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ORIGINAL RESEARCH ARTICLE

Opioid Use After Hospital Care due to Hip Fracture Among Community-Dwelling Persons With and Without Alzheimer's Disease

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Abstract

Background Hip fractures are common among persons with Alzheimer's disease (AD), but problems in pain assessment may lead to insufficient analgesia after hospitalization.

Objective We investigated the prevalence of opioid use in the 6 months after discharge from hospital care due to hip fracture among community-dwellers with and without AD.

Setting and method The Medication use and Alzheimer's disease (MEDALZ) cohort was used for this study, consisting of all community-dwelling persons newly diagnosed with AD during 2005–2011 in Finland and their comparison persons without AD matched on age, sex, and region of residence at the time of AD diagnosis. Data were collected from nationwide healthcare registers.

Main outcome measures We investigated opioid use versus non-use in persons with and without AD in the 6 months after discharge from hospital care due to hip fracture.

Results Altogether 2342 persons with AD and 1615 persons without AD, discharged to community settings within ≤ 120 days after a hip fracture, were included. A higher percentage of persons with AD used opioids compared to those without AD, 39.5% [95% confidence interval (CI) 37.5–41.5] versus 31.2% (95% CI 28.9–33.5). Persons with AD used more frequently strong opioids during the first 3 months and buprenorphine during the 6-month period, and used weak opioids less frequently after the first month after discharge compared to those without AD.

Conclusions Frequent opioid use after hospital care due to hip fracture may indicate increased attention to pain among persons with AD. Nevertheless, the benefits and harms of opioid use should be evaluated regularly in community-dwelling older persons.

Key Points

Persons with Alzheimer's disease used opioids more frequently than persons without Alzheimer's disease after hospital discharge after hip fracture.

Pain and need for opioid use should be evaluated regularly after hospital care.

During opioid use, careful monitoring of the adverse effects and events of opioids is needed.

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1 Introduction

Alzheimer's disease (AD) is the most common cognitive disorder and is increasing in prevalence globally as the population ages [1]. One key aspect of health among persons with AD is falls and subsequent fractures. Persons with AD are at a high risk of falling and have a two- to threefold increased risk of hip fracture compared to those without AD [2, 3].

Aphasia and decline of cognitive functioning in AD lead to difficulties in expressing pain verbally, and therefore, the assessment and management of pain may be challenging [4]. In addition, pain can be a contributory cause to neuropsychiatric symptoms, such as aggression and agitation [5], and also for delirium [6]. Previously, suspicions of inadequate pain treatment in persons with AD and other dementias have been raised, as findings of less frequent analgesic use compare to other older adults have been common [7–10]. However, more recent studies indicate more frequent use of paracetamol, but less frequent use of nonsteroidal anti-inflammatory drugs (NSAIDs) among community dwellers with cognitive disorders compared to other older adults [11, 12]. Reports on opioid use have been more inconsistent, but a higher prevalence of opioid use, strong opioid use, and long-term opioid use have also been found among persons with cognitive disorders compared to those without [12–16].

Previous studies have also reported less opioid use after a hip fracture in hospital care among persons with dementia compared to other hip-fracture patients [8, 15, 17–19]. In the days following the fracture, opioids have been used by more than 70% of people with and without dementia [15], but by fewer and at lower doses in those with dementia [8, 15, 17]. However, among older adults with a hip fracture, pain is still experienced by 42% until 4 months and by 13–25% until 1 year [20, 21]. Among the population in general, opioid use can be frequent even a year after hip fracture surgery [22]. To our knowledge, there are no previous studies describing the use of opioids after discharge to community settings among hip-fracture patients with cognitive disorders.

1.1 Aim of the Study

The aim of this study was to investigate the prevalence of opioid use in the 6 months after discharge from hospital care due to hip fracture among community-dwelling persons with and without AD.

1.2 Ethics Approval

All data from the registers were pseudonymized prior to being submitted to the research group. Participants were not contacted in any way, and according to Finnish legislation, ethics committee approval was therefore not required. The study protocol was approved by the register maintainers [the Social Insurance Institution of Finland (SII), Statistics Finland, and the National Institute of Health and Welfare].

2 Method

This study is part of the nationwide, register-based Medication use and Alzheimer's disease (MEDALZ) cohort. The cohort contains all community-dwelling persons who received a clinically verified diagnosis of AD during 2005–2011 in Finland ($N = 70{,}718$). For each person with AD, a comparison person without AD was matched on age, sex, and region of residence at the time of AD diagnosis ($N = 70{,}718$). The MEDALZ cohort has been described in more detail elsewhere [23].

The MEDALZ cohort contains data from several nationwide healthcare registers [the Prescription Register (1995–2015), Special Reimbursement Register (1972–2015), and Hospital Discharge Register (1972–2015)] and data on socioeconomic position from Statistics Finland [24–26]. Persons with AD were identified from the Special Reimbursement Register maintained by the SII. The register contains data on all persons who are eligible for special reimbursements for drugs for chronic illnesses, including AD. Reimbursement for antidementia drugs requires an AD diagnosis based on the National Institute of Neurological and Communicative Diseases and Stroke/Alzheimer's Disease and Related Disorders Association (NINCDS-ADRDA) [27] and Diagnostic and Statistical Manual of Mental Disorders 4th edition (DSM-IV) criteria [28], including a computed tomography or magnetic resonance imaging scan, and confirmation of the diagnosis by a neurologist or a geriatrician. A certificate of the fulfillment of the diagnostic criteria is submitted to the SII, where an expert in this field grants the special reimbursement if the criteria are met. Finnish national guidelines recommend treating all persons with AD with antidementia drugs unless specifically contraindicated [29]. Reimbursement is granted to persons with mild-to-moderate AD, but is not withdrawn when the disease progresses.

For this study, persons having a hip fracture after AD diagnoses/corresponding matching date between January 1, 2011 and until June 30, 2015 were identified. We collected data on hip fractures from the national Hospital Discharge Register, based on the International Classification of Diseases (ICD), with the following ICD-10 codes: S72.0 (fracture neck of femur), S72.1 (peritrochanteric fracture), and S72.2 (subtrochanteric fracture). Persons with a previous hip fracture were identified with the corresponding ICD-8 and ICD-9 codes, and they were excluded to restrict analyses to incident cases. The positive predictive value (PPV) for AD

diagnoses is 97.1 [30], and the PPV for hip fracture is 98 [31].

As the purpose was to investigate opioid use after discharge from hospital care, persons who died during continuous hospital care or within 3 days after discharge were excluded. To ensure follow-up for potential opioid use in outpatient care, further exclusions were made: we excluded persons who were still in hospital care (any hospital care, including acute care hospitals and community hospitals providing rehabilitation) 120 days after hip fracture, those who had less than 10 days of follow-up after discharge, and those who did not purchase any drugs within 60 days after discharge, which was considered as an indicator of institutionalization. Exclusions are described in detail in Fig. 1.

The follow-up in this study was divided into two parts. A pre-fracture period covered 6 months before a hip fracture and a post-discharge period covered 6 months after discharge from hospital care after a hip fracture (Fig. 2a). Between these pre-fracture and post-discharge periods was time spent in hospital care (including surgical care and rehabilitation), during which drug use is not recorded in the Prescription Register and, thus, cannot be assessed in this study. The follow-up in the post-discharge period ended on death, end of the follow-up (December 31, 2015), and, for comparison persons, if they were diagnosed with AD, whichever came first.

Drug use was obtained from the Prescription Register, which includes data on all reimbursed prescription drug purchases from Finnish pharmacies. In Finland, opioids

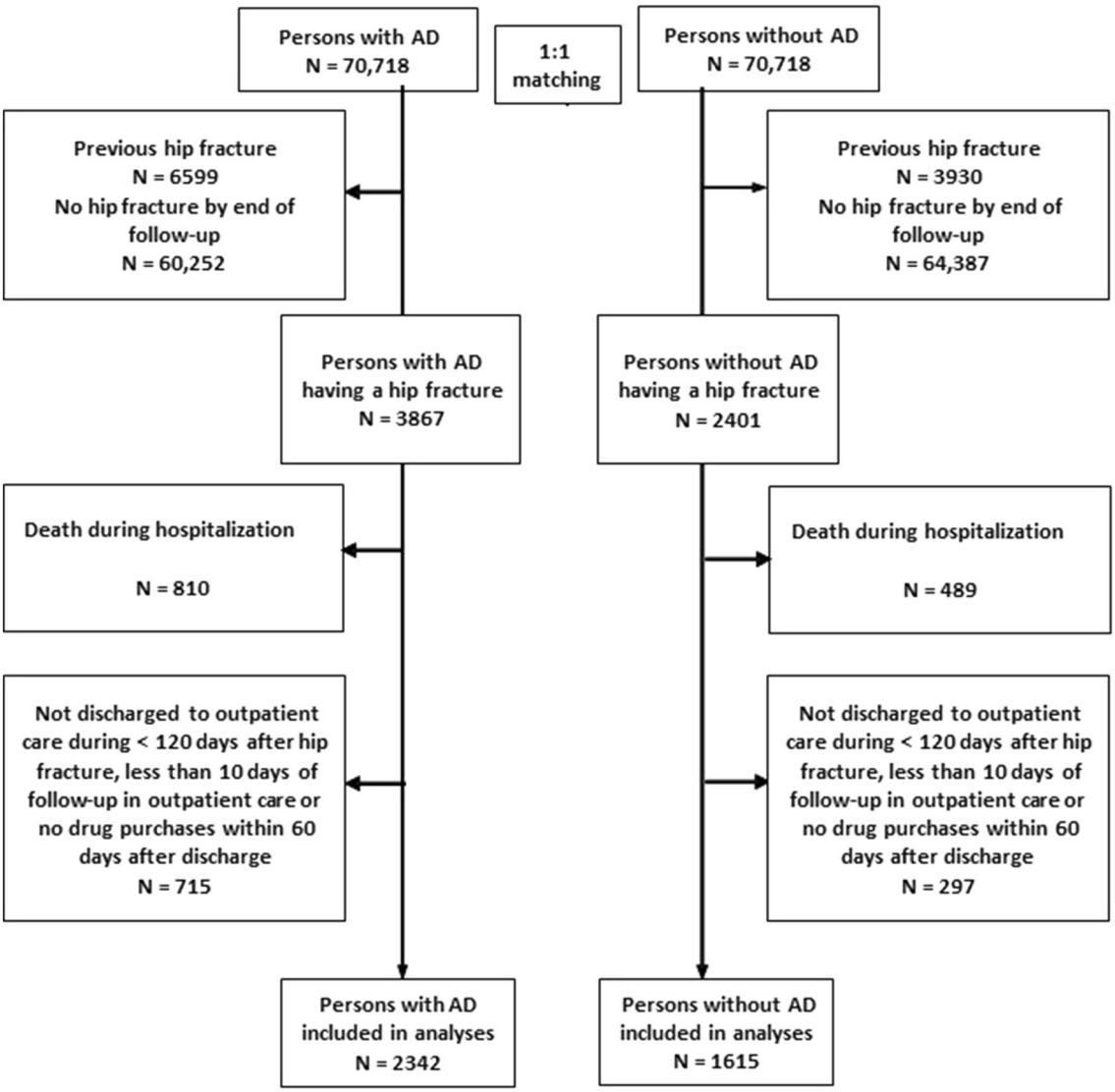

Fig. 1 The formation of the study sample. Persons having a hip fracture after AD diagnoses/corresponding matching date, between January 1, 2011 and until June 30, 2015, were identified. *AD* Alzheimer's disease

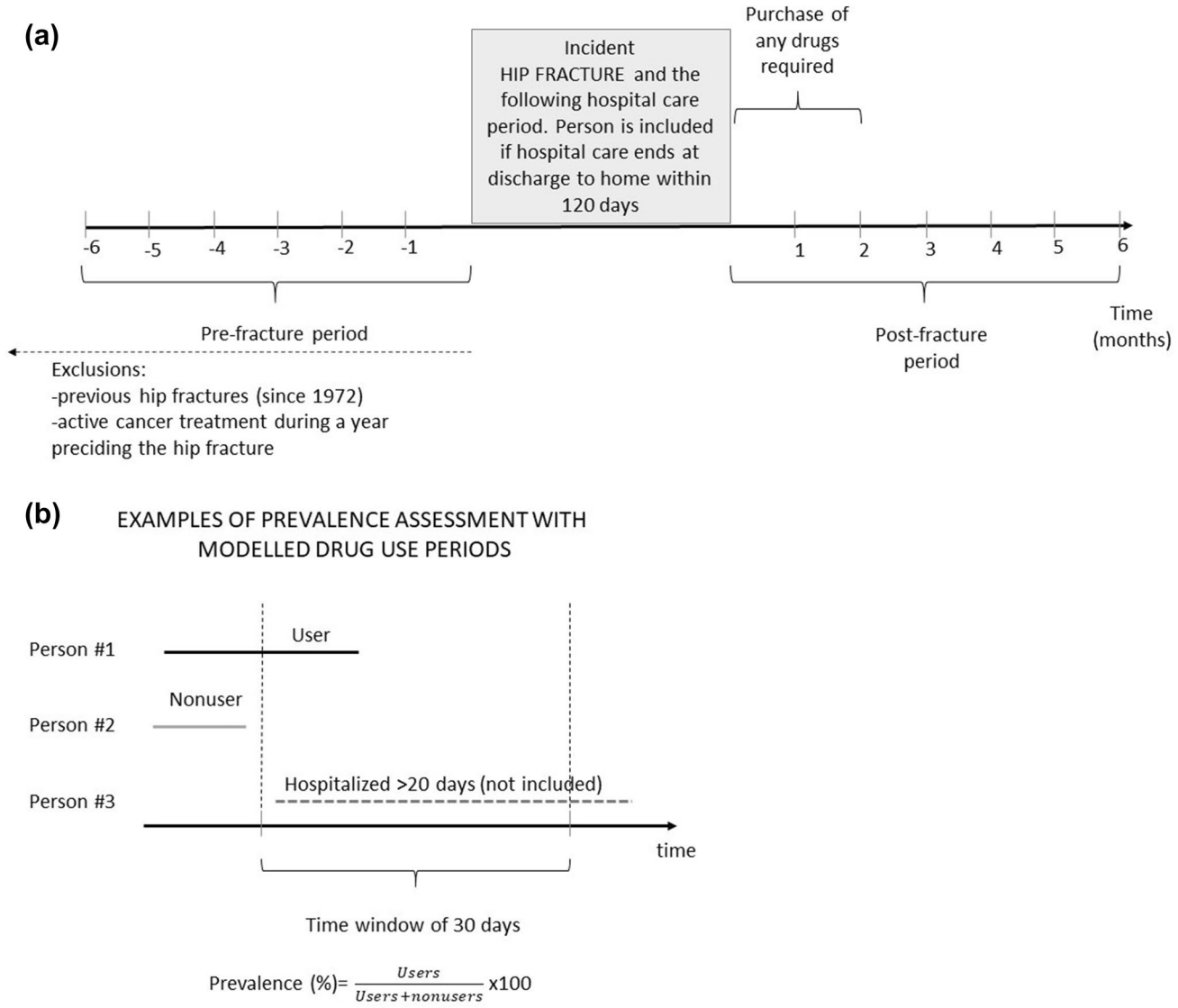

Fig. 2 **a** Study design graph. **b** Definition of opioid use within a 30-day time window. Opioid users were required to have ≥ 1 day of opioid use in the time window, according to modeled drug use periods. Opioid use was only assessed among those who had ≥ 10 days of follow-up within the 30-day window, due to hospital care periods and mortality

are only available with prescription and opioids are reimbursed, with few exceptions. Products containing paracetamol and codeine were not reimbursed prior to June 2010, which is why we restricted our analyses only on hip fractures from 2011 onward. Drugs used during hospital stays are not recorded in this register and were not analyzed in this study. Drugs in the Prescription Register were categorized according to the World Health Organization (WHO) Anatomical Therapeutic Chemical (ATC) classification system [32]. Opioids (N02A) were categorized into weak opioids [tramadol (N02AX02) and codeine (N02AA59)], partial opioid agonists [buprenorphine (N02AE01)], and strong opioids [oxycodone (N02AA05), fentanyl (N02AB03), morphine (N02AA01), hydromorphone (N02AA03), dextropropoxyphene (N02AC04), and pentazocine (N02AD01)]. Drug use periods for each opioid were modeled with a previously validated mathematical method, 'from purchases to drug use periods', PRE2DUP [33, 34]. The method calculates drug use periods based on sliding averages of daily dose in defined daily doses (DDDs) and according to individual drug use patterns. It takes into account time spent in hospital care (when drugs are provided by the caring unit and not recorded in the register), stockpiling of drugs, and changing dose during use.

Opioid use prevalence was investigated during the pre-fracture period and the post-discharge period. Opioid use was assessed in 30-day time windows as 'used' (at least 1 day) versus 'not used,' based on modeled drug use data

(Fig. 2b). Opioid use was only assessed among those who had at least 10 days of follow-up in the time window (i.e., censoring those hospitalized for more than 20 days of the period and excluding those who had died). Thus, the sample size varies in each time window. For the post-discharge period, also the proportion of those who used opioids at any time point during the period was calculated separately.

The analyses on factors associated with opioid use after hip fracture were adjusted for covariates associated with opioid use and hip fracture (Supplementary Table 1; see the electronic supplementary material). The Special Reimbursement Register and Hospital Discharge Register were utilized to identify asthma or chronic obstructive pulmonary disease (COPD), any cardiovascular disease, active cancer, diabetes (type 1 and type 2), and rheumatoid arthritis and other connective tissue diseases, until the date of hip fracture. Any cardiovascular disease was defined as one or more of the following: arterial hypertension, coronary artery disease, chronic heart failure, or chronic arrhythmia. Prosthetic replacement of knee or hip was identified from the Hospital Discharge Register with the Finnish version of the Nordic Medico-Statistical Committee (NOMESCO) Classification for Surgical Procedures (NCSP). Bisphosphonate use (M05BA, M05BB), from the Prescription Register, was utilized as a proxy for osteoporosis and measured as ever used before the hip fracture.

The Prescription Register was utilized to identify the use of other drugs during the month before hip fracture: non-opioid analgesics, antiepileptics, and psychotropics. Psychotropic drugs were defined as benzodiazepines and related drugs (N05BA, N05CD, and N05CF), antidepressants (N06A), and antipsychotics (N05A, excluding lithium). Of non-opioid analgesics, paracetamol, ibuprofen, and ketoprofen are also available as over-the-counter products in Finland in small package sizes, which are not recorded in the Prescription Register.

Socioeconomic position was defined as the highest occupational position recorded in population censuses for study persons in their middle age (45–55 years old). Socioeconomic position was based on classification by Statistics Finland, and it was categorized into four classes: the highest class included entrepreneurs and higher clerical workers; the medium class included lower clerical workers and employees; and the lowest class included unemployed persons, retirees, and students. Persons with unknown socioeconomic class and those with missing data at Statistics Finland (1.9% of the cohort) were combined in the class 'unknown.'

All statistical analyses were performed using SPSS (version 24.0; IBM Corp., Armonk, New York, USA). Characteristics between persons with and without AD were compared with chi-squared tests for categorical variables. We considered $P \leq 0.05$ as statistically significant. The median, with interquartile range (IQR), was calculated for continuous variables.

Logistic regression models were used to investigate factors associated with the use of opioids, weak opioids, buprenorphine, and strong opioids in the post-discharge period (Supplementary Table 2; see the electronic supplementary material). The results were expressed as odds ratios (ORs) with 95% confidence intervals (CIs). The analyses were adjusted for the following factors: AD, sex, age (< 80 vs. ≥ 80 years), time since AD diagnosis (categorized as 0 to < 3, 3 to < 6, 6 to < 9, and 9 years or more), socioeconomic position (high, medium, low, or unknown), asthma/COPD, rheumatoid arthritis, diabetes, history of stroke, active cancer, epilepsy, cardiovascular disease, endoprosthesis, osteoporosis, history of fracture, substance abuse, use of psychotropics, antiepileptics or non-opioid analgesics, and the length of hospital stay (categorized as 0–7, 8–14, 15–21, 22–28, 29–35, or 36 days or more). In the sensitivity analyses, we investigated opioid use after hospital care among persons with and without AD who were discharged after a hip fracture in 0–21 days and 22–120 days to further analyze the effect of length of stay on opioid use.

3 Results

In this study, there were 2342 persons with and 1615 persons without AD who had a new hip fracture. The mean age was 84 years [standard deviation (SD) 6.4 years] for persons with AD and 87 years (SD 5.1 years) for persons without AD. Women comprised 79% of persons with AD and 80% of persons without AD. The median time from the AD diagnoses/corresponding matching date for comparison persons to having a hip fracture was 1365 days (IQR 814–1950) among persons with AD and 1554 days (IQR 963–2225) among persons without AD. After the discharge from hospital care due to hip fracture, 506 persons (12.7%) died within the first 6 months after discharge: 341 persons with AD and 165 persons without AD.

Opioid use was more frequent among persons with AD, with 39.5% (95% CI 37.5–41.5) using after hip fracture in comparison to 31.2% (95% CI 28.9–33.5) (Table 1). Opioid users were more likely to have AD, cardiovascular disease, history of fracture, and osteoporosis and were in a lower socioeconomic position. In addition, opioid users more often used psychotropics, antiepileptics, and non-opioid analgesics in the pre-fracture period. Nonusers more likely had hip or knee endoprosthesis and were more likely in a high socioeconomic position. Among persons with AD, the proportion of opioid users after hip fracture became larger in later annual cohorts compared to earlier cohorts. In 2011, 32.7% of persons with AD were opioid users compared to

Table 1 Characteristics of users and nonusers of opioids in a 6-month post-fracture period among persons with and without AD

Female sex	Without AD			With AD		*P* value
	Opioid user *N* = 503 *N* (%)	Nonuser *N* = 1112 *N* (%)	*P* value	Opioid user *N* = 925 *N* (%)	Nonuser *N* = 1417 *N* (%)	
Female sex	403 (80.1)	881 (79.2)	0.681	746 (80.6)	1102 (77.8)	0.095
Age, years			0.553			0.078
< 65	0	0		9 (1.0)	11 (0.8)	
65–74	12 (2.4)	18 (1.6)		54 (5.8)	109 (7.7)	
75–84	168 (33.4)	367 (33.0)		363 (39.2)	600 (42.3)	
≤ 85	323 (64.2)	727 (65.4)		499 (53.9)	697 (49.2)	
Socioeconomic position			0.214			0.056
High	152 (30.2)	395 (35.5)		284 (30.7)	488 (34.4)	
Medium	310 (61.6)	635 (57.1)		563 (60.9)	831 (58.6)	
Low	33 (6.6)	68 (6.1)		63 (6.8)	88 (6.2)	
Unknown	8 (1.6)	14 (1.3)		15 (1.6)	10 (0.7)	
Asthma/COPD	64 (12.7)	121 (10.9)	0.282	105 (11.4)	136 (9.6)	0.172
Rheumatoid arthritis	44 (8.7)	73 (6.6)	0.117	56 (6.1)	67 (4.7)	0.160
Diabetes	112 (22.3)	206 (18.5)	0.080	144 (15.6)	283 (20.0)	0.007
Cardiovascular disease	397 (78.9)	793 (71.3)	0.001	629 (68.0)	916 (64.6)	0.094
Previous stroke	66 (13.1)	152 (13.7)	0.765	114 (12.3)	145 (10.2)	0.115
Epilepsy	14 (2.8)	28 (2.5)	0.756	29 (3.1)	34 (2.4)	0.282
Endoprosthesis*	270 (53.7)	599 (53.9)	0.944	461 (49.8)	820 (57.9)	< 0.001
History of fracture	164 (32.6)	344 (30.9)	0.504	347 (37.5)	464 (32.7)	0.018
Osteoporosis	144 (28.6)	211 (19.0)	< 0.001	203 (21.9)	222 (15.7)	< 0.001
Active cancer	28 (5.6)	55 (4.9)	0.601	53 (5.7)	59 (4.2)	0.083
History of substance abuse	13 (2.6)	21 (1.9)	0.367	24 (2.6)	36 (2.5)	0.936
*Use of drugs***						
Psychotropics	226 (44.9)	391 (35.2)	< 0.001	598 (64.6)	833 (58.8)	0.004
Antiepileptics	54 (10.7)	61 (5.5)	< 0.001	78 (8.4)	79 (5.6)	0.007
Non-opioid analgesics	243 (48.3)	335 (30.1)	< 0.001	454 (49.1)	462 (32.6)	< 0.001
Length of hospital stay			0.399			< 0.001
0–7 days	54 (10.7)	98 (8.8)		211 (22.8)	177 (12.5)	
8–14 days	62 (12.3)	137 (12.3)		152 (16.4)	169 (11.9)	
15–21 days	86 (17.1)	169 (15.2)		166 (17.9)	252 (17.8)	
22–28 days	86 (17.1)	171 (15.4)		117 (12.6)	205 (14.5)	
29–35 days	51 (10.1)	123 (11.1)		82 (8.9)	150 (10.6)	
36 days or more	164 (32.6)	414 (37.2)		197 (21.3)	464 (32.7)	
Year of hip fracture			0.722			< 0.001
2011	99 (19.7)	253 (22.8)		181 (19.6)	372 (26.3)	
2012	124 (24.7)	264 (23.7)		217 (23.5)	365 (25.8)	
2013	109 (21.7)	240 (21.6)		243 (26.3)	305 (21.5)	
2014	118 (23.5)	245 (22.0)		187 (20.2)	267 (18.8)	
2015	53 (10.5)	110 (9.9)		97 (10.5)	108 (7.6)	

AD Alzheimer's disease, *COPD* chronic obstructive pulmonary disease

*Of knee or hip joint

**Last 0–30 days in pre-fracture period

47.3% in 2015. Among persons without AD, the increase in proportion was smaller, from 28.1% in 2011 to 32.5% in 2015 ($P = 0.254$).

In the pre-fracture period, there were no significant differences in opioid use between persons with AD and those without AD. During the post-discharge period, persons

with AD used opioids more often than persons without AD (Fig. 3a). Weak opioids were more likely used by persons without AD after the first month in the post-discharge period (Fig. 3b), whereas buprenorphine was more frequently used by persons with AD during the entire post-discharge period (Fig. 3c). Strong opioid use was more frequent among persons with AD during the first 3 months of the post-discharge period (Fig. 3d). Of the persons who used any opioids in the post-discharge period, 37.2% of persons with AD and 44.7% without AD had used opioids in the pre-fracture period.

In sensitivity analyses on the effect of length of hospital stay, we compared those discharged after a hip fracture in 0–21 days with those staying in the hospital for 22–120 days. Of the persons who were discharged in 0–21 days, 46.9% (95% CI 44.0–49.9) of persons with AD and 33.3% (95% CI 29.7–37.2) without AD used opioids in the post-discharge period. Of the persons who were discharged in 22–120 days, 32.6% (95% CI 30.0–35.3) of persons with AD and 29.8% (95% CI 27.1–32.7) of persons without AD used opioids in the post-discharge period.

AD was associated with the use of buprenorphine [adjusted OR (aOR) 2.02, 95% CI 1.67–2.45] and strong opioids (aOR 1.70, 95% CI 1.38–2.09), but inversely associated with the use of weak opioids (aOR 0.56, 95% CI 0.46–0.69) (see Supplementary Table 2).

4 Discussion and Conclusion

Our main finding was that persons with AD frequently used opioids after discharge from hospital care due to hip fracture. Strong opioid use during the first 3 months and buprenorphine use throughout the post-discharge period were significantly more frequent in persons with AD, whereas weak opioids were significantly less frequently used in the AD group, compared to persons without AD. To our knowledge, this is the first study to investigate the use of opioids after discharge from hospital care after hip fracture among persons with a verified diagnosis of AD.

Paracetamol is recommended as a first-line analgesic after discharge from hospital after hip fracture [29], and opioid use in older adults should ideally be reserved for management of severe acute pain [35]. Decisions to continue treatment with opioids are done based on individual assessment of pain. However, opioid use can still be common 1 year after hip fracture surgery [22]. Pain assessment is essential in monitoring pain treatment and for decisions to continue, taper, or discontinue opioid therapy [36–38]. Among persons with cognitive disorders, however, assessment of pain can be challenging [5]. Self-report is important in mild-to-moderate AD, but observational pain scales, such as Pain Assessment in Advanced Dementia (PAINAD) and Pain Assessment Checklist for Seniors with Limited Ability to Communicate (PACSLAC) [39, 40], become more useful as the disease progresses [5, 41, 42]. Frequent use of opioids months after the hip fracture among persons with AD in this study may indicate the challenges of pain assessment. However, whether regular pain assessment has been carried out could not be evaluated in this study. Similarly, indication for opioid use could not be assessed through the registers utilized in this study. Thus, it is possible that some persons used opioids for pain unrelated to the hip fracture.

Studies on the use of opioids after hospital care for hip fractures are rare. Previous studies have reported the use of opioids among persons with AD in hospital care or in nursing homes after a hip fracture, and have described possible undertreatment of pain among persons with dementia [8, 15, 17, 18]. Persons with dementia who had had a hip fracture received less treatment with opioids in hospital care [8, 15, 17, 18] and less treatment with paracetamol and opioids [15] compared to persons without dementia. In contrast, we found more frequent use of buprenorphine and strong opioids among persons with AD. While it is possible that differences exist between prescribing patterns of different countries, the contrast between previous studies and ours is likely to reflect the difference in treatment setting, i.e., between inpatient hospital care and the community. Persons with AD who are discharged to community settings might thus benefit from closer monitoring of their opioid treatment. In our study, persons with AD also had shorter hospital stays compared to persons without AD, which is in line with previous research [43]. However, adjusting for length of stay did not change our results. In our sensitivity analyses stratified by length of hospital stay, persons with AD still used significantly more opioids than those without AD. One possible explanation for this finding is that a larger proportion of persons with AD are clients of residential and home care and so their pain is attended to more frequently. In addition, research in recent decades may have increased attention to pain management in persons with dementia. This may be reflected in previous findings of similar or even higher prevalence rates of analgesic and opioid use among community dwellers with dementia, when compared to other older adults [12–16]. Moreover, we found that among persons with AD, the proportion of opioid users after hip fracture increased steadily by almost 15 percentage points from 2011 to 2015. Increased use of opioids among persons with cognitive disorders has been previously reported among community-dwelling Finns, as well as in Finnish, Norwegian, and Canadian long-term care facilities [12, 44–46]. Whether these trends persist over time should be a subject for future studies.

In our study population, buprenorphine was almost solely used as transdermal patches. We found that buprenorphine use was significantly more frequent in persons with AD throughout the post-discharge period, which is in accordance with previous findings where studies have described

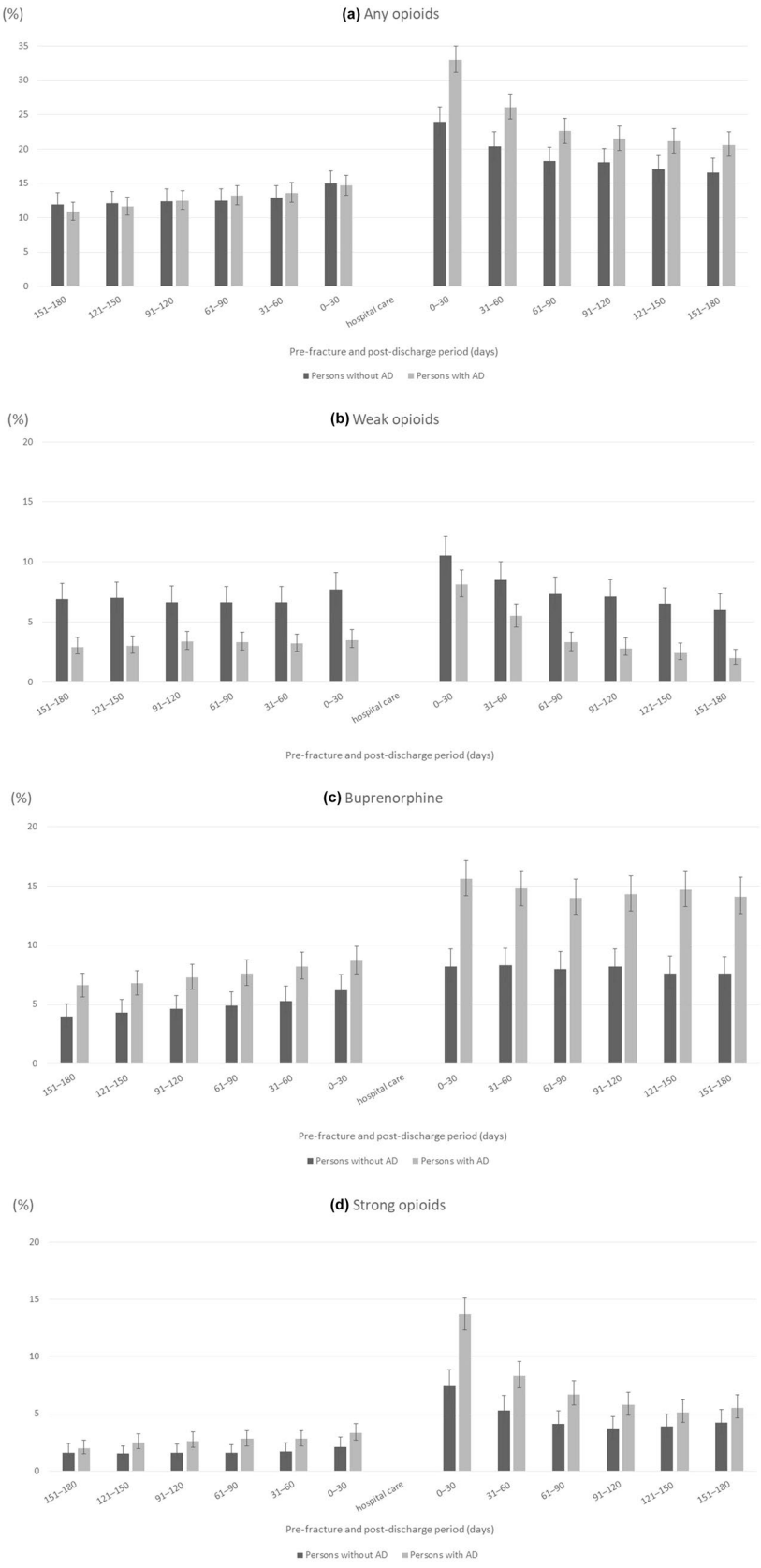

Fig. 3 Prevalence of opioid use among persons with and without AD in pre-fracture and post-discharge periods: **a** any opioids, **b** weak opioids, **c** buprenorphine, and **d** strong opioids. *AD* Alzheimer's disease

longer persistence on transdermal opioids compared with oral ones [47, 48] and more frequent use of transdermal opioids among community-dwellers with dementia [12, 20]. In addition, long-term opioid use has been strongly associated with transdermal opioid use among persons with AD [14]. Similarly, dementia has previously been reported as a risk factor for chronic opioid use after total hip arthroplasty [49]. Transdermal opioid treatment may be preferred due to difficulties in the ingestion of oral medicines, and particularly in patients with moderate to severe AD [50]. Treatment schemes of transdermal buprenorphine, i.e., change every 7 days, may provide additional ease of use, for example, reducing administration time and staffing requirements in home care services and in residential care [51]. In addition, it may not be surprising that buprenorphine is preferred over weak opioids among persons with AD; weak opioids may commonly induce constipation and drug–drug interactions, and have genetic variation in efficacy [34, 52]. Use of tramadol may be problematic among older people, as it can cause central nervous system adverse effects, and thus, tramadol is recommended to be avoided in older adults [33]. Further, antidepressant use, which may increase the serotonergic adverse effects of tramadol, is common among persons with AD [53]. However, clinicians should be aware that buprenorphine adverse effects, such as somnolence, may be more pronounced among concomitant antidepressant users with dementia [54, 55]. Regular assessment of pain and the need for opioids, as well as the benefits and harms of opioid therapy, should be conducted, regardless of the route of administration.

The main strength of our study was the nationwide coverage of all community-dwelling persons with a clinically verified AD diagnosis from several years. Our results are generalizable to prescription opioid use and to older persons with and without AD, due to the nationwide registers with good coverage and validity [56], although some differences between countries may exist. In this study, the diagnosis of hip fracture is reliably recorded in the Hospital Discharge Register data [31]. The diagnosis of AD cases can be considered reliable due to the diagnosis requirements of the SII [30]. However, mixed cases of AD with features of vascular or Lewy body dementia may be included if AD was considered the main contributor to the symptoms. In addition to previously mentioned strengths, our register-based results are not prone to recall bias, which can be a problem in interview-based studies.

A limitation of this study was that we were not able to analyze opioid usage in different stages of AD because the Special Reimbursement register does not include the severity of the disease. The registers do not contain data on pain severity or non-pharmacological treatments for pain, and thus, it is not possible to assess the adequacy of the provided pharmacotherapy. Moreover, we were not able to estimate opioid dose during each 30-day time window, and this is therefore an important topic for future research. In addition, we were not able to analyze opioid use during hospital care or if persons were discharged to institutions which provide medications, i.e., are not recorded in the Prescription Register. However, persons without outpatient follow-up and those who did not purchase any drugs within 3 months following discharge were not included in our study. The results of our study may at least partly be explained by country-specific prescribing patterns, and should thus be replicated in other countries.

Persons with AD more frequently used opioids than persons without AD after hospital discharge after hip fracture, and thus, our study could not confirm low or undertreatment of pain after hospitalization due to hip fracture in persons with AD. Frequent opioid use after hospital care due to hip fracture may indicate increased attention to pain among persons with AD. Nevertheless, pain and the benefits and harms of opioid use should be evaluated regularly in community-dwelling older persons after hospitalization due to hip fracture.

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Compliance with Ethical Standards

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Conflict of Interest HT, JT, and AT have participated in research projects funded by Janssen and Eli Lilly, with grants paid to the institution where they were employed. JT has received personal fees from the Finnish Medicines Agency (Fimea), European Medicines Agency (EMA), Eli Lilly, Janssen-Cilag, Lundbeck, and Otsuka, and has received grants from the Stanley Foundation and Sigrid Jusélius Foundation. SH has received fees from the Swedish Research Council. AH has been supported by the Alfred Kordelin Foundation and Borg Foundation. All other authors (EL, MT, and AMT) declare no conflicts of interest.

Ethical Approval Participants were not contacted in any way, and according to Finnish legislation, ethics committee approval was therefore not required.

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