusion), a fall-risk questionnaire [29]. Medical history and medication use, including drug type, daily dose, frequency of use, and duration of use were registered. Collected data were verified with records from the patient's general physician and local pharmacist. Furthermore, the assessment included a physical examination, physical performance tests, and a blood sample. The blood sample was used for measuring 25-hydroxyvitamin D levels, and to screen for hematologic, electrolyte, and liver and kidney function abnormalities. During the baseline assessment and at the follow-up research OPC visit, participants completed questionnaires on generic Health Related Quality of Life (HRQoL). HRQoL was measured using the Dutch versions of the EuroQol five dimensions [30], and the Short Form-12 version 2 [31], at baseline and at 12 months-follow-up. A detailed description of the study protocol can be found elsewhere [26].

Randomization

Participants were randomized to one of the treatment arms, the intervention group versus 'care as usual', using a web-based variable block randomization program that was available 24 hours a day. Randomization using the trial website was done by the research physician. A block randomization with a block size of 4 was used. Due to the nature of the intervention, participants, research physicians, and care-givers could not be blinded to group assignment.

Intervention

All participants received a structured medication assessment. In the 'care as usual' group, the medication was not changed. In the intervention group, FRIDs were withdrawn where possible. The single intervention consisted of a systematic FRIDs assessment combined with FRIDs-withdrawal or modification, when safely possible. FRIDs, as defined in the

literature[18-21,26], were discontinued, reduced or substituted with potentially safer drugs in the intervention group if deemed safely possible. A complete list of FRIDs, based on current literature, is shown in Table 1. For each drug, the research physician assessed whether the initial indication still existed. Proposed changes in medication were discussed with a senior geriatrician, and if necessary with the prescribing physician. The participant's General Practitioner (GP), and the prescribing physician if other than the GP were informed of any changes in medication. For each drug modification, the research physician followed the standardized instructions of the Dutch National Formulary [32], and a clinical pharmacologist was available for advice when needed. A research nurse offered counselling, evaluated possible negative effects via a standardized telephone follow-up, and discussed any problems regarding the drug modification with the research physician and geriatrician.

All participants with follow-up were included in the intention-to-treat analyses. Regarding the per protocol analyses, the intervention group included both participants in whom FRID withdrawal/substitution was successful and participants in whom FRID withdrawal was not necessary or safely possible. In the event of more than one attempted FRID withdrawal, the successful withdrawal/substitution of at least one FRID was considered successful. The control group only included the participants in the "care as usual" group in whom we did not withdraw/substitute FRIDs during the first research OPC visit.

Definition and measurement of falls

A fall was defined as coming to rest unintentionally on the ground or a lower level with or without losing consciousness, but not induced by acute medical conditions, *e.g.*, stroke, or exogenous factors such as a traffic accident [33]. The history of falls was ascertained during a structured interview with the use of a falls questionnaire [29].

All participants received a Falls Calendar for reporting falls during a one-year follow-up period. Falls were recorded weekly on the Falls Calendars, which had to be returned every three months. The first GP consultation and first ED visit because of a fall were also collected from abovementioned Falls Calendars and medical records. Follow-up started two weeks after completed intervention or two weeks after initial research OPC visit when no intervention was performed.

Laboratory values

Non-fasting blood samples were collected at the baseline assessment. Vitamin D deficiency was defined as serum 25(OH)D < 50 nmol/l [34,35]. Anaemia was defined as haemoglobin levels < 8.1 mmol/L for men and < 7.5 mmol/L for women.

Statistical analyses

All analyses were performed using the Statistical Package of the Social Sciences (SPSS version 17.0, Chicago, Ill.). A p-value of < 0.05 was used as threshold for statistical significance.

After sample size calculations, our aim was to include a total number of 620 participants in the study, 310 in the control group and 310 in the intervention group [26]. Calculation of the required sample size was based on the assumption that the annual cumulative incidence of further falling is 50% without intervention [36], a 15% drop-out rate (including death) [1], drug withdrawal being possible in 50% of the participants in the intervention group and a 50% decrease of further falls among participants with successful withdrawal [24]. A single-sided test with an alpha level of 0.05 and a beta of 0.2 indicated that 310 patients in each group would be sufficient in order to detect a 25% decrease of participants reporting further falls in the intervention group [26].

Data were analyzed according to the intention-to-treat principle (primary), and per-protocol (secondary). The per-protocol analysis only included participants without a protocol violation as mentioned above. The hazard ratios for falling were calculated using a Cox-regression model. Herein, the time between the start of follow-up and the first fall served as the primary outcome measure. The time between the start of follow-up and the second fall, first GP consultation and first ED visit because of a fall were also analyzed. Differences in cumulative incidence of falls, GP consultations and ED visit were analyzed using Poisson regression, adjusted for overdispersion because of interdependence among the dependent variable (falls). Subgroup analyses were performed, assessing the separate effect of cardiovascular and psychotropic drug withdrawal.

Predefined models were constructed in order to adjust for age, gender and other potential confounders. Potential predefined confounders that were considered for inclusion in the multivariate model were MMSE, BMI, the Charlson Comorbidity index, vitamin D deficiency, anemia HRQoL, physical performance, number of drugs, the number of FRIDs, smoking, alcohol intake, history of recurrent falls, use of walking aid, urinary incontinence, vision problems, fear of falling, and dizziness. Confounders that led to a change in the regression coefficient (B) of 10% or more were retained in the multivariate-adjusted regression model.

RESULTS

In total, 7,081 ED visitors were screened for possible trial participants, of whom 3,294 were not eligible, and 1,954 refused to participate. Subsequently, 612 participants were randomized in the IMPROveFALL study (Figure 1). Randomization resulted in 293 participants being allocated to the control group and 319 participants to the intervention group (Figure 1). For the intention-to-treat analyses, 21 participants in the control group and 11 participants in the intervention group were excluded due to withdrawal from study or death. For the per protocol analyses, 9 participants in the control group and 66 participants in the intervention group were excluded due to protocol violations (Figure 1).

The mean age of participants was 76 years, and 62% of the study population was female. No differences in baseline characteristics were noted between the intervention and control group (Table 2). The mean number of drugs and FRIDs used at baseline were six ± three and four ± two, respectively. Figure 2 (and supplementary eTable 1) specifies number of participants compliant to attempted interventions according to FRID categories; the supplementary eTable 1 includes the specific drug types. Participants using multiple types of FRIDs, e.g. psychotropic and cardiovascular FRIDs, are presented in both categories. Notably, in 40% of all FRIDs, 62% of cardiovascular FRIDs, 32% of psychotropic FRIDs, and 78% of other FRIDs, an intervention was not deemed possible or necessary. Of all attempted FRID-withdrawals 35% failed (37% of cardiovascular FRID interventions, 48% of psychotropic FRID interventions, and 31% of other FRID interventions), either due to non-compliance or due to a return of the primary reason for which the drug had initially been prescribed.

The percentage of participants using ≥ 3 FRIDs at baseline was 72% in the control group and 70% in the intervention group; these percentages did not decrease after 1 year

follow-up, 75% and 70% respectively (Figure 3). Furthermore, 66 participants (22%) in the intervention group and 68 (25%) in the control group used a higher number of FRIDs after 12 months of follow-up than they used at baseline (Supplementary eTable 2), due to new prescriptions of FRIDs during the follow-up year.

The number of participants in the control group (n=91; 34%) and intervention group (n=115; 37%) experiencing a fall during the one-year follow-up did not differ significantly (p = 0.33). Similarly, the number of participants in the control group (n=38; 14%) and intervention group (n=50; 16%) experiencing a recurrent fall during the one-year follow-up did not differ significantly (p = 0.45). The number of fallers requiring a GP consultation (n=46; 17% vs. 36; 12%, p=0.07) or ED visit (n=21; 8% vs. 16; 5%, p=0.22) did not differ significantly.

The mean number of falls during follow-up in the control group was 0.83 and the mean number of falls in the intervention group was 0.80 (p = 0.88). The mean number of GP consultations because of a fall were 0.21 and 0.16 respectively, p=0.25; and the mean number of ED visits because of a fall were 0.08 and 0.06 respectively, p=0.51.

In the intention-to-treat analysis, cox-regression analyses adjusted for age and gender showed that FRIDs withdrawal had no significant effect on the time to first fall (hazard ratio [HR] 1.17; 95% confidence interval [CI] 0.89-1.54), or on the time to the second fall (HR 1.19; 95% CI 0.78-1.82) (Table 3). Similarly, no significant effect on the time to the first GP consultation because of a fall (HR 0.66; 95% CI 0.42-1.06) or the time to the first ED visit because of a fall (HR 0.85; 95% CI 0.43-1.68) was found (Table 3). Subgroup analyses of cardiovascular and psychotropic FRIDs withdrawal were similar, except for a significantly increased time until the first GP consultation because of a fall after cardiovascular FRIDs withdrawal (HR 0.57; 95% CI 0.34-0.93). The per-protocol analyses did not alter the results.

Poisson regression analyses showed FRIDs withdrawal did not have a significant effect on the cumulative incidence of falls (β -0.05; 95% confidence interval [CI] -0.52- 0.42), or on the cumulative incidence of GP consultations (β -0.28; 95% CI -0.75- 0.18) or ED visits (β -0.22; 95% CI -0.88- 0.44) because of a fall. Subgroup analyses of cardiovascular and psychotropic FRIDs withdrawal were again similar, and per protocol analyses did not alter these results (Supplementary eTable 3).

During the 12-months follow-up, 28 participants in the control group and 27 participants in the intervention group sustained an injurious fall ($p = 0.64$). Seven participants in the control group and six participants in the intervention group sustained a fracture because of a fall ($p = 0.66$). Two participants, both in the control group, sustained a traumatic brain injury because of a fall ($p = 0.14$).

Six participants died in the control group, causes were a ruptured coronary artery during a coronary angiography [1], kidney failure [1], oesophageal cancer [1], leukaemia [1], motor vehicle collision [1], and unknown [1]. Thirteen participants died in the intervention group, causes were sepsis [4], cancer [3], cerebrovascular accident [2], encephalopathy [1], heart failure [1], and unknown [2] ($p = 0.15$). Looking at the separate causes of death the distribution of these deaths appear to be coincidental and not due to adverse effects of drug withdrawal.

DISCUSSION

In the present randomized controlled trial we found that a structured medication assessment including withdrawal of FRIDs as a single intervention did not lead to a reduction of further falls in community dwelling elderly who visited the ED because of a fall. In the intervention group, 35% of all attempted FRID-withdrawals failed, and at one year follow-up the percentage of participants using ≥ 3 FRIDs remained at 70%. Moreover, 22% of the participants used a higher number of FRIDs after 12 months of follow-up than they used at baseline. This indicates that FRID withdrawal or modification is difficult to maintain over one year, in a population of complex, multimorbid older fallers.

There are several possible explanations for our main findings. First, in the last decade, falls prevention guidelines including instructions on fall-risk increasing drugs, and drug withdrawal- have been incorporated into usual care in the Netherlands, this may well have blunted the effect of the intervention. Second, in our intervention group a large proportion of FRIDs was prescribed adequately and thus withdrawal was not appropriate. Third, a large proportion of the participants in the intervention group was not compliant with the intervention, especially concerning psychotropic drugs withdrawal. Finally, when analyzing the participants in the successful withdrawal group individually, it was apparent that even when one or more FRIDs were successfully withdrawn, reduced, or substituted, several participants were prescribed additional FRIDs during the follow-up year by their GP or other specialist, often for new conditions.

Our results are in contrast with previous studies, where the withdrawal of FRIDs has been shown to be safely possible and effective [20,23-25]. These studies, however, used different intervention approaches. In a study by Pit *et al.* the intervention was carried out by the participants' GP, thereby probably increasing and sustaining the number of successful

withdrawals due to the more substantial doctor-patient relationship [25]. Campbell *et al.* performed a psychotropic drug withdrawal intervention that was complete and double-blinded, demonstrating the effectiveness of total psychotropic drug withdrawal on preventing falls in the short term (44 weeks) [24]. However, as in our study, compliance was difficult to maintain.

In our study, we observed a tendency towards fewer fall-related GP-visits in the intervention group, which was significant in the cardiovascular-drug withdrawal subgroup. Most studies associate psychotropic drugs with a greater fall risk [19,21], however, a greater fall-risk reduction after withdrawal of cardiovascular drugs has been reported before [20]. Furthermore, a recent large study found that antihypertensive medications were associated with an increased risk of serious fall injuries [37].

A major strength of this study is that current recommendations regarding falls prevention studies were followed [38], i.e., addressing a single intervention in a randomized controlled trial. Furthermore, participants included were high-risk fallers, i.e., older men and women who visited the ED because of a fall. In this target group even a small reduction of their fall risk might prevent loss of independence. However, the following limitations should be taken into account when interpreting our results. First, recruiting participants proved challenging, the recruitment-period lasted 4 years despite enrolling 6 hospitals. Possible reasons for refusing to participate have been reported previously [39]. Most common reasons for refusal were the added burden of additional visits to the hospital; highly independent older adults feeling “too healthy”; and personal opinions regarding the cause of the fall. Second, possibly the method of reporting falls was not as accurate as anticipated; as mentioned above, the intervention group reported as many falls as the control group, but the numbers of healthcare visits because of a fall (which were verified with GP records) were higher in the control group. Possibly fall incidence is better monitored with weekly phone calls instead of

self-report calendars [40]. Third, as mentioned before, in the intervention group compliance with FRIDs withdrawal was limited. This might be improved if the prescribing physician performs the withdrawal, as was the case in the study by Pit *et al.* [25]. Further research into the method of implementation of the intervention is warranted, e.g. in a setting with a more substantial doctor-patient relationship.

We found that withdrawal or modification of FRIDs in our study population was often not successful. Non-compliance was a significant factor; this may have affected our outcome, but also mirrors clinical practice. In this population of complex multimorbid patients visiting an ED because of a fall our single intervention approach of FRIDs-withdrawal was not effective in reducing falls.

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Author contributions

NvdV, EvL, KH, TvdC, PP, and EvB designed the study, obtained funding and recruited participating centres. NB, NvdV, KH, OdV, FMR, and TvdC, supervised conduct of trial, screening of records, and collected data. NB, NvdV, OdV, EvL, FMR, EvB, TvdC, PL, and PP, analyzed and interpreted data. NB, NvdV, and OdV, drafted the manuscript, and all authors contributed substantially to its revision. All authors approved the final version of the manuscript. NB had full access to all the data in the study and takes full responsibility for the integrity of the data and the accuracy of data analysis.

Trial collaborators participated in the screening of potential participants, and collecting trial data. Sponsor's role: None.

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Trial registration

Netherlands Trial Register NTR1593.

Conflicts of interest disclosure

The authors declare no conflict of interest.

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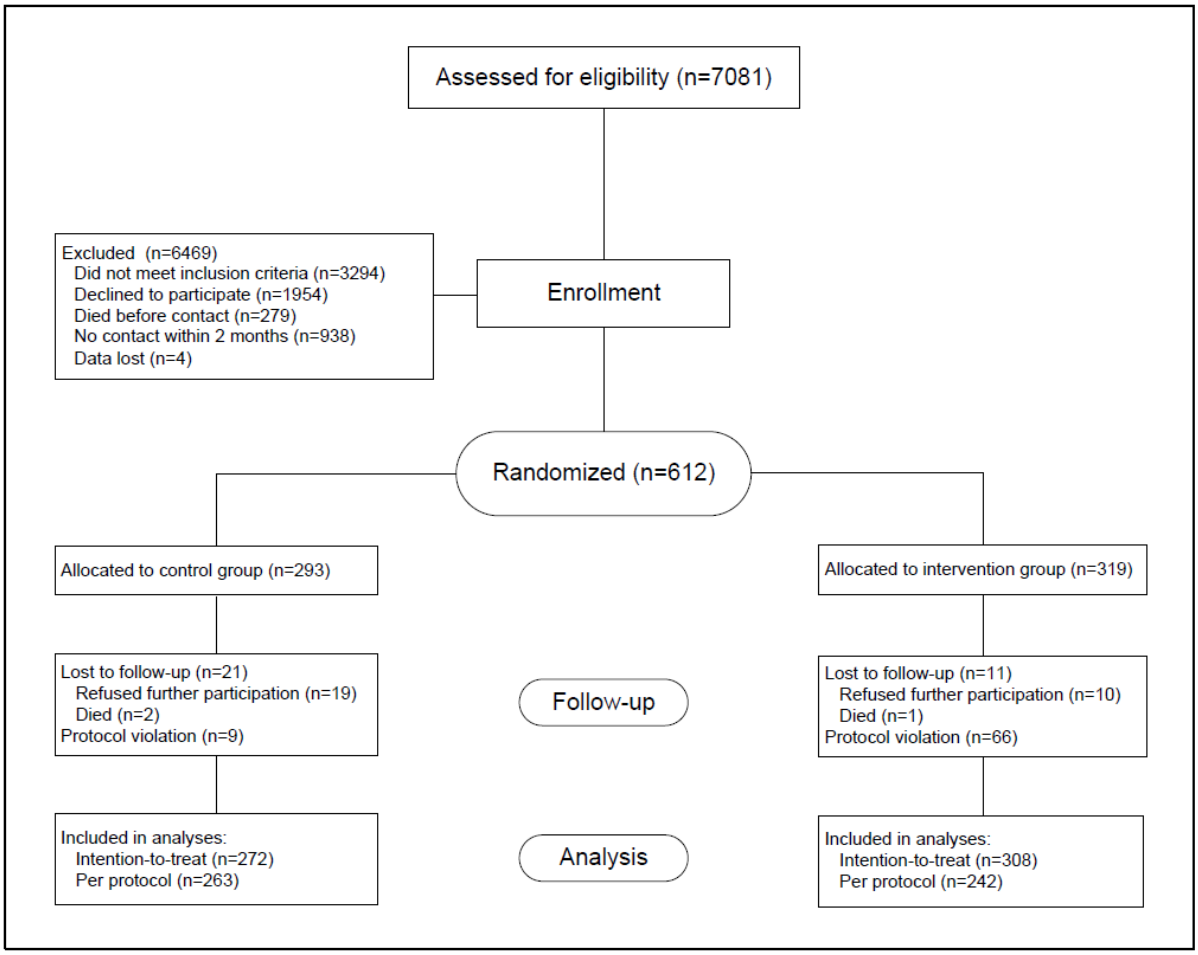
FIGURES & TABLES

Figure 1. Flowchart of study participants



*Of the participants that died during follow-up, most were included in the analyses, except for two in the usual care and one in the intervention group.

Table 1. Fall-risk increasing drugs

Drug category	Drug type	Therapeutic subgroups	ATC code
Psychotropic	Analgesics	Opioids	N02A
	Anti-epileptic	Barbiturates, fatty-acid derivatives, carboxamide derivatives, other	N03
	Anti-Parkinson	Dopaminergics, anticholenergics	N04
	Neuroleptics	Dopamine D2-receptor agonists and serotonin dopamine receptor antagonists	N05A
	Anxiolytics & Sedative/Hypnotics	Benzodiazepines and others	N05B N05C
	Antidepressants	Tricyclic antidepressants, selective serotonin reuptake inhibitors, serotonin-norepinephrine reuptake inhibitors and monoamine oxidase inhibitors	N06
	Other	Anti-vertigo agents	N07CA
Cardiovascular	Cardiac therapy	Digitalis, anti-arrhythmics, nitrates	C01
	Anti-hypertensives	Alpha-adrenoceptor blockers, centrally acting antihypertensives	C02
	Diuretics	Thiazide diuretics, loop diuretics	C03
	Beta-blockers		C07
	Calcium-channel blockers		C08
	ACE/Angiotensin-II inhibitors		C09
	HMG CoA reductase inhibitors		C10AA
Other drugs	Gastro-Intestinal	Anticholinergics Hypoglycemics	A03AA A10
	Urogenital system	α –blockers, spasmolytics	G04BD G04CA
	Anti-inflammatory	Steroids Non-steroidal anti-inflammatory drugs (NSAID) Anti-gout	H02AB, R01AD B01AC06/08, M01A M04
	Muscle relaxant	Hydroquinine	M09AA
	Pulmonary	Sympathomimetics, cough suppressants, anti-histaminics	R03AC, R05DA, R06A

*According to study protocol [26]. ATC, Anatomical Therapeutic Chemical.

Table 2. Baseline characteristics

	Control n = 293	Intervention n = 319
Demographics		
Age (year)	76.4 ± 6.6	76.5 ± 7.2
Gender (female)	182 (62)	198 (62)
MMSE	27.0 ± 2.4	27.0 ± 2.3
BMI (m^2/kg)	27.6 ± 4.7	27.6 ± 4.6
Home care	69 (24)	82 (26)
Fall risk factors		
Charlson Comorbidity Index	1.9 ± 1.6	1.9 ± 1.6
Number of drugs	6.4 ± 3.3	6.3 ± 3.3
Number of FRIDs	3.9 ± 2.0	3.9 ± 2.1
History of recurrent falls	128 (44)	148 (46)
Use of walking aid	72 (27)	78 (27)
Urinary incontinence	37 (13)	52 (16)
Vision problems	85 (30)	98 (32)
Nycturia	177 (60)	181 (57)
Fear of falling	104 (36)	118 (37)
Dizziness	75 (26)	102 (32)
Indoor fall	107 (37)	148 (46)
Smoking	37 (13)	34 (11)
Alcohol intake (≥ 3 units/day)	33 (11)	34 (11)
Functional status		
Activities of Daily Living	0.80 ± 4.5	0.80 ± 3.3
Instrumental Activities of Daily Living	1.39 ± 5.4	1.37 ± 4.0
Biochemical		
Vitamin D deficiency	119 (41)	135 (42)
Anemia	34 (13)	58 (19)

Continuous data are shown as mean values ± standard deviation, categorical data as number with percentage. MMSE, Mini-Mental State Examination; BMI, Body Mass Index; FRID, Fall-Risk Increasing Drugs.

Figure 2. Specification of attempted FRID withdrawals in intervention group

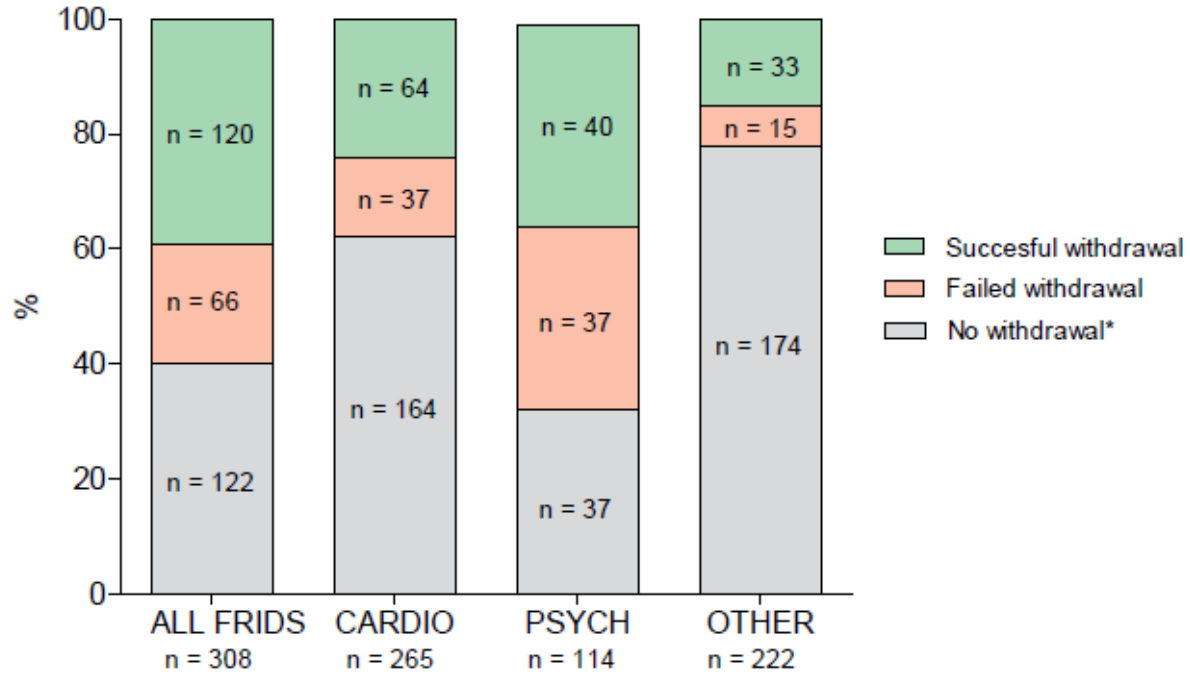


Figure 2 illustrates the number and percentage of participants where FRIDs withdrawal was not necessary or safely possible*, the failed withdrawals and the successful withdrawals; according to FRID categories (All, cardiovascular, psychotropic and other FRIDs) in the intervention group. Participants using multiple types of FRIDs, e.g. psychotropic and cardiovascular FRIDs are presented in both categories. FRID: Fall-Risk Increasing Drugs. CARDIO: cardiovascular FRIDs. PSYCH: psychotropic FRIDs. OTHER: other FRIDs. Data are shown as percentage of participants.

Figure 3. Amount of FRIDs at baseline and follow-up

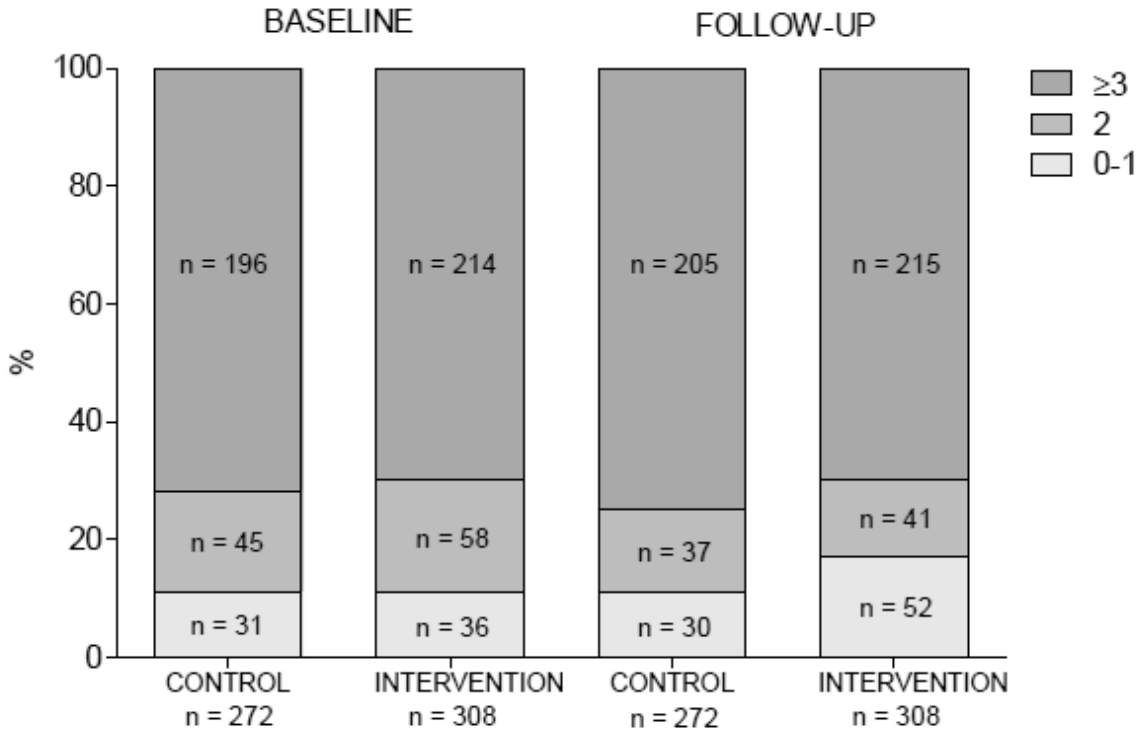


Figure 3 illustrates the number FRIDs being used at baseline and follow-up by participants in the control and intervention groups. FRID: Fall-Risk Increasing Drugs. Data are shown as number and percentage of participants.

Table 3. Cox-regression analyses including subgroup analyses

	Intention to treat			Per protocol		
	HR	**95% CI**	***p*-value**	**HR**	**95% CI**	***p*-value**
All FRIDs						
First fall	1.17	0.89; 1.54	0.27	1.19	0.89; 1.60	0.24
Second fall	1.19	0.78; 1.82	0.41	1.26	0.80; 1.99	0.31
GP consultation	0.66	0.42; 1.06	0.09	0.61	0.37; 1.02	0.06
ED visit	0.85	0.43; 1.68	0.64	0.78	0.37; 1.63	0.50
Cardiovascular FRIDs						
First fall	1.10	0.82; 1.49	0.51	1.12	0.81; 1.54	0.49
Second fall	1.21	0.78; 1.88	0.41	1.31	0.81; 2.12	0.27
GP consultation	0.57	0.34; 0.93	0.03	0.52	0.30; 0.91	0.02
ED visit	0.77	0.38; 1.58	0.48	0.68	0.31; 1.50	0.34
Psychotropic FRIDs						
First fall	1.28	0.84; 1.94	0.26	1.44	0.91; 2.29	0.12
Second fall	1.17	0.64; 2.15	0.60	1.37	0.71; 2.67	0.35
GP consultation	0.74	0.37; 1.48	0.40	0.88	0.42; 1.85	0.74
ED visit	0.78	0.28; 2.16	0.64	0.93	0.32; 2.69	0.89

Adjusted for age and gender. FRID, fall-risk increasing drug.