Drugs & Aging (2022) 39:811–827
https://doi.org/10.1007/s40266-022-00972-9

ORIGINAL RESEARCH ARTICLE

Correlates of Opioid Use Among Ontario Long-Term Care Residents and Variation by Pain Frequency and Intensity: A Cross-sectional Analysis

Anita Iacono[1] · Michael A. Campitelli[2] · Susan E. Bronskill[2,3,4] · David B. Hogan[5] · Andrea Iaboni[6,7] · Laura C. Maclagan[2] · Tara Gomes[2,3,8,9] · Mina Tadrous[2,4,9] · Charity Evans[10] · Andrea Gruneir[2,11] · Qi Guan[2,3] · Thomas Hadjistavropoulos[12] · Cecilia Cotton[13] · Sudeep S. Gill[2,14] · Dallas P. Seitz[2,15] · Joanne Ho[16,17] · Colleen J. Maxwell[1,2,18]

Accepted: 26 July 2022 / Published online: 17 August 2022

Abstract

Background Chronic non-cancer pain is common among older residents of long-term care (LTC) homes and often poorly recognized and treated. With heightened concerns regarding opioid prescribing in recent years, it is important to examine the current prevalence of opioid use and its association with resident characteristics to help identify those potentially at risk of medication harms as well as suboptimal pain management.

Objectives The aims were to estimate the prevalence and correlates of opioid use among non-palliative LTC residents and explore variation in opioid prevalence and correlates across strata defined by pain frequency and intensity.

Methods We conducted a population-based cross-sectional study of all older (aged > 65 years) LTC residents (excluding those with cancer or receiving palliative care) in Ontario, Canada during 2018–2019. Health administrative databases were linked with standardized clinical assessment data to ascertain residents' health and pain characteristics and their opioid and other medication use. Modified Poisson regression models estimated unadjusted and adjusted associations between residents' characteristics and opioid use, overall and across strata capturing pain frequency and intensity.

Results Among 75,020 eligible residents (mean age 85.1 years; 70% female), the prevalence of opioid use was 18.5% and pain was 29.4%. Opioid use ranged from 12.2% for residents with no current pain to 55.7% for those with severe pain. In adjusted models, residents newly admitted to LTC (adjusted risk ratio [aRR] = 0.60, 95% confidence interval [CI] 0.57–0.62) and with moderate to severe cognitive impairment (aRR = 0.69, 95% CI 0.66–0.72) or dementia (aRR = 0.76, 95% CI 0.74–0.79) were significantly less likely to receive an opioid, whereas residents with select conditions (e.g., arthritis, aRR = 1.37, 95% CI 1.32–1.41) and concurrently using gabapentinoids (aRR = 1.80, 95% CI 1.74–1.86), benzodiazepines (aRR = 1.33, 95% CI 1.28–1.38), or antidepressants (aRR = 1.31, 95% CI 1.27–1.35) were significantly more likely to receive an opioid. The associations observed for residents newly admitted, with dementia, and concurrently using gabapentinoids, benzodiazepines, or antidepressants were largely consistent across all pain strata.

Conclusions Our findings describe resident sub-groups at potentially higher risk of adverse health outcomes in relation to both opioid use and non-use. LTC clinical and policy changes informed by research are required to ensure the appropriate recognition and management of non-cancer pain in this setting.

✉ Colleen J. Maxwell
colleen.maxwell@uwaterloo.ca

Extended author information available on the last page of the article

Key Points

In this population-based cross-sectional study of Ontario long-term care (LTC) residents (without cancer and not receiving palliative care), almost one in five were dispensed an opioid during 2018–2019 and just under one third had some level of pain. Opioid prevalence increased with pain frequency/intensity, though almost half of residents with severe pain were not dispensed an opioid, nor were they more likely to receive non-opioid analgesics.

Generally, across all pain levels, residents newly admitted to LTC and those with dementia were significantly less likely to receive an opioid, whereas residents concurrently using other high-risk medications (gabapentinoids, benzodiazepines, or antidepressants) were more likely to be dispensed an opioid.

Study findings suggest resident sub-groups potentially at greater risk for harm because of opioid use, as well as some who may be potentially vulnerable to poorly recognized or managed pain.

1 Introduction

Opioids are often prescribed to long-term care (LTC) residents for non-cancer pain [1], with prevalence estimates for this indication ranging from 19.6% [2] to 32% [3]. Pain management in this care setting is challenging as healthcare providers must carefully balance the risks and benefits of opioid therapy in older, more vulnerable individuals. Beyond their advanced age, LTC residents typically present with high levels of cognitive impairment, multimorbidity, frailty, and polypharmacy [4]. These characteristics, along with age-associated physiological, pharmacokinetic, and pharmacodynamic changes, increase their risk for opioid-related adverse events, including cognitive dysfunction, sedation, falls, and clinically important drug interactions [5–7].

Nonetheless, relatively higher opioid prescribing in LTC may be expected given the high burden of pain in this population [1]. Prevalence estimates of non-cancer pain among LTC residents range from approximately 25–50%, depending on the study population, pain measure, and time period examined [8–11]. For some residents in pain, opioids may be an appropriate alternative when other therapies are contraindicated or ineffective [12–15]. Further, it is well-known that pain is poorly recognized and treated in the LTC setting, despite awareness of the adverse health and quality-of-life consequences of inadequate pain control [13, 16]. Though not yet explored, it is possible that the under-treatment of pain among LTC residents has increased in recent years because of increased concern about opioid misuse and heightened monitoring of prescribing practices across care settings [17].

Research suggests that up to one quarter of LTC residents with severe pain do not receive any analgesic or adjuvant therapy [1]. Residents with cognitive and/or communication impairment appear to be at particular risk for both the under-recognition and under-treatment of pain [1, 3, 8, 18–21]. In addition to distress related to uncontrolled pain, it can also lead to a worsening of residents' cognitive and functional status [11, 22]. Among those with dementia, it may manifest as agitation and/or aggression, encouraging the prescription of antipsychotics and other high-risk medications [23, 24]. Less is known about how other resident characteristics, including frailty [2], common co-occurring conditions and medications, and recency of LTC admission (a potential indicator of changing patterns in opioid prescribing in the community or other care settings related to the opioid crisis), influence the use of opioids in LTC. Understanding opioid use in relation to these resident characteristics, in addition to their assessed pain symptoms, may help to identify those at heightened risk of medication harms and/or sub-optimal pain management and thus adverse health and quality-of-life outcomes. This is particularly true for Canadian LTC settings where there have been no population-based investigations of the prevalence and correlates of opioid use. Further compounding clinical uncertainty in this area is the fact that Canada is yet to develop national clinical practice guidelines for the management of non-cancer pain [25] that specifically address the unique considerations of LTC residents.

We utilized linked clinical and health administrative databases for all older LTC residents in Ontario (excluding those with cancer and/or receiving palliative care) to (1) estimate the overall prevalence and correlates of opioid use during 2018–2019, with a focus on several resident characteristics not previously examined, and (2) explore variation in the prevalence and correlates of opioid use across strata defined by pain frequency and intensity. In addressing these objectives, we sought to identify resident sub-groups potentially at greater risk for harm because of opioid use as well as those potentially vulnerable to poorly recognized or managed pain. We hypothesized that opioid use would be higher among residents with more frequent/intense pain and pain-related

indices, but lower among those of advanced age, with higher levels of cognitive impairment, frailty, and/or polypharmacy.

2 Methods

2.1 Study Design, Setting, and Data

Using linked health administrative and clinical databases from Ontario (Canada's most populous province), we conducted a population-based cross-sectional study of prescription opioid use among older adults residing within all LTC homes (also termed nursing homes in the US and elsewhere). LTC homes in Ontario are distinct from assisted living/retirement homes with admission restricted to those with provincial health insurance who require 24-h nursing and personal care, assistance with activities of daily living (ADL), on-site supervision or monitoring to ensure safety or well-being, and care that cannot be met through other community-based services. The publicly funded provincial health insurance program covers most LTC costs and provides residents with coverage for prescription medications listed on a provincial formulary or through an exceptional access program, hospital care, and physician services. Interactions with these healthcare sectors are captured in provincial health databases (see Supplemental Table S1 in the electronic supplementary material). Clinical data for Ontario LTC residents are captured in the Canadian Institute for Health Information's (CIHI's) Continuing Care Reporting System. Full assessments are mandatory upon admission to LTC, annually thereafter, and following significant changes in health status. They are conducted using the Resident Assessment Instrument-Minimum Data Set Version 2.0 (RAI-MDS 2.0), a validated tool which provides a standardized and comprehensive evaluation of a resident's health status, functional limitations, and care needs [26, 27]. These databases were linked using encoded identifiers and analyzed at ICES and have been extensively used to examine prescription medication use and health issues in LTC [2, 4, 28].

ICES (formerly the Institute for Clinical Evaluative Sciences) is an independent, non-profit research institute whose legal status under Ontario's health information privacy law allows it to collect and analyze healthcare and demographic data, without consent, for health system evaluation and improvement.

2.2 Study Population

We included all adults aged 66 years and older in Ontario who resided in an LTC home at some point between April 1, 2018 and March 31, 2019. Residents were identified upon their earliest full clinical assessment during this study period (index assessment). Among the 88,941 residents identified, we excluded those with an active cancer diagnosis recorded on the RAI-MDS 2.0 (n = 7411; 8.3%) or who received palliative care in the past 6 months (n = 6230; 7.0%) as our focus was on the correlates of opioid use for non-cancer pain. We also excluded residents with no drug claims in the 12 months prior to the index assessment (n = 156; 0.18%), those aged greater than 105 years or with an invalid sex (n = 73; 0.08%), and residents identified as comatose at their index assessment (n = 51; 0.06%). Our final study population contained 75,020 residents from 627 unique LTC homes.

2.3 Opioid Use

The Ontario Drug Benefit (ODB) database was used to obtain opioid medication claims, which included information on the dispensation date, type of opioid dispensed (codeine, fentanyl, hydromorphone, morphine, and oxycodone), and the prescription duration in days. To focus on opioids used to manage pain, we excluded claims where these drugs were used to treat opioid use disorders (e.g., methadone), as a cough suppressant, or in antidiarrheals (see Supplemental Table S2 in the electronic supplementary material). Using these claims, we identified LTC residents dispensed opioids at their index date (i.e., RAI-MDS 2.0 assessment date), defined as a duration of opioid therapy (estimated using the dispensation date and days of medication supplied) that overlapped or included their index assessment date.

2.4 Covariates

Resident characteristics examined as correlates of opioid use were selected based on previous literature [1, 2, 9, 29] and clinical relevance as determined by the research team. Of particular interest in the current study were understudied characteristics relevant to our understanding of pain management in this care setting, including recency of LTC admission, frailty and specific co-occurring conditions and medications.

2.4.1 Sociodemographic

Resident age and sex were determined from the Ontario Registered Persons Database. The RAI-MDS 2.0 index assessment was differentiated as occurring at LTC home entry (i.e., assessment completed with input from the multidisciplinary care team within 14 days of admission to LTC) versus annually or in response to a health status change.

2.4.2 Pain Symptom Items

We derived a categorical pain measure from index RAI-MDS 2.0 items on pain symptom frequency and intensity assessed over the past week, coded as follows: 0 (no pain), 1 (less than daily mild-moderate pain), 2 (daily mild-moderate pain), and 3 (any frequency of severe pain). For these items, assessors are instructed to rely on resident self-report when possible, consult family and staff, and observe the resident for any signs or symptoms of pain. Compared to the validated RAI-MDS 2.0 pain scale [30], we collapsed any frequency of severe pain in the highest category to better capture cases where opioid use may be deemed more appropriate. We also summarized assessment items describing the site of pain (e.g., back, bone, hip/joint, incisional, soft tissue).

2.4.3 Health Status

Data from the index RAI-MDS 2.0 assessment were used to derive validated scales of resident frailty [4], cognitive [31] and ADL performance [32], depressive symptoms [33], and aggressive behaviors [34]. These commonly used scales are described in detail in Supplemental Table S3 (see the electronic supplementary material). Frailty was identified using a 72-item frailty index based on the accumulated deficits approach where for each resident, the proportion of health deficits present are divided by the number considered. The deficits considered in this index included measures of psychosocial well-being, mood, cognitive and functional status, and health conditions. As in previous work [4], those with greater than 30% of potential deficits present were categorized as frail. Residents with a depression rating scale score of 3 or greater were categorized as having clinically relevant depressive symptoms.

2.4.4 Co-occurring Health Conditions and Medications

Items on the index RAI-MDS 2.0 assessment were used to determine the presence of pain-related health conditions (musculoskeletal, recent fractures, pressure ulcers, surgical wounds, oral disease, and foot problems) [3, 9, 35], dementia, and other chronic diseases. The latter included conditions that may increase the likelihood for opioid use for reasons other than pain control (e.g., to manage dyspnea associated with chronic obstructive pulmonary disease [COPD] or congestive heart failure). The CIHI Discharge Abstract Database and National Ambulatory Care Reporting System identified inpatient admissions and emergency department visits in the 90 days prior to assessment, respectively. The ODB database was used to obtain non-opioid medication claims where the duration of therapy overlapped or included residents' index assessment date. We used these claims to quantify the number of unique non-opioid medications concurrently dispensed to each resident and to determine the concurrent use of benzodiazepines, antipsychotics, antidepressants including trazodone, gabapentinoids (pregabalin, gabapentin), non-opioid analgesics (acetaminophen, non-steroidal anti-inflammatory drugs [NSAIDs]), and oral corticosteroids (sometimes used as adjuvant therapy for pain).

2.5 Statistical Analysis

Given the large sample size, standardized differences were used to compare resident characteristics between those dispensed and not dispensed an opioid at their index assessment, overall and across pain symptom strata. Standardized differences greater than 10% were interpreted as meaningful differences between groups [36].

We used Poisson regression models, modified to analyze binary outcomes [37], to examine the association between resident characteristics and opioid use. Our models included a robust sandwich variance estimator to account for the clustering of residents within LTC homes [38]. Given our outcome (prevalent opioid use) was relatively common, especially among residents with more frequent/intense pain symptoms, this method yields unbiased estimates of our parameter of interest, the risk ratio (RR), and appropriate 95% confidence intervals (CIs). Both unadjusted models and models adjusting for a selection of resident characteristics were explored. We built our final adjusted model in a staged approach by adding in clusters of similar variables sequentially to evaluate any collinearity issues (assessed by an examination of the robustness of covariate estimates as new measures were entered and variance inflation factor [VIF] values, which indicated no relevant collinearity concerns). Then, to develop a parsimonious model, we removed any non-significant factors except for age and concurrent drug use as we wanted to retain these in our final models for comparative purposes (i.e., to allow a relative comparison of associations across pain strata adjusting for similar resident factors). Stratified analyses, specified a priori, were conducted among residents assessed as experiencing no pain, less than daily mild-moderate pain, daily mild-moderate pain, and any frequency of severe pain. To further support our stratified models, we examined models for the total sample incorporating interaction terms between our four-level pain measure and key covariates of interest, including cognitive impairment, new admission to LTC home, frailty, and co-occurring use of select central nervous system medications (e.g., benzodiazepines, gabapentinoids).

We applied a Bonferroni correction in assessing statistical significance to address concerns of multiple testing (with bolding of model estimates to illustrate this corrected level of statistical significance). All analyses were two-tailed.

SAS version 9.4 (SAS Institute Inc.) was used to conduct all analyses.

Our study received ethics approval by the University of Waterloo Human Research Ethics Committee (# 42355).

3 Results

Among the 75,020 residents meeting inclusion criteria, the mean age was 85.1 years (±8.1), and most were female (70.0%) (Table 1). A high proportion of residents were categorized as frail (58.7%), had moderate to greater cognitive impairment (66.1%), required at least extensive ADL assistance (84.0%), and were prescribed five or more unique non-opioid medications (75.7%). The proportion of residents assessed as having any pain was 29.4% (21.2% with less than daily mild-moderate pain, 5.7% with daily mild-moderate pain, and 2.5% with any severe pain). Almost half of residents were assessed as having at least one pain-related condition, with arthritis the most common (45.5%). An estimated 18.5% of residents were dispensed an opioid at their index assessment date, with the most common being hydromorphone (68.7% of opioid dispensations) followed by codeine (16.8%), oxycodone (6.8%), morphine (5.3%), and fentanyl (2.6%). For essentially all residents (99%), prevalent opioid use represented an opioid dispensed within the LTC setting. Additional details regarding opioid type, dose, and use prior to and post the index dispensation are provided in Supplemental Table S2 (see the electronic supplementary material). Most residents (73.9%) were dispensed an opioid dose of < 50-mg morphine equivalents, with higher doses evident among those with more frequent and severe pain (e.g., 24.9% of residents in severe pain vs. 9.8% with no pain were dispensed an opioid dose of ≥ 90-mg morphine equivalents). Most residents (81.6%) were dispensed an opioid in both the week prior to and post their index opioid dispensation (suggesting more than a one-time use at index date), though this proportion declined slightly for those with more frequent/severe pain (72.4%). Among those dispensed an opioid, 46.6% were assessed as having no pain and 32.2% with less than daily mild-moderate pain.

Residents receiving an opioid were more likely to be female and assessed as having pain (all levels) and pain-related conditions, frailty, ADL dependency, clinically meaningful depressive symptoms, anxiety, and select chronic conditions (e.g., congestive heart failure, peripheral vascular disease, COPD). They were also more likely to be receiving ten or more unique non-opioid medications, benzodiazepines, antidepressants, gabapentinoids (pregabalin and gabapentin), acetaminophen, and NSAIDs. Those dispensed an opioid were, however, less likely to be newly admitted to the LTC home or to have moderate to severe cognitive impairment or a diagnosis of dementia (Table 1). Among newly admitted residents, 60.7% were admitted from home, 27.3% from acute care, 5.3% from a different LTC home, and 6.7% from another setting. Prevalent opioid use was lowest for those admitted from home (10.3%) and higher for those admitted from other settings (e.g., 20.7% for acute care). Resident characteristics not associated with opioid use included age, presence of aggressive behaviors, recent hospitalization, and antipsychotic use.

Within the total cohort, following adjustment for relevant covariates, including pain (Table 2), there was a significantly lower likelihood for opioid use among male residents (adjusted RR [aRR] = 0.92, 95% CI 0.89–0.95), those newly admitted to LTC (aRR = 0.60, 95% CI 0.57–0.62), those with cognitive impairment (aRR = 0.69, 95% CI 0.66–0.72 for moderate to severe impairment), and those diagnosed with Parkinson's disease (aRR = 0.90, 95% CI 0.85–0.95). When a dementia diagnosis was substituted for the cognitive performance score in this model, the adjusted association for dementia was similar (aRR = 0.76, 95% CI 0.74–0.79). Conversely, residents were significantly more likely to be dispensed an opioid if they were assessed as having pain, especially of high frequency and/or intensity (e.g., aRR = 3.21, 95% CI 2.99–3.44 for any severe pain), ADL dependency (aRR = 1.40, 95% CI 1.32–1.48), or select pain-related chronic conditions (including arthritis, aRR = 1.37, 95% 1.32–1.41, a recent fracture, aRR = 1.26, 95% CI 1.18–1.33, and serious pressure ulcer, aRR = 1.32 95% CI 1.25–1.39). In the adjusted model, the presence of frailty, depressive symptoms, and a few other health conditions (osteoporosis, COPD) showed significant, though modest, positive associations with opioid use. Concurrent use of benzodiazepines (aRR 1.33, 95% CI 1.28–1.38), antidepressants (aRR 1.31, 95% CI 1.27–1.35), gabapentinoids (aRR 1.80, 95% CI 1.74–1.86), NSAIDs (aRR 1.18, 95% CI 1.10–1.26), or oral corticosteroids (aRR 1.13, 95% CI 1.06–1.21) was also associated with a higher likelihood of opioid use.

Table 3 and Figs. 1, 2, and 3 present the adjusted associations between residents' characteristics and opioid use stratified by pain symptom level (see Supplemental Tables S4–S7 for the unadjusted associations for each of the pain strata). All interaction terms investigated were statistically significant ($p < 0.0001$). The crude prevalence of opioid use ranged from 12.2% for residents with no pain to 55.7% for those with any severe pain. Across all pain strata, there was a reduced likelihood of receiving an opioid for residents newly admitted to LTC. For the no and lowest pain strata only, residents with mild or moderate to severe cognitive impairment were significantly less likely to be dispensed an opioid. Models with dementia substituted for the cognitive performance scale showed that residents with this diagnosis were significantly less likely to receive an opioid across all strata except for the severe pain sub-group (Tables S4–S7).

Table 1 Ontario LTC resident characteristics by prevalent opioid use at index assessment, April 2018–March 2019

Characteristic	Total cohort Number (%)[a] (*N* = 75,020)	Number (%) prescribed opioids[b] (*N* = 13,896; 18.5%)	Number (%) not prescribed opioids[b] (*N* = 61,124; 81.5%)	Std diff.
Demographics				
Age, mean (±SD)	85.1 (±8.1)	84.9 (±8.2)	85.2 (±8.1)	0.03
66–75	10,736 (14.3)	2153 (15.5)	8583 (14.0)	0.04
76–85	24,423 (32.6)	4516 (32.5)	19,907 (32.6)	0
86+	39,861 (53.1)	7227 (52.0)	32,634 (53.4)	0.03
Sex				
Female	52,496 (70.0)	10,511 (75.6)	41,985 (68.7)	0.16
Male	22,524 (30.0)	3385 (24.4)	19,139 (31.3)	0.16
Entry LTC assessment	22,511 (30.0)	3152 (22.7)	19,359 (31.7)	0.20
Health status				
Pain symptom frequency/intensity				
No pain	52,999 (70.6)	6474 (46.6)	46,525 (76.1)	0.64
Less than daily mild-moderate pain	15,876 (21.2)	4470 (32.2)	11,406 (18.7)	0.31
Daily mild-moderate pain	4268 (5.7)	1906 (13.7)	2362 (3.9)	0.35
Any frequency of severe pain	1877 (2.5)	1046 (7.5)	831 (1.4)	0.30
Resident frailty				
Not frail/pre-frail	30,976 (41.3)	4852 (34.9)	26,124 (42.7)	0.16
Frail	44,044 (58.7)	9044 (65.1)	35,000 (57.3)	0.16
Cognitive performance scale (score)				
Intact/borderline intact (0, 1)	13,137 (17.5)	3469 (25.0)	9668 (15.8)	0.23
Mild impairment (2)	12,262 (16.3)	2293 (16.5)	9969 (16.3)	0.01
Moderate to severe impairment (3, 4)	35,441 (47.2)	5651 (40.7)	29,790 (48.7)	0.16
Severe to very severe impairment (5, 6)	14,180 (18.9)	2483 (17.9)	11,697 (19.1)	0.03
ADL performance (score)				
Independent/some assistance (0–2)	12,031 (16.0)	1871 (13.5)	10,160 (16.6)	0.09
Extensive assistance (3, 4)	41,302 (55.1)	7176 (51.6)	34,126 (55.8)	0.08
Dependent (5, 6)	21,687 (28.9)	4849 (34.9)	16,838 (27.5)	0.16
Depression Rating Scale (score)				
No clinically relevant depressive symptoms (0–2)	54,876 (73.1)	9035 (65.0)	45,841 (75.0)	0.22
Clinically relevant depressive symptoms (3+)	20,144 (26.9)	4861 (35.0)	15,283 (25.0)	0.22
Aggressive behaviors scale (score)				
None (0)	42,270 (56.3)	7971 (57.4)	34,299 (56.1)	0.03
Mild-moderate (1–4)	26,742 (35.6)	4840 (34.8)	21,902 (35.8)	0.02
Moderate-severe (5+)	6008 (8.0)	1085 (7.8)	4923 (8.1)	0.01
Pain-related conditions				
Arthritis	34,147 (45.5)	8255 (59.4)	25,892 (42.4)	0.35
Osteoporosis	23,490 (31.3)	4987 (35.9)	18,503 (30.3)	0.12
Any fracture in past 180 days	3589 (4.8)	1125 (8.1)	2464 (4.0)	0.17
Serious pressure ulcer	4503 (6.0)	1430 (10.3)	3073 (5.0)	0.20
Surgical wounds	1750 (2.3)	618 (4.4)	1132 (1.9)	0.15
Oral disease[c]	4475 (6.0)	1021 (7.3)	3454 (5.7)	0.07
Foot problems[d]	17,248 (23.0)	3931 (28.3)	13,317 (21.8)	0.15
Other chronic conditions				
Dementia	49,398 (65.8)	7690 (55.3)	41,708 (68.2)	0.27
Diabetes	20,743 (27.6)	3937 (28.3)	16,806 (27.5)	0.02
Arteriosclerotic heart disease	11,760 (15.7)	2488 (17.9)	9272 (15.2)	0.07
Congestive heart failure	9224 (12.3)	2116 (15.2)	7108 (11.6)	0.11
Peripheral vascular disease	4282 (5.7)	1122 (8.1)	3160 (5.2)	0.12

Table 1 (continued)

Characteristic	Total cohort Number (%)[a] (*N* = 75,020)	Number (%) prescribed opioids[b] (*N* = 13,896; 18.5%)	Number (%) not prescribed opioids[b] (*N* = 61,124; 81.5%)	Std diff.
COPD	11,036 (14.7)	2635 (19.0)	8401 (13.7)	0.14
Parkinson's disease	5080 (6.8)	863 (6.2)	4217 (6.9)	0.03
Anxiety disorder	10,281 (13.7)	2415 (17.4)	7866 (12.9)	0.13
Recent hospital use				
ED visit and/or inpatient admission in past 90 days	18,566 (24.7)	3849 (27.7)	14,717 (24.1)	0.08
Concurrent medications used on index date				
Number of unique non-opioid medications used				
0–4	18,248 (24.3)	2094 (15.1)	16,154 (26.4)	0.28
5–9	36,372 (48.5)	6336 (45.6)	30,036 (49.1)	0.07
10+	20,400 (27.2)	5466 (39.3)	14,934 (24.4)	0.32
Benzodiazepines	7082 (9.4)	2094 (15.1)	4988 (8.2)	0.22
Antipsychotics	18,324 (24.4)	3321 (23.9)	15,003 (24.5)	0.02
Antidepressants (including trazodone)	43,701 (58.3)	9553 (68.7)	34,148 (55.9)	0.27
Gabapentinoid (pregabalin and/or gabapentin)	8668 (11.6)	3593 (25.9)	5075 (8.3)	0.48
Acetaminophen[e]	31,331 (41.8)	6635 (47.7)	24,696 (40.4)	0.15
Non-steroidal anti-inflammatories[e]	2246 (3.0)	691 (5.0)	1555 (2.5)	0.13
Oral corticosteroids	2265 (3.0)	599 (4.3)	1666 (2.7)	0.09

ADL activities of daily living, *COPD* chronic obstructive pulmonary disease, *ED* emergency department, *LTC* long-term care, *ODB* Ontario Drug Benefit, *SD* standard deviation, *Std diff.* standardized difference (estimates > 0.10 represent meaningful difference between comparison groups)

[a]Cohort excludes residents receiving palliative care in 6 months prior to index date and/or with cancer diagnosis at index date

[b]Data are presented as number (column percentage)

[c]Oral disease included presence of any of following in 7 days prior to index assessment: mouth pain, broken/loose/carious teeth, inflamed gums/swollen, bleeding gums/oral abscesses/ulcers/rashes

[d]Foot problems included presence of any of following in 7 days prior to index assessment: corns/callouses/bunions/hammer toes/overlapping toes/pain/structural problems, infection of the foot, open lesions of the foot

[e]Represent underestimate of actual use in LTC given exposures are not fully captured by ODB claims.

Male residents were significantly less likely to receive an opioid among the no pain stratum only.

Across all pain strata, there was a higher likelihood of opioid use for residents concurrently using benzodiazepines or gabapentinoids. The associations observed for the concurrent use of benzodiazepines and gabapentinoids (and other drug classes positively associated with opioid use in the total cohort) were more pronounced among the no pain group. Residents who were frail were significantly more likely to receive an opioid among the no pain stratum only. For many of the other characteristics observed to have a significant association with opioid use in the total cohort, most remained significant correlates of opioid use within the two lowest pain symptom strata (no pain and less than daily mild-moderate pain) and showed a less pronounced association with opioid use as pain frequency and severity increased. One exception was the presence of clinically relevant depressive symptoms, which was significantly associated with opioid use among residents in the no pain and severe pain strata.

Descriptive data regarding the pain site noted for residents assessed with pain and associated opioid use are presented in Supplemental Table S8. Pain sites reflective of musculoskeletal conditions (e.g., back, hip, and joint pain) were particularly prevalent and associated with opioid use.

To further illustrate the relevance of cognitive impairment to opioid use for pain management, Fig. 4a presents the adjusted prevalence of opioid use by residents' cognitive status and assessed pain. Opioid use increased with pain symptom frequency and intensity and was generally lower with increasing cognitive impairment across all pain levels. The exception was the slight increase in the adjusted prevalence of opioid use for residents with severe to very severe cognitive impairment (especially evident for residents assessed with any severe pain). We also examined the adjusted prevalence of opioid use among residents assessed as having no pain, according to their cognitive impairment level and number of pain-related conditions (Fig. 4b). Similar findings, though relatively lower adjusted opioid prevalence estimates overall, were observed. These two figures

Table 2 Associations between Ontario LTC resident characteristics and prevalent opioid use at index assessment, April 2018–March 2019

Characteristic	% Prescribed opioids[b]	Unadjusted RR[c] (95% CI)	Adjusted RR[c] (95% CI)
Total cohort[a]	18.5		
Age group, ref. = 66–75	20.1		
76–85	18.5	0.93 (0.89–0.98)	1.02 (0.98–1.07)
86+	18.1	**0.93 (0.89–0.97)**	1.03 (0.99–1.08)
Sex, ref. = Female	20.0		
Male	15.0	**0.75 (0.73–0.78)**	**0.92 (0.89–0.95)**
Entry LTC assessment, ref. = No	20.5		
Yes	14.0	**0.65 (0.62–0.69)**	**0.60 (0.57–0.62)**
Pain symptom frequency/intensity, ref. = No pain	12.2		
Less than daily mild-moderate pain	28.2	**2.35 (2.26–2.45)**	**2.00 (1.92–2.08)**
Daily mild-moderate pain	44.7	**3.88 (3.68–4.09)**	**2.89 (2.75–3.04)**
Any frequency of severe pain	55.7	**4.60 (4.26–4.96)**	**3.21 (2.99–3.44)**
Resident frailty, ref. = Not frail/pre-frail	15.7		
Frail	20.5	**1.30 (1.25–1.35)**	**1.11 (1.07–1.16)**
Cognitive performance scale (score),[d] ref. = Intact/borderline intact (0,1)	26.4		
Mild impairment (2)	18.7	**0.71 (0.67–0.74)**	**0.82 (0.78–0.86)**
Moderate to severe impairment (3,4)	15.9	**0.60 (0.57–0.62)**	**0.69 (0.66–0.72)**
Severe to very severe impairment (5,6)	17.5	**0.67 (0.63–0.71)**	**0.75 (0.71–0.80)**
ADL performance (score), ref. = Independent/some assistance (0–2)	15.6		
Extensive assistance (3,4)	17.4	**1.16 (1.10–1.22)**	**1.10 (1.05–1.15)**
Dependent (5,6)	22.4	**1.57 (1.48–1.67)**	**1.40 (1.32–1.48)**
Depression rating scale (score), ref. = No clinically relevant depressive symptoms (0–2)	16.5		
Clinically relevant depressive symptoms (3+)	24.1	**1.43 (1.38–1.47)**	**1.08 (1.04–1.11)**
Arthritis	24.2	**1.69 (1.64–1.75)**	**1.37 (1.32–1.41)**
Osteoporosis	21.2	**1.25 (1.21–1.29)**	**1.10 (1.07–1.13)**
Any fracture in past 180 days	31.3	**1.67 (1.56–1.78)**	**1.26 (1.18–1.33)**
Serious pressure ulcer	31.8	**1.77 (1.68–1.86)**	**1.32 (1.25–1.39)**
Surgical wounds	35.3	**1.89 (1.75–2.04)**	1.11 (1.03–1.20)
Oral disease	22.8	**1.18 (1.11–1.26)**	1.09 (1.03–1.16)
Foot problems	22.8	**1.33 (1.27–1.38)**	1.06 (1.02–1.10)
Congestive heart failure	22.9	**1.24 (1.19–1.29)**	1.05 (1.01–1.09)
Peripheral vascular disease	26.2	**1.37 (1.30–1.45)**	1.05 (1.00–1.10)
COPD	23.5	**1.29 (1.24–1.34)**	**1.10 (1.06–1.13)**
Parkinson's disease	17.0	0.93 (0.87–0.98)	**0.90 (0.85–0.95)**
Benzodiazepines	29.6	**1.65 (1.58–1.72)**	**1.33 (1.28–1.38)**
Antipsychotics	18.1	0.97 (0.94–1.01)	1.02 (0.99–1.06)
Antidepressants (including trazodone)	21.9	**1.51 (1.46–1.56)**	**1.31 (1.27–1.35)**
Gabapentinoids (pregabalin and/or gabapentin)	41.5	**2.59 (2.50–2.68)**	**1.80 (1.74–1.86)**
Acetaminophen	21.2	**1.24 (1.19–1.30)**	0.98 (0.94–1.01)
Non-steroidal anti-inflammatories	30.8	**1.63 (1.51–1.75)**	**1.18 (1.10–1.26)**
Oral corticosteroids	26.4	**1.41 (1.32–1.52)**	**1.13 (1.06–1.21)**

ADL activities of daily living, *CI* confidence interval, *COPD* chronic obstructive pulmonary disease, *LTC* long-term care, *ref.* reference, *RR* risk ratio

[a] N = 75,020, excludes residents receiving palliative care in 6 months prior to index date and/or with cancer diagnosis at index date

[b] Data are presented as row percentage

[c] Derived from modified Poisson regression models (estimates in bold were statistically significant after Bonferroni correction), with robust standard errors accounting for clustering of residents, full model adjusted for all variables listed

[d] In adjusted model with dementia substituted for cognitive performance score, dementia (n = 49,398) = 15.6% dispensed opioids and adjusted RR = **0.76 (0.74–0.79)**

Table 3 Associations between Ontario LTC resident characteristics and prevalent opioid use at index assessment by pain frequency and intensity, April 2018–March 2019

Characteristic	RAI-MDS 2.0 pain symptom frequency/intensity			
	No pain[a] *N* = 52,999; 70.6%	Less than daily mild-mod. pain[a] *N* = 15,876; 21.2%	Daily mild-mod. pain[a] *N* = 4268; 5.7%	Any frequency of severe pain[a] *N* = 1877; 2.5%
	aRR[b] (95% CI)	aRR[b] (95% CI)	aRR[b] (95% CI)	aRR[b] (95% CI)
Opioid use	12.2%	28.2%	44.7%	55.7%
Age group, ref. = 66–75				
76–85	1.00 (0.93–1.08)	1.05 (0.97–1.13)	0.91 (0.84–0.99)	0.99 (0.89–1.11)
86+	1.04 (0.97–1.12)	1.02 (0.94–1.10)	0.88 (0.81–0.96)	0.94 (0.85–1.04)
Sex, male	**0.87 (0.83–0.92)**	0.92 (0.87–0.97)	0.94 (0.87–1.02)	1.06 (0.98–1.16)
Entry LTC assessment	**0.54 (0.50–0.58)**	**0.56 (0.52–0.60)**	**0.65 (0.60–0.70)**	**0.78 (0.71–0.86)**
Frail	**1.19 (1.11–1.27)**	1.05 (0.98–1.14)	0.97 (0.88–1.07)	1.10 (0.97–1.24)
Cognitive performance scale (score), ref. = Intact/borderline Intact (0,1)				
Mild impairment (2)	**0.74 (0.69–0.80)**	**0.85 (0.79–0.91)**	0.98 (0.89–1.08)	0.88 (0.77–0.99)
Moderate to severe impairment (3, 4)	**0.57 (0.53–0.62)**	**0.75 (0.71–0.81)**	0.89 (0.82–0.97)	0.85 (0.74–0.97)
Severe to very severe impairment (5, 6)	**0.62 (0.56–0.68)**	0.87 (0.79–0.96)	0.90 (0.80–1.02)	1.06 (0.90–1.25)
ADL performance (score), ref. = Independent/some assistance (0–2)				
Extensive assistance (3, 4)	**1.15 (1.06–1.24)**	1.12 (1.04–1.22)	1.02 (0.93–1.12)	1.02 (0.89–1.17)
Dependent (5, 6)	**1.55 (1.41–1.70)**	**1.39 (1.26–1.53)**	1.18 (1.06–1.32)	1.09 (0.92–1.28)
Clinically relevant depressive symptoms (DRS 3+)	**1.13 (1.07–1.19)**	1.02 (0.97–1.08)	1.07 (0.99–1.15)	**1.19 (1.09–1.30)**
Arthritis	**1.60 (1.52–1.68)**	**1.25 (1.19–1.32)**	1.09 (1.02–1.16)	**1.15 (1.06–1.25)**
Osteoporosis	**1.10 (1.06–1.15)**	**1.09 (1.04–1.15)**	1.07 (1.00–1.15)	1.08 (0.99–1.18)
Any fracture in past 180 days	**1.66 (1.45–1.90)**	**1.23 (1.11–1.37)**	1.15 (1.04–1.27)	1.07 (0.98–1.18)
Serious pressure ulcer	**1.47 (1.35–1.60)**	**1.29 (1.20–1.39)**	**1.18 (1.08–1.30)**	1.17 (1.05–1.29)
Surgical wounds	1.30 (1.08–1.55)	1.22 (1.08–1.38)	1.03 (0.92–1.16)	1.00 (0.87–1.16)
Oral disease	1.12 (1.01–1.24)	1.12 (1.04–1.21)	1.04 (0.92–1.18)	1.00 (0.87–1.15)
Foot problems	**1.11 (1.05–1.18)**	1.08 (1.03–1.14)	0.94 (0.87–1.01)	0.96 (0.88–1.05)
Congestive heart failure	1.07 (1.00–1.15)	1.08 (1.02–1.15)	0.96 (0.88–1.05)	1.04 (0.94–1.15)
Peripheral vascular disease	1.09 (1.01–1.19)	1.07 (0.98–1.16)	1.06 (0.96–1.18)	0.93 (0.81–1.07)
COPD	**1.12 (1.05–1.18)**	**1.12 (1.05–1.18)**	1.10 (1.02–1.19)	1.01 (0.93–1.09)
Parkinson's disease	0.92 (0.84–1.01)	0.87 (0.79–0.96)	0.90 (0.79–1.03)	0.78 (0.63–0.97)
Benzodiazepines	**1.43 (1.34–1.53)**	**1.29 (1.21–1.38)**	**1.24 (1.15–1.33)**	**1.22 (1.13–1.32)**
Antipsychotics	1.07 (1.02–1.13)	0.99 (0.94–1.04)	0.90 (0.83–0.97)	0.97 (0.86–1.09)
Antidepressants (including trazodone)	**1.47 (1.40–1.54)**	**1.26 (1.20–1.33)**	**1.18 (1.11–1.27)**	1.02 (0.94–1.12)
Gabapentinoids (pregabalin and/or gabapentin)	**2.31 (2.19–2.44)**	**1.67 (1.58–1.75)**	**1.33 (1.24–1.42)**	**1.44 (1.32–1.57)**
Acetaminophen	0.99 (0.93–1.05)	0.97 (0.92–1.03)	**0.87 (0.81–0.94)**	0.93 (0.86–1.02)
Non-steroidal anti-inflammatories	**1.56 (1.39–1.75)**	1.09 (0.97–1.23)	1.00 (0.89–1.13)	0.96 (0.83–1.10)
Oral corticosteroids	**1.26 (1.13–1.40)**	1.14 (1.02–1.28)	1.07 (0.94–1.22)	0.87 (0.71–1.07)

ADL activities of daily living, *aRR* adjusted risk ratio, *CI* confidence interval, *COPD* chronic obstructive pulmonary disease, *DRS* depression rating scale, *LTC* long-term care, *mod.* moderate, *RAI-MDS 2.0* Resident Assessment Instrument-Minimum Data Set Version 2.0, *ref.* reference

[a]Excludes residents receiving palliative care in 6 months prior to index date and/or with cancer diagnosis at index date

[b]Derived from modified Poisson regression models (estimates in bold were statistically significant after Bonferroni correction), with robust standard errors accounting for clustering of residents and adjusted for all variables listed

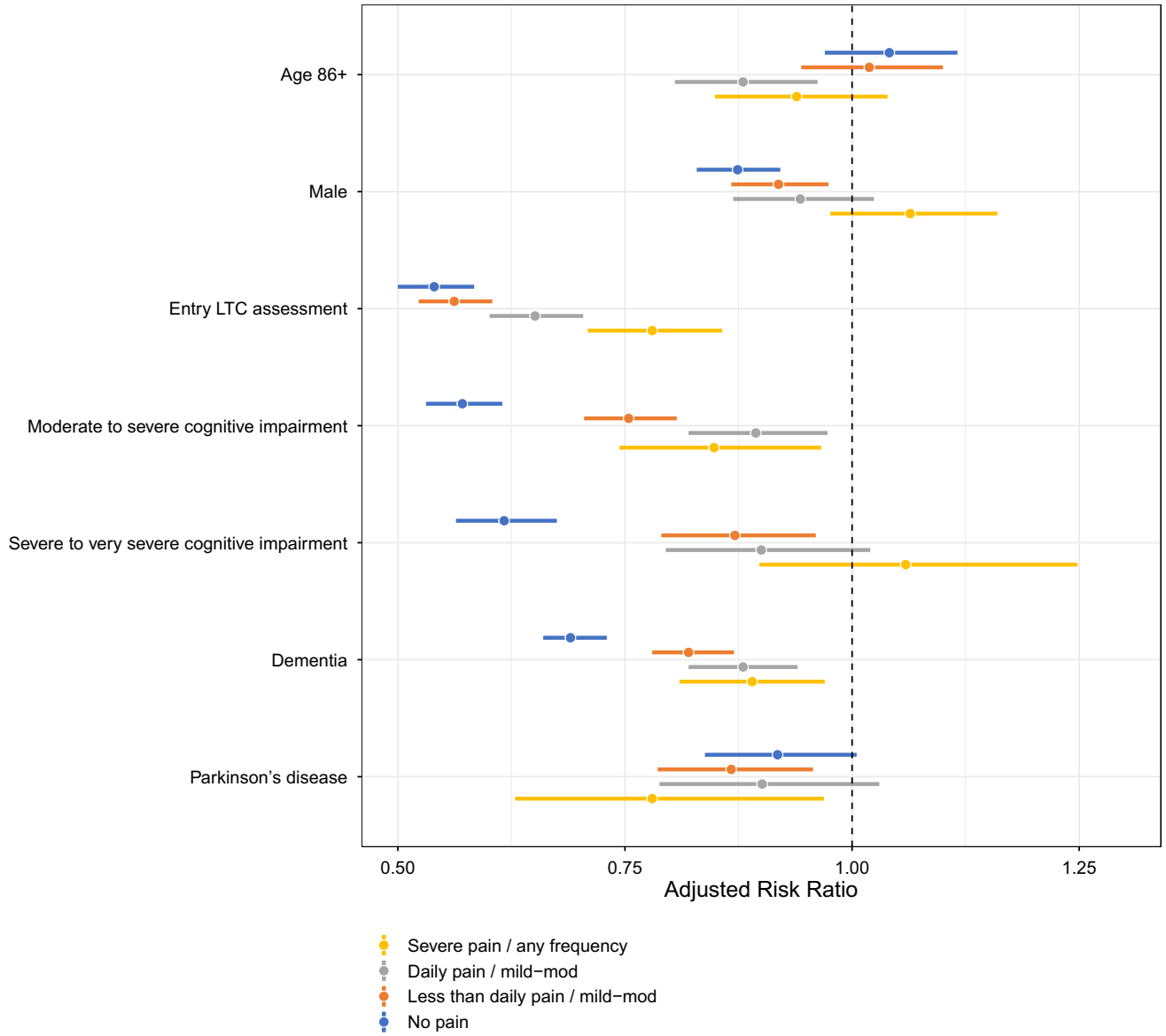

Fig. 1 Adjusted risk ratio for opioid use associated with sociodemographic and clinical characteristics, stratified by pain frequency and intensity, among Ontario long-term care (LTC) residents

also show that the adjusted prevalence of opioid use was as high as 16.7% among cognitively intact residents assessed with no pain and 10.2% among those with both no assessed pain and no pain-related conditions.

4 Discussion

In this population-based cross-sectional study of Ontario LTC residents assessed between 2018 and 2019, the overall prevalence of opioid use was 18.5% and pain was 29.4%. Among residents assessed with pain, most (72.1%) had less than daily mild-moderate pain. Opioid prevalence was lowest, but still notable (12.2%), among residents assessed as having no pain. Though the likelihood for receiving an opioid increased with pain symptom frequency and intensity (up to 55.7% for residents with severe pain), nearly half of residents with severe pain were not dispensed an opioid, with no evidence to suggest that these residents were more likely to receive non-opioid analgesics. Residents newly admitted to LTC and those with moderate to severe cognitive impairment or with a diagnosis of dementia were significantly less likely to receive an opioid. Opioid use was, however, more prevalent among residents concurrently using specific central nervous system medications, including gabapentinoids, benzodiazepines, and antidepressants. With a few exceptions

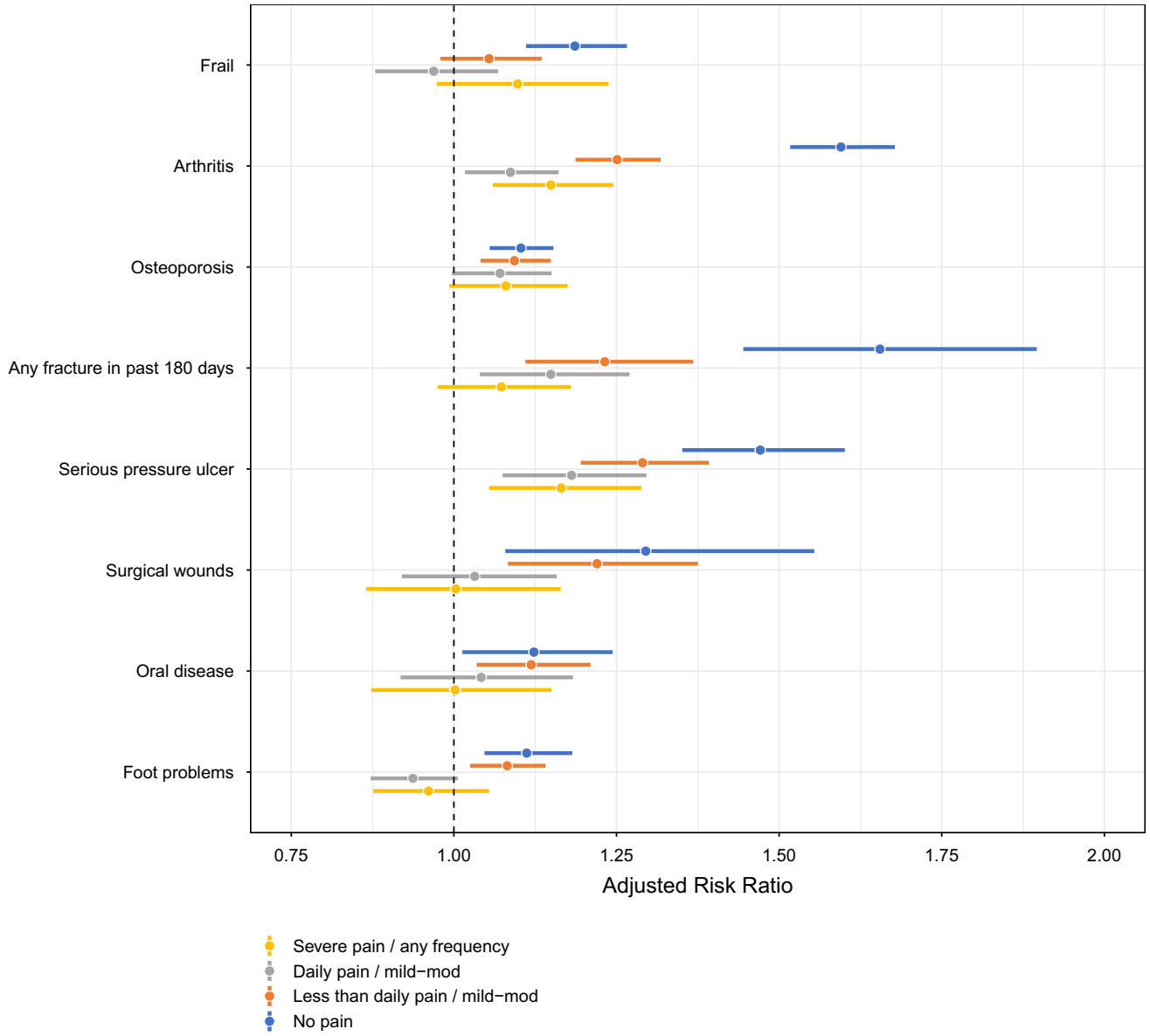

Fig. 2 Adjusted risk ratio for opioid use associated with pain-related conditions, stratified by pain frequency and intensity, among Ontario long-term care residents

(e.g., cognitive impairment), these associations were consistent across all pain strata.

Our prevalence estimate of non-cancer pain is consistent with that observed for US nursing home residents [3]. However, our prevalence of opioid use is lower than estimates reported for LTC residents internationally (30–32% [3, 39]), including a 2015 investigation of all (palliative and non-palliative) older nursing home residents in Denmark (~ 42%) [40], and that observed for Ontario LTC residents in 2017 (19.6% [2]). As hypothesized, when examined by pain strata, our opioid estimates followed a similar pattern (i.e., higher prevalence with higher pain severity) to that shown in a recent US nursing home study [1].

The finding of a lower likelihood of opioid use for residents newly admitted to LTC (evident even among those with severe pain) raises concerns regarding possible discontinuity in the assessment, recognition, and/or treatment of pain among older adults during care transitions (e.g., from home to hospital to LTC). Gilmore-Bykovskyi et al. [41] found that 23% of persons with dementia who were prescribed an analgesic in hospital experienced a potentially abrupt discontinuation when discharged to skilled nursing facilities. It is also possible that heightened concern and oversight of opioid prescribing in the community [25] is contributing to a reduced prevalence of opioid use among those entering LTC more recently [17]. Among residents

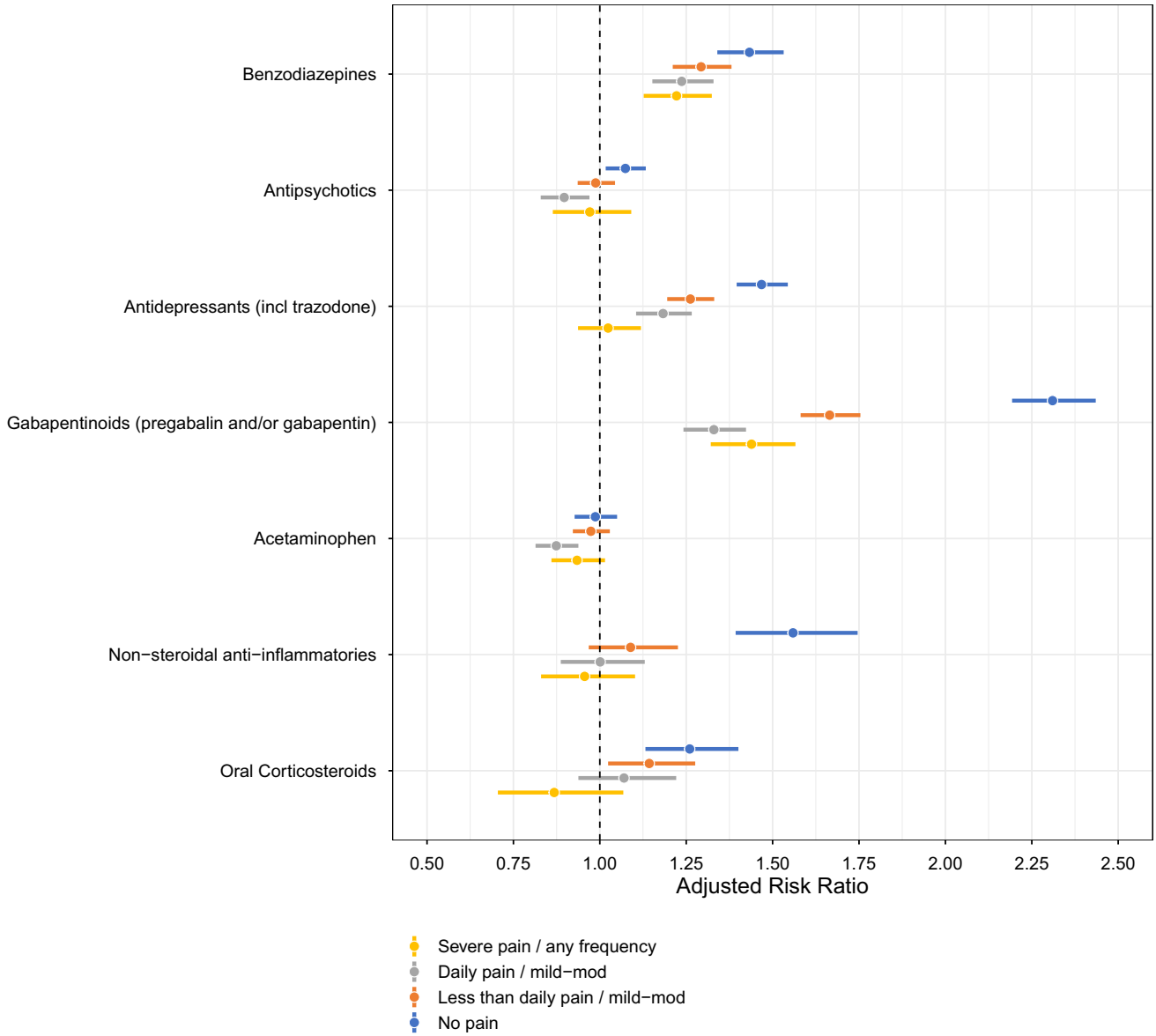

Fig. 3 Adjusted risk ratio for opioid use associated with select drug classes, stratified by pain frequency and intensity, among Ontario long-term care residents. *Incl* including

newly admitted, most (67%) came from home. This group had the lowest prevalence of opioid use relative to those coming from acute care or other settings. Though this observation may support the latter interpretation, there may be other plausible clinical reasons for lower opioid use among residents coming from home. Additional research is needed to understand the up-stream drivers and appropriateness of analgesic and other pain management strategies among older adults entering LTC, given potential concerns about timely medication reconciliation and pain assessment among those newly admitted to LTC [42].

Consistent with previous research [1, 3, 8, 18–21], we showed a lower prevalence of opioid use among residents with higher levels of cognitive impairment or with a diagnosis of dementia. While it is well recognized that pain is often poorly detected among residents who face challenges in expressing and/or communicating their pain symptoms to staff and family [1, 3, 8, 18–20], this does not fully explain the lower use of opioids evident among residents with dementia across pain strata. There may be a reluctance to use opioids for pain management, even when otherwise indicated, among those with dementia because of concerns about medication risks [7, 42]. We did observe a slightly higher adjusted prevalence of opioid use for residents with the highest level of cognitive impairment and pain intensity. This may reflect the use of opioids for comfort (end-of-life)

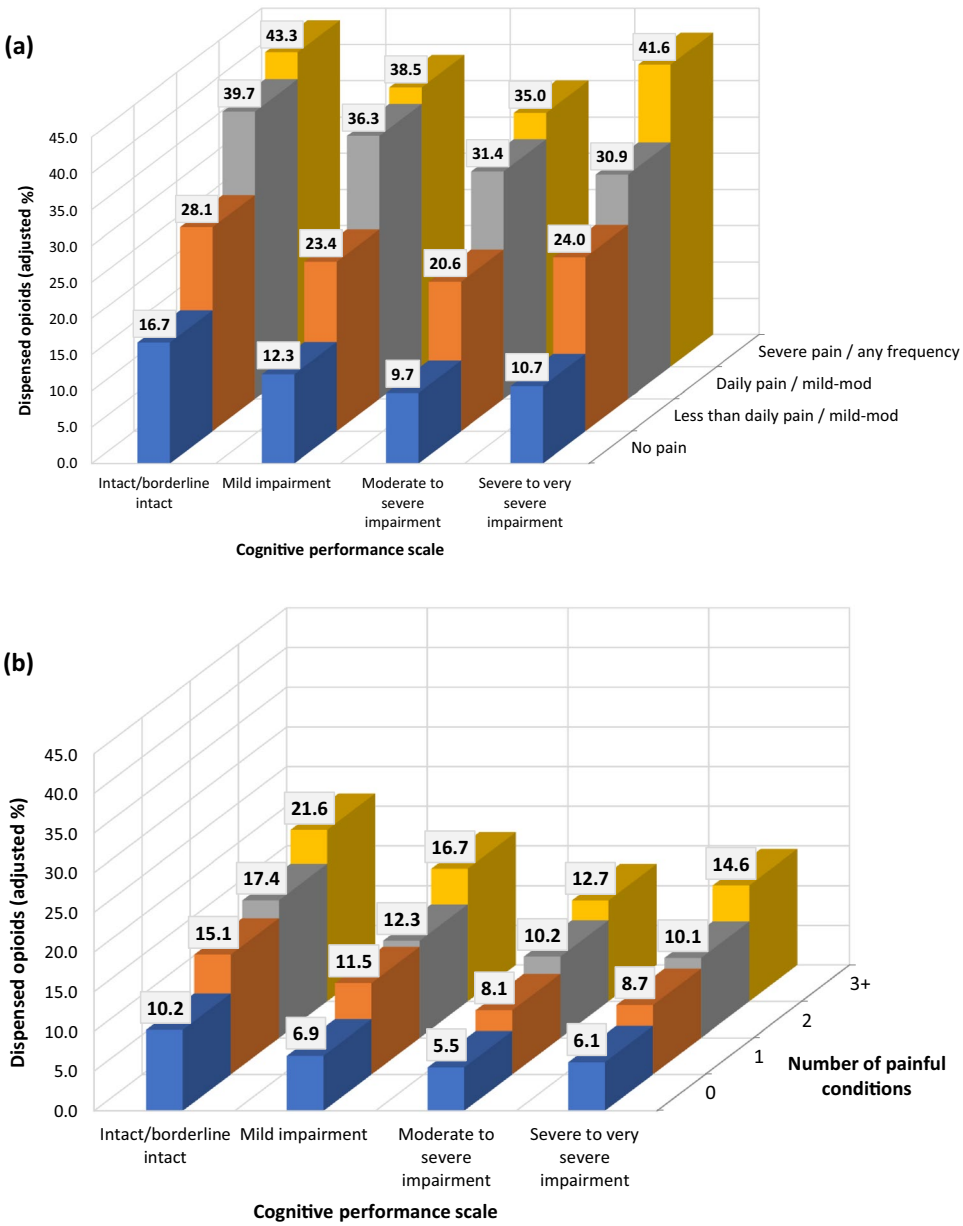

Fig. 4 **a** Adjusted prevalence of opioid use by cognitive impairment level and pain frequency and intensity, among Ontario long-term care residents. **b** Adjusted prevalence of opioid use by cognitive impairment level and number of pain-related conditions, among Ontario long-term care residents assessed as having no pain

care in residents with advanced dementia. In the total cohort, residents with Parkinson's disease were significantly less likely to receive an opioid. Few studies have examined Parkinson's disease as a relevant correlate of opioid or other analgesic use [29], despite the high prevalence of pain, unique management considerations, and potential for undertreatment among persons with this neurodegenerative disorder [43–45]. What underlies the lower prevalence of opioid use among residents with neurodegenerative disorders could include the under-recognition of pain, clinical uncertainty, and/or concerns about drug interactions and adverse events.

Frailty status has been relatively unexplored in LTC studies of analgesic use [2] despite being associated with pain and pain-related conditions [46] and its relevance to understanding the balance between benefit and risk for many medications [42, 47, 48]. Contrary to our hypothesis, frailty showed a statistically significant though modest positive association with opioid use overall and among residents assessed with no pain. The observation that this association was not more pronounced is encouraging from a risk perspective as the presence of frailty may exacerbate age-related changes in pharmacokinetics and pharmacodynamics [47], predisposing older residents to drug–drug and drug–disease interactions and poorer health outcomes. However, given the high prevalence of frailty among LTC residents [49], and our observation of an increased likelihood for concurrent use of other central nervous system medications among residents dispensed opioids, additional studies on the impact

of frailty on opioid-related health outcomes in this population are warranted.

It is particularly challenging to interpret the associations observed between residents' characteristics and opioid use in the no pain group. Some of these findings may reflect potentially inappropriate use, though previous studies have raised concerns about the validity and reliability of the RAI-MDS 2.0 pain items, especially for residents with cognitive and/or communication difficulties [50–53]. It is plausible that the no pain group includes a mix of residents with undetected pain, effectively treated pain, and truly no pain as well as those receiving opioids for other indications. This is supported by our findings showing a meaningful variation in the adjusted prevalence of opioid use by residents' cognitive performance level and number of pain-related conditions in those assessed as having no pain with the RAI-MDS 2.0.

Contrary to our hypothesis, we showed significant positive associations between the use of several medication classes, most notably the use of gabapentinoids, benzodiazepines, and antidepressants, and opioid use across all pain strata. As mentioned above, this concurrent use of multiple central nervous system medications among older residents, also noted elsewhere [1], is worrisome given the potential for elevated risks of significant drug interactions and adverse drug effects (e.g., increased sedation, confusion, falls, and mortality) in this population [5, 7, 54–57]. There is also emerging data that the coronavirus disease 2019 (COVID-19) pandemic may be contributing to an increased likelihood for potentially inappropriate concurrent use of opioids, gabapentinoids, and various psychotropic medications among LTC residents [28]. The indications for (including empirical data on the prevalence of neuropathic pain [58, 59]), and appropriateness of, concurrent use of opioids with gabapentinoids and/or benzodiazepines in the LTC setting are priority areas for future research.

Regarding the other medications examined, we found no significant associations between the receipt of an antipsychotic and opioid use, overall and across pain strata. These findings suggest that residents not receiving an opioid (including those in severe pain) were not necessarily more likely to receive an antipsychotic, though additional research on the inter-relationships between sub-optimal pain management, resident behaviors, and potentially inappropriate antipsychotic use are needed [60]. Among residents assessed with any pain, there were generally weak to no associations observed between the receipt of other analgesics and opioid use.

Our population-based data, capturing all non-palliative residents of Ontario LTC homes, and our stratified analyses illustrating the relevance of residents' characteristics to opioid use across levels of their assessed pain, are important strengths of our study. The richness of the clinical assessment items linked to provincial prescription drug claims and other administrative data allowed us to conduct a comprehensive exploration of a diverse range of potential correlates of opioid use, including several not previously explored. Though our stratified analyses help to inform our understanding of resident sub-groups at risk for opioid-related harms or potential sub-optimal management of daily or severe chronic pain, the RAI-MDS 2.0 pain items are known to underestimate the prevalence of pain, especially among residents with cognitive and/or communication difficulties [51–53]. As such, it is likely that pain frequency and severity were underestimated across all four pain strata. We also did not have access to data regarding non-pharmacological pain treatments. A further limitation is the absence of data regarding the indications for use or non-use of an opioid, which precludes us from making definite conclusions regarding the appropriateness of opioid prescribing. The prescription claims measures do not necessarily reflect whether a medication was taken as directed (though medication use is carefully supervised by clinicians in LTC) and may not capture some common non-prescription analgesics. Our cross-sectional design also limits our interpretation regarding the direction of some observed associations. Though population-based, our findings may not be generalizable to older adults receiving care in the community or LTC in other regions.

5 Conclusions

Notwithstanding the potential limitations of the RAI-MDS 2.0 pain items, our findings suggest that older adults newly admitted to LTC and with dementia are significantly less likely to be dispensed an opioid, even in the presence of more frequent or intense pain. Regardless of pain symptom level, residents receiving an opioid are significantly more likely to be exposed to multiple and potentially worrisome drug combinations, including the concurrent use of gabapentinoids and benzodiazepines. Our observations regarding opioid use among residents with no assessed pain and/or no pain-related conditions also indicate potentially inappropriate use in need of further investigation. Our findings echo those of others [42] calling for significant clinical and policy changes in LTC to improve the recognition, assessment, and management of non-cancer pain. The increasing prevalence of pain and clinical complexity of LTC residents also illustrates the urgency for robust investigations of the safety and effectiveness of pain management strategies in this care setting.

Supplementary Information The online version contains supplementary material available at https://doi.org/10.1007/s40266-022-00972-9.

Acknowledgements We thank IQVIA Solutions Canada Inc. for use of their Drug Information File. We wish to acknowledge Christina Diong, MSc., for her assistance with the original cohort creation. Please contact the authors for any supplemental information related to the study such as the study protocol, analysis plan, or analytic code.

Author contributions CM, MC, and SB conceived and designed the study. MC carried out the statistical analysis with supervision by CM and CC. AI (lead author), CM, MC, and DH drafted the initial manuscript. All authors made substantial contributions to the interpretation of data, critically reviewed the manuscript for important intellectual content, approved the final manuscript submitted for consideration, and agree to be accountable for all aspects of the work in relation to its accuracy and integrity. MC and CM had full access to the study databases.

Declarations

Funding This research was funded by the Canadian Institutes of Health Research (CIHR) through two operating grants (Exploring frailty and its role in the assessment of high-risk medications and risk of poor health outcomes in vulnerable populations—MOP-136854 and Understanding and optimizing opioid use in long-term care—PJT-168914). This study was supported by ICES, which is funded by an annual grant from the Ontario Ministry of Health (MOH) and the Ministry of Long-Term Care (MLTC). Parts of this material are based on data and/or information compiled and provided by the Canadian Institute for Health Information (CIHI). However, the analyses, conclusions, opinions, and statements expressed herein are solely those of the authors and do not reflect those of the funding or data sources; no endorsement by ICES, the MOH, MLTC, or CIHI is intended or should be inferred.

Sponsor's role The study sponsors provided the operating costs and infrastructure to support the research. No funding bodies had any role in the study design, data collection, analysis, decision to publish, or preparation of the manuscript.

Conflict of interest The authors have no conflicts of interest to report.

Ethics approval This study received ethics clearance by the University of Waterloo Human Research Ethics Committee (# 42355).

Consent to participate Not applicable.

Consent for publication Not applicable.

Availability of data and material The dataset from this study is held securely in coded form at ICES. While legal data sharing agreements prohibit ICES from making the dataset publicly available, access may be granted to those who meet pre-specified criteria for confidential access, available at http://www.ices.on.ca/DAS (email: das@ices.on.ca).

Code availability The full dataset creation plan and underlying analytic code are available from the authors upon request, understanding that the computer programs may rely upon coding templates or macros that are unique to ICES and are therefore either inaccessible or may require modification.

References

1. Lapane KL, Hume AL, Morrison RA, Jesdale BM. Prescription analgesia and adjuvant use by pain severity at admission among nursing home residents with non-malignant pain. Eur J Clin Pharmacol. 2020;76(7):1021–8.
2. Iaboni A, Campitelli MA, Bronskill SE, Diong C, Kumar M, Maclagan LC, Gomes T, Tadrous M, Maxwell CJ. Time trends in opioid prescribing among Ontario long-term care residents: a repeated cross-sectional study. CMAJ Open. 2019;7(3):E582–98.
3. Hunnicutt JN, Chrysanthopoulou SA, Ulbricht CM, Hume AL, Tjia J, Lapane KL. Prevalence of long-term opioid use in long-stay nursing home residents. J Am Geriatr Soc. 2018;66(1):48–55.
4. Maclagan LC, Maxwell CJ, Gandhi S, Guan J, Bell CM, Hogan DB, Daneman N, Gill SS, Morris AM, Jeffs L, Campitelli MA, Seitz D, Bronskill SE. Frailty and potentially inappropriate medication use at nursing home transition. J Am Geriatr Soc. 2017;65(10):2205–12.
5. Al-Qurain AA, Gebremichael LG, Khan MS, Williams DB, Mackenzie L, Phillips C, Russell P, Roberts MS, Wiese MD. Opioid prescribing and risk of drug-opioid interactions in older discharged patients with polypharmacy in Australia. Int J Clin Pharm. 2021;43(2):365–74.
6. Jassal M, Egan G, Dahri K. Opioid prescribing in the elderly: a systematic review. J Pharm Technol. 2020;36(1):28–40.
7. The 2019 American Geriatrics Society Beers Criteria® Update Expert Panel. American Geriatrics Society 2019 updated AGS Beers Criteria® for potentially inappropriate medication use in older adults. J Am Geriatr Soc. 2019;67(4):674–694.
8. Dube CE, Morrison RA, Mack DS, Jesdale BM, Nunes AP, Liu SH, Lapane KL. Prevalence of pain on admission by level of cognitive impairment in nursing homes. J Pain Res. 2020;13:2663–72.
9. Hunnicutt JN, Ulbricht CM, Tjia J, Lapane KL. Pain and pharmacologic pain management in long-stay nursing home residents. Pain. 2017;158(6):1091–9.
10. Hunnicutt JN, Hume AL, Ulbricht CM, Tjia J, Lapane KL. Long-acting opioid initiation in US nursing homes. Pharmacoepidemiol Drug Saf. 2019;28(1):31–8.
11. Lapane KL, Quilliam BJ, Chow W, Kim M. The association between pain and measures of well-being among nursing home residents. J Am Med Dir Assoc. 2012;13(4):344–9.
12. Abdulla A, Adams N, Bone M, Elliott AM, Gaffin J, Jones D, Knaggs R, Martin D, Sampson L, Schofield P; British Geriatric Society. Guidance on the management of pain in older people. Age Ageing. 2013;42(Suppl 1):i1–57.
13. Edelman LS, Hemmert R. Opioid use in long-term care: guidelines and policy recommendations. J Gerontol Nurs. 2019;45(9):5–10.
14. Oscanoa TJ, Lizaraso F, Carvajal A. Hospital admissions due to adverse drug reactions in the elderly. A meta-analysis. Eur J Clin Pharmacol. 2017;73(6):759–70.
15. Vranken MJM, Schutjens MDB, Mantel-Teeuwisse AK. The double opioid crisis: a call for balance. Pharmacoepidemiol Drug Saf. 2019;28(1):1–3.
16. Helvik AS, Bergh S, Benth JS, Selbaek G, Husebo BS, Tevik K. Pain in nursing home residents with dementia and its association to quality of life. Aging Ment Health. 2021;1–11: Online ahead of print. https://doi.org/10.1080/13607863.2021.1947968
17. Herr K, Arnstein P. The opioid epidemic and persistent pain management in older adults. J Gerontol Nurs. 2016;42(12):3–4.

18. Achterberg WP, Erdal A, Husebo BS, Kunz M, Lautenbacher S. Are chronic pain patients with dementia being undermedicated? J Pain Res. 2021;14:431–9.
19. La Frenais F, Vickerstaff V, Cooper C, Livingston G, Stone P, Sampson EL. Factors influencing prescription and administration of analgesic medication: a longitudinal study of people with dementia living in care homes. Int J Geriatr Psychiatry. 2021;36(9):1354–61.
20. Mehta HB, Kuo YF, Raji M, Li S, Westra J, Goodwin JS. Time trends in opioid use by dementia severity in long-term care nursing home residents. J Am Med Dir Assoc. 2021;22(1):124–31.
21. Nunes AP, Zhao D, Jesdale WM, Lapane KL. Multiple imputation to quantify misclassification in observational studies of the cognitively impaired: an application for pain assessment in nursing home residents. BMC Med Res Methodol. 2021;21(1):132.
22. Cadogan MP, Edelen MO, Lorenz KA, Jones M, Yosef J, Hascall T, Simon B, Harker JO, Ferrell B, Saliba D. The relationship of reported pain severity to perceived effect on function of nursing home residents. J Gerontol A Biol Sci Med Sci. 2008;63(9):969–73.
23. Greenblatt HK, Greenblatt DJ. Use of antipsychotics for the treatment of behavioral symptoms of dementia. J Clin Pharmacol. 2016;56(9):1048–57.
24. Husebo BS, Ballard C, Sandvik R, Nilsen OB, Aarsland D. Efficacy of treating pain to reduce behavioural disturbances in residents of nursing homes with dementia: cluster randomised clinical trial. BMJ. 2011;343: d4065.
25. Busse JW, Craigie S, Juurlink DN, Buckley DN, Wang L, Couban RJ, Agoritsas T, Aki EA, Carrasco-Labra A, Cooper L, Cull C, da Costa BR, Frank JW, Grant G, Iorio A, Persaud N, Stern S, Tugwell P, Vandvik PO, Guyatt GH. Guideline for opioid therapy and chronic noncancer pain. CMAJ. 2017;189(18):E659–66.
26. Canadian Institute for Health Information, Continuing Care Reporting System (CCRS) RAI-MDS 2.0© Output Specifications Manuel, 2019-2020. Ottawa, Ont.: CIHI, 2019. https://secure.cihi.ca/estore/productFamily.htm?pf=PFC3942&lang=en&media=0
27. Hirdes JP, Poss JW, Caldarelli H, Fries BE, Morris JN, Teare GF, Reidel K, Jutan N. An evaluation of data quality in Canada's Continuing Care Reporting System (CCRS): secondary analysis of Ontario data submitted between 1996–2011. BMC Med Inform Decis Mak. 2013;13:27.
28. Campitelli MA, Bronskill SE, Maclagan LC, Harris DA, Cotton CA, Tadrous M, Gruneir A, Hogan DB, Maxwell CJ. Comparison of medication prescribing before and after the COVID-19 pandemic among nursing home residents in Ontario, Canada. JAMA Netw Open. 2021;4(8): e2118441.
29. Lapane KL, Quilliam BJ, Chow W, Kim MS. Pharmacologic management of non-cancer pain among nursing home residents. J Pain Symptom Manage. 2013;45(1):33–42.
30. Fries BE, Simon SE, Morris JN, Flodstrom C, Bookstein FL. Pain in U.S. nursing homes: validating a pain scale for the minimum data set. Gerontologist. 2001;41(2):173–179.
31. Hartmaier SL, Sloane PD, Guess HA, Koch GG, Mitchell CM, Phillips CD. Validation of the minimum data set cognitive performance scale: agreement with the mini-mental state examination. J Gerontol A Biol Sci Med Sci. 1995;50A(2):M128–33.
32. Morris JN, Fries BE, Morris SA. Scaling ADLs with the MDS. J Gerontol A Biol Sci Med Sci. 1999;54(11):M546–53.
33. Burrows AB, Morris JN, Simon SE, Hirdes JP, Phillips C. Development of a Minimum Data Set-based depression rating scale for use in nursing homes. Age Ageing. 2000;29(2):165–72.
34. Perlman CM, Hirdes JP. The aggressive behavior scale: A new scale to measure aggression based on the Minimum Data Set. J Am Geriatr Soc. 2008;56(12):2298–303.
35. Woo KY, Sears K, Almost J, Wilson R, Whitehead M, VanDenKerkhof EG. Exploration of pressure ulcer and related skin problems across the spectrum of health care settings in Ontario using administrative data. Int Wound J. 2017;14(1):24–30.
36. Austin PC. Balance diagnostics for comparing the distribution of baseline covariates between treatment groups in propensity-score matched samples. Stat Med. 2009;28(25):3083–107.
37. Zou G. A modifed poisson regression approach to prospective studies with binary data. Am J Epidemiol. 2004;159(7):702–6.
38. Zou GY, Donner A. Extension of the modifed poisson regression model to prospective studies with correlated binary data. Stat Methods Med Res. 2013;22(6):661–70.
39. Roitto HM, Kautiainen H, Aalto UL, Öhman H, Laurila J, Pitkälä KH. Fouteen-year trends in the use of psychotropic medications, opioids and other sedatives among institutionalized older people in Helsinki, Finland. J Am Med Dir Assoc. 2019;20(3):305–11.
40. Jensen-Dahm C, Zakarias JK, Gasse C, Waldemar G. Geographical variation in opioid use in elderly patients with dementia: a nationwide study. J Alzheimers Dis. 2019;70(4):1209–16.
41. Gilmore-Bykovskyi AL, Block L, Hovanes M, Mirr J, Kolanowski A. Analgesic use patterns among patients with dementia during transitions from hospitals to skilled nursing facilities. Res Gerontol Nurs. 2019;12(2):61–9.
42. Lapane KL, Dubé C, Hume AL, Tjia J, Jesdale BM, Pawasauskas J, Khodyakov D. Priority-setting to address the geriatric pharmacoparadox for pain management: a nursing home stakeholder delphi study. Drugs Aging. 2021;38(4):327–40.
43. Karnik V, Farcy N, Zamorano C, Bruno V. Current status of pain management in Parkinson's disease. Can J Neurol Sci. 2020;47(3):336–43.
44. Mylius V, Möller JC, Bohlhalter S, de Andrade DC, Lloret SP. Diagnosis and management of pain in Parkinson's disease: a new approach. Drugs Aging. 2021;38(7):559–77.
45. Qureshi AR, Rana AQ, Malik SH, Rizvi SFH, Akhter S, Vannabouathong C, Sarfraz Z, Rana R. Comprehensive examination of therapies for pain in Parkinson's disease: a systematic review and meta-analysis. Neuroepidemiology. 2018;51(3–4):190–206.
46. Saraiva MD, Suzuki GS, Lin SM, de Andrade DC, Jacob-Filho W, Suemoto CK. Persistent pain in a risk factor for frailty: a systematic review and meta-analysis from prospective longitudinal studies. Age Ageing. 2018;47(6):785–93.
47. Hogan DB, Maxwell CJ. Frailty and unintended risks of medications. Curr Epidemiol Rep [Epidemiology of Aging Section] 2020; https://doi.org/10.1007/s40471-020-00226-5
48. Woodford HJ, Fisher J. New horizons in deprescribing for older people. Age Ageing. 2019;48(6):768–75.
49. Ng R, Lane N, Tanuseputro P, Mojaverian N, Talarico R, Wodchis WP, Bronskill SE, Hsu AT. Increasing complexity of new nursing home residents in Ontario, Canada: a serial cross-sectional study. J Am Geriatr Soc. 2020;68(6):1293–300.
50. Cadogan MP, Schnelle JF, Yamamoto-Mitani N, Cabrera G, Simmons SF. A minimum data set prevalence of pain quality indicator: is it accurate and does it reflect differences in care processes? J Gerontol A Biol Sci Med Sci. 2004;59(3):281–5.
51. Cohen-Mansfield J. The adequacy of the minimum data set assessment of pain in cognitively impaired nursing home residents. J Pain Symptom Manage. 2004;27(4):343–51.
52. Fisher SE, Burgio LD, Thorn BE, Allen-Burge R, Gerstle J, Roth DL, Allen SJ. Pain assessment and management in cognitively impaired nursing home residents: association of certified nursing assistant pain report, Minimum Data Set pain report, and analgesic medication use. J Am Geriatr Soc. 2002;50(1):152–6.
53. Wu N, Miller SC, Lapane K, Roy J, Mor V. The quality of the quality indicator of pain derived from the minimum data set. Health Serv Res. 2005;40(4):1197–216.
54. Bronskill SE, Campitelli MA, Iaboni A, Herrmann N, Guan J, Maclagan LC, Watt J, Rochon PA, Morris AM, Jeffs L, Bell CM, Maxwell CJ. Low-dose trazodone, benzodiazepines, and

fall-related injuries in nursing homes: a matched-cohort study. J Am Geriatr Soc. 2018;66(10):1963–71.
55. Gomes T, Juurlink DN, Antoniou T, Mamdani MM, Paterson JM, van den Brink W. Gabapentin, opioids, and the risk of opioid-related death: a population-based nested case–control study. PLoS Med. 2017;14(10): e1002396.
56. Gomes T, Greaves S, van den Brink W, Antoniou T, Mamdani MM, Paterson JM, Martins D. Juurlink DN Pregabalin and the risk for opioid-related death: a nested case–control study. Ann Intern Med. 2018;169(10):732–4.
57. Macri JC, Iaboni A, Kirkham JG, Maxwell C, Gill SS, Vasudev A, Whitehead M, Seitz DP. Association between antidepressants and fall-related injuries among long-term care residents. Am J Geriatr Psychiatry. 2017;25(12):1326–36.
58. Mbrah AK, Nunes AP, Hume AL, Zhao D, Jesdale BM, Bova C, Lapane KL. Prevalence and treatment of neuropathic pain diagnoses among U.S. nursing home residents. Pain. 2021. https://doi.org/10.1097/j.pain.0000000000002525 (Online ahead of print)
59. Zhao D, Shridharmurthy D, Alcusky MJ, Yuan Y, Nunes AP, Hume AL, Baek J, Lapane KL. The prevalence and factors associated with antiepileptic drug use in US nursing home residents. Drugs Aging. 2020;37(2):137–45.
60. Rajkumar AP, Ballard C, Fossey J, Orrell M, Moniz-Cook E, Woods RT, Murray J, Whitaker R, Stafford J, Knapp M, Romeo R, Woodward-Carlton B, Khan Z, Testad I, Corbett A. Epidemiology of pain in people with dementia living in care homes: longitudinal course, prevalence and treatment implications. J Am Med Dir Assoc. 2017;18(5):453.e1-453.e6.

Authors and Affiliations

Anita Iacono[1] · Michael A. Campitelli[2] · Susan E. Bronskill[2,3,4] · David B. Hogan[5] · Andrea Iaboni[6,7] · Laura C. Maclagan[2] · Tara Gomes[2,3,8,9] · Mina Tadrous[2,4,9] · Charity Evans[10] · Andrea Gruneir[2,11] · Qi Guan[2,3] · Thomas Hadjistavropoulos[12] · Cecilia Cotton[13] · Sudeep S. Gill[2,14] · Dallas P. Seitz[2,15] · Joanne Ho[16,17] · Colleen J. Maxwell[1,2,18]

1 School of Public Health Sciences, University of Waterloo, 200 University Avenue West, Waterloo, ON N2L 3G1, Canada

2 ICES, Toronto, ON, Canada

3 Institute of Health Policy, Management and Evaluation, Dalla Lana School of Public Health, University of Toronto, Toronto, ON, Canada

4 Women's College Research Institute, Women's College Hospital, Toronto, ON, Canada

5 Division of Geriatric Medicine, Department of Medicine, Cumming School of Medicine, University of Calgary, Calgary, AB, Canada

6 KITE Research Institute, Toronto Rehabilitation Institute, University Health Network, Toronto, ON, Canada

7 Department of Psychiatry, University of Toronto, Toronto, ON, Canada

8 Unity Health, Toronto, ON, Canada

9 Leslie Dan Faculty of Pharmacy, University of Toronto, Toronto, ON, Canada

10 College of Pharmacy and Nutrition, University of Saskatchewan, Saskatoon, SK, Canada

11 Department of Family Medicine, University of Alberta, Edmonton, AB, Canada

12 Department of Psychology and Centre on Aging and Health, University of Regina, Regina, SK, Canada

13 Department of Statistics and Actuarial Science, University of Waterloo, Waterloo, ON, Canada

14 Department of Medicine, Queen's University, Kingston, ON, Canada

15 Department of Psychiatry, Cumming School of Medicine, University of Calgary, Calgary, AB, Canada

16 Department of Medicine, McMaster University, Hamilton, ON, Canada

17 Schlegel Research Institute for Aging, Waterloo, ON, Canada

18 School of Pharmacy, University of Waterloo, Waterloo, ON, Canada