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1 **Title: Psychotropic drug use in community-dwelling elderly people – characteristics of**
2 **persistent and incident users**

3

4 **Authors:**

5 Maria Rikala^{1,2}, Maarit Jaana Korhonen³, Raimo Sulkava^{4,5}, Sirpa Hartikainen^{1,6,7}

6 ¹ Kuopio Research Centre of Geriatric Care, University of Eastern Finland, Kuopio, Finland

7 ² School of Pharmacy/Social Pharmacy, University of Eastern Finland, Kuopio, Finland

8 ³ Department of Pharmacology, Drug Development and Therapeutics, University of Turku,
9 Turku, Finland

10 ⁴ Institute of Public Health and Clinical Nutrition, University of Eastern Finland, Kuopio,
11 Finland

12 ⁵ Department of Neurology, Kuopio University Hospital, Kuopio, Finland

13 ⁶ School of Pharmacy/Clinical Pharmacology and Geriatric Pharmacotherapy, University of
14 Eastern Finland, Kuopio, Finland

15 ⁷ Leppävirta Health Centre, Leppävirta, Finland

16

17 **Corresponding author:**

18 Maria Rikala

19 School of Pharmacy, University of Eastern Finland, PO Box 1627, 70211 Kuopio, Finland,

20 Phone +358 40 3553125, Fax +358 17 162242, e-mail: maria.rikala@uef.fi

21

22 **WORDS:** 3099

23 **KEY WORDS:** psychotropic drugs, persistent use, incidence, elderly

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25

1 **ABSTRACT**

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3 **PURPOSE** This prospective cohort study aimed to analyze psychotropic drug use in
4 community-dwelling elderly people over a 3-year period and characterize persons most
5 susceptible to persistent and incident use.

6 **METHODS** Data on demographics, health status, cognition, functional capacity and drug use
7 were gathered by interviews at baseline (2004) and in three follow-ups (2005–2007) in a
8 population-based sample of 700 community-dwelling people aged ≥ 75 years. Characteristics
9 associated with persistent and incident use were identified using Cox proportional-hazards
10 regression.

11 **RESULTS** At baseline, 38% (n=269) of the participants used psychotropic drugs. Of them,
12 60% (n=162) reported use in all three follow-ups, whereas 22% (n=59) discontinued use.
13 Among the baseline users of antipsychotics (n=40), antidepressants (n=83) and
14 benzodiazepines (n=219), respectively 43%, 51% and 55% reported use in all three follow-
15 ups. The characteristics associated with persistent use of psychotropic drugs included
16 concomitant use of psychotropic drugs, regular use of psychotropic drugs, increasing age and
17 good self-rated health. Among the baseline nonusers of psychotropic drugs (n=431), 20%
18 (n=88) initiated use during the follow-up. Incident use of psychotropic drugs was associated
19 with increasing GDS scores, MMSE score ≤ 24 , number of visits to physician ≥ 6 ,
20 moderate/poor self-rated health and moderate/poor life satisfaction.

21 **CONCLUSIONS** Psychotropic drugs, particularly benzodiazepines, are frequently used for
22 extended periods in community-dwelling people aged ≥ 75 years. Persons with multiple
23 psychotropic drugs and regular pattern of use are most susceptible to persistent use.
24 Characteristics associated with incident use include depressive symptoms, cognitive decline
25 and poor general health.

1 **INTRODUCTION**

2

3 Psychotropic drugs are extensively used in the elderly [1–3]. In Finland, more than one-third
4 of community-dwelling people aged ≥ 75 years use at least one psychotropic drug [2]. A major
5 concern surrounding psychotropic drug use is the potential for unfavorable outcomes.

6 Specifically, use of benzodiazepines, antidepressants and antipsychotics has been associated
7 with an increased risk of falls [4, 5]. Other concerns related to benzodiazepine use include
8 dependence [6] and cognitive decline [7]. Moreover, use of antipsychotics may increase
9 mortality among elderly people with dementia [8, 9].

10

11 In general, psychotropic drugs are recommended to be used for a limited period of time in the
12 elderly. Specifically, benzodiazepines should not be used for longer than two or four weeks
13 [6] and antidepressant use should be discontinued 12 months after achieving remission from
14 depression [10]. Furthermore, periodic attempts to reduce or discontinue antipsychotic use are
15 suggested in people with dementia [11]. However, extended periods of psychotropic drug use
16 are indicated in certain psychiatric disorders, such as schizophrenia [12] and recurrent major
17 depression [10].

18

19 Although the guidelines recommend limited duration, several studies indicate that
20 psychotropic drugs are frequently used for extended periods, particularly among elderly
21 people [13–16]. The occurrence of use deemed as persistent ranges from 4.5% to 21.5% in
22 general elderly population [17–24] and from 39% to 70% in elderly users of psychotropic
23 drugs [17, 20, 21, 23–25]. Besides differences in the study populations and drugs considered,
24 heterogeneity may result from variations in the definition (from 90 days up to 6 years) and the

1 method of assessment of persistent use (retrospective self-reports, consecutive interviews,
2 pharmacy claims databases).

3

4 Identification of characteristics associated with persistent use of psychotropic drugs would aid
5 health care professionals to recognize high-risk patients. Since new users frequently end up as
6 persistent users [26], also characteristics related to incident use need to be specified. Although
7 several studies have investigated the occurrence and determinants of persistent and incident
8 use of psychotropic drugs among elderly people [17–28], few considered other drugs than
9 benzodiazepines [17, 24] or focused on people aged ≥ 75 years [19]. In addition, the majority
10 of the studies were conducted in 1980s or in early 1990s [17–21, 27, 28]. Furthermore, some
11 follow-up studies analyzed only those surviving until the end of the follow-up [19, 24],
12 potentially excluding those with the highest risk for persistent and incident use. This
13 prospective cohort study aimed to analyze psychotropic drug use over a 3-year period in
14 community-dwelling people aged ≥ 75 years. In addition, persons most susceptible to
15 persistent and incident use were characterized.

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1 **METHODS**

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3 **Study population**

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5 The current study was based on the data from the population based GeMS (Geriatric
6 Multidisciplinary Strategy for the Good Care for the Elderly) intervention study. Initially, a
7 random sample of 1000 persons aged ≥ 75 years (born before 1 November 1928) living in the
8 City of Kuopio, Finland was selected from the census data of the City of Kuopio. These
9 persons were randomly assigned to intervention (n=500) and control (n=500) groups. The
10 baseline examination was performed in 2004, with follow-ups in three consecutive years in
11 2005, 2006 and 2007. Of the initial sample, 162 refused, two had moved, 81 lived in
12 institutional settings and 55 died before baseline. The remaining 700 community-dwelling
13 participants were included in the analysis. During the study period, 119 participants were lost
14 to follow-up because of death (n=100), refusal (n=17), moving (n=1) or not being able to
15 contact (n=1).

16

17 **Data collection**

18

19 The study protocol has been described more detailed elsewhere [29]. Briefly, the participants
20 of the intervention group underwent a Comprehensive Geriatric Assessment (CGA) at the
21 baseline (2004) and in the 1-year (2005) and 2-year (2006) follow-ups. The CGA included a
22 clinical examination, medication assessment and interventions to improve nutritional state and
23 functional capacity by a team of two physicians (trainees in geriatrics), three study nurses,
24 two physiotherapists and a nutritionist. In addition to the CGA, the participants in the
25 intervention and control groups were interviewed annually (2004–2007) by three study nurses

1 to assess demographic characteristics, health status, cognition, functional capacity and drug
2 use.

3

4 The study nurses interviewed the participants either in a municipal health center or at
5 participants' homes, using a structured questionnaire. The Mini-Mental State Examination
6 (MMSE) was used to assess cognitive performance [30]. The Geriatric Depression Scale
7 (GDS15) was employed as a screening instrument for depressive symptoms [31]. Limitations
8 in instrumental activities of daily living (IADL) were screened by the scale developed by
9 Lawton and Brody [32]. Years of education, living situation (alone, with someone), self-rated
10 health (good, fairly good, moderate, fairly poor, poor), self-rated life satisfaction (very
11 satisfied, satisfied, unsatisfied, very unsatisfied) and the number of visits to physician during
12 the year preceding the baseline interview were self-reported by the participants. Information
13 on history of psychosis was based on the medical records of the municipal health center and
14 participants own report. If the participant was unable to answer (e.g. due to dementia), a
15 caregiver or home nursing staff responded instead.

16

17 During study nurses' annual interviews (2004–2007), the participants were asked to specify
18 all the prescription and over-the-counter drugs they were currently taking. Each time the
19 information was confirmed from prescriptions, drug packages and medical records of the
20 municipal health center. Drugs used daily, several times a week or at regular intervals (e.g.
21 long-acting injectable antipsychotics) were defined as regular drugs, while other drugs were
22 considered to be "as needed" drugs. All drugs were coded according to the Anatomical
23 Therapeutic Chemical (ATC) classification system recommended by World Health
24 Organization [33].

25

1 **Psychotropic drugs**

2

3 In the current study, psychotropic drugs were defined as antipsychotics (N05A),
4 benzodiazepines (N05B, N05C excluding buspirone, hydroxyzine, valerian and melatonin)
5 and antidepressants (N06A, N06CA01) according to the ATC-classification [33]. A user of a
6 psychotropic drug refers to a participant who was using at least one psychotropic drug either
7 regularly or “as needed” based on the data collected by the study nurses.

8

9 **Statistical analyses**

10

11 Characteristics of users and nonusers of psychotropic drugs at baseline were compared using
12 the Pearson χ^2 -test for categorical variables and the Mann-Whitney U test for continuous
13 variables. Baseline characteristics associated with persistent (event: discontinuation) and
14 incident use of psychotropic drugs were identified among 700 community-dwelling
15 participants using Cox proportional-hazards regression. Discontinuation occurred when a
16 baseline user did not report any use of psychotropic drugs in a follow-up, whereas initiation
17 occurred when a baseline nonuser reported any use of psychotropic drugs in a follow-up.
18 Survival time was censored at the end of 2007 for participants who did not experience the
19 event during the study period. For the participants who were lost to follow-up without
20 experiencing the event (n= 48 in discontinuation analysis and n=55 in initiation analysis), the
21 survival time was censored at the end of the loss year. The most important reason for loss to
22 follow-up was death in both analyses (88% and 78% of those lost to follow-up respectively).
23 Psychotropic drugs were analyzed together because of the high frequency of concomitant use
24 (e.g. benzodiazepine and antidepressant) and switching between therapeutic categories (e.g.
25 from benzodiazepine to antipsychotic).

1 The baseline characteristics included in the Cox proportional-hazards regression analyses are
2 presented in the Table 1. A threshold of ≤ 24 for MMSE scores was used to define cognitive
3 decline and a threshold of ≤ 6 for IADL scores to indicate impairment. Self-rated health was
4 dichotomized into good (includes good and fairly good) and moderate/poor (includes
5 moderate, fairly poor and poor). Self-rated life satisfaction was divided into excellent
6 (includes very satisfied) and moderate/poor (includes satisfied, unsatisfied and very
7 unsatisfied). The number of non-psychotropic drugs included both regularly and “as needed”
8 taken drugs. Age and GDS15 scores were treated as continuous variables. History of
9 psychosis was not included in the analyses because of the low number of participants affected
10 ($n=20$). The participants of the intervention and control groups were analyzed together
11 because the group assignment was not associated with discontinuation of psychotropic drug
12 use ($HR=1.09$; 95% CI 0.65–1.82), nor with the initiation of use ($HR=0.90$; 95% CI 0.59–
13 1.36). In addition, the intervention had minor effects on the prevalence of use of
14 antipsychotics, benzodiazepines and antidepressants [29]. Nevertheless, group assignment
15 was included in the models as a design variable.

16
17 Both crude and adjusted Cox proportional-hazards regression analyses were performed. The
18 proportional-hazards assumption for each categorical variable was evaluated by comparing
19 adjusted survival curves between categories. The participants missing data on the chosen
20 variables were excluded from the analyses except for GDS15 scores, the values for which
21 were imputed with the mean value (2) for the whole study population. Data management and
22 statistical analyses were performed using Statistical Package for Social Sciences (SPSS),
23 version 14.0 (SPSS Inc., Chicago, USA).

24

25

1 **Ethical issues**

2

3 Written informed consent was obtained from the participants or their family members or their
4 caregivers. The study protocol was approved by the Research Ethics Committee of the
5 Hospital District of Northern Savo as required by the Finnish legislation.

6

7 **RESULTS**

8

9 **Psychotropic drug use at baseline**

10

11 At baseline, 38 % (n=269) of the community-dwelling participants used at least one
12 psychotropic drug. The majority of them (68%, n=183) were using psychotropic drugs on a
13 regular basis. Benzodiazepines were the most commonly used category (31%, n=219),
14 followed by antidepressants (12%, n=83) and antipsychotics (6%, n=40). Of the users of
15 psychotropic drugs, every third (28%, n=76) used at least two psychotropic drugs.

16

17 Compared with the nonusers, the users of psychotropic drugs were older, more commonly
18 women and lived more commonly alone (Table 1). In addition, the users and nonusers
19 differed in terms of health status, cognition, functional capacity and drug use. Of the users of
20 psychotropic drugs, 19 had a history of psychosis of the following types: schizophrenic (n=6),
21 paranoid (n=7), depressive (n=4), reactive (n=1) and unclassified (n=1).

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1 **Persistent use of psychotropic drugs**

2

3 Of the baseline users of psychotropic drugs (n=269), 60% (n=162) reported use in all three
4 follow-ups (Table 2). The majority of these persistent users had a regular pattern of use at
5 baseline (n=120) and in each three follow-ups (n=126, n=130 and n=135 respectively). Over
6 half (n=85) of the persistent users reported use of at least two therapeutic categories during
7 the follow-up either in the same year (concomitant use) or in different years (switch between
8 therapeutic categories). Of the persistent users of psychotropic drugs, 8% (n=13) had a history
9 of psychosis, 14% (n=22) had GDS15 scores ≥ 5 and 27% (n=43) had MMSE scores ≤ 24 .

10 When the baseline users of antipsychotics, antidepressants and benzodiazepines were
11 analyzed separately, 43%, 51% and 55% respectively, reported use in all three follow-ups
12 (Table 3).

13

14 Of the baseline users of psychotropic drugs (n=269), 22% (n=59) discontinued all
15 psychotropic drugs during the follow-up (Table 2). In adjusted Cox proportional-hazards
16 regression analysis, oldest persons, users of at least two psychotropic drugs, regular users of
17 psychotropic drugs and people with good self-rated health were less likely to discontinue use
18 (Table 4), representing the characteristics associated with persistent use. Hazard ratios (HR)
19 were materially the same (differed less than 10% from the reported HRs) after removing the
20 variables number of psychotropic drugs and pattern of psychotropic drug use from the model,
21 except for education (HR=1.36; 95% CI 0.77–2.41), number of non-psychotropic drugs ≥ 9
22 (HR=1.13; 95% CI 0.61–2.08), MMSE scores ≤ 24 (HR=0.96; 95% CI 0.44–2.09) and IADL
23 scores ≤ 6 (HR=0.85; 95% CI 0.42–1.72).

24

25

1 **Incident use of psychotropic drugs**

2

3 Among the baseline nonusers of psychotropic drugs (n=431), 20% (n=88) initiated
4 psychotropic drug use during the follow-up (Table 2). Of the initiated drugs, the majority
5 were benzodiazepines (n= 44), followed by antidepressants (n=22) and antipsychotics (n=8).
6 In addition, 14 participants initiated psychotropic drugs at least from two therapeutic
7 categories (e.g. benzodiazepine and antipsychotic). When the baseline nonusers of
8 antipsychotics, antidepressants and benzodiazepines were analyzed separately, 7% , 10% and
9 17% respectively, initiated use during the follow-up (Table 3).

10

11 In adjusted Cox proportional-hazards regression analysis, characteristics associated with
12 incident use of psychotropic drugs included increasing GDS15 scores, MMSE score ≤ 24 ,
13 number of visits to physician ≥ 6 , moderate/poor self-rated health, and moderate/poor life
14 satisfaction (Table 4).

15

16 **DISCUSSION**

17

18 The current study found a high prevalence of psychotropic drug use in community-dwelling
19 people aged ≥ 75 years. Despite increasing awareness of potential adverse effects and the
20 guidelines recommending limited duration, psychotropic drugs were frequently used for
21 extended periods. Specifically, 60% of the baseline users of psychotropic drugs reported use
22 in three following years. In addition, every fifth baseline nonuser initiated psychotropic drug
23 use during the study period, the majority of them reporting use also in the next follow-up.

24

1 Extended periods of psychotropic drug use are indicated in certain psychiatric disorders.
2 Precisely, life-long antipsychotic therapy is suggested for patients with schizophrenia and
3 delusional disorder [12]. At least three years of antidepressant therapy is recommended for
4 patients with recurrent major depression [10]. In addition, extended periods of
5 antidepressant therapy may be necessary to prevent recurrence among patients with
6 panic disorder, generalized anxiety disorder or obsessive compulsive disorder [34, 35].
7 However, persistent use of psychotropic drugs consisted more of benzodiazepines than
8 antipsychotics and antidepressants. Specifically, every fifth community-dwelling participant
9 used benzodiazepines during the whole study period. This is of concern since
10 benzodiazepines should not be used for longer than two or four weeks in elderly people,
11 because of adverse effects, dependency and limited efficacy in continuous use [6].

12
13 Persistent use of psychotropic drugs was specifically associated with use of at least two
14 psychotropic drugs and regular pattern of use. The hazard ratios were materially the same
15 after adjusting for several factors reflecting poor mental and general health, suggesting that
16 the associations were not confounded by participants' health status. Moreover, the findings
17 are consistent with previous research. Precisely, extended periods of benzodiazepine use have
18 been reported among people with more than one benzodiazepine and among people with
19 frequent/daily pattern of use [14, 36]. Therefore, risk for persistent use needs to be considered
20 before prescribing an additional psychotropic drug to an elderly person. Moreover,
21 recommendations to avoid regular use of benzodiazepines [6] should be strongly emphasized
22 when aiming to decrease the risk for persistent use.

23
24 Consistent with the findings of previous studies [17, 24, 27, 28], people with depressive
25 symptoms were more likely to initiate psychotropic drug use. In addition, incident use was

1 associated with lower MMSE scores, which may largely explain the high prevalence of
2 psychotropic drug use among elderly people with dementia [2, 3]. Other characteristics
3 associated with incident use included frequent visits to physician, moderate/poor self-rated
4 health and moderate/poor life-satisfaction, suggesting that initiation of psychotropic drugs is
5 also related to physical morbidity, non-specific symptoms and drug seeking behavior.
6 However, these associations may involve residual confounding by some unmeasured
7 conditions, such as insomnia and anxiety.

8
9 In contrast to previous research, female gender was not related to persistent [19, 22, 25] or
10 incident use [24, 27, 28] of psychotropic drugs. Conflicting findings may result from
11 differences in drugs considered and participants' age, the majority of the previous studies
12 focusing on benzodiazepines and people aged ≥ 65 years. In addition, some follow-up studies
13 analyzed only those surviving until the end of the follow-up [19, 24], potentially leading to
14 over-representation of healthy men in a study population. Furthermore, some studies
15 compared persistent users with never users [19, 23], and therefore their results may reflect
16 determinants of use in general, rather than persistent use. In fact, a number of studies have
17 detected that female gender has minor influence on duration of psychotropic drug use among
18 prevalent users [17, 20, 24], supporting the findings of the current study.

19
20 Besides characteristics considered here, psychotropic drug use may be related to health
21 system characteristics. For example, both incident and persistent use of benzodiazepines has
22 been associated with a high number of prescribing physicians [22, 28]. The finding could
23 partly explain the frequency of persistent use in Finland, where many different physicians are
24 typically involved in each patient's care. In Finland, it is also common that physicians renew
25 psychotropic prescriptions without meeting the patient [37]. Persistent use of psychotropic

1 drugs may also arise from patient attitudes. Negative perceptions against discontinuation are
2 typically attributed to fear of recurrence, feeling of being unable to manage without, and
3 underestimation of potential adverse effects [38–40]. On the other hand, primary care
4 physicians may be pessimistic about successful discontinuation and encounter multiple
5 barriers when trying to interfere in a patient’s benzodiazepine use [41].

7 **Methodological considerations**

8
9 The annually collected data offered a great opportunity to prospectively analyze longitudinal
10 patterns of psychotropic drug use at an individual level. Furthermore, the self-reported data on
11 drug use can be considered valid since the information was confirmed from the prescriptions,
12 drug packages and medical records. In addition, the self-reported data was in agreement with
13 the information extracted from the Finnish Prescription Register (includes reimbursable drugs
14 dispensed in the Finnish community pharmacies) with κ values of 0.84 for antipsychotics,
15 0.88 for antidepressants and 0.70 for benzodiazepines [42]. A further advantage of the study
16 was the fact that not only the survivors, but also those who were lost to follow-up during the
17 study period were included in the analyses.

18
19 The study has some limitations. To begin with, the study may have overestimated the
20 occurrence of persistent use (if a participant had a long gap in psychotropic drug use between
21 the follow-ups) and underestimated the occurrence of both persistent use (if a participant
22 happened to have a gap in psychotropic drug use at the time of the follow-up) and incident
23 use (if a participant used psychotropic drug between the follow-ups). The study was further
24 limited by the fact that at the beginning of the follow-up the sample of psychotropic drug
25 users was a mixture of short-term and long-term users. Therefore, the characteristics of

1 persistent users identified in this study may differ from those identified in a sample of new
2 users [15, 26].

3
4 Some additional limitations need to be considered regarding the Cox proportional-hazards
5 regression analyses. The study could not take into consideration some potential characteristics
6 of persistent and incident users, such as insomnia and anxiety. In addition, the study used only
7 baseline measurements for time-dependent variables. This may have biased the associations
8 for variables with a tendency to vary over time, such as self-rated health and self-rated life
9 satisfaction. Nevertheless, use of time-dependent Cox proportional-hazards regression was
10 not considered appropriate because the potential variation in time-dependent variables may be
11 affected by other variables included in the analyses [43].

12

13 **CONCLUSIONS**

14

15 Psychotropic drugs, particularly benzodiazepines, are frequently used for extended periods in
16 community-dwelling people aged ≥ 75 years. Persons with multiple psychotropic drugs and
17 regular pattern of use are most susceptible to persistent use. Characteristics associated with
18 incident use include depressive symptoms, cognitive decline and poor general health. Further
19 research is needed to evaluate whether the characteristics of persistent and incident users vary
20 between antipsychotics, antidepressants and benzodiazepines.

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1 **CONFLICTS OF INTEREST**

2

3 The authors declare that they have no conflicts of interest

4

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6

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Table 1. Characteristics of community-dwelling users (n=269) and nonusers (n=431) of psychotropic drugs at baseline

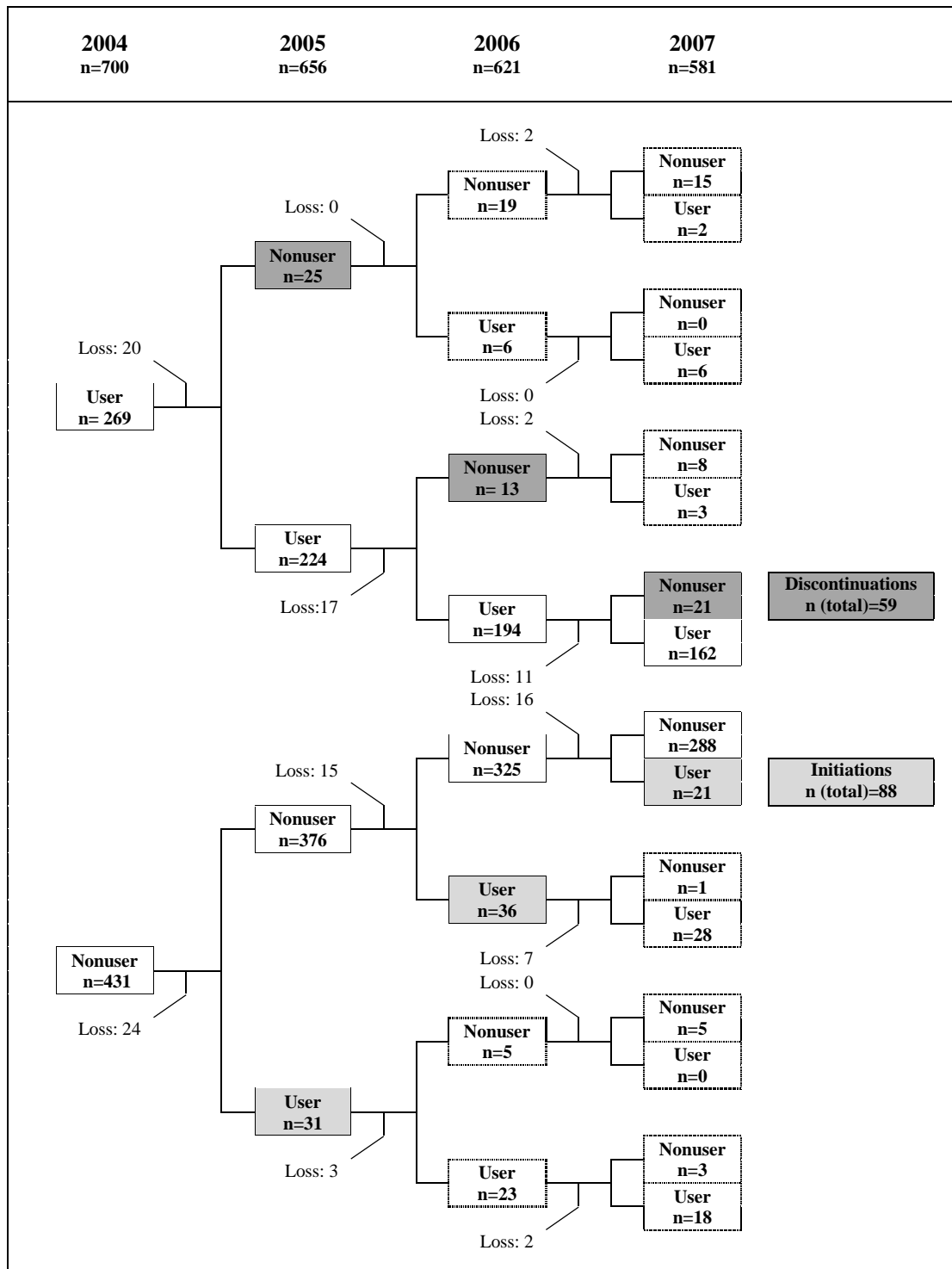
CHARACTERISTICS		Users	Nonusers	p*
		n=269	n=431	
Gender	women (n, %)	213 (79)	273 (63)	0.000
Age (years)	mean (SD)	81.7 (4.8)	80.2 (4.4)	0.000
Living alone	yes (n, %)	174 (65)	228 (53)	0.002
Years of education	0–6 (n, %)	127 (49)	215 (51)	0.594
GDS15 (0–15)	mean (SD)	2.3 (2.2)	1.3 (1.6)	0.000
MMSE (0–30)	≤24 (n, %)	76 (29)	94 (22)	0.044
IADL (0–8)	≤6 (n, %)	114 (43)	128 (30)	0.000
Number of visits to physician	≥6 (n, %)	59 (22)	69 (16)	0.043
Self-rated health	moderate or poor (n, %)	177 (66)	220 (51)	0.000
Self-rated life satisfaction	moderate or poor (n, %)	184 (69)	250 (58)	0.005
Number of non-psychotropic drugs	≥9 (n, %)	72 (27)	56 (13)	0.000
Number of psychotropic drugs	≥2 (n, %)	76 (28)	0	
Pattern of psychotropic drug use	regular (n, %)	183 (68)	0	

* Pearson's χ^2 -test for category variables and Mann-Whitney U test for continuous variables

GDS15=Geriatric Depression Scale, MMSE=Mini-Mental State Examination, IADL=Instrumental Activities of Daily Living

Missing data: years of education (n=18), GDS15 (n=11), MMSE (n=6), IADL (n=13), number of visits to physician (n=10), self-rated health (n=2), self-rated life satisfaction (n=2)

Table 2. Psychotropic drug use over a 3-year period in the community-dwelling baseline users (n=269) and nonusers (n=431)



Loss=Lost to follow-up because of death, refusal, moving or not being able to contact

Table 3. Antipsychotic, antidepressant and benzodiazepine use over a 3-year period in the community-dwelling baseline users and nonusers

	Antipsychotics	Antidepressants	Benzodiazepines
	n (%)	n (%)	n (%)
BASELINE USERS	40	83	219
Discontinued use	14 (35)	32 (39)	59 (27)
Remained as user	17 (43)	42 (51)	121 (55)
Loss to follow-up*	9	9	39
BASELINE NONUSERS	660	617	481
Initiated use	44 (7)	62 (10)	81 (17)
Remained as nonuser	512 (78)	453 (73)	339 (70)
Loss to follow-up*	104	102	61

* Lost to follow-up because of death, refusal, moving or not being able to contact

Table 4. Characteristics associated with persistent use of psychotropic drugs (event: discontinuation) in community-dwelling baseline users (n= 269)

Characteristics		n	Crude*		Adjusted**	
			HR	95% CI	HR	95% CI
Gender	men	56	1.00		1.00	
	women	213	0.94	0.51–1.74	0.68	0.32–1.45
Age	per year	269	0.95	0.90–1.01	0.92	0.86–0.99
Living alone	no	95	1.00		1.00	
	yes	174	1.29	0.74–2.24	1.84	0.97–3.51
Years of education	≥7	133	1.00		1.00	
	0–6	127	1.12	0.67–1.87	1.74	0.96–3.13
GDS15	per score (0–15)	262	0.85	0.74–0.99	0.95	0.81–1.11
MMSE	25–30	189	1.00		1.00	
	≤24	76	0.72	0.39–1.34	1.12	0.50–2.50
IADL	7–8	149	1.00		1.00	
	≤6	114	0.75	0.44–1.29	1.05	0.50–2.21
Number of visits to physician	0–5	205	1.00		1.00	
	≥6	59	1.41	0.80–2.48	1.40	0.77–2.55
Self-rated health	good	91	1.00		1.00	

	moderate or poor	177	1.47	0.83–2.62	1.92	1.01–3.68
Self-rated life satisfaction	excellent	84	1.00		1.00	
	moderate or poor	184	0.80	0.46–1.39	0.64	0.35–1.17
Number of non-psychotropic drugs	0–8	197	1.00		1.00	
	≥9	72	1.21	0.69–2.12	0.99	0.52–1.87
Number of psychotropic drugs	1	193	1.00		1.00	
	≥2	76	0.26	0.11–0.60	0.26	0.10–0.70
Pattern of psychotropic drug use	as needed	86	1.00		1.00	
	regular	183	0.39	0.23–0.65	0.47	0.26–0.84

HR=hazard ratio, CI=Confidence Interval, GDS15=Geriatric Depression Scale, MMSE=Mini-Mental State Examination, IADL=Instrumental Activities of Daily Living

* Cox proportional-hazards regression (adjusted for group assignment, participants with missing data are excluded).

** Cox proportional-hazards regression (adjusted for group assignment and the other variables listed in the Table 2. Participants missing data on the chosen variables (n=23) are excluded from the analysis except for GDS15 scores, the values for which were imputed with the mean value for the whole study population).

Table 5. Characteristics associated with incident use of psychotropic drugs in community-dwelling baseline nonusers (n=431)

Characteristics		n	Crude*		Adjusted**	
			HR	95% CI	HR	95% CI
Gender	men	158	1.00			
	women	273	1.35	0.85–2.13	1.15	0.67–1.97
Age	per year	431	1.04	0.99–1.08	1.01	0.96–1.06
Living alone	no	203	1.00		1.00	
	yes	228	1.49	0.97–2.30	1.29	0.80–2.08
Years of education	≥7	207	1.00		1.00	
	0–6	215	1.11	0.73–1.70	0.96	0.61–1.52
GDS15	per score (0–15)	427	1.32	1.20–1.44	1.22	1.08–1.37
MMSE	25–30	335	1.00		1.00	
	≤24	94	3.09	2.02–4.73	2.49	1.49–4.16
IADL	7–8	296	1.00		1.00	
	≤6	128	2.14	1.39–3.28	1.29	0.75–2.22
Number of visits to physician	0–5	357	1.00		1.00	
	≥6	69	2.03	1.26–3.25	1.94	1.16–3.25
Self-rated health	good	210	1.00		1.00	

	moderate or poor	220	2.49	1.57–3.97	1.85	1.12–3.04
Self-rated life satisfaction	good	180	1.00		1.00	
	moderate or poor	250	2.33	1.43–3.78	1.82	1.04–3.17
Number of non-psychotropic drugs	0–8	375	1.00		1.00	
	≥9	56	2.30	1.40–3.74	1.41	0.81–2.45

HR=hazard ratio, CI=Confidence Interval, GDS15=Geriatric Depression Scale, MMSE=Mini-Mental State

Examination, IADL=Instrumental Activities of Daily Living

* Cox proportional-hazards regression (adjusted for group assignment, participants with missing data are excluded).

** Cox proportional-hazards regression (adjusted for group assignment and the other variables listed in the Table 3. Participants missing data on the chosen variables (n=23) are excluded from the analysis except for GDS15 scores, the values for which were imputed with the mean value for the whole study population).