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Original Article

Symptoms Associated with Long-term Benzodiazepine Use in Elderly Individuals Aged 65 Years and Older: A Longitudinal Descriptive Study☆

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SUMMARY

Background: Recent epidemiologic studies have shown that the use of psychotropics is associated with many symptoms and may result in dependence and tolerance among elderly individuals. The aim of this study was to describe the symptoms related to withdrawal or dose reduction of long-term benzodiazepine (BZD) or BZD-related drugs (RDs) use and to compare them with nonuse of these drugs in community-dwelling individuals aged 65 and older.

Methods: The study was a *post hoc* analysis embedded in a 12-month randomized, controlled fall-prevention trial that included withdrawal of BZDs and RDs. The participants ($n = 248$) in the intervention group were divided into the following four groups according to their use of BZDs/RDs at baseline and follow-up: (1) withdrawal (WG), (2) reduction (RG), (3) unchanged (UG), and (4) nonusers (NUG). Differences in symptom changes were compared between and within these four groups.

Results: Using BZD/RD was associated with numerous symptoms at baseline and during the intervention. At follow-up, those symptoms reduced significantly among all participants. However, there were no significant differences between the groups in the changes of symptoms during the follow-up. Self-perceived health improved in only NUG ($p < 0.001$), but not in the other groups (WG, RG, and UG).

Conclusion: Withdrawal or reduction of BZD/RD produced positive effects on physical, psychological, or cognitive symptoms among all participants, but no differences between the groups were detected. We recommend that clinical goals should be carefully assessed against the risks of long-term BZD/RD use, and that withdrawal interventions should be initiated for community-dwelling users aged 65 and older, especially those long-term users who may already be experiencing adverse drug effects.

1. Introduction

Benzodiazepines and BZD-related drugs (BZDs/RDs) are widely prescribed[1] and long-term BZD/RD use is common. However, psychotropics tend to be overprescribed and overused in patients aged 65 years and older, the age group most vulnerable to their adverse effects. Use of psychotropics is common among patients with memory disturbances or dementia[2]. In Europe, the prevalence of BZD/RD use is about 2–3% in the general population, whereas its prevalence in the aged individuals varies between 10% and 42% worldwide[3].

Primary insomnia and anxiety are the most common clinical indications for prescribing BZD or RD; however, this is associated with certain risks. Cross-sectional and longitudinal studies show that BZD/RD use among the elderly population is associated with sedation, sleep disorders, depression, psychomotor and cognitive

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impairments, motor vehicle accidents, and increased risk of falls and fall-related injuries[4–6].

Long-term BZD/RD use may result in dependence and tolerance. These risks are especially high among individuals aged 85 years or over, and among those with cognitive impairment, poor health, mental disorders, previous use of BZDs/RDs, concomitant antidepressant use, multiple drug use, and multiple chronic and psychiatric diseases[6].

In this study, an intervention implemented by our research team included a one-time individual counseling session followed by a group lecture about the risks of adverse effects from BZD/RD use, and recommendations to reduce or stop long-term BZD/RD use[7]. Using the trial data, we carried out a *post hoc* analysis and assessed whether withdrawal or reduction of BZDs/RDs would be associated with changes in physical, psychological, or cognitive abilities in individuals aged 65 years and older.

2. Materials and methods

2.1. Participants and study design

Participants ($n = 591$) were 65 years or older in a multifactorial, randomized, controlled fall-prevention trial lasting 12 months (registered in ClinicalTrials.gov, ID = NCT00247546). The trial has been previously described in more detail[8]. The number of regular users of BZDs/RDs decreased significantly by 35% in the intervention group and correspondingly increased by 4% in the controls[7]. Participants ($n = 248$) belonging to the intervention group and participating in follow-up examinations formed the study group for the present study's longitudinal analyses. The use of BZD/RD was not randomized (Fig. 1). Ethics approval was obtained from the Ethics Committee of Satakunta Hospital District and written informed consent from the participants was also obtained.

For the longitudinal analyses, participants were divided into four groups according to their usage of BZDs/RDs at the baseline and after the 12-month intervention: (1) those participants who totally stopped BZD/RD used formed the withdrawal group (WG); (2) those who reduced BZD/RD use formed the reduction group (RG); (3) those who did not change their BZD/RD use formed the unchanged group (UG); and (4) those not using BZD/RD at baseline and after 12 months formed the nonuser group (NUG). Interventions (geriatric assessment, guidance, lectures, and psychosocial support) performed in all groups were identical.

At the baseline and after the 12-month intervention, a senior clinical geriatrician (M.S.) collected drug-utilization data (1) by interviewing the participants, and (2) from the medical records. All participants were asked to take their prescriptions and pillboxes of regularly or irregularly used drugs to the interviews. For those who had higher Geriatric Depression Scale (GDS) scores, the geriatrician prescribed antidepressant treatment with caution. Antidepressant treatment was started only if the participant was diagnosed to suffer from major depression. Drugs were coded using a Finnish translation of the Anatomical Therapeutic Chemical (ATC) Classification System[9]. BZDs and RDs consisted of medications included in the following ATC codes: N05BA, N05CD, N05CF, A03CA, N03AE01, R06AE53, and N06CA01. Participants received individually designed withdrawal program by the geriatrician. The program has been previously described in more detail[7].

The participants' physical symptoms were measured at baseline and during the follow-up examination. These used structured questions about palpitation, hand tremor, incontinence, dizziness while walking and dizziness while arising, tendency to fall, and heavy perspiration without physical exercise. For every symptom, participants were asked: "Have you had the following symptoms during the most recent 14 days, and if so, how frequently?" The occurrence and frequency of these symptoms were rated on scales covering the following four frequencies: 1 = not at all; 2 = every now and then; 3 = almost daily; and 4 = daily. Psychological and cognitive symptoms were ascertained from questions about insomnia, lack of confidence while walking, unwillingness and powerlessness, tiredness and weakness, anxiety, memory loss, and global cognitive abilities. For every symptom, participants were asked: "Have you had the following symptoms during the most recent 14 days, and if so, how frequently?" For statistical analyses, answers in symptom items were combined into two categories (yes/no), because of the small numbers of observations in some of the categories.

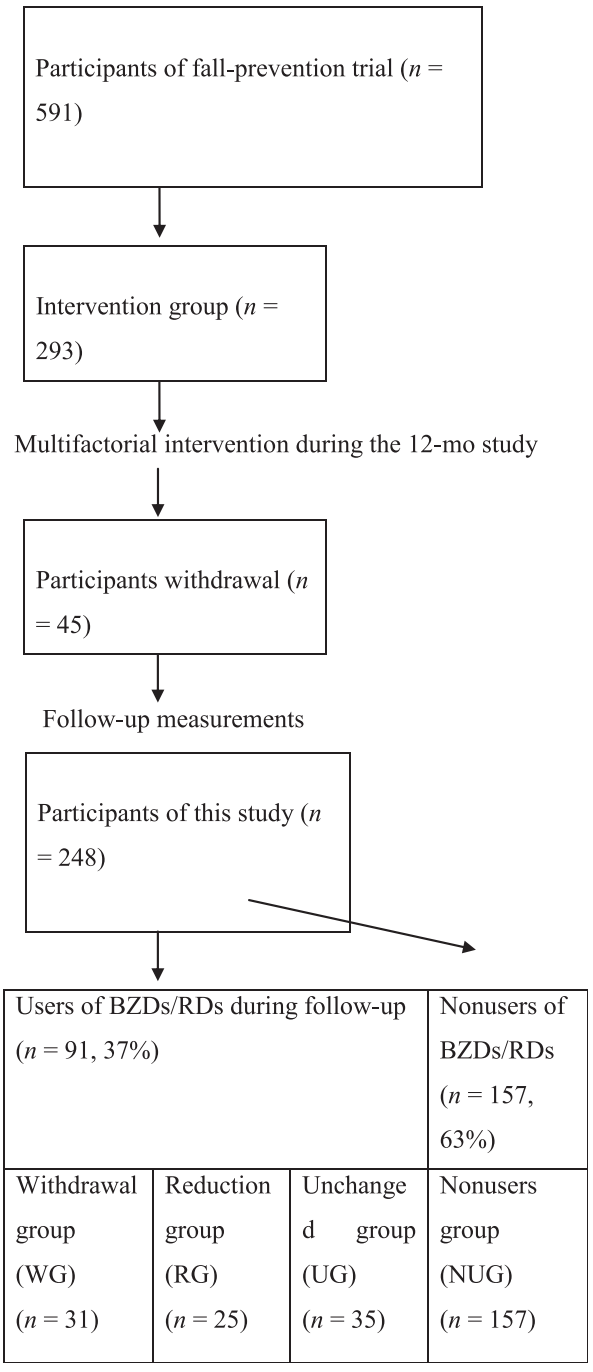

Fig. 1. Flowchart for the identification of participants from the longitudinal fall-prevention trial. BZDs = benzodiazepine; RDs = BZD-related drugs.

In addition, questions were asked concerning quality of life satisfaction, loneliness, and self-perceived health. These were measured with five-point scales. *Life satisfaction:* 1 = very unsatisfied; 2 = unsatisfied; 3 = neither satisfied nor unsatisfied; 4 = satisfied; and 5 = very satisfied; *Loneliness:* 1 = never; 2 = seldom; 3 = every now and then; 4 = often; and 5 = constantly; *Self-perceived health:* 1 = very poor; 2 = poor; 3 = neither poor nor good; 4 = good; and 5 = very good. In the statistical analyses, self-perceived health was combined into three categories (1 = good; 2 = moderate; and 3 = poor), because of the small numbers of observations in some of the categories.

Global cognitive abilities were measured with the Mini-Mental State Examination (MMSE)[10]. Scores and subcomponents were used to derive categories and additional clinical information on cognitive impairment: 1 = moderate (score = 17–24); 2 = normal (score = 25–30). The MMSE includes the serial sevens test (range = 0–5) and the recall test (range = 0–3). The number of depressive symptoms was measured with the GDS-30[11]. It is categorized as follows: 1 = a small number of depressive symptoms (score = 0–10), or 2 = a high number of depressive symptoms (score = 11–30). The Berg Balance Scale[12] was used as a measure of functional balance: 1 = decreased (score = 0–44); 2 = good (score = 45–56).

2.2. Data analyses

Data were analyzed on an intention-to-treat basis[13]. The differences in categorical background variables between users and nonusers of BZDs/RDs and among the four groups (WG, RG, UG, and NUG) were analyzed using Chi-square test or Fisher exact test. The Mann–Whitney *U* test and the Kruskal–Wallis test were used to test the differences in continuous background variables between the groups.

Table 1
Baseline characteristics of participants in the intervention group by changes in BZD/RD use during the intervention.

	Intervention group (n = 248)				
	Users of BZDs/RDs at baseline (n = 91)			Nonusers of BZDs/RDs at baseline	p^*
	Withdrawal group (n = 31)	Reduction group (n = 25)	Unchanged group (n = 35)	Nonusers group (n = 157)	
	n (%)	n (%)	n (%)	n (%)	
Sex					
Male	3 (10)	1 (4)	3 (9)	27 (17)	0.186
Female	28 (90)	24 (96)	32 (91)	130 (83)	
Age					
65–74 (y)	17 (55)	18 (72)	18 (51)	109 (69)	0.105
≥75 (y)	14 (45)	7 (28)	17 (49)	48 (31)	
Marital status					
Single	2 (6)	1 (4)	1 (3)	12 (8)	0.416
Married or cohabiting	17 (55)	12 (48)	11 (31)	65 (41)	
Widowed, divorced, or legally separated	12 (39)	12 (48)	23 (66)	80 (51)	
Living circumstances					
Alone	13 (42)	13 (52)	23 (66)	89 (57)	0.261
With a spouse or other person(s)	18 (58)	12 (48)	12 (34)	68 (43)	
Living place					
Home	29 (94)	22 (88)	34 (97)	155 (99)	0.028
Sheltered housing	2 (6)	3 (12)	1 (3)	2 (1)	
Number of prescribed medications					
<4	13 (42)	8 (32)	12 (34)	88 (56)	0.022
≥4	18 (58)	17 (68)	23 (66)	69 (44)	
Diseases					
Cardiovascular diseases	21 (68)	17 (68)	28 (80)	106 (68)	0.537
Musculoskeletal disorders	19 (61)	17 (68)	25 (71)	105 (67)	0.859
Pulmonary diseases	5 (16)	6 (24)	5 (14)	27 (17)	0.789
Malignancies	2 (6)	2 (8)	2 (6)	7 (4)	0.718
Psychiatric disease	5 (16)	4 (16)	6 (17)	1 (1)	<0.001
Neurological disease	5 (16)	6 (24)	5 (14)	24 (15)	0.708
MMSE (range, 0–30)					
25–30	28 (90)	24 (96)	29 (83)	142 (92)	0.318
17–24	3 (10)	1 (4)	6 (17)	13 (8)	
GDS (range, 0–30)					
0–10	28 (93)	18 (75)	24 (71)	137 (89)	0.011
11–30	2 (7)	6 (25)	10 (29)	17 (11)	
BBS (range, 0–56)					
45–56	2 (6)	2 (8)	5 (14)	15 (10)	0.729
0–44	29 (94)	23 (92)	30 (86)	142 (90)	
Age[a] (y)	74.0 (68.0–77.0)	72.0 (68.0–76.0)	74.0 (70.0–77.0)	72.0 (69.0–75.0)	0.631
Number of prescribed medications[a]					
Regularly	4.0 (2.0–6.0)	5.0 (2.0–7.0)	5.0 (3.0–6.0)	3.0 (1.0–5.0)	0.002
Irregularly	2.0 (1.0–4.0)	2.0 (1.0–4.0)	2.0 (1.0–3.0)	1.0 (0–2.0)	<0.001
Number of diseases[a]	4.0 (3.0–5.0)	4.0 (2.0–6.0)	4.0 (3.0–6.0)	3.0 (2.0–4.0)	0.008
MMSE[a]	28.0 (27.0–29.0)	28.0 (26.0–29.0)	27.0 (26.0–29.0)	28.0 (27.0–29.0)	0.491
GDS[a]	4.5 (3.0–7.0)	4.5 (3.0–10.5)	5.5 (2.0–12.0)	3.0 (1.0–6.0)	0.011
BBS[a]	54.0 (50.0–55.0)	53.0 (48.0–55.0)	53.0 (48.0–55.0)	53.0 (50.0–55.0)	0.696

* Statistical significance for the difference between the groups (WG, RG, UG, and NUG).
[a] Median (lower quartile–upper quartile).
BBS = Berg Balance Scale; BZDs/RDs = benzodiazepines or related drugs; GDS = Geriatric Depression Scale; MMSE = Mini-Mental State Examination.

Baseline differences between the groups were assessed using logistic regression. During follow-up, the changes in GDS-30 and MMSE sum scores, serial sevens, and recall tests within the groups and the changes between the groups were analyzed using analysis of covariance. The changes in symptoms within the groups and the differences in changes between the groups (interaction effect group × time) were analyzed by logistic regression analyses using generalized estimation equations to account for correlations between repeated measurements[14]. An exchangeable correlation structure was used in the analyses.

The results of logistic models were quantified by calculating odds ratios (ORs) for dichotomous outcome variables and cumulative ORs (CORs) for ordinal outcome variables, including their 95% confidence intervals (95% CI). The p values of 0.05 and less were considered statistically significant. All p values were calculated with two-sided tests, and no adjustments were made for multiplicity. Analyses were performed with the SAS System for Windows, version 9.1 (SAS Institute Inc., Cary, NC, USA).

3. Results

3.1. Baseline characteristics and symptoms in the intervention group

The four groups (WG, RG, UG, and NUG) differed significantly from each other in some baseline characteristics (Table 1). Psychiatric diagnoses were more common in WG, RG, and UG than in NUG, and the participants in these groups had more diseases and depressive symptoms and used more prescribed medications than participants in NUG. At the baseline, insomnia was more common in WG than in NUG (OR = 5.9; 95% CI = 1.8–19.2, $p = 0.003$). Anxiety was less common (OR = 0.3, 95% CI = 0.1–1.0, $p = 0.049$), but loneliness was more common (OR = 3.1, 95% CI = 1.0–9.2, $p = 0.041$) in WG than in UG.

Participants who used BZDs/RDs regularly (15%) or irregularly (29%) mostly did so to treat sleep disorders. More women and older persons used BZDs/RDs than men or the younger participants. The most common drug was zopiclone and the others were temazepam, zolpidem, and oxazepam. One third of the intervention group withdrew from regular use and almost one third withdrew from irregular use[7].

3.2. Changes in symptoms during the intervention

There were no differences in the changes of symptoms between the groups. Therefore, symptoms were not analyzed separately within the groups. The analyses were adjusted for group and confounding factors (living place, number of prescribed medications, number of diseases, and a high number of depressive symptoms).

Those participated in the intervention had less palpitation, hand tremors, dizziness while walking and arising, falling tendency, and heavy perspiration without physical exercise at follow-up than at baseline. Significant changes were also detected in some psychological/cognitive symptoms. Insomnia, lack of confidence with walking, unwillingness and powerlessness, tiredness and weakness, and anxiety decreased during follow-up (Table 2). These symptoms were reduced among those who managed to withdraw their BZDs/RDs or reduce their use during the intervention (data not shown).

Self-perceived health improved in NUG (COR = 2.5, 95% CI 1.6–2.8, $p < 0.001$). In WG, the change of self-perceived health was not statistically significant (COR = 1.7, 95% CI = 0.7–4.0, $p = 0.211$), which was also the case in RG (COR = 0.9, 95% CI = 0.3–2.3, $p = 0.767$) and in UG (COR = 0.7, 95% CI = 0.3–1.4, $p = 0.283$; Table 3).

A significant difference in these changes in self-perceived health was found between WG, RG, UG, and NUG (interaction effect group × time, $p < 0.001$) after adjustment for confounding factors.

Table 2
Symptoms in the intervention group at baseline and after the 12-month intervention by changes in the participant's BZD/RD use during the intervention.

Physical symptoms	Baseline *n* (%)	Follow-up *n* (%)	Adjusted[a] OR for change (95% CI)	*p**
Palpitation	107 (47)	72 (32)	0.5 (0.4–0.7)	<0.001
Tremor of hands	66 (29)	45 (20)	0.6 (0.4–0.8)	<0.001
Incontinence	90 (40)	72 (32)	0.7 (0.5–0.9)	0.012
Dizziness while walking	114 (49)	82 (36)	0.6 (0.4–0.7)	<0.001
Dizziness while arising	127 (55)	86 (37)	0.4 (0.3–0.6)	<0.001
Tendency to fall	64 (28)	13 (6)	0.1 (0.1–0.3)	<0.001
Heavy perspiration without physical exercise	93 (39)	63 (27)	0.5 (0.4–0.7)	<0.001
Psychological/cognitive symptoms				
Insomnia	167 (68)	71 (31)	0.6 (0.4–0.8)	<0.001
Lack of confidence with walking	106 (46)	161 (70)	0.5 (0.4–0.7)	<0.001
Unwillingness and powerlessness	116 (50)	97 (42)	0.7 (0.5–1.0)	0.035
Tiredness and weakness	133 (58)	94 (41)	0.5 (0.3–0.6)	<0.001
Anxiety	61 (27)	41 (18)	0.5 (0.4–0.8)	0.006
Memory loss	146 (63)	131 (57)	0.8 (0.5–1.1)	0.099
Life satisfaction	58 (24)	56 (23)	1.0 (0.7–1.6)	0.889
Loneliness	147 (61)	145 (60)	1.0 (0.7–1.3)	0.901
	Median (lower quartile–upper quartile)		Adjusted mean difference (95% CI)	*p*
MMSE	28.0 (27.0–29.0)	28.0 (27.0–29.0)	−0.23 (−1.2 to 0.7)	0.638
Serial sevens[b]	5.0 (4.0–5.0)	5.0 (4.0–5.0)	−0.17 (−0.8 to 0.4)	0.575
Recall[c]	2.0 (1.0–3.0)	2.0 (2.0–3.0)	0.03 (−0.4 to 0.5)	0.869
GDS[d]	4.0 (2.0–8.0)	2.0 (1.0–5.0)	0.12 (−1.9 to 2.1)	0.908
BBS	53.0 (50.0–55.0)	54.0 (51.0–56.0)	−1.2 (−2.5 to 0.1)	0.074

* Statistical significance for the change between the baseline and the follow-up among all participants.
[a] Adjusted for group, living place, prescribed medications (regularly and irregularly), number of diseases, and a high number of depressive symptoms; OR < 1 indicates decrease in the symptoms. There were no differences in the changes of symptoms between the groups.
[b] Serial sevens test of MMSE (range, 0–5).
[c] Recall test of MMSE (range, 0–3).
[d] Adjusted for group, living place, prescribed medications (regularly and irregularly), and number of diseases.
BBS = Berg Balance Scale; BZDs/RDs = benzodiazepines or related drugs; CI = confidence interval; GDS = Geriatric Depression Scale; MMSE = Mini-Mental State Examination; OR = odds ratio.

Table 3
Self-perceived health in the intervention group at baseline and after the 12-month intervention by changes in BZD/RD use during the intervention within the groups.

	Baseline			Follow-up			COR (95% CI)	p^*
	Good	Moderate	Poor	Good	Moderate	Poor		
	n (%)	*n* (%)	*n* (%)	*n* (%)	*n* (%)	*n* (%)		
WG	4 (13)	23 (74)	4 (13)	9 (29)	17 (55)	5 (6)	1.7 (0.7–4.0)	0.211
RG	5 (20)	18 (72)	2 (8)	7 (28)	14 (56)	4 (16)	0.9 (0.3–2.3)	0.767
UG	8 (24)	21 (62)	5 (15)	6 (18)	22 (65)	6 (18)	0.7 (0.3–1.4)	0.283
NUG	35 (23)	104 (68)	13 (9)	66 (43)	76 (50)	10 (7)	2.5 (1.6–2.8)	<0.001

Significant difference in the changes of the symptoms between the groups was found in self-perceived health (interaction effect group × time, $p < 0.001$).
* Statistical significance for the change between the baseline and the follow-up within the groups.
BZDs/RDs = benzodiazepines or related drugs; CI = confidence interval; COR = cumulative odds ratio; NUG = nonusers group ($n = 157$); RG = reduction group ($n = 25$); UG = unchanged group ($n = 35$); WG = withdrawal group ($n = 31$).

The change in self-perceived health in NUG was significantly different than that for UG (interaction effect group × time, $p = 0.002$). No other statistically significant differences between the groups were detected. In addition, WG and RG were compared with UG. There were no significant differences between the user groups WG and RG compared with UG during follow-up.

4. Discussion

The results showed self-perceived health improving significantly among those not using BZDs/RDs during the intervention and slightly among individuals withdrawing or reducing BZD/RD use. However, the study sample was quite small, and the use of BZD/RD was not randomized; therefore, the tendency for improved self-perceived health should be taken into consideration. Further analyses of subpopulations (among those aged ≥ 75 or with a higher risk of adverse effects of BZDs/RDs) were not possible due to the small number of individuals in this study.

More than half of the participants were 65–74 years of age and their health was quite good. In the younger aged participants, BZD/RD use may be a smaller risk factor for adverse effects and events than for those of more advanced age, more chronic diseases, and/or poorer general health. The results might have been different if more frail and older participants had been included, as the compensative reserve capacity reduces and pharmacodynamics and pharmacokinetics change with aging.

Our study was part of a randomized, controlled trial and based on secondary analyses[15]. Many variables were measured using standardized and internationally validated rating scales, though some of the participants' symptoms, such as life satisfaction, loneliness, and self-perceived health were assessed using Likert-type scales. Answers to symptom-item questions were combined into two or three categories, and those scales are not sensitive for changes.

At baseline, women and persons living in sheltered housing formed a greater proportion of the users, and they received more medications, had more depressive symptoms and diagnoses. In addition, their balance was worse and they were older. To control for these confounders, we adjusted multivariable models. Even after adjustments, more of the BZD/RD users suffered from insomnia, indicating that long-term BZD/RD use does not normalize the self-perceived quality of sleep[16].

Withdrawers had fewer depressive symptoms and they had been less anxious than nonwithdrawers at baseline. Differences in these symptoms might explain why some participants could withdraw while others could not. The intervention is based on the participants' willingness to discontinue or reduce their BZD use[17]. It may be that those who managed to discontinue their BZD use will have a better perception of health than the others. This may also influence the results on the reduced symptomatology.

However, because of the retrospective categorization of WG, RG, UG, and NUG, it is possible that those participants with the most symptoms related to indications of (short term) BZDs/RDs were not able to reduce their use of BZDs/RDs because of increased symptoms related to BZDs/RDs withdrawal[18,19]. Many participants' opinion was that withdrawal or reduction of BZD/RD will cause more problems than the use of the medication.[17]

Multiple physical, psychological, and cognitive symptoms were reduced in the fall-prevention trial's intervention group. Because the intervention consisted of evidence-based psychosocial support and physical exercise components[19], the results are consistent with and extend related prior research and theory. These symptoms were reduced among those who managed to withdraw their BZDs/RDs or reduce their use during the intervention. After adjusting for the confounders, only self-perceived health tended to improve in the WG and in the group reducing their use of BZDs/RDs. However, a significant positive change occurred in BZDs/RD nonusers, indicating that the tendency to improve in the WG and RG may not be solely due to the withdrawal or reduction of these drugs. A holistic intervention may have affected them at least partly.

There is a need for further education regarding psychotropics use by primary-care physicians/family physicians[4,20]. To maximize the benefits and minimize the risks of psychotropic drug use in older people[20,21], clinicians should be aware of the prevalence, dependence, and evidence of serious adverse effects from BZD/RD use and the benefits of withdrawal or dose reduction. It is recommended that psychotropic drugs should be prescribed with caution, balancing benefits and risks. They should be used in small doses and for short periods, assessing carefully and continuously the indications for use and need for them. The indications for long-term BZD or RD use should be carefully assessed, and withdrawal interventions should be targeted to long-term users experiencing adverse effects from these drugs.

References

1. Nelson J, Chouinard G. Guidelines for the clinical use of benzodiazepines: pharmacokinetics, dependency, rebound and withdrawal. Canadian Society for Clinical Pharmacology. *Can J Clin Pharmacol.* 1999;6:69–83.
2. Hartikainen S, Rahkonen T, Kautiainen H, et al. Kuopio 75+ Study: does advanced age predict more common use of psychotropics among the elderly? *Int Clin Psychopharmacol.* 2003;18:163–167.
3. Voshaar RC, Couvée JE, van Balkom AJ, et al. Strategies for discontinuing long-term benzodiazepine use: meta-analysis. *Br J Psychiatry.* 2006;189:213–220.
4. Pimlott NJ, Hux JE, Wilson LM, et al. Educating physicians to reduce benzodiazepine use by elderly patients: a randomized controlled trial. *CMAJ.* 2003;168:835–839.
5. Hartikainen S, Lönnroos E, Louhivuori K. Medication as a risk factor for falls: critical systematic review. *J Gerontol A Biol Sci Med Sci.* 2007;62:1172–1181.
6. Barker MJ, Greenwood KM, Jackson M, et al. Cognitive effects of long-term benzodiazepine use: a meta-analysis. *CNS Drugs.* 2004;18:37–48.
7. Salonoja M, Salminen M, Aarnio P, et al. One-time counselling decreases the use of benzodiazepines and related drugs among community-dwelling older persons. *Age Ageing.* 2010;39:313–319.

8. Sjösten NM, Salonoja M, Piirtola M, et al. A multifactorial fall prevention programme in home-dwelling elderly people: a randomized-controlled trial. *Public Health*. 2007;121:308–318.
9. Classification of drugs (ATC) and the defined daily doses (DDD) Lääkelaitos. 2005 (in Finnish), edited by Tinna Voipio. ISSN 1455–2698.
10. Folstein MF, Folstein SE, McHugh PR. "Mini-mental state". A practical method for grading the cognitive state of patients for the clinician. *J Psychiatr Res*. 1975;12:189–198.
11. Yesavage JA, Brink TL, Rose TL, et al. Development and validation of a geriatric depression screening scale: a preliminary report. *J Psychiatr Res*. 1982–1983;17:37–49.
12. Berg KO, Wood-Dauphinee SL, Williams JI, et al. Measuring balance in the elderly: validation of an instrument. *Can J Public Health*. 1992;83:S7–S11.
13. Hollis S, Campbell F. What is meant by intention to treat analysis? Survey of published randomised controlled trials. *BMJ*. 1999;319:670–674.
14. Hosmer DW, Lemeshow S. *Applied Logistic Regression*. 2nd ed. New York, NY: John Wiley & Sons Inc; 2000.
15. Boslaugh S. *Secondary Data Sources for Public Health: A Practical Guide*. Cambridge, UK: Cambridge University Press; 2007.
16. Beland SG, Preville M, Dubois MF, et al. Benzodiazepine use and quality of sleep in the community-dwelling elderly population. *Aging Ment Health*. 2010;14:843–850.
17. Cook JM, Biyanova T, Masci C, et al. Older patient perspectives on long-term anxiolytic benzodiazepine use and discontinuation: a qualitative study. *J Gen Intern Med*. 2007;22:1094–1100.
18. Cook JM, Marshall R, Masci C, et al. Physicians' perspectives on prescribing benzodiazepines for older adults: a qualitative study. *J Gen Intern Med*. 2007;22:303–307.
19. Parr JM, Kavanagh DJ, Young RM, et al. Views of general practitioners and benzodiazepine users on benzodiazepines: a qualitative analysis. *Soc Sci Med*. 2006;62:1237–1249.
20. Barker MJ, Greenwood KM, Jackson M, et al. Persistence of cognitive effects after withdrawal from long-term benzodiazepine use: a meta-analysis. *Arch Clin Neuropsychol*. 2004;19:437–454.
21. Taipale HT, Bell JS, Uusi-Kokko M, et al. Sedative load among community-dwelling people aged 75 years and older: a population-based study. *Drugs Aging*. 2011;28:913–925.