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Fourteen-Year Trends in the Use of Psychotropic Medications, Opioids, and Other Sedatives Among Institutionalized Older People in Helsinki, Finland

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1	14-Year Trends in the Use of Psychotropic Medications, Opioids, and Other Sedatives among
2	Institutionalized Older People in Helsinki, Finland
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26 **Abstract**

- 27 Objectives: The use of psychotropic drugs in long-term care (LTC) is very common, despite their
- 28 known adverse effects. The prevalence of opioid use is growing among older adults. This study
- 29 aimed to investigate trends in the prevalence of psychotropics, opioids, and sedative load in a LTC
- 30 setting over a 14-year period. We also explored the interaction of psychotropic and opioid use
- 31 according to residents' dementia status in nursing home (NH) and assisted living facility (ALF)
- 32 settings.
- 33 *Design*: Four cross-sectional studies.
- 34 Setting: institutional settings in Helsinki, Finland.
- 35 *Participants*: Older residents in NHs in 2003 (n=1987), 2011 (n=1576), and 2017 (n=791) and in
- 36 ALFs in 2007 (n=1377), 2011 (n=1586), and 2017 (n=1624).
- 37 *Measures:* Comparable assessments were conducted among LTC residents at four time-points over
- 38 14 years. The prevalence of regular psychotropics, opioids, and other sedatives and data on
- 39 demographics and diagnoses were collected from medical records.
- 40 Results: Disabilities and severity of dementia increased in both settings over time. The prevalence
- of all psychotropics decreased significantly in NHs (from 81% in 2003 to 61% in 2017), whereas in
- 42 ALFs there was no similar linear trend (65% in 2007 and 64% in 2017). There was a significant
- increase in the prevalence of opioids in both settings, being 30% in NHs and 22% in AFLs in 2017.
- Residents with dementia used less psychotropics and opioids than those without dementia in both
- settings and at each time-point.
- 46 Conclusions/Implications: NHs show a favorable trend in psychotropic drug use, but the rates of
- 47 psychotropic use remain high in both NHs and ALFs. In addition, the rates of opioid use have
- 48 almost tripled, leading to a high sedative load among LTC residents. Clinicians should carefully
- 49 consider the risk-to-benefit ratio when prescribing in LTC.

Introduction

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The use of psychotropic drugs in long-term care (LTC) is very common. In studies published from 2004 to 2017, the prevalence of use of any psychotropic drug has varied between 52% and 80% in nursing homes (NHs)²⁻⁶ and between 53% and 68% in assisted living facilities (ALFs)^{7,8}. The prevalence of any psychotropic is higher among LTC residents with dementia than among their peers with normal cognition. 9,10 There have been concerns of the potential adverse effects related to psychotropic medication such as falls and cognitive decline. 11,12 Higher use of healthcare services and greater mortality have also been suggested. 13,14 Psychotropic use has been associated with lower quality of life. 15 Few studies have examined the long-term trends in the use of psychotropics in LTC settings. In NHs of the United States, use of antipsychotics decreased after OBRA 87,16 whereas the use of antidepressants increased between 1996 and 2006.¹⁷ In 2018 data from the National Partnership Program in the United States showed a significant reduction of antipsychotic use between 2011-2018 being 14.8% nationwide¹⁸. In Finnish NHs the use of antipsychotics, anxiolytics, and hypnotics decreased between 2003 and 2011.¹⁹ However, less is known about the trends in later years. The prevalence of opioid use has been growing in the older population, ²⁰ and also in NHs over the years. 19,21 In a recent study, the use of opioids has not decreased from 2007 to 2016 among older people, and their use is highest among disabled Medicaid beneficiaries. ²² High use could be problematic because older adults are prone to falls, cognitive decline, and delirium. ²³⁻²⁵ Concomitant use of psychotropic medications and opioids may results in a high sedative load among vulnerable LTC residents. The aim of this study was to examine trends in prevalence of psychotropic medications and opioids in institutionalized older adults in Helsinki over a 14-year period. We also explored the interaction of psychotropic and opioid use according to residents' dementia status in NH and ALF settings.

Methods

78 Study participants

This study combined data from four comparable cross-sectional studies exploring medication use and nutrition in institutional settings in Helsinki. The studies were conducted among all NH residents of Helsinki in 2003 (n=1987), 2011 (n=1576), and 2017 (n=791) and among all ALF residents of Helsinki in 2007 (n=1377), 2011 (n=1586), and 2017 (n=1624). All residents aged 65 years and older were invited to participate. The 2003, 2011, and 2017 samples comprised 94%, 81%, and 68% of the total NH population, and the 2007, 2011, and 2017 samples 66%, 64%, and 62% of the total ALF population, respectively. The nonparticipants were those suffering from moderate-severe dementia (CDR 2-3) and not having a close proxy to give informed consent, refusals, or those not providing a complete medication list.

In Finland, ALFs provide round the clock care with a registered nurse in charge. This is similar to the care provided in NHs, but ALFs are designed to resemble residents' own home environment to a greater extent. ALFs include both apartments and group homes for people with dementia. However, the number of registered nurses is lower in ALFs than in traditional NHs. The number of NH beds in Helsinki has significantly declined from 2003 to 2017, and this has been compensated by an increase in the number of ALF beds. The national recommendation for minimum staffing levels in 24-hour care is 0.6 employees per resident in NHs and 0.5 in ALFs.

Measures

All medications were classified using the Anatomical Therapeutic Chemical (ATC) classification system. ²⁶ Psychotropic medications included antipsychotics (N05A), antidepressants (N06A),

anxiolytics (N05B), and hypnotics and sedatives (N05C). Opioids (N02A) were further categorized as weak opioids (codeine, buprenorphine, tramadol) and strong opioids (morphine, fentanyl, oxycodone). The use of paracetamol (N02BE01) and nonsteroidal anti-inflammatory drugs (NSAIDs) (M01A) was also included to illustrate the overall use of pain medication. In addition, we report the use of Alzheimer medication (N06D), including cholinesterase inhibitors (N06DA) and/or memantine (N06DX01), because they are often used for neuropsychiatric symptoms alternatively to psychotropics.²⁷ In addition to psychotropics and opioids, we defined, for the purpose of the analysis, also other medications that contribute to sedative load, including pregabalin (N03AX16), gabapentin (N03AX12), carbamazepine (N03AF01), oxcarbazepine (N03AF02), and valproic acid (N03AG01). Medication use was considered regular if there was a documented regular sequence of administration. Only regularly used medications were considered when comparing the prevalence at each time-point. Medication use was reported as using/not using. Dosages were not calculated.

The Charlson Comorbidity Index²⁸ was used to calculate each resident's burden of comorbidity. We trained thoroughly nurses in each setting to collect data and perform the assessments. The nurses used Clinical Dementia Rating (CDR)²⁹ to grade the severity of dementia and Mini Nutritional Assessment (MNA)³⁰ to assess and grade each resident's nutritional state. Resident's mobility was assessed by the MNA item and categorized to either 0="unable to get out of a bed, a chair, or a wheelchair without the assistance of another person" or 1="able to get out of bed or a chair without help".

126 **Statistics** 127 Significance for the unadjusted hypothesis of linearity between cohorts was evaluated by using the Cochran-Armitage test for trend or analysis of variance with an appropriate contrast. 128 129 Number of medications used was calculated using a Poisson regression model and proportion of opioids users was evaluated using a logistic model. The models included gender, age, Charlson 130 131 comorbidity index, and ability to move independently as covariates. The bootstrap method was used 132 when the theoretical distribution of the test statistics was unknown or in the case of violation of 133 assumptions (e.g. non-normality). The normality of variables was evaluated with the Shapiro-Wilk W-test. All analyses were performed using STATA 15.1 (StataCorp, College Station, TX, USA). 134 135 Statement of ethics 136 137 The study protocol was approved by the Ethics Committee of the University of Helsinki. Written informed consent was obtained from each participant and in case of significant cognitive decline 138 139 (CDR 2 or 3) from their closest proxy. 140 **Results** 141 142 NH and ALF residents were more disabled in their mobility and had more often dementia in the 143 latter cohorts (Tables 1 and 2). The severity of cognitive decline increased over time in both settings according to the CDR memory item. The proportion of males increased over time in both facilities. 144 145 Mean age, comorbidities, or nutritional status did not change significantly over time. The prevalence of psychotropic medication use declined significantly in the NHs (p<0.001), 146 147 whereas in ALFs there was no linear trend (p=0.15). The prevalence of regular psychotropic 148 medication use in NHs fell from 81.3 % in 2003 to 60.9% in 2017. In ALFs, the prevalence 149 remained more stable, being 64.6% in 2007 and 63.6% in 2017. In NHs, the use of antipsychotic

medication dropped from 42.7% to 32.7%, whereas in ALFs the use of antipsychotic medication

151 increased from 27.3% to 34.0%. Also the use of antidepressants dropped from 44.9% to 32.7% in 152 NHs. In ALFs, the prevalence of antidepressants increased from 39.3% to 46.3% in 2011 and dropped again to 37.5% in 2017. The prevalence of anxiolytic use dropped from 40.9 % to 14.4% in 153 154 NHs, and in ALFs from 24.1% to 9.6%. The use of hypnotics also decreased significantly in NHs from 11.3% to 6.1%, whereas in ALFs there was a significant increase from 10.2% to 17.2%. 155 The prevalence of regular opioid use increased linearly in both NHs and ALFs over the years 156 (p<0.001). In NHs, the prevalence of regular opioid use increased from 11.7% in 2003 to 30.2% in 157 2017. In ALFs, the increase was from 8.6% in 2007 to 21.6% in 2017. The largest increase in 158 159 prevalence was observed in strong opioids in NHs, where the prevalence increased from 1.9% to 160 14.9%. The use of NSAIDs decreased significantly in both groups, being minimal in 2017; 0.8% in NHs 161 162 and 0.5% in ALFs. Paracetamol was widely used and its prevalence increased significantly in NHs 163 from 34.3% in 2003 to 51.6% in 2017, whereas its use in ALFs did not change significantly, being 38.6% in 2017. The prevalence of pregabalin or gabapentin use in NHs increased from 0.6% to 164 165 9.1%. In ALFs, the corresponding increase was from 2.2% to 6.9%. The prevalence of Alzheimer medication increased significantly for both groups (p<0.001). One in three NH residents and half of 166 ALF residents were administered Alzheimer medication in 2017. 167 168 The overall sedative load decreased significantly in NH residents (p<0.001), from 84.6% in 2003 to 69.1% in 2017. In ALFs, no significant change occurred in the prevalence of sedative medication. 169 170 When the psychotropic users were stratified according to diagnosis of dementia, in NHs both people 171 with and without dementia showed significant decrease in the prevalence of psychotropic use over 172 the 14-year follow-up (p<0.001 for cohort), whereas people with dementia used less psychotropics 173 (p<0.001 for dementia), and among them the use decreased more rapidly (p<0.001 for interaction) (Figure 1a). There was no similar interaction in ALFs (p<0.001 for cohort, p=0.004 for dementia, 174

p=0.41 for interaction) (Figure 1a). In NHs the whole cohort showed significant decrease in the use of antipsychotics over the 14-year follow-up (p<0.001 for cohort), whereas people with dementia used less antipsychotics than those without dementia (p=0.026 for dementia). There was no interaction (p=0.060 for interaction) (Figure 1b). In ALFs the use of antipsychotics increased over time and people with dementia used more antipsychotics than those without dementia (p<0.001 for cohort, p<0.001 for dementia and p=0.024 for interaction) (Figure 1b). In NHs the whole cohort showed significant decrease in the use of anxiolytics and hypnotics over the 14-year follow-up (p<0.001 for cohort), whereas people with dementia used less anxiolytics and hypnotics (p<0.001 for dementia). There was no interaction among people with and without dementia (p=0.38 for interaction) (Figure 1c). In ALFs the use of anxiolytics and hypnotics also decreased over time and people with dementia used less anxiolytics and hypnotics than those without dementia (p<0.001 for cohort, p<0.001 for dementia and p=0.37 for interaction) (Figure 1b). In NHs the whole cohort showed significant decrease in the use of antidepressants over the 14-year follow-up (p<0.001 for cohort). People with dementia used less antidepressants than those without dementia (p<0.001 for dementia). People without dementia showed more rapid decrease in antidepressants that those with dementia (p=0.0015 for interaction) (Figure 1d). In ALFs the use of antidepressants showed an overall trend of increase in the whole cohort (p<0.001 for cohort). People with dementia used less antidepressants than those without dementia (p=0.022 for dementia). There was no interactions (p=0.35 for interaction) (Figure 1d). When the opioids users in NHs were stratified according to diagnosis of dementia, the whole cohort showed significant increase in the use of opioids over the 14-year period (p<0.001 for cohort). People with dementia used less opioids (p<0.001 for dementia), and the use increased more rapidly among them compared to those without dementia (p<0.001 for interaction) (Figure 2). In ALFs, the residents with dementia used less opioids, but the use increased over time; there was, however, no interaction (p<0.001 for cohort, p<0.001 for dementia, p=0.65 for interaction). In NHs, both groups

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showed significant decreases in the prevalence of overall sedative medication use over the 14-year follow-up (p<0.001 for dementia, p<0.001 for cohort, p<0.039 for interaction) (Figure 3). In ALFs, people with dementia used less sedatives (p<0.001 for dementia), with the use increasing significantly over time (p<0.001), but there was no interaction (p=0.058).

Our study demonstrated important trends in the use of psychotropic medications and opioids over

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Discussion

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the past 14 years in LTC in Helsinki. The prevalence of psychotropic medication decreased significantly in NHs, but not in ALFs. There was a considerable increase in the prevalence of opioids in both settings. The changes detected may partly reflect the changes in resident profile: both dementia and mobility disabilities are more prevalent and more severe in latter cohorts and the difference between these two settings has diminished. An important strength of our study is the large sample size and comparable data at each of the four time-points. Residents were assessed by well-trained nurses in 2003, 2007, 2011, and 2017 using the same data collection instruments and methodology, resulting in high validity of data. Our assessments were cross-sectional. We were not able to follow the same resident at different timepoints, because the mean time spent in LCT in Helsinki is less than two years. Another strength of the study is that medication use was taken directly from each resident's medication administration chart, ensuring that only medication actually taken was included in the analysis. Moreover, we only considered medication that was taken regularly. However, it has been shown that psychotropic medication may also be administered on a pro re nata basis, so our results might underestimate the actual use of these medications. ¹⁰ Another limitation is that response rates have significantly decreased over the years in NHs. The non-responders are mainly people with moderate-severe dementia and not having a proxy. Thus, the estimates of increases in dementia and disability are

225 probably underestimates. In addition, the organization of long-term care has changed over time challenging the comparability of NHs. The number of NH beds has significantly decreased whereas 226 the increasing number of beds in ALFs have replaced them. However, all available residents living 227 228 in Helsinki long-term care were included. 229 The results of this study are fairly in line with other recent studies examining the growing trend of opioid use in LTC.^{31, 21} However, the opioid use in LTC in Helsinki is still lower than among 230 disabled Medicaid beneficiaries in the United States (quarterly use 39%).²¹ The increased use of 231 opioids around the world may reflect the overall "opioid epidemic", i.e. the marked rise in opioid 232 use in general populations.³² On the other hand it has also been noted that pain assessment and 233 management are suboptimal among patients with dementia in NHs.³³ At the end-of-life care the use 234 of opioids and psychotropics is often appropriate.³⁴ However, according to RAI data on the study 235 population, the number of residents in terminal care is very small $(0.6\%)^{35}$ and has not significantly 236 increased over time. The use of other painkillers seem to become favourable since the use of 237 NSAIDs has almost disappeared and the use of paracetamol has increased. However, the fairly high 238 concomitant use of gabapentinoids may predispose residents to falls.³⁶ 239 While the changes in the use of opioid medications were consistent with other recent studies, the 240 changes in the use of psychotropic medication were found to be more complex. A systematic review 241 and meta-analysis reported a small increase in antipsychotic medication in LTC residents with 242 dementia from 1991 to 2013,³⁷ whereas other studies have reported a decrease in the use of 243 antipsychotic medication, albeit an increase in the use of antidepressants. 18,38,39 The prevalence of 244 antipsychotic use in our sample is more than double compared to the latest figures in the U.S.¹⁸ 245 In our study, the use of psychotropic medication in NHs decreased significantly, but this trend was 246 247 not seen in ALFs. This could be partly because the residents in ALFs were more mobile, with less advanced dementia, and they may have suffered more often from neuropsychiatric symptoms than 248

the residents of NHs. Another possible explanation is that in Finland the staff in NHs includes more registered nurses than in AFLs, thus having a better pharmacologic education and ability to assess the possible benefits and adverse effects of psychotropic medication. The training of nurses has been shown to improve physicians' prescribing practices in LTC. 40 Antipsychotics are often used to treat neuropsychiatric symptoms of dementia even though the evidence of their effectiveness is limited⁴¹ and the guidelines suggest non-pharmacological treatments as the first line choise. ⁴² Even though the use of Alzheimer medication increased significantly over the years, it did not decrease the use of antipsychotics in ALFs. It has also been suggested that older adults with dementia may express pain as neuropsychiatric symptoms, such as agitation and aggression, 43,44 and that treating pain systematically reduces these symptoms. 45 The steep rise in the use of opioids in both settings could reflect better pain recognition and clinicians' efforts to optimize pain management to reduce neuropsychiatric symptoms among residents with dementia. Alarming is that the concomitant use of antipsychotic medication remains high and even keeps increasing at the same time in ALFs. In our study, residents with dementia used less psychotropics and opioids and had a lower sedative load than residents without dementia. People without dementia admitted to LTC probably suffer from stroke, depression, other psychiatric illnesses, and disabling musculoskeletal diseases that cause pain, increasing their use of various psychotropics. 46 People with chronic mental health conditions such as schizophrenia are likely to require psychotropic medication, although the dosage may need to be readjusted as they age. To our knowledge, this is the first study with over 10-year follow-up investigating trends in the use of both psychotropic medication and opioids among institutionalized older adults. Our study both confirms earlier findings and provides novel data regarding the prevalence of psychotropic and opioid use in LTC. The increasing use of Alzheimer medication or opioids has not significantly

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273 decreased the use of psychotropics. Instead these medication changes have led to polypharmacy 274 among vulnerable long term care population. **Conclusions/Relevance** 275 276 Although the prevalence of psychotropics has decreased over the last 14 years in NHs, the rates of 277 psychotropic use remain high in both NHs and ALFs. In addition, the rates of opioid use have almost tripled, leading to a high sedative load among vulnerable LTC residents. Clinicians should 278 279 carefully consider the risk-to-benefit ratio when prescribing in LTC. Strategies for regular medication reviews and deprescribing in LTC are required. 280 281 Another finding with practical implications is that the LTC population profile has changed over 282 time. Residents are more disabled and the severity of dementia has increased. This is key 283 information for both clinicians and policy-makers to consider when planning LTC in the future. As 284 the dementia disease progresses there are often changes in behavior implicating timely assessments 285 and adjustments in person-centered care. 286

The authors declare that they have no conflicts of interest relevant to this report.

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References

- Janus S, van Manen J, IJzerman M, Zuidema S. Psychotropic drug prescriptions in
 Western European nursing homes. Int Psychogeriatr. 2016:11:1775-1790.
- Hosia-Randell H, Pitkälä K. Use of Psychotropic Drugs in Elderly Nursing Home
 Residents with and without Dementia in Helsinki, Finland. Drugs Aging 2005;22:793 800.
 - 3. Selbaek G, Kirkevold Ø, Engedal K. The prevalence of psychiatric symptoms and behavioural disturbances and the use of psychotropic drugs in Norwegian nursing homes, Int J Geriatr Psychiatry 2007;22:843-849.
 - 4. Richter T, Mann E, Meyer G, et al. Prevalence of psychotropic medication use among German and Austrian nursing home residents: a comparison of 3 cohorts. J Am Med Dir Assoc 2012;13:187.e7–187.e13.
 - 5. Rolland Y, Andrieu S, Crochard A, et al. Psychotropic Drug Consumption at Admission and Discharge of Nursing Home Residents. J Am Med Dir Assoc 2012;13:407.e7 407.e12.
 - 6. Helvik A, Šaltytė Benth J, Wu B, et al. Persistent use of psychotropic drugs in nursing home residents in Norway. BMC Geriatr 2017;17:52.
 - 7. Crotty M, Whitehead C, Rowett D, et al. An outreach intervention to implement evidence based practice in residential care: a randomized controlled trial [ISRCTN67855475]. BMC Health Serv Res 2004;4:6.
 - 8. Stafford AC, Alswayan MS, Tenni, PC. Inappropriate prescribing in older residents of Australian care homes. J Clin Phar Ther 2011;36:33-44.
 - 9. Schulze J, van den Bussche H, Glaeske G, et al. Impact of safety warnings on antipsychotic prescriptions in dementia: nothing has changed but the years and the substances. Eur Neuropsychopharmacol 2013;23:1034-1042.

315	10. Allers K, Dörks M, Schmiemann G, et al. Antipsychotic drug use in nursing home
316	residents with and without dementia: keep an eye on the pro re nata medication. Int Clin
317	Psychopharmacol 2017;32:213-218.
318	11. Schneider LS, Dagerman K, Insel PS, et al. Efficacy and adverse effects of atypical
319	antipsychotics for dementia: meta-analysis of randomized, placebo-controlled trials. Am
320	J Geriatr Psychiatry 2006;14:191-210.
321	12. Olazarán J, Valle D, Serra JA, et al. Psychotropic medications and falls in nursing
322	homes: a cross-sectional study. J Am Med Dir Assoc 2013;14:213-217.
323	13. Schneider LS, Dagerman KS, Insel P, et al. Risk of death with atypical antipsychotic
324	drug treatment for dementia: meta-analysis of randomized placebo-controlled trials.
325	JAMA 2005;294:1934-1943.
326	14. Kales HC, Valenstein M, Kim HM, et al. Mortality risk in patients with dementia treated
327	with antipsychotics versus other psychiatric medications. Am J Psychiatry
328	2007;164:1568-1576.
329	15. Galik E, Resnick B. Psychotropic medication use and association with physical and
330	psychosocial outcomes in nursing home residents. J Psychiatr Ment Health Nurs
331	2013;20:244-252.
332	16. Garrard J, Chen V, Dowd B. The impact of the 1987 federal regulations on the use of
333	psychotropic drugs in Minnesota nursing homes. Am J Public Health 1995;85:771-776.
334	17. Hanlon JT, Handler SM, Castle NG. Antidepressant prescribing in US nursing homes
335	between 1996 and 2006 and its relationship to staffing patterns and use of other
336	psychotropic medications. J Am Med Dir Assoc 2010:11:320-324.

18. National Partnership to Improve Dementia Care in Nursing Homes: Antipsychotic

Medication Use Data Report. Available at:

337

339	https://www.nhqualitycampaign.org/files/Antipsychotic_Medication_Use_Report.pdf
340	Accessed on December 12, 2018.
341	19. Pitkala KH, Juola A, Hosia H, et al. Eight-Year Trends in the Use of Opioids, Other
342	Analgesics, and Psychotropic Medications Among Institutionalized Older People in
343	Finland. J Am Med Dir Assoc 2015;16:973-978.
344	20. Atluri S, Sudarshan G, Manchikanti L. Assessment of the trends in medical use and
345	misuse of opioid analgesics from 2004 to 2011. Pain Physician 2014;17:E119-E128.
346	21. La Frenais FL, Bedder R, Vickerstaff J, et al. Temporal Trends in Analgesic Use in
347	Long-Term Care Facilities: A Systematic Review of International Prescribing. Am
348	Geriatr Soc 2018;66:376-382.
349	22. Jeffery MM, Hooten WM, Henk HJ, et al. Trends in opioid use in commercially insured
350	and Medicare Advantage populations in 2007-16: retrospective cohort study, BMJ
351	2018;362:k2833.
352	23. Wright RM, Roumani YF, Boudreau R, et al. Effect of central nervous system
353	medication use on decline in cognition in community-dwelling older adults: findings
354	from the Health, Aging And Body Composition Study. J Am Geriatr Soc 2009;57:243-
355	250.
356	24. Laurila JV, Laakkonen ML, Tilvis RS, et al. Predisposing and precipitating factors for
357	delirium in a frail geriatric population. J Psychosom Res 2008;65:249-254.
358	25. Chou R, Turner JA, Devine EB, et al. The effectiveness and risks of long-term opioid
359	therapy for chronic pain: a systematic review for a National Institutes of Health
360	Pathways to Prevention Workshop. Ann Intern Med 2015;162:276-286.
361	26. WHO Collaborating Centre for Drug Statistics Methodology. The Anatomical
362	Therapeutic Chemical Classification System. ATC/DDD Index 2018. Available at:
363	https://www.whocc.no/atc_ddd_index/. Accessed on August 30, 2018.

364	27. Memory Disorders. Current Care Guidelines. Working group appointed by the Finnish
365	Medical Society Duodecim, Societas Gerontologica Fennica, Finnish Geriatricians, the
366	Finnish Neurological Society, Finnish Psychogeriatric Association and the Finnish
367	Association for General Practice. Available at:
368	http://www.kaypahoito.fi/web/kh/suositukset/suositus?id=hoi50044. Accessed on
369	August 30, 2018.

- 28. Charlson ME, Pompei P, Ales KL, et al. A new method of classifying prognostic comorbidity in longitudinal studies: development and validation. J Chronic Dis 1987;40:373-383.
- 29. Hughes CP, Berg L, Danziger WL, et al. A new clinical scale for the staging of dementia. Br J Psychiatry 1982;140:566-572.
- 30. Guigoz Y, Lauque S, Vellas BJ. Identifying the elderly at risk for malnutrition. The Mini Nutritional Assessment. Clin Geriatr Med 2002;18:737–757.
- 31. Sandvik R, Selbaek G, Kirkevold O, et al. Analgesic prescribing patterns in Norwegian nursing homes from 2000 to 2011: trend analyses of four data samples. Age Ageing 2016;45:54–60.
- 32. Humphreys K. Avoiding globalisation of the prescription opioid epidemic. Lancet 2017;390:437-439.
- 33. Lichtner V, Dowding D, Esterhuizen P, et al. Pain assessment for people with dementia: a systematic review of systematic reviews of pain assessment tools. BMC Geriatr 2014;14:138.
- 34. Jansen K, Haugen DF, Pont L, Ruths S. Safety and Effectiveness of Palliative Drug

 Treatment in the Last Days of Life-A Systematic Literature Review. J Pain Symptom

 Manage. 2018;55:508-521.e3.

35. Laakkonen ML, Finne-Soveri UH, Noro A, et al. Advance orders to limit therapy in 67 long-term care facilities in Finland. Resuscitation 2004;61:333-339.

- 36. Shanthanna H, Gilron I, Rajarathinam M, et al. Benefits and safety of gabapentinoids in chronic low back pain: A systematic review and meta-analysis of randomized controlled trials. PLoS Medicine. 2017;14:e1002369.
- 37. Kirkham J, Sherman C, Velkers C, et al. Antipsychotic Use in Dementia: Is There a Problem and Are There Solutions? Can J Psychiatry. 2017;62:170-181.
- 38. Ruths S, Sørensen PH, Kirkevold Ø, et al. Trends in psychotropic drug prescribing in Norwegian nursing homes from 1997 to 2009: a comparison of six cohorts, Int J Geriatr Psychiatry 2013;28:868-876.
- 39. Vasudev A, Shariff SZ, Liu K, et al. Trends in Psychotropic Dispensing Among Older Adults with Dementia Living in Long-Term Care Facilities: 2004-2013, Am J Geriatr Psychiatry 2015;23:1259-1269.
- 40. Pitkälä KH, Juola AL, Kautiainen H, et al. Education to reduce potentially harmful medication use among residents of assisted living facilities: a randomized controlled trial. J Am Med Dir Assoc 2014;15:892-898.
- 41. Sink KM, Holden KF, Yaffe K. Pharmacological treatment of neuropsychiatric symptoms of dementia: a review of the evidence. JAMA 2005;293:596-608.
- 42. American Geriatrics Society: Ten Things Clinicians and Patients Should Question.

 Available at: http://www.choosingwisely.org/wp-content/uploads/2015/02/AGS-Choosing-Wisely-List.pdf. Accessed on December 12, 2018.
- 43. Tosato M, Lukas A, van der Roest HG, et al. Association of pain with behavioral and psychiatric symptoms among nursing home residents with cognitive impairment: results from the SHELTER study. Pain 2012;153:305-310.

412	44. Rajkumar AP, Ballard C, Fossey J, et al. Epidemiology of Pain in People With Dementia
413	Living in Care Homes: Longitudinal Course, Prevalence, and Treatment Implications. J
414	Am Med Dir Assoc 2017;18:453.e1-453.e6.
415	45. Husebo BS, Ballard C, Sandvik R, et al. Efficacy of treating pain to reduce behavioural
416	disturbances in residents of nursing homes with dementia: cluster randomised clinical
417	trial. The BMJ 2011;343:d4065.
418	46. Aalto UL, Roitto HM, Finne-Soveri H et al. Use of Anticholinergic Drugs and its
419	Relationship With Psychological Well-Being and Mortality in Long-Term Care
420	Facilities in Helsinki. J Am Med Dir Assoc. 2018;19:511-515.
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437 Figure 1a. Mean number of psychotropics used by NH and ALF residents with and without dementia from 2003 to 2017. 438 439 Figure 1b. Mean number of antipsychotics used by NH and ALF residents with and without 440 441 dementia from 2003 to 2017. 442 Figure 1c. Mean number of anxiolytics and hypnotics used by NH and ALF residents with and 443 444 without dementia from 2003 to 2017. 445 Figure 1d. Mean number of antidepressants used by NH and ALF residents with and without 446 dementia from 2003 to 2017. 447 448 449 Figure 2. The percentage of opioid users among NH and ALF residents with and without dementia 450 from 2003 to 2017. 451 452 Figure 3. Mean number of sedatives used by NH and ALF residents with and without dementia 453 from 2003 to 2017.