

REVIEW

Psychotropic drug prescriptions in Western European nursing homes

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ABSTRACT

Background: Despite the numerous warnings of European and national drug agencies as well as clinical guidelines since the year 2004, psychotropic drugs are still frequently used in dementia. A systematic review comparing the use of psychotropic drugs in nursing homes from different European countries is lacking.

Objective: The aim of this study was to examine prescription rates of psychotropic drug use in nursing home patients between different Western European countries since the first warnings were published.

Methods: A literature review was performed and the various psychotropic prescribing rates in European nursing homes were investigated. The prescription rates of antipsychotic and antidepressants were pooled per country. Other classes of psychotropic drugs could not be pooled because of the limited number of studies found.

Results: Thirty-seven studies on antipsychotic drug use and 27 studies on antidepressant drug use conducted in 12 different European countries. The antipsychotic use in nursing homes ranged from 12% to 59% and antidepressant use from 19% to 68%. The highest rates of antipsychotic drug prescription were found in Austria, Ireland, and Belgium while for antidepressants in Belgium, Sweden, and France.

Conclusions: Despite warnings about the side effects and recommendation to focus on non-pharmacological interventions, antipsychotics and antidepressants are commonly used drugs in nursing homes. The data suggest that Norway does best with regards having a low antipsychotic drug usage. Studies are needed to explain the differences between Norway and other European countries.

Key words: dementia, psychopharmacology, nursing homes

Introduction

In Europe, one in five elderly people with functional limitations receive long-term care in an institution (Onder *et al.*, 2012). More than half of these elderly are diagnosed with dementia (Lithgow *et al.*, 2012; Hoffmann *et al.*, 2014) and frequently suffer from some type of neuropsychiatric symptoms over the course of the disease (Steinberg *et al.*, 2008). Resulting challenging behaviors include verbal and physical aggression, agitation, psychotic symptoms, sleep disturbances, depression, oppositional behavior, and wandering (Brodaty and Arasaratnam,

2012). Currently, only few pharmacologic options are available for the management of neuropsychiatric symptoms. However, patients with dementia are regularly prescribed psychotropic drugs. The prescription numbers are striking (Wetzels *et al.*, 2011), taking into account the limited effectiveness of psychotropic drugs for the treatment of neuropsychiatric symptoms and the severe side effects experienced by this patient group (Zuidema *et al.*, 2006). These side effects include sedation, negative impact on (psycho) motor function – walking and swallowing, accelerated cognitive decline, and risk of falling. Most controversial is the treatment of neuropsychiatric symptoms with antipsychotics (Ballard *et al.*, 2009; Harding and Peel, 2013). Antipsychotics are associated with an increased risk of extrapyramidal effects, stroke, pneumonia, and death. Other psychotropic drugs

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such as antidepressants, anxiolytics, hypnotics, or anti-dementia drugs also have side effects and are therefore hardly a better alternative (Trinh *et al.*, 2003; Sink *et al.*, 2005). The prescription of psychotropic drugs in nursing homes is frequent (Wetzels *et al.*, 2011), even though the US Food and Drug Administration (FDA) published warnings and required changes to the prescribing information for risperidone already in 2003 (Banerjee, 2009). In 2004, the European Medicines Agency (EMA) also issued a public advice about an increased risk of cerebrovascular adverse events and mortality in elderly patients with dementia receiving olanzapine (Banerjee, 2009). These warnings by the EMA continued during the following years (European Medicines Agency, 2008; Ballard *et al.*, 2010). Also national drug agencies in the United Kingdom (UK), Italy, Spain, France, and other countries issued warnings about the increased risk of mortality associated with antipsychotics between 2004 and 2005 (Gallini *et al.*, 2014). Additionally, drug safety warnings have been published in some countries (Janssen-Cilag GmbH, 2004; Lilly Pharma, 2004). Furthermore, clinical practice guidelines in European countries recommend that psychological and social approaches should be the first treatment option of neuropsychiatric symptoms, followed by pharmacological recommendations as second-line treatment (Gauthier *et al.*, 2010; Azermi *et al.*, 2012). Since the warnings, there are several studies describing psychotropic drug use in parts of Europe but comparative studies across Europe are scarce (Foebel *et al.*, 2014). Studies have mainly been conducted on a national level to estimate the prescription rates of psychotropic drugs as for example in the Netherlands (Wetzels *et al.*, 2010). These data present a highly prevalent and persistent antipsychotic drug use (Wetzels *et al.*, 2010; van der Spek *et al.*, 2015). However, to our knowledge there is no systematic review comparing the use of psychotropic drugs in nursing homes from different Western European countries. A comparison of Western European data can highlight the countries in which a low prevalence of antipsychotic drugs already exists and therefore might serve as example for other countries on how to achieve lower prescription rates. We choose to limit our search for Western European countries (including Scandinavian countries), since it is expected that these countries are more comparable to each other. An earlier study already demonstrated substantial differences in prevalences of inappropriate medication use in nursing homes between Western and Eastern European countries (Fialová *et al.*, 2005). Therefore, including only Western European countries will lead to a more

straightforward comparison. The aim of this study was to examine prescription rates of psychotropic drug use in patients living in nursing homes between different Western European countries since the first warnings were published.

Method

A literature search was performed in Scopus, Pubmed, and Web of Science in October 2015. The search string included the following keywords: psychotropic, antipsychotics, antidepressants, anxiolytics, hypnotics, anti-dementia drugs, dementia/Alzheimer's, nursing home, country. A total of 19 Western European countries were used in the search string. Several database features such as truncation, proximity operators, and phrase searching were used (if available in the search engine) to increase the relevancy of retrieval of the free text search. The search was limited to abstracts published between January 2004 and October 2015. Abstracts, titles, and where necessary the whole paper was screened by the author (SJ) for the following inclusion criterion: living in a nursing home, data collection took place after 2003. Studies in which patients were selected on certain disease characteristics, such as specific target groups (e.g. patients with a depression), were excluded.

Data extraction

Information from the studies was extracted on country, study methods, year, inclusion criteria, and number of participants. The data about psychotropic drug use from cross-sectional and longitudinal studies was extracted. The "pro re nata" use was not included. From the longitudinal (cohort and interventional studies), the first measurement (baseline assessment) was used for the analysis. Psychotropic drugs were divided into the groups of known antipsychotics, antidepressants, anxiolytics, hypnotics, anti-dementia agents according to the Anatomical Therapeutic Classification (ATC) (World Health Organization, 2015). Besides the psychotropic drug, patient characteristics, as described in the papers, were acquired. This was done in order to see whether the samples from the various studies were similar.

Data analysis

The authors tabulated the study design, place, outcomes, and results. Drug prescription rates were pooled by country. Therefore, a meta-analysis of prevalence was undertaken for binary

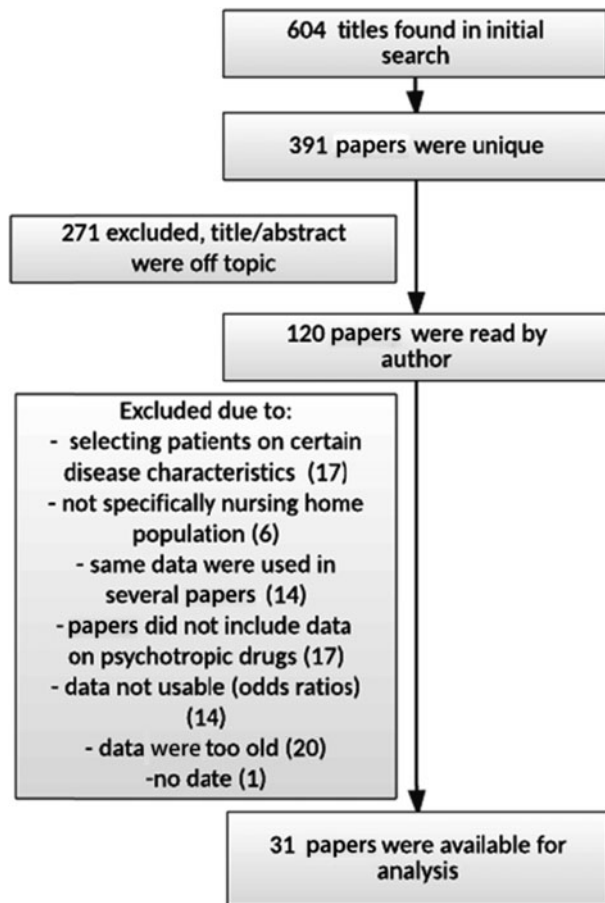


Figure 1. Search results.

outcomes. Proportions were subjected to a double arcsine transformation to stabilize the variance, following the recommendations of Barendregt *et al.* (Barendregt *et al.*, 2013). Pooled percentages and 95% confidence intervals from the selected studies are graphed by drug. The relationship between antipsychotic and antidepressant drug use was examined by computing the correlation coefficient. The study period is extracted from the papers and is averaged for the period over which the (baseline) data were collected. All analyses were carried out using the IBM SPSS Statistics 22 and Excel 2013.

Results

The process of selecting papers for the review is illustrated in Figure 1. The literature search yielded 604 hits of which 390 papers were unique. These abstracts were read by the author (SJ). Of these 390 unique studies, 276 were excluded because the title/abstract indicated it to be off-topic. Of the remaining 114 papers, 17 papers selected patients on certain disease characteristics and were therefore excluded. In six papers, the authors

did not differentiate between people living in the community or nursing homes. Fourteen papers were excluded because the data were previously reported and subsequently used in several papers. Another 17 papers were excluded because they did not have data on psychotropic drug prevalence. Furthermore, 20 papers needed to be excluded because data collection took place before 2003. One paper was excluded because the authors did not mention the year of data collection. Finally, a total of 31 papers were available for analysis. Three papers contained data on more than one country and there are considered as individual studies.

Initially, we searched for all psychotropic drugs. However, more than half of the relevant papers did not provide any data regarding anxiolytics, hypnotics, or anti-dementia drugs. Due to the amount of missing data, these drug groups were not further analyzed. However, 38 studies had data on antipsychotic drug use and 28 studies on antidepressant drug use. These data were analyzed further.

Description of the studies

The selected studies were conducted in Norway (eight studies) (Barca *et al.*, 2010; Testad *et al.*, 2010; Bergh *et al.*, 2011; Husebo *et al.*, 2011; Helvik *et al.*, 2014; Iden *et al.*, 2014; Mjørud *et al.*, 2014; Borza *et al.*, 2015), Germany (six studies) (Kuske *et al.*, 2009; Majic *et al.*, 2010; Richter *et al.*, 2012; Hundertmark, 2013; de Mauleon *et al.*, 2014), Sweden (five studies) (Johnell and Fastbom, 2012; Gustafsson *et al.*, 2013a; Gustafsson *et al.*, 2013b; de Mauleon *et al.*, 2014; Midlov *et al.*, 2014), the Netherlands (five studies) (Eggermont *et al.*, 2009; Wetzels *et al.*, 2010; Volicer *et al.*, 2013; de Mauleon *et al.*, 2014; Zwijsen *et al.*, 2014), France (four studies) (Rolland *et al.*, 2009; Cool *et al.*, 2014; de Mauleon *et al.*, 2014; Laffon de Mazieres *et al.*, 2015), UK (four studies) (Testad *et al.*, 2010; Shah *et al.*, 2011; de Mauleon *et al.*, 2014; Stewart *et al.*, 2014), Finland (two studies) (de Mauleon *et al.*, 2014; Pitkala *et al.*, 2015), Austria (two studies) (Testad *et al.*, 2010; Richter *et al.*, 2012), Spain (two studies) (Olazaran *et al.*, 2013; de Mauleon *et al.*, 2014), Ireland (one study) (Barry *et al.*, 2015), Belgium (one study) (Bourgeois *et al.*, 2012), and Italy (one study) (Toscani *et al.*, 2013). Of these studies, 17 were cross-sectional. These studies collected their data from national databases or via surveys. Furthermore, the data of eight studies were extracted from the baseline measurement of intervention studies or randomized controlled

trials. The remaining 16 studies were cohort studies. The study population in the 41 studies consisted of nursing home residents with a mean age of 84 years (SD 2), of which 73% are female (SD 5.7). The sample sizes varied considerably between studies from $N = 38$ to $N = 86,721$ participants. The mean number of participants in these studies was 3,109 (SD 13,466).

The studies differed regarding to the selection of patients. In 17 studies, there was no selection of cognitively impaired nursing home residents. The remaining 24 studies, however, included only patients with the diagnosis of dementia. In those studies, dementia was diagnosed by a physician/expert assessment (Husebo *et al.*, 2011; Wetzels *et al.*, 2011; de Mauleon *et al.*, 2014; Zwijsen *et al.*, 2014; Barry *et al.*, 2015), notes in patient files (Eggermont *et al.*, 2009; Hundertmark, 2013), or various scales. The Clinical Dementia Rating scale was used by four studies to determine the prevalence of dementia in the patients (Kuske *et al.*, 2009; Testad *et al.*, 2010; Bergh *et al.*, 2011; Helvik *et al.*, 2014) and the Gottfries' Scale in two Swedish studies (Gustafsson *et al.*, 2013a; Gustafsson *et al.*, 2013b). Other studies used the German version of the Mini-Mental State Examination (MMSE) to confirm the existing medical diagnosis (Majic *et al.*, 2010), the Cognitive Performance Scale (CPS) (Volicer *et al.*, 2013), the Functional assessment staging (FAST) (Testad *et al.*, 2010; Toscani *et al.*, 2013), and the Global Deterioration Scale (GDS) (Testad *et al.*, 2010; Wetzels *et al.*, 2010) to select patients with dementia.

Comparison between European countries

The pooled percentage of antipsychotic use was 27% (95% CI 27–28) and the pooled percentage of antidepressant use was 40% (95% CI 40–41) of the study population. The antipsychotic use in nursing homes ranged from 12% to 59% and antidepressants from 19% to 68% (see Table 1). The highest use of antipsychotics was found in Austria, Ireland, and Belgium while Belgium, Sweden, and France showed highest use of antidepressants (see Table 2). In the selected group of studies with dementia patients only, the highest antipsychotic drug use was prescribed in Spain, Austria, and Germany (see Figure 2). In the mixed group, the highest ranking countries are Belgium, Sweden, and France. In the selected group of studies with dementia patients only, the highest antidepressant drug use was prescribed in Sweden, Ireland, and Norway (see Figure 3). In the mixed group, the highest ranking countries are Belgium, Sweden, and France.

A Pearson correlation coefficient was computed to assess the relationship between antipsychotic and antidepressant drug use in studies selecting patients with dementia. Although there was a slight negative correlation between the two drugs for studies selecting patients with dementia visible of $r = -0.2$ ($N = 13$), no statistically significant correlation between the two drugs was observed. In studies selecting nursing home patients, no significant correlation between the two drugs was seen either ($r = -0.1$, $N = 11$, $p = ns$).

Discussion

In this systematic review, we compared the differences in prescribing rates of antipsychotic and antidepressant drugs between Western European countries. The highest rates of antipsychotic drug prescription were found in Austria, Ireland, and Belgium while the highest rates for antidepressants were seen in Belgium, Sweden, and France.

This study gives interesting insights in the antipsychotic and antidepressant drug use between European countries. Especially since we differentiate between studies including nursing home patients in general and studies including patients with dementia. Unlike other countries, Norway has a relatively low antipsychotic drug use for studies selecting dementia patients and studies with a mixed population. Whereas Sweden has a high antipsychotic and antidepressant drug use when one looks at the studies including nursing home patients. This is surprising, since its overall antipsychotic drugs use is one of the lowest in Europe for patients suffering from dementia. Altogether, Norway and Sweden had a relatively low antipsychotic drug use for studies selecting dementia patients.

Overall, large differences between countries and between studies were found. Differences between countries with regards to the care organization could explain the differences in drug use. For example, the Dutch situation in nursing homes differs from similar institutions in other European countries. Dutch nursing homes have more expertise since only specialists in elderly care medicine are responsible for the medical treatment (Schols *et al.*, 2004). Due to this expertise, patients are more likely to receive extended medical treatment in the nursing homes instead of being transferred to hospitals (Houttekier *et al.*, 2010). Therefore, the Dutch nursing home population might differ from other European countries. Additionally, European variation of physicians prescribing habits can be related to the presence of accessibility, financial incentives, and the effect

Table 1. Description of the studies included

	STUDY, YEAR (LOCATION)	STUDY PERIOD (AVERAGE)	METHOD	INCLUSION CRITERIA	N	MEAN AGE (SD)	FEMALE %	ANTI- PSYCHOTIC (%)	ANTI- DEPRESSANT (%)	PATIENT GROUP	DEMENTIA RATING
1.	De Mauleon <i>et al.</i> (2014) (Germany)	2011	Cohort	≥65 years old, living in nursing home between 1–3 months, diagnosis of dementia, MMSE ≤24	119	84*	74*	47.1		Patients with dementia	Diagnosis of dementia by expert assessment
2.	Hundertmark (2013) (Germany)	2009	Cross- sectional	ability to communicate	74	82	68	47.3	35.1	Patients with dementia	Chart diagnosis
3.	Richter <i>et al.</i> (2012) (Germany)	2004	Cross- sectional	≥70 years old, ability to walk, living in the nursing home for ≥ 3 months	2,367	86	81	28.4	20.1	Nursing home patients	–
4.	Richter <i>et al.</i> (2012) (Germany)	2005	Intervention	living in nursing home	1,125	87	85	28.4	20.4	Nursing home patients	–
5.	Majic <i>et al.</i> (2010) (Germany)	2009	Cross- sectional	Clinical dementia rating, MMSE, living in nursing home	304	82	71	52.3	30.3	Patients with dementia	MMSE with a threshold value of ≤ 24 to confirm the existing medical diagnosis
6.	Kuske <i>et al.</i> (2009) (Germany)	2005	Intervention	diagnosis of dementia with a Clinical Dementia Rating Scale ≥ 1	210	81	76	30.0		Patients with dementia	CDR
7.	De Mauleon <i>et al.</i> (2014) (UK)	2011	Cohort	≥65 years old, living in nursing home between 1–3 months, diagnosis of dementia, MMSE ≤24	76	84*	74*	32.9		Patients with dementia	Diagnosis of dementia by expert assessment

Table 1. Continued

	STUDY, YEAR (LOCATION)	STUDY PERIOD (AVERAGE)	METHOD	INCLUSION CRITERIA	N	MEAN AGE (SD)	FEMALE %	ANTI- PSYCHOTIC (%)	ANTI- DEPRESSANT (%)	PATIENT GROUP	DEMENTIA RATING
8.	Stewart <i>et al.</i> (2014) (UK)	2011	Cross-sectional	Living in nursing home ≥ 2 weeks	301	84	66	19.9	32.6	Nursing home patients	–
9.	Shah <i>et al.</i> (2011) (UK)	2008	Cross-sectional	≥ 65 years old	4,269	85	74	21.7		Nursing home patients	–
10.	Testad <i>et al.</i> (2010) (UK)	2004	Intervention	Dementia according to CDR	302	81	37	48.0	28.8	Patients with dementia	CDR
11.	De Mauleon <i>et al.</i> (2014) (Sweden)	2011	Cohort	≥ 65 years old, living in nursing home between 1–3 months, diagnosis of dementia, MMSE ≤ 24	84	84*	74*	11.9		Patients with dementia	Diagnosis of dementia by expert assessment
12.	Midlov <i>et al.</i> (2014) (Sweden)	2008	Cohort	≥ 65 years old, living in nursing home, without language difficulties	177	84	71	49.7		Patients with dementia	Chart diagnosis
13.	Gustafsson <i>et al.</i> (2013a) (Sweden)	12–2005	Intervention	living in nursing home	344	82	71	38.4	52.3	Nursing home patients	–
14.	Gustafsson <i>et al.</i> (2013b) (Sweden)	2007	Cross-sectional	≥ 65 years old, dementia according to Gottfries' cognitive scale score of less 24 points	2019	85	70	25.5	49.1	Patients with dementia	Gottfries scale
15.	Johnell and Fastbom (2012) (Sweden)	2008	Cross-sectional	≥ 65 years old, living in nursing home	86,721	86	70		43.9	Nursing home patients	–
16.	Borza <i>et al.</i> (2015) (Norway)	2004	Cohort	≥ 50 years old, living in nursing home ≥ 2 weeks	1,158	85	73		38.1	Nursing home patients	–
17.	Mjørud <i>et al.</i> (2014) (Norway)	2011	Cohort	Living in nursing home ≥ 4 weeks, not terminally ill	198	87	79	14.6	67.7	Nursing home patients	–

Table 1. Continued

	STUDY, YEAR (LOCATION)	STUDY PERIOD (AVERAGE)	METHOD	INCLUSION CRITERIA	N	MEAN AGE (SD)	FEMALE %	ANTI- PSYCHOTIC (%)	ANTI- DEPRESSANT (%)	PATIENT GROUP	DEMENTIA RATING
18.	Helvik <i>et al.</i> (2014) (Norway)	2004	Cohort	Living in nursing home ≥ 2 weeks, Clinical Dementia Rating scale ≥ 1	932	85	74	25.9	39.1	Patients with dementia	CDR
19.	Iden <i>et al.</i> (2014) (Norway)	2011	Cohort	recently admitted patients (a stay shorter than 3 months) to LTC, having an expected lifetime longer than 3 months	88	87	59		34.3	Nursing home patients	–
20.	Husebo <i>et al.</i> (2011) (Norway)	2009	Intervention	≥ 65 years old, dementia according Diagnostic and Statistical Manual of Mental Disorders (4 th edition) clinically relevant behavioral disturbances	177	87	74	27.0		Patients with dementia	Diagnosis of dementia
21.	Bergh <i>et al.</i> (2011) (Norway)	2009	Cohort	dementia defined as a Clinical Dementia Rating scale > 0.5	169	85	69	21.9	42.6	Patients with dementia	CDR
22.	Testad <i>et al.</i> (2010) (Norway)	2004	Intervention	Dementia according to FAST	163	86	72	19.0	45.5	Patients with dementia	FAST
23.	Barca <i>et al.</i> (2010) (Norway)	2005	Cohort	Living in nursing home ≥ 2 weeks	872	85	74	20.9	37.9	Nursing home patients	–
24.	Laffon de Maziere <i>et al.</i> (2015) (France)	2011	Cross-sectional	Living in nursing home	6,275	84	74	24.4		Nursing home patients	–
25.	Cool <i>et al.</i> (2014) (France)	2011	Cross-sectional	not terminally ill	974	86	72	26.5	43.1	Nursing home patients	–

Table 1. Continued

	STUDY, YEAR (LOCATION)	STUDY PERIOD (AVERAGE)	METHOD	INCLUSION CRITERIA	N	MEAN AGE (SD)	FEMALE %	ANTI- PSYCHOTIC (%)	ANTI- DEPRESSANT (%)	PATIENT GROUP	DEMENTIA RATING
26.	De Mauleon <i>et al.</i> (2014) (France)	2011	Cohort	≥65 years, living in nursing home between 1–3 months, diagnosis of dementia, MMSE ≤24	49	84*	74*	26.5		Patients with dementia	Diagnosis of dementia by expert assessment
27.	Rolland <i>et al.</i> (2009) (France)	2008	Cross- sectional	Living in nursing home	4,896	86	74	27.5		Nursing home patients	–
28.	Pitkala <i>et al.</i> (2015) (Finland)	2011	Cross- sectional	≥65 years old	1,576	85	77	27.8	42.1	Nursing home patients	–
29.	De Mauleon <i>et al.</i> (2014) (Finland)	2011	Cohort	≥65 years old, living in nursing home between 1–3 months, diagnosis of dementia, MMSE ≤24	122	84*	74*	29.5		Patients with dementia	Diagnosis of dementia by expert assessment
30.	Barry <i>et al.</i> (2015) (Ireland)	2011	Cross- sectional	living in nursing home ≥4 weeks, diagnosis of dementia	42	82	57	38.1	40.5	Patients with dementia	Diagnosis of dementia
31.	De Mauleon <i>et al.</i> (2014) (Spain)	2011	Cohort	≥65 years old, living in nursing home between 1–3 months, diagnosis of dementia, MMSE ≤24	113	84*	74*	54.0		Patients with dementia	Diagnosis of dementia by expert assessment
32.	Olazaran <i>et al.</i> (2013) (Spain)	2011	Cross- sectional	living in nursing home	4,502	84	73	25.4	18.6	Nursing home patients	–
33.	Richter <i>et al.</i> (2012) (Austria)	2007	Cross- sectional	≥70 years old, living in nursing home ≥3 months	1,844	81	73	45.9	36.8	Nursing home patients	–
34.	Testad <i>et al.</i> (2010) (Austria)	2004	Intervention	Dementia according to GDS	38	81	74	52.6	31.6	Patients with dementia	GDS

Table 1. Continued

	STUDY, YEAR (LOCATION)	STUDY PERIOD (AVERAGE)	METHOD	INCLUSION CRITERIA	N	MEAN AGE (SD)	FEMALE %	ANTI- PSYCHOTIC (%)	ANTI- DEPRESSANT (%)	PATIENT GROUP	DEMENTIA RATING
35.	Bourgeois <i>et al.</i> (2012) (Belgium)	2005	Cross-sectional	living in nursing home	1,730	85	78	32.9	49.5	Nursing home patients	–
36.	De Mauleon <i>et al.</i> (2014) (the Netherlands)	2011	Cohort	≥65 years old, living in nursing home between 1–3 months, diagnosis of dementia, MMSE ≤24	113	84*	74*	35.4		Patients with dementia	Diagnosis of dementia by expert assessment
37.	Volicer <i>et al.</i> (2013) (the Netherlands)	2009	Cross-sectional	≥65 years old, CPS score of least 1, assessment performed at least 3 months after admission	1,562	84	71	30.7		Patients with dementia	CPS
38.	Wetzels <i>et al.</i> (2010) (the Netherlands)	2006	Cohort	living in nursing home ≥4 weeks, Diagnosed with (DSM-IV) criteria by the nursing home physician, no life-threatening diseases at the moment of inclusion	290	84	78	32.0	25.0	Patients with dementia	Diagnosis of dementia, first author checked eligibility and diagnosis of all participants
39.	Zwijzen <i>et al.</i> (2014) (the Netherlands)	2011	Intervention	Living in nursing home, dementia diagnosis	659	84	70	27.9	32.2	Patients with dementia	Diagnoses of dementia

Table 1. Continued

	STUDY, YEAR (LOCATION)	STUDY PERIOD (AVERAGE)	METHOD	INCLUSION CRITERIA	N	MEAN AGE (SD)	FEMALE %	ANTI- PSYCHOTIC (%)	ANTI- DEPRESSANT (%)	PATIENT GROUP	DEMENTIA RATING
40.	Eggermont <i>et al.</i> (2009) (the Netherlands)	2005	Cross- sectional	≥70 years old, diagnosis of dementia or presence of cognitive impairment reported in medical chart, MMSE score between 10–24, without acute psychiatric disorders	206	85	87	21.4	18.9	Patients with dementia	Diagnosis of dementia or presence of cognitive impairment reported in the medical chart
41.	Toscani <i>et al.</i> (2013) (Italy)	2008	Cohort	living in nursing home, FAST score ≥7, expected survival ≥2 weeks according to primary doctor's clinical judgment	245	85	87	29.8	20.8	Patients with dementia	FAST

*Mean age and Gender only published for the total study population and not per country.

Table 2. Antipsychotic and antidepressant drug use per country (number of studies, pooled percentage, 95% confidence intervals)

	ANTIPSYCHOTIC DRUG USE						ANTIDEPRESSANT DRUG USE					
	ALL STUDIES		STUDIES WITH DEMENTIA ONLY		STUDIES WITH MIXED SAMPLE		ALL STUDIES		STUDIES WITH DEMENTIA ONLY		STUDIES WITH MIXED SAMPLE	
	N	POOLED % (95% CIs)	N	POOLED % (95% CIs)	N	POOLED % (95% CIs)	N	POOLED % (95% CIs)	N	POOLED % (95% CIs)	N	POOLED % (95% CIs)
Germany	6	31 (29–32)	4	45 (41–49)	2	28 (27–30)	4	21 (20–22)	2	30 (26–35)	2	20 (19–21)
UK	3	31 (30–33)	2	43 (38–48)	2	21 (20–23)	2	30 (27–34)	1	28 (23–34)	1	32 (27–37)
Sweden	4	28 (26–29)	3	26 (24–28)	1	37 (32–43)	3	43 (42–43)	2	47 (45–50)	1	43 (42–43)
Norway	7	25 (24–26)	4	24 (22–27)	3	21 (19–24)	6	39 (38–41)	3	39 (37–42)	3	39 (37–41)
France	4	25 (25–26)	1	26 (14–38)	3	25 (25–26)	1	42 (39–45)	–	–	1	42 (39–45)
Finland	2	27 (25–30)	1	29 (21–37)	1	27 (25–30)	1	41 (39–43)	–	–	1	41 (39–43)
Austria	2	45 (42–47)	1	49 (33–65)	1	44 (42–47)	2	36 (34–38)	1	30 (16–46)	1	36 (34–38)
Belgium	1	32 (30–35)	–	–	1	32 (30–35)	1	48 (45–50)	–	–	1	48 (45–50)
Spain	2	26 (24–27)	1	51 (42–61)	1	25 (24–26)	1	18 (17–20)	–	–	1	18 (17–20)
Ireland	1	36 (22–51)	1	36 (22–51)	–	–	1	29 (24–54)	1	39 (24–54)	–	–
The Nether-lands	5	29 (27–31)	5	29 (27–31)	–	–	4	27 (25–30)	4	27 (25–30)	–	–
Italy	1	29 (24–35)	1	29 (24–35)	–	–	1	21 (16–26)	1	20 (16–26)	–	–

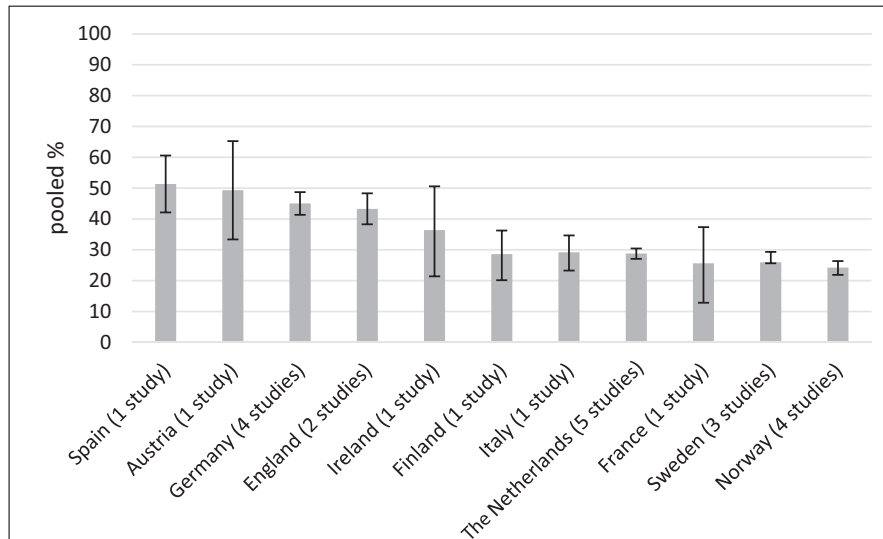


Figure 2. Comparison of the pooled percentages of patients prescribed antipsychotics between European countries of studies selecting patients with dementia.

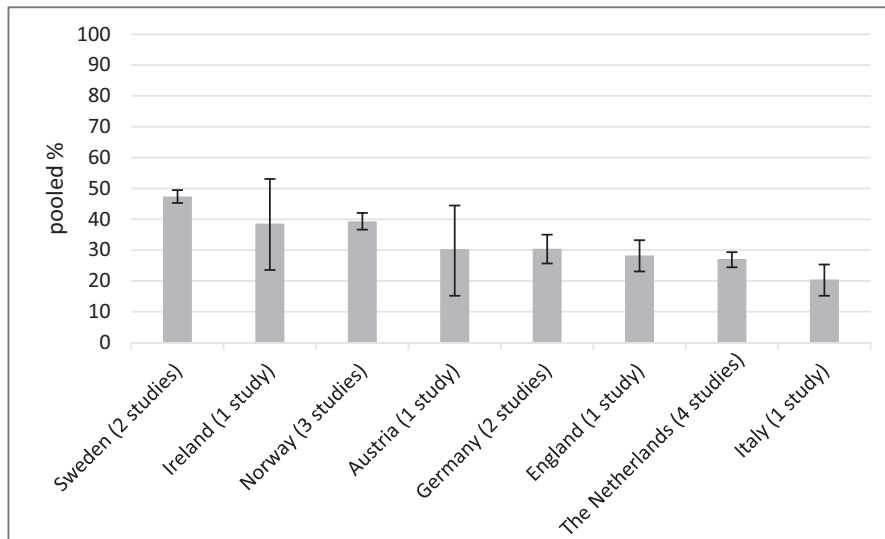


Figure 3. Comparison of the pooled percentages of patients prescribed antidepressants between European countries of studies selecting patients with dementia.

of culture (Sturm *et al.*, 2007). In our search, we did not use age as a criterion; therefore, the population of patients might not be elderly in all cases, but it might increase the chance that the results mirror the actual nursing home population better. Differences between studies could also be explained by differences between nursing homes. The existence of considerable variation in the antipsychotic drug use between various nursing homes in the Netherlands was already found by Kleijer (Kleijer *et al.*, 2014). In his study, Kleijer found an even larger variability of antipsychotic drug prescription (5%–52%) compared to our results. He demonstrated that variability was related to nursing home characteristics rather

than differences in prevalence of neuropsychiatric symptoms among these facilities. This indicates differences in institutional prescribing cultures.

In parallel to the strengths of the study, such as the fairly large sample size of most studies and the representation of nursing home populations of 12 countries, there are several limitations which need to be considered when interpreting the findings. First, the studies have different inclusion criteria and do not always provide a comprehensive overview of important patient characteristics of behavior, stage dementia, and cognition. Therefore, the groups might differ. Differences in patient characteristics might explain the differences in antipsychotic and antidepressant

drug use. In addition, there could be a selection at the ward level, since wards participating in research are not randomly chosen. Chances are that wards with low use are more eager to join cohort or cross-sectional studies, since they do not expect a lot of intervention to lower psychotropic drug prescription. Therefore, in intervention studies, wards participate who expect a lot of the intervention and have a somewhat higher psychotropic drug use at baseline. It is unclear whether this plays a big role. Second, due to the differences in study designs the sample sizes in the studies reviewed vary widely. Our results may include rates of individual nursing homes or rates across several facilities. Therefore, our results might be exaggerate individual organizational practices rather than representing an individual country. Third, most of the studies did not differentiate between subgroups of antipsychotics and antidepressants. For instance, no data are provided about the frequency of typical and atypical antipsychotics. A cross-European comparison would have been interesting because recommendations in national guidelines to use (a)typical antipsychotics are different.

Psychotropic drugs are commonly used drugs in nursing homes, even though the use of these drugs is continuously discussed. The EMA as well as several clinical guidelines warn about adverse events for several psychotropic drugs for years. From these reports, one can expect that physicians working in nursing homes consciously try to reduce psychotropic drugs. However, this study showed that at least antipsychotics and antidepressants are widely used. Others have already shown that warnings of international drug authorities on antipsychotic drug use in dementia patients do not impact overall prescription behavior (Schulze *et al.*, 2013). It has been suggested that evidence-based guidelines are not considered as adequate for daily practice by physicians (McCleery and Fox, 2012). Therefore, more practice-based recommendations for appropriate drug prescription are needed to lower the high antipsychotic drug use, such as the one recently developed practice guidelines for antipsychotic drug use (Zuidema *et al.*, 2015). Further studies are also required to identify the best strategies to implement these recommendations in order to reduce psychotropic drugs in nursing homes. Additionally, due to the limited information about the patient characteristics in the studies found, we could not thoroughly explain the differences seen between European countries. The studies from Sweden and Norway had a lower antipsychotic drug use; however, no significant association was found. Therefore, more studies are needed to explain the differences between this

Nordic countries and other Western European countries.

Conflict of interest

None.

Description of the authors' roles

SJ designed the study and developed the search protocol with input from JvM and SZ. SJ conducted the review. SJ extracted and analyzed the data under supervision of JvM and SZ. SJ drafted the paper. JvM, SZ, and MIJ commented on the drafts and advised in various stages of the research. All authors have been involved in drafting the paper critically for important intellectual content, and have given final approval of the version to be published.

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