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Psychotropic drug use in community-dwelling people with young-onset dementia: two-year course and determinants

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ABSTRACT

Objectives: The aim of this study was to describe the course of psychotropic drug use in people with young-onset dementia and to explore possible associations with age, sex, dementia severity, dementia subtype and neuropsychiatric symptoms.

Methods: Psychotropic drug use was studied in 198 community-dwelling persons participating in the Needs in Young-onset Dementia study. Data about psychotropic drug use were retrieved at baseline, as well as at 6, 12, 18 and 24 months and was classified into five groups (antiepileptics, antipsychotics, anxiolytics, hypnotics/sedatives and antidepressants) and quantified as 'present' or 'absent'. Generalized Estimating Equation modeling and chi-square tests were used to study associations between the determinants and psychotropic drug use.

Results: There was a statistically significant increase in the prevalence of psychotropic drug use from 52.3% to 62.6% during the course of the study. Almost three-quarters (72.4%) of the participants were treated with any psychotropic drug during the study, and more than one-third (37.4%) received psychotropic drugs continuously. Antipsychotics were used continuously in more than 10% of the participants and antidepressants in more than 25%. Increasing age was positively associated ($p = .018$) with psychotropic drug use at baseline, while apathy symptoms were negatively associated ($p = .018$).

Conclusions: Despite the recommendations of various guidelines, the prolonged use of psychotropic drugs in community-dwelling people with young-onset dementia is high. Therefore, more attention is needed to timely evaluate psychotropic drug use and the introduction of self-management programs for caregivers should be encouraged to support caregivers in dealing with the neuropsychiatric symptoms caused by the dementia.

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Introduction

Psychotropic drugs are frequently prescribed to people with dementia. These psychotropic drugs are used for the treatment of neuropsychiatric symptoms, such as psychosis, agitation, aggression and depressive symptoms and include antipsychotics, antidepressants, mood stabilizers and anxiolytics/hypnotics (Masopust, Protopopova, Valis, Pavelek, & Klimova, 2018). A recent Dutch study of general practices showed a prevalence rate of 28.7% for these psychotropic drugs, which affect brain activities associated with mental processes and behavior (Borsje, Lucassen, Wetzels, Pot, & Koopmans, 2018). It is often believed by health care professionals that neuropsychiatric symptoms that develop during the course of dementia can only be treated successfully with psychotropic drugs (Cornege-Blokland, Kleijer, Hertogh, & van Marum, 2012). However, the Dutch Association of Elderly Care Physicians' multidisciplinary guideline for managing these symptoms in dementia states that none of these psychotropic drugs have substantial evidence supporting their effectiveness in reducing neuropsychiatric symptoms in dementia (Tariot et al., 2006; Zuidema et al., 2018). Furthermore, research on the effect of psychotropic drugs on neuropsychiatric symptoms in dementia mainly considers people with late-onset dementia.

Of the antipsychotics, haloperidol shows a minor effect on agitation or psychotic symptoms (Tariot et al., 2006). The newer antipsychotics are better tolerated but show less effectiveness in reducing psychotic behavior in elderly people with dementia (Masopust et al., 2018). Studies on the effectiveness of psychotropic drugs show only small effects which are clinical not relevant and sometimes these effects are only found in sub analysis (Brodaty et al., 2005; Rabinowitz et al., 2004; Schneider et al., 2003). However, research in the late nineties showed some effect of risperidone in the treatment of agitation in elderly with dementia but there were also warnings about side effects such as extrapyramidal symptoms and somnolence (Katz et al., 1999; Lavretsky & Sultzer, 1998). In a case report especially extrapyramidal symptoms were found to be probably a risk

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symptom for the development of a neuroleptic malignant syndrome (Gerritsen, de Jonghe-Rouleau, & Stienstra-Liem, 2004). Despite this limited effectiveness of psychotropic drugs in persons with dementia, the use sometimes remains necessary in the event of severe agitation or psychotic behavior. Additionally, antidepressant treatment shows little or no reduction in depressive symptoms and benzodiazepines have major disadvantages when used in people with dementia, such as deterioration of cognitive functions, sedation and a risk of falls (Banerjee et al., 2011; Dudas, Malouf, McCleery, & Dening, 2018; Tampi & Tampi, 2014; Zuidema et al., 2018).

Psychotropic drug use, especially the use of antipsychotics, is becoming increasingly controversial due to the known increased risk of stroke, death and many other side effects in older people with dementia (Kales et al., 2012; Nielsen, Lolk, Rodrigo-Domingo, Valentin, & Andersen, 2017; Ray, Chung, Murray, Hall, & Stein, 2009; Rochon et al., 2008). Despite these side effects, barriers to discontinuing their use are high due to the presumed chance of reoccurrence of the neuropsychiatric symptoms (Azermai, Vander Stichele, Van Bortel, & Elseviers, 2014).

A Dutch study on the course of neuropsychiatric symptoms in community-dwelling people with dementia showed that persistence of these symptoms was high over a two-year period (Aalten, de Vugt, Jaspers, Jolles, & Verhey, 2005). Approximately 70% of people with dementia live at home in the Netherlands and have a general practitioner as the main consultant for dementia-related problems. A study on involuntary treatment, including psychotropic drug use, showed that general practitioners experience a more positive attitude towards prescribing psychotropic drugs compared to other healthcare professionals (Mengelers et al., 2018).

Psychotropic drug use in community-dwelling people with so-called young-onset dementia, defined as disease onset before the age of 65, is also high despite the recommendations of all international and national dementia guidelines to use psychosocial interventions as a first-line intervention (Koopmans et al., 2014). Earlier research showed that general practitioners mainly needed support in the management of neuropsychiatric symptoms and knowledge on where to find local services (Foley, Boyle, Jennings, & Smithson, 2017). For the support of persons with young-onset dementia this is even of more importance as they are cared for at home for a longer period compared to those with late-onset dementia (Bakker et al., 2013a).

Our Needs in Young-onset Dementia (NeedYD) study showed that in community-dwelling people with young-onset dementia, 52% of the study participants used at least one psychotropic drug (Koopmans et al., 2014). Furthermore, caregivers for persons with young-onset dementia consult their general practitioner more often than late-onset dementia caregivers do because these caregivers experience more psychological or emotional problems than caregivers of persons with late-onset dementia (Lim et al., 2018). This can contribute to the prescribing of psychotropic drugs to people with young-onset dementia. The current study investigates the two-year course of psychotropic drug use of the NeedYD cohort.

In late-onset dementia, dementia severity has been found to be positively associated with psychotropic drug use, but Koopmans et al. did not find this relationship in young-onset dementia (Calvo-Perxas et al., 2012; Koopmans et al., 2014). Additionally, in late-onset dementia, no differences in the use of antipsychotics have been found between people with Alzheimer's disease (AD), vascular dementia (VaD) and frontotemporal dementia (FTD) (Calvo-Perxas et al., 2012).

To our knowledge, no studies have examined the course of psychotropic drug use and its possible association with dementia severity or dementia subtypes in community-dwelling persons with young-onset dementia while findings highlight the importance of obtaining more insight into this course. Therefore, the aim of this study is to describe the course of the different groups of psychotropic drugs in persons with young-onset dementia living at home and to explore possible associations with age, sex, disease severity, dementia subtype and neuropsychiatric symptoms.

Methods

Study design and selection

This study used data from the NeedYD study, of which the study protocol has been described earlier (van Vliet et al., 2010). For the current longitudinal study, data from 198 of the 215 participants with the three most common diagnoses: AD, FTD and VaD, including mixed dementia of the NeedYD study, who still lived at home were used. Analysis of psychotropic drug use was performed with 174 participants who had a complete two-year follow-up. The use of antiepileptics by four participants with known epilepsy was excluded from the analyses. Baseline assessments took place in 2007 and 2008. Participants were recruited from three university medical centers, regional hospitals, mental health services and day-care facilities specialized in persons with young-onset dementia (van Vliet et al., 2010). Diagnoses of dementia subtype were established according to the criteria of McKhann, the NINDS-AIREN criteria, the consensus on clinical diagnostic criteria of FTD and the consensus on clinical dementia subtypes (American Psychiatric Association [APA], 2000; Erkinjuntti, 1994; McKeith, 2006; McKhann et al., 1984; Mesulam, Grossman, Hillis, Kertesz, & Weintraub, 2003; Neary et al., 1998). Persons who were not able to sign a written informed consent were asked to give oral consent, and their legal representative gave written consent (van Vliet et al., 2010).

The study protocol was approved by the Medical Ethics Committee of the University Medical Center Maastricht. The local Ethics Committees of the participating institutions also consented (van Vliet et al., 2010).

Primary outcome

Data about psychotropic drug use were retrieved from interviews with the primary caregiver at baseline (T1) and 6, 12, 18 and 24 (T5) months after baseline and checked against available pharmacists' medication lists and pillboxes (van Vliet et al., 2010). Psychotropic drug use was classified based on the Anatomical Therapeutic Chemical Classification

Table 1. Definition of prevalence rates and (dis)continuation of psychotropic drug use.

Prevalence rate	Number of persons with psychotropic drug use at assessment, percentage of total group ($N = 174$)
Continuation	Ratio of persons using psychotropic drugs at follow-up to those using on the previous assessments
Discontinuation	Ratio of persons using psychotropic drugs at one assessment but not at the next assessment
New onset	Persons using psychotropic drugs at the assessment but not at the previous assessment, percentage of total group ($N = 174$)
Two-year continuation rate	Number of persons who used psychotropic drugs at all assessments, percentage of total group ($N = 174$)
Cumulative use	Proportion of persons who received psychotropic drugs at baseline or during follow-up ($N = 174$)
Cumulative new onset	Proportion of persons who did use psychotropic drugs at one assessment but not at baseline ($N = 174$)

Table 2. Baseline findings.

	Total ($N = 198$)	Complete follow-up ($N = 174$)
Mean age, years (SD)	60.9 (5.5)	60.9 (5.6)
Sex, male *N* (%)	105 (53)	92 (52.9)
Dementia Subtypes		
Alzheimer's disease *N* (%)	122 (61.6)	106 (60.9)
Vascular dementia *N* (%)	34 (17.2)	31 (17.8)
Frontotemporal dementia *N* (%)	42 (21.2)	37 (21.3)
Dementia stage (GDS[a])	$N = 183$	$N = 166$
Mild *N* (%)	31 (16.9)	30 (18.1)
Moderate *N* (%)	120 (65.6)	112 (67.5)
Severe *N* (%)	32 (17.5)	24 (14.5)
Neuropsychiatric Inventory,[b] mean	($N = 195$)	($N = 171$)
Psychosis (SD)	2.33 (4.5)	2.47 (4.6)
Hyperactivity (SD)	10.17 (10.9)	10.37 (11.0)
Affective symptoms (SD)	3.55 (4.9)	3.66 (4.9)
Apathy (SD)	8.84 (8.2)	8.80 (8.3)
Psychotropic Drug Use		
Antipsychotics (N05A) *N* (%)	28 (14.4)	27 (15.5)
Anxiolytics (N05B) *N* (%)	18 (9.2)	16 (9.2)
Hypnotics/sedatives (N05C) *N* (%)	9 (4.6)	9 (5.2)
Antidepressants (N06A) *N* (%)	71 (36.4)	65 (37.4)
Antiepileptics (N03A) *N* (%)	9 (7.5)	9 (5.2)
Total psychotropic drug use[c] *N* (%)	100 (50.5)	92 (52.9)

[a]GDS = Global Deterioration Scale; mild (stage 2 + 3), moderate (4 + 5) and advanced (6 + 7).
[b]Neuropsychiatric Inventory items were grouped into four neuropsychiatric sub-syndromes as suggested by the European Alzheimer Disease Consortium.
[c]Total psychotropic drug use = the use of at least one type of psychotropic drug.

(Nordic Council on Medicines, 1990). Psychotropic drugs were categorized into five groups: N03A (antiepileptics), N05A (antipsychotics), N05B (anxiolytics), N05C (hypnotics/sedatives) and N06A (antidepressants). As needed medication and anti-dementia drugs were excluded from the analysis.

Determinants

The *dementia subtypes* AD, VaD and FTD were included. The Global Deterioration Scale (GDS) was used to assess *dementia severity*. This widely used and validated instrument rates dementia severity from (1) no cognitive decline to (7) very severe cognitive decline (Reisberg, Ferris, de Leon, & Crook, 1982). *Neuropsychiatric symptoms* were assessed with the Dutch version of the Neuropsychiatric Inventory, a valid rating scale for neuropsychiatric symptoms in dementia (Cummings et al., 1994; Kat et al., 2002). The frequency (0–4) and severity scores (1–3) of the Neuropsychiatric Inventory items are multiplied, resulting in a score ranging from 0 to 12.

Statistical analysis

The prevalence rate, continuation, discontinuation and new onset of psychotropic drug use were calculated using the same criteria as in the study by Wetzels, Zuidema, de Jonghe, Verhey, and Koopmans (2011) (Table 1). Psychotropic drug use was categorized as 'present' or 'absent'. When a person used more than one drug from the same subgroup, this was only registered as 'present'. Persons with a complete medication registration at all five assessments were included for evaluation.

Dementia severity was categorized as mild (GDS 2,3), moderate (GDS 4,5) or advanced dementia (GDS 6,7). Neuropsychiatric Inventory items were grouped into four neuropsychiatric sub-syndromes (Aalten et al., 2008). These sub-syndromes are psychosis (summed scores of delusions, hallucinations and night-time behavioral disturbances; range 0–36), hyperactivity (summed scores of agitation, euphoria, disinhibition, irritability and aberrant motor behavior; range 0–60), affective symptoms (summed scores of depression and anxiety; range 0–24) and apathy (summed scores of apathy, sleep-time and night-time disturbances and appetite/eating disorder; range 0–36). We included all Neuropsychiatric Inventory scores, including those who are regarded as not clinical relevant (below 4), because low scores on, for example, delusions, hallucinations and night-time disturbances can ultimately result in a clinically relevant score on sub-syndrome psychosis.

Statistical analysis was performed using the Statistical Package for Social Sciences (SPSS) software, version 22.2.0.01 (2013) (IBM SPSS Statistics, IBM Corporation, Chicago, IL). Age, sex, dementia subtype, GDS and neuropsychiatric symptoms were described by calculating means or proportions. Analyses with chi-square or *t* test were performed to determine whether there was an association of psychotropic drug use with each of the determinants at baseline. To compare age, sex, dementia severity, neuropsychiatric symptoms and psychotropic drug use of the persons with a complete two-year evaluation (completers) with persons who did not have complete psychotropic drug use information (non-completers), chi-square test and Fischer exact test were used for categorical variables and Mann-Whitney test for continuous variables because the assumptions for parametric testing were not met. Repeated logistic regression analysis was performed with Generalized Estimating Equation (GEE) modeling to examine the course of psychotropic drug use (Zeger & Liang, 1986). Interaction terms for sex, age, dementia subtype, GDS and neuropsychiatric symptoms were added to test the hypothesis that the association between time and total psychotropic drug use was different for these determinants. Finally, we explored the Cox proportional hazard ratio if age or sex influenced the course of psychotropic drug use. A p value of $<.05$ was considered statistically significant based on two-sided tests.

Results

We included 174 of the 198 persons of the NeedYD study who had a complete two-year follow-up period. The mean

Table 3. Course of psychotropic drug use ($N = 174$).

	First interval				Second interval				Third interval				Fourth interval			
	T1[a]	Continuation[b]	Discontinuation[c]	New onset[d]	T2	Continuation[b]	Discontinuation[c]	New onset[d]	T3	Continuation[b]	Discontinuation[c]	New onset[d]	T4	Continuation[b]	Discontinuation[c]	New onset[d]	T5
% Antipsychotics	**15.5**	81.5	18.5	8.8	**20.1**	80.0	20.0	5.8	**20.7**	97.2	2.8	10.1	**28.2**	79.6	20.4	6.4	**27.0**
% Anxiolytics	**9.2**	62.5	37.5	5.1	**10.3**	88.9	11.1	3.8	**12.6**	77.3	22.7	2.6	**12.1**	95.2	4.8	4.6	**15.5**
% Hypnotics/sedatives	**5.2**	66.7	33.3	1.8	**5.2**	55.6	44.4	3.6	**6.3**	72.7	27.3	1.2	**5.7**	60.0	40.0	1.2	**4.6**
% Antidepressants	**37.4**	87.7	12.3	5.5	**36.2**	87.3	12.7	8.1	**36.8**	90.6	9.4	8.2	**38.5**	95.5	4.5	12.1	**44.3**
% Antiepileptics	**5.2**	88.9	11.1	1.8	**7.9**	66.7	33.3	1.2	**6.3**	92.9	7.1	3.1	**8.6**	93.3	6.7	1.3	**9.2**
% Total psychotropic drug use[e]	**52.3**				**55.2**				**53.4**				**59.8**				**62.6**

[a]T1–T5: 6 months assessments, (T1 = baseline).
[b]Continuation: the ratio of psychotropic drug users/users previous assessment.
[c]Discontinuation: the ratio of non-psychotropic drug users/users previous assessment.
[d]New onset: the ratio of psychotropic drug users/non-users at previous assessment.
[e]Total psychotropic drug use: the use of at least one type of psychotropic drug.

Table 4. Two-year psychotropic drug use ($N = 174$).

	Baseline	Two-year continuation	Cumulative	
			Use[a]	New onset[b]
Antipsychotics *N* (%)	27 (15.5)	18 (10.3) [66.7][c]	37.4 %	21.3 %
Anxiolytics *N* (%)	16 (9.2)	8 (4.6) [50.0][c]	21.3 %	12.1 %
Hypnotics/sedatives *N* (%)	9 (5.2)	2 (1.1) [22.2][c]	11.5 %	6.3 %
Antidepressants *N* (%)	65 (37.4)	44 (25.3) [67.7][c]	51.7 %	14.4 %
Antiepileptics *N* (%)	9 (5.2)	4 (2.3) [44.4][c]	10.3 %	6.3 %
Total psychotropic drug use[d] *N* (%)	91 (52.3)	65 (37.4) [72.2][c]	72.4 %	21.4 %

[a]Cumulative use: proportion who received psychotropic drugs at baseline or during follow-up.
[b]Cumulative new onset: proportion who did not use psychotropic drugs at baseline but at any of the next assessments.
[c][Percentage of baseline users].
[d]Total psychotropic drug use: the use of at least one type of psychotropic drugs.

Table 5. Two-year course of psychotropic drug use, Cox proportional hazard ratio's ($N = 174$).

							95.0% CI for Exp(B)	
	B	SE	Wald	df	Sig.	Exp(B)	Lower	Upper
Assessments								
Baseline[a]								
6 months	.120	.109	1.198	1	.274	1.127	.910	1.397
12 months	.480	.122	.154	1	.695	1.049	.826	1.331
18 months	.315	.142	4.946	1	.026	1.370	1.038	1.808
24 months	.415	.146	8.073	1	.004	1.515	1.137	2.017
Age at baseline	.065	.026	6.419	1	.011	1.067	1.015	1.122
Sex, female	.338	.266	1.613	1	.204	1.402	.832	2.361

[a]Reference.

age was 61 years, and most persons were male (Table 2). The most common dementia subtype was AD, and the majority of persons were in a moderate stage of dementia. Non-completers had a more advanced disease stage compared to that of completers.

Psychotropic drug use

At baseline, more than half of the persons were prescribed at least one psychotropic drug, and this increased during the two-year follow-up by more than 10% (Table 3). Cumulative psychotropic drug use was present in almost three-quarters of the persons, while continuous psychotropic drug use was present in 37.4% of the persons (Table 4). Antipsychotic medication and antidepressants had the highest prevalence rates and showed the highest increase during the study at 11.5% and 6.9%, respectively. Hypnotics were the only psychotropic drugs that decreased during the two-year follow-up.

Determinants of psychotropic drug use

Chi-square analyses revealed that older persons received more psychotropic drugs (hazard ratio [HR] = 1.061; CI 1.010–1.114) ($p = .018$) for each year of higher age and this relationship remained during follow-up (Table 5). Persons who scored higher on the Neuropsychiatric Inventory subsyndrome apathy received fewer psychotropic drugs (hazard ratio [HR] = 0.963; CI 0.933–0.993) ($p = .018$) at baseline. No other associations were found for gender, diagnosis, global deterioration score or Neuropsychiatric Inventory

Table 6. Psychotropic drug use: univariate analysis.

	Use		Course[a]	
Determinants	Chi-Square (df)	*p* Value	Chi-Square (df)	*p* Value
Age	5.635 (1)	.018	1.426 (4)	.840
Gender	0.606 (1)	.436	1.772 (4)	.778
Diagnosis	0.249 (2)	.883	10.707 (8)	.219
GDS[b]	2.755 (2)	.252	9.470 (8)	.304
NPI[c]				
Psychosis	2.188 (1)	.139	4.506 (4)	.342
Hyperactivity	2.398 (1)	.122	2.710 (4)	.607
Affective	0.643 (1)	.423	7.733 (4)	.102
Apathy	5.637 (1)	.018	4.492 (4)	.344

[a]Interaction with time.
[b]Global Deterioration Scale.
[c]Neuropsychiatric Inventory.

sub-syndrome scores psychosis, hyperactivity or affective and psychotropic drug use (Table 6).

Discussion

To our knowledge, this is the first study that reports on the course of psychotropic drug use in community-dwelling persons with young-onset dementia. During the two-year follow-up period, 72% of them were treated with a psychotropic drug.

The prescriptions of antipsychotics and antidepressants were the highest, and new prescriptions for antipsychotics and antidepressants were found in 21.3% and 14.4% of persons, respectively. Despite the Dutch guidelines that recommend a maximum use of 3 months, we found that 10% of the persons were treated with antipsychotics continuously (Zuidema et al., 2018). We know from a study in Dutch nursing homes that appropriate prescription of psychotropic drugs according to guidelines is difficult, as only 10% of the prescriptions were appropriate, including 58% for a correct duration of therapy (van der Spek et al., 2016).

The increase in antipsychotics in our sample is remarkable, since in community-dwelling elderly with dementia, it was previously found that the use of antipsychotic medication remained stable over three years (Boucherie et al., 2017). Although that study cannot be compared directly with our study, it raises the question of whether there is a different prescription pattern for persons with young-onset dementia compared to that for elderly persons with dementia. Another study found that clinically relevant scores on sub-syndrome psychosis were present in 10% of community-dwelling persons with late-onset dementia (Borsje et al., 2018). We found that in approximately 20% the cumulative score on the sub-syndrome psychosis was four or more, which is considered clinically relevant. Our baseline findings and the increase in antipsychotic prescriptions are more than expected, and it seems unlikely that the increase in antipsychotics is due to an increase in dementia severity. The cumulative use of antipsychotics was approximately 37% in the two-year follow-up which means that the number of participants using antipsychotics more than doubled (2.4 times) during our follow-up. Research in young-onset Alzheimer's dementia has shown no positive association of delusions, depression or anxiety with increasing dementia severity (Tanaka et al., 2015). Furthermore, we also found that the two-year dementia progression in the NeedYD cohort was limited to less than one point on the GDS (Gerritsen et al., 2018).

Depression or depressive symptoms are common in people with young-onset dementia, with prevalence rates of 65%, and sometimes they are one of the earliest symptoms of dementia (Draper & Withall, 2016; Rosness, Barca, & Engedal, 2010). This likely explains why approximately one in three people used antidepressants at baseline. However, we found no association between the Neuropsychiatric Inventory sub-syndrome affective symptoms score and psychotropic drug use, suggesting that antidepressants were not prescribed for persons with only depressive symptoms. Törmälehto et al. found that the use of antidepressants in home-dwelling people with late-onset Alzheimer's dementia was weakly correlated with the score on the Neuropsychiatric Inventory or the score on the depression scale that was used (Tormalehto, Martikainen, Bell, Hallikainen, & Koivisto, 2017). Research shows that antidepressants should have no place in people with dementia and mild or moderate depressive symptoms because this treatment shows little or no reduction in depressive symptoms and has little impact on activities in daily life (Banerjee et al., 2011; Dudas et al., 2018; Zuidema et al., 2018).

Persons with higher Neuropsychiatric Inventory sub-syndrome apathy scores received significantly fewer psychotropic drugs. However, the increase during the two-year follow-up was the same for them as it was for those with high scores on psychosis or affective symptoms. Contrary to our findings, Appelhof et al. found higher psychotropic drug use in institutionalized young persons with dementia and high neuropsychiatric symptoms apathy scores compared with those of persons with late-onset dementia (Appelhof et al., 2019). It remains unclear why these findings differ.

Each increasing year of age was associated with an approximately 7% higher chance of receiving psychotropic drugs at baseline, but also during the two-year follow-up (Table 5). This finding is consistent with the multivariate baseline analysis of Koopmans et al. (2014) on this cohort in which increase of one year of age was associated with a likelihood of 8% more psychotropic drug use. Studies concerning psychotropic drug use report more often on associations with disease progression, however, we found one study reporting a higher likelihood of the use of psychotropic drugs in older participants (Kester, Unutzer, Hogan, & Huang, 2017). Lornstad, Aaroen, Bergh, Benth, and Helvik (2019) found that younger age in late-onset dementia was related to a higher odds for persistant use of antipsychotics or antidepressants (Lornstad et al., 2019).

Dementia subtype showed no association with psychotropic drug use, as has also been found in late-onset dementia (Calvo-Perxas et al., 2012). It is known that caregivers of young people with dementia experience more distress due to neuropsychiatric symptoms in their care-dependent family member than do caregivers of elderly people with dementia. In addition, neuropsychiatric symptoms in people with young-onset dementia might have a greater impact due to stronger physically appearance, and therefore they are experienced as more threatening by caregivers, resulting in potentially prescribing psychotropic drugs in all dementia subtypes, as it is comprehensible that they ask the general practitioner for help (Arai, Matsumoto, Ikeda, & Arai, 2007). It is understandable that

general practitioners have little experience with psychological approaches to managing neuropsychiatric symptoms in dementia and even less experience with neuropsychiatric symptoms in people with young-onset dementia; therefore, general practitioners prescribe psychotropic drugs more easily (Mengelers et al., 2018). The Dutch general practitioners guideline for the management of dementia advises that psychosocial interventions are provided by a day-care or a mental health center, which means that one must be motivated to be referred to such establishments (Moll van Charante, Vernooij-Dassen, Boswijk, Stoffels, & Luning-Koster, 2012). Furthermore, the guideline advises the use of antipsychotics only in acute situations. In a double-blind placebo-controlled study in treating psychosis in elderly patients with Alzheimer's dementia, there was no significant difference between the treatment with quetiapine or haloperidol and placebo. Some effect was found for decreasing agitation on all three treatments but quetiapine showed a significant higher change compared with placebo (Tariot et al., 2006). Also a study on elderly patients with Alzheimer's dementia showed no benefit on depressive symptoms of sertraline or mirtazapine compared with placebo (Banerjee et al., 2011). The authors suggested to reconsider the use of these antidepressants because the increased risk of adverse events in using these drugs. This suggestion is subscribed by the Cochrane review of Dudas et al. (2018) who found that there is limited evidence to support the efficacy on antidepressants for the treatment of depression in people with dementia (Dudas et al., 2018). Self-management programs which have already shown effectiveness in caregivers of people with late-onset, early-stage dementia, might also help to support caregivers of people with young-onset dementia in the management of neuropsychiatric symptoms (Boots, de Vugt, Kempen, & Verhey, 2018).

Earlier findings in this cohort showed no negative effect of antipsychotic drug use on the course of memory loss or dementia severity but it is suggested that psychotropic drug use in young-onset nursing home residents, causes a decrease in the quality of life (Appelhof et al., 2017; Gerritsen et al., 2018). However, studies about the (negative) effects of psychotropic drug use in people with young-onset dementia are scarce. Moreover, we know that despite the newer generation antipsychotics, the risk of serious side effects remains present (Belvederi Murri et al., 2015).

In most countries there are limited opportunities for respite care in young-onset dementia, because most services for dementia care are not age appropriate or opening hours are inconvenient (Bakker et al., 2013b). Despite Dutch special day-care units, specialized memory clinics and a care standard, all helping in providing psychological or physically support for caregivers the use of psychotropic drugs remains substantial but it is assumed that the use was even more without these facilities.

Limitations

Some limitations of this study need to be discussed. We did not consider the indications for the prescription of psychotropic drug use, the dosages or the severity of symptoms such as genuine depressive disorder versus depressive symptoms at the time of prescription. We would have gained more insight if the relationship between indications and neuropsychiatric symptoms was known. Another limitation is the lack of information on psychotropic drug use between assessments, resulting in missing data regarding the initiation or ceasing of particular drugs. Consequently, this causes either an overestimation of continuous use or an underestimation of new-onset use. At last, regarding the analysis of the baseline GDS and Neuropsychiatric Inventory scores a possible issue might be that changes in those scores during follow-up could have resulted in different associations with psychotropic drug use. Concerning non-completers, they had significantly more advanced dementia than did completers. This could have influenced the outcome of psychotropic drug use. However, we did not find a difference in the Neuropsychiatric Inventory scores between completers and non-completers. Anti-dementia drugs can be used in people with dementia and problem behavior due to psychosis. However, this indication is limited to people with Lewy Body dementia experiencing psychosis or people with Parkinson related psychosis. Both categories were not included in this study, but it is unknown if some of the participants got anti-dementia drugs because of behavioral problems. Also, in 2007 and 2008 the years of baseline assessment in this cohort, the use of anti-dementia drugs for behavioral problems was not yet common in clinical practice (Campbell et al., 2008).

Conclusion

This study emphasizes that psychotropic drugs are often prescribed in community-dwelling persons with young-onset dementia and that these drugs are also used for prolonged periods of time, which is not in line with current guidelines. Therefore, more attention must be paid to following the guidelines and frequently evaluating the use of psychotropic drugs and discontinuing their use whenever possible (van der Spek et al., 2018).

The finding of this study that more than 50% of the people were using psychotropic drugs and that this use increased over time underscores the need to reduce psychotropic drug use in the home situation by having easily available psychosocial interventions.

We suggest further research on the side effects of psychotropic drug use in persons with young-onset dementia.

Indication, evaluation and therapy duration can be improved by introducing repeated medication reviews (Massot Mesquida et al., 2019; van der Spek et al., 2018). Perhaps this is also achievable for general practitioners in the treatment of young persons with dementia.

The development and evaluation of self-management programs for caregivers of people with young-onset dementia has to be promoted to investigate if caregivers of people with young-onset dementia also could benefit from such a program.

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