Time trends in opioid prescribing among Ontario long-term care residents: a repeated cross-sectional study

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Abstract:	Background: Opioids are an important pain therapy, but their use may be associated with adverse events in frail and cognitively impaired long-term care (LTC) residents. The objective of this study was to investigate trends in opioid prescribing among Ontario LTC residents over time, given the paucity of data for this setting. Methods: We used linked clinical and health administrative databases to conduct a population-based, repeated cross-sectional study of opioid use among Ontario LTC residents between April 1, 2009 and March 31, 2017. We identified prevalent opioid use by drug type, dose, and co-prescription with benzodiazepines and within certain subgroups including

	frail residents and those with dementia. Log-binomial regression was used to quantify the percentage change between the 2009/10 and 2016/17 fiscal years. Results: Among an average of 76,147 LTC residents per year, the prevalence of opioid use increased from 15.8% in 2009/10 to 19.6% in 2016/17 ($p<0.001$). Over the study period, the use of hydromorphone increased by 235.6%, while use of all other opioid agents decreased. The use of high-dose opioids (>90 milligrams of morphine equivalents) and the co-prescription of opioids with benzodiazepines decreased significantly by 17.4% ($p<0.001$) and 23.6% ($p<0.001$), respectively. Increases in opioid prevalence were more notable in frail residents (38.3% vs. 18.9% for non-frail; $p<0.001$) and those with dementia (39.2% vs. 21.9% for no dementia; $p<0.001$). Interpretation: Trends in opioid prescribing within Ontario LTC facilities demonstrate increasing use of opioids, particularly in frail and cognitively impaired residents, and a large shift towards using hydromorphone.

The RECORD statement – checklist of items, extended from the STROBE statement, that should be reported in observational studies using routinely collected health data.

	Item No.	STROBE items	Location in manuscript where items are reported	RECORD items	Location in manuscript where items are reported
Title and abstract					
	1	(a) Indicate the study's design with a commonly used term in the title or the abstract (b) Provide in the abstract an informative and balanced summary of what was done and what was found	See Title Page and Abstract section	RECORD 1.1: The type of data used should be specified in the title or abstract. When possible, the name of the databases used should be included. RECORD 1.2: If applicable, the geographic region and timeframe within which the study took place should be reported in the title or abstract. RECORD 1.3: If linkage between databases was conducted for the study, this should be clearly stated in the title or abstract.	See Title Page and Abstract section
Introduction					
Background rationale	2	Explain the scientific background and rationale for the investigation being reported	See Introduction section		
Objectives	3	State specific objectives, including any prespecified hypotheses	See Introduction section (lines 145-148)		
Methods					
Study Design	4	Present key elements of study design early in the paper	See 'Study Design, Setting, and Data' portion of the Methods section.		
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	See Methods section, mainly the 'Study Design, Setting, and Data' portion.		

Participants	6	*(a) Cohort study* - Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up *Case-control study* - Give the eligibility criteria, and the sources and methods of case ascertainment and control selection. Give the rationale for the choice of cases and controls *Cross-sectional study* - Give the eligibility criteria, and the sources and methods of selection of participants *(b) Cohort study* - For matched studies, give matching criteria and number of exposed and unexposed *Case-control study* - For matched studies, give matching criteria and the number of controls per case	a) See 'Study Population' portion of the Methods section. b) Not applicable.	RECORD 6.1: The methods of study population selection (such as codes or algorithms used to identify subjects) should be listed in detail. If this is not possible, an explanation should be provided. RECORD 6.2: Any validation studies of the codes or algorithms used to select the population should be referenced. If validation was conducted for this study and not published elsewhere, detailed methods and results should be provided. RECORD 6.3: If the study involved linkage of databases, consider use of a flow diagram or other graphical display to demonstrate the data linkage process, including the number of individuals with linked data at each stage.	See 'Study Population' portion of the Methods section for 6.1, 6.2, and 6.3.
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable.	See 'Medication Use' and 'Resident Characteristics' portions of the Methods Section.	RECORD 7.1: A complete list of codes and algorithms used to classify exposures, outcomes, confounders, and effect modifiers should be provided. If these cannot be reported, an explanation should be provided.	See 'Online Supplement, eTable 2' for a complete list of opioid medications considered.
Data sources/ measurement	8	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	See 'Medication Use' and 'Resident Characteristics' portions of the Methods Section.		

Bias	9	Describe any efforts to address potential sources of bias	See 'Statistical Analysis' portion of the Methods section.		
Study size	10	Explain how the study size was arrived at	Not applicable.		
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen, and why	See 'Statistical Analysis' portion of the Methods section.		
Statistical methods	12	(a) Describe all statistical methods, including those used to control for confounding (b) Describe any methods used to examine subgroups and interactions (c) Explain how missing data were addressed (d) *Cohort study* - If applicable, explain how loss to follow-up was addressed *Case-control study* - If applicable, explain how matching of cases and controls was addressed *Cross-sectional study* - If applicable, describe analytical methods taking account of sampling strategy (e) Describe any sensitivity analyses	See 'Statistical Analysis' portion of the Methods section for a) and b). c) There were no missing data in the study to address. d) Our cross-sectional study design included all LTC residents in a given study year and did not employ a sampling strategy to select study participants.		
Data access and cleaning methods		..		RECORD 12.1: Authors should describe the extent to which the investigators had access to the database population used to create the study population. RECORD 12.2: Authors should provide	See 'Author contributions' portion of the Acknowledgements section of 12.1. Not applicable –

				information on the data cleaning methods used in the study.	12.2
Linkage		..		RECORD 12.3: State whether the study included person-level, institutional-level, or other data linkage across two or more databases. The methods of linkage and methods of linkage quality evaluation should be provided.	See 'Study Design, Setting, and Data' portion of the Methods section for 12.3.
Results					
Participants	13	(a) Report the numbers of individuals at each stage of the study (*e.g.*, numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed) (b) Give reasons for non-participation at each stage. (c) Consider use of a flow diagram	See 'Study Population' portion of the Methods section (lines 165-175) for a). See 'Study Population' portion of the Methods section for b).	RECORD 13.1: Describe in detail the selection of the persons included in the study (*i.e.,* study population selection) including filtering based on data quality, data availability and linkage. The selection of included persons can be described in the text and/or by means of the study flow diagram.	See 'Study Population' portion of the Methods section.
Descriptive data	14	(a) Give characteristics of study participants (*e.g.*, demographic, clinical, social) and information on exposures and potential confounders (b) Indicate the number of participants with missing data for each variable of interest (c) *Cohort study* - summarise follow-up time (*e.g.*, average and total amount)	See 'Online Supplement, eTable 3' for a). No missing data for b). c) Study was cross-sectional and there was no follow-up time.		
Outcome data	15	*Cohort study* - Report numbers of outcome events or summary measures over time *Case-control study* - Report numbers in each exposure category, or summary measures of exposure	See Results section.		

		Cross-sectional study - Report numbers of outcome events or summary measures			
Main results	16	(a) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (e.g., 95% confidence interval). Make clear which confounders were adjusted for and why they were included (b) Report category boundaries when continuous variables were categorized (c) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	See Results section and Tables 1 and 2 for a), b), and c).		
Other analyses	17	Report other analyses done—e.g., analyses of subgroups and interactions, and sensitivity analyses	See Results section and Table 2.		
Discussion					
Key results	18	Summarise key results with reference to study objectives	See Interpretation section.		
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias	See limitations portion of the Interpretation section.	RECORD 19.1: Discuss the implications of using data that were not created or collected to answer the specific research question(s). Include discussion of misclassification bias, unmeasured confounding, missing data, and changing eligibility over time, as they pertain to the study being reported.	See limitations portion of the Discussion section.
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant	See Interpretation section.		

		evidence			
Generalisability	21	Discuss the generalisability (external validity) of the study results	Given the cross-sectional nature of the study and its population-based nature, there are minimal impacts to external validity.		
Other Information					
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	See 'Funding' and 'Sponsor's Role' portion of the Acknowledgements section on the manuscript title page(s).		
Accessibility of protocol, raw data, and programming code		..		RECORD 22.1: Authors should provide information on how to access any supplemental information such as the study protocol, raw data, or programming code.	See Acknowledgements section on the manuscript title page(s).

*Reference: Benchimol EI, Smeeth L, Guttmann A, Harron K, Moher D, Petersen I, Sørensen HT, von Elm E, Langan SM, the RECORD Working Committee. The REporting of studies Conducted using Observational Routinely-collected health Data (RECORD) Statement. *PLoS Medicine* 2015; in press.

Time trends in opioid prescribing among Ontario long-term care residents: a repeated cross-sectional study

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Author Contributions: AI, MC, SB, and CM conceived and designed the study. MC, CD, and MK carried out the statistical analysis. AI**,** MC, SB, and CM drafted the manuscript. All authors contributed to the interpretation of data and critical revisions of the manuscript for important intellectual content. MC and SB had full access to the study databases and are the guarantors of the study.

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ABSTRACT

Background: Opioids are an important pain therapy, but their use may be associated with adverse events in frail and cognitively impaired long-term care (LTC) residents. The objective of this study was to investigate trends in opioid prescribing among Ontario LTC residents over time, given the paucity of data for this setting.

Methods: We used linked clinical and health administrative databases to conduct a population-based, repeated cross-sectional study of opioid use among Ontario LTC residents between April 1, 2009 and March 31, 2017. We identified prevalent opioid use by drug type, dose, and co-prescription with benzodiazepines and within certain subgroups including frail residents and those with dementia. Log-binomial regression was used to quantify the percentage change between the 2009/10 and 2016/17 fiscal years.

Results: Among an average of 76,147 LTC residents per year, the prevalence of opioid use increased from 15.8% in 2009/10 to 19.6% in 2016/17 ($p<0.001$). Over the study period, the use of hydromorphone increased by 235.6%, while use of all other opioid agents decreased. The use of high-dose opioids (>90 milligrams of morphine equivalents) and the co-prescription of opioids with benzodiazepines decreased significantly by 17.4% ($p<0.001$) and 23.6% ($p<0.001$), respectively. Increases in opioid prevalence were more notable in frail residents (38.3% vs. 18.9% for non-frail; $p<0.001$) and those with dementia (39.2% vs. 21.9% for no dementia; $p<0.001$).

Interpretation: Trends in opioid prescribing within Ontario LTC facilities demonstrate increasing use of opioids, particularly in frail and cognitively impaired residents, and a large shift towards using hydromorphone.

INTRODUCTION

Prescribers of opioid medications in long-term care (LTC) settings face difficulties balancing appropriate pain management with the potential risks of these therapies in vulnerable older adults. While pain is highly prevalent among LTC residents,(1, 2) reliable pain assessment in LTC is clinically challenging, particularly in those with dementia who may have trouble expressing their pain management needs.(3) As a result, poor recognition and under-treatment of pain in individuals with cognitive impairment in LTC settings is a well-described phenomenon.(4, 5)

While under-treatment of pain is one concern, the use of opioids in older adults is also associated with side effects and adverse events.(6) Pharmacokinetic changes, such as age-related decline in renal function and drug metabolism, place older adults at increased risk of sedation or opioid overdose.(6) Older adults are also more vulnerable to events such as falls (7) and respiratory depression.(8) Furthermore, polypharmacy is common in the LTC population, increasing the risk of exposure to clinically significant drug interactions, including the concurrent use of opioids with benzodiazepines which is associated with an elevated risk of overdose and death.(9, 10)

Nonetheless, opioids are an important intervention for the pharmacologic management of moderate to severe pain in older adults,(11) with 22% of all older adults in Ontario prescribed an opioid.(12) Prescribers have a number of choices about opioid treatment, including the selection of the agent, duration of action, and dosing.(6) Internationally, there is considerable variation in opioid prescribing patterns in LTC, both in terms of drug selection and dosing, although recent trends indicate increased opioid use in LTC, particularly in people with dementia.(13)

In response to wider concerns around opioid use in the community, there have been a number of initiatives over the past decade focused on improving pain assessment and treatment, and on providing guidelines for appropriate and safer opioid prescribing.(11, 14-17) Recent Canadian guidelines for the management of chronic non-cancer pain recommend avoiding escalation of daily doses above 90 milligrams of morphine equivalents (MME), and avoiding co-prescription of opioids with benzodiazepines.(16) Furthermore, the 2011 Ontario Narcotics Safety Awareness Act increased the surveillance of prescription opioids by introducing a provincial prescription monitoring program for community prescribers.(18) To date, Canadian guidelines have not directly addressed the unique and clinically challenging issues facing opioid prescribing in LTC.

In an era when opioid use is highly scrutinized in other populations, it is unclear whether these guidelines or legislative changes have had an impact on the opioid prescribing habits of LTC

physicians. Towards addressing the sparseness of data in this area, we examined trends over time in the prescribing of opioids for LTC residents in Ontario.

METHODS

Study Design, Setting, and Data

We conducted a population-based, repeated cross-sectional study of opioid use among LTC residents from Ontario, Canada between April 1, 2009 and March 31, 2017. The study used clinical and health administrative databases which were linked using unique encoded identifiers and analyzed at ICES (see **eTable 1** for a description of the databases). These databases have been used extensively to study medication use in the LTC setting.(19-22) In Ontario, the majority of the cost of LTC is covered by the publicly-funded provincial health system. Additionally, all residents have universal access to prescription medications, physician services, and hospital care. The study used data authorized under section 45 of Ontario's Personal Health Information Protection Act, which does not require review by a Research Ethics Board.

Study Population

The Continuing Care Reporting System LTC database includes clinical assessment data on all residents collected using the validated Resident Assessment Instrument Minimum Data Set version 2.0 (RAI-MDS 2.0) tool.(23) Mandatory full clinical assessments are completed on LTC admission, annually, and following any significant health status change. We identified all 1,030,310 full clinical assessments with the RAI-MDS 2.0 during our study period among residents aged 66 years and older. Assessments where the resident had no medication claims in the past year (N=8,399; 0.82%), had used palliative care services in the inpatient or outpatient setting in the past 6 months (N=42,986; 4.17%), or had a concurrent diagnosis of cancer noted in the RAI-MDS 2.0 (N=89,751; 8.71%) were excluded. As the use of opioids in palliative care and cancer pain are clearly indicated, our study focused on non-cancer and non-palliative LTC residents. The remaining 889,174 assessments were grouped into study years (from April 1 to the following March 31 to align with provincial data reporting cycles) and we selected one assessment per resident for each year, giving preference to the earliest assessment. The final study population comprised 609,177 residents across eight study years.

Medication use

We used the Ontario Drug Benefit (ODB) database to ascertain all opioid and benzodiazepine drug claims whereby a course of therapy (estimated using the date dispensed plus

days supplied) overlapped or included the RAI-MDS 2.0 assessment date. An assessment could have had multiple opioid claims meeting this definition. A list of all opioid medications included can be found in **eTable 2**. We used previously described methods to compute the combined total daily dose in MMEs for all opioid prescriptions at assessment date.(24)

Measures captured at each assessment date included the proportion of residents prescribed any opioid, as well as the proportion receiving specific opioid agents (codeine, hydromorphone, morphine, fentanyl, and oxycodone), different formulations (long-acting and short-acting), a total daily dose greater than 90 MMEs, and opioids co-prescribed with benzodiazepines.

Resident Characteristics

Age and sex at assessment date was determined using the Ontario Registered Persons database. The RAI-MDS 2.0 data were used to identify assessments with a concurrent diagnosis of Alzheimer's disease or other dementia.(25) Assessment items from the RAI-MDS 2.0 were also used to compute a validated measure of resident frailty,(26, 27) which included 72 deficits covering multiple domains of health (disease diagnoses, functional status, psychosocial well-being, cognition, and communication). In accordance with previous work,(26-28) residents with greater than 30% of potential deficits were defined as frail. A measure of pain frequency in the RAI-MDS 2.0 was used to identify residents experiencing daily pain, less than daily pain, or no pain in the 7 days prior to assessment. Finally, the RAI-MDS 2.0 was used to distinguish full assessments performed upon entry to LTC versus on-going full assessments (occurring annually or after significant health status changes) thereafter.

Statistical Analysis

To summarize any changes that occurred over the eight year study period, we compared the patterns of each opioid dispensing measure between the first (2009/10) and last (2016/17) study year using log-binomial regression models to calculate the percentage change. Adjusted models included age, sex, dementia diagnosis, frailty, and LTC assessment type to control for any changes in the LTC population across the study period. Pain frequency was not included in the adjusted models as pain may have been modified by opioid use. As individuals could have been included in multiple study years, we used generalized estimating equations to account for the correlated nature of the data.(29)

For the annual measure of the proportion of residents receiving any opioid at assessment date, we stratified the above analyses by age (≤85 years vs. >85 years), sex, dementia diagnosis,

resident frailty, pain frequency at assessment (any pain vs. no pain), and LTC assessment type (entry vs. on-going assessment) and ran interaction tests to assess for any effect modification.

Analyses were conducted using SAS version 9.4 (SAS Institute Inc.). All statistical tests were 2-tailed and we defined $p<0.05$ as the level of statistical significance.

RESULTS

Trends in opioid prescribing

Our study population comprised an average of 76,147 LTC residents per study year (see **eTable 3** for resident characteristics at each year). The prevalence of any opioid prescription in LTC increased from 15.8% in 2009/10 to 19.6% in 2016/17 (**Figure 1**), a significant 23.8% increase (p-value <0.001) in opioid prevalence over the eight year period (**Table 1**). After adjusting for age, sex, frailty status, dementia diagnosis, and LTC assessment type (entry vs. on-going), this represented a 30.3% increase in opioid prevalence during the study period. After adjustment, the use of most opioid agents decreased over this time frame, including a 26.1% reduction in codeine, a 39.8% reduction in fentanyl, and a 36.8% reduction in oxycodone. However, there was a coinciding 235.6% increase (from 3.7% in 2009/10 to 11.8% in 2016/17) in hydromorphone prescribing. While the use of both opioid formulations increased significantly, the increase was larger for short-acting formulations (42.4% increase vs. a 13.1% increase for long-acting formulations).

Trends in safer opioid prescribing

The overall, adjusted use of high-dose opioids (total daily dose >90 MME) decreased significantly by 17.4% (p-value <0.001), from a prevalence in all residents of 4.8% in 2009/10 to 3.6% in 2016/17 (**Table 1**). Among opioid users in 2016/17, 18.3% of residents had a total daily dose >90 MME (vs. 30.2% in 2009/10), while 70.5% had a total daily dose <50 MME (vs. 60.3% in 2009/10).

The proportion of all residents co-prescribed opioids and benzodiazepines decreased from 4.8% in 2009/10 to 3.4% in 2016/17, a significant 23.6% reduction (p-value <0.001) over the study period after adjustment. Among only residents who were prevalent opioid users, this represented a 43.3% reduction in the proportion of residents also prescribed a benzodiazepine (30.6% in 2009/10 vs. 17.4% in 2016/17).

Trends in opioid prescribing by LTC resident characteristics

After adjustment, the percent increase in opioid prevalence over the study period was significantly greater for residents >85 years (vs. residents ≤85 years; p-value = 0.003 for interaction),

residents with dementia (vs. residents without dementia; p-value <0.001 for interaction), frail residents (vs. non-frail residents; p-value <0.001 for interaction), and residents assessed as having no pain (vs. residents assessed as having pain; p-value <0.001 for interaction) (**Table 2**). While there was a 39.2% increase in opioid prevalence in individuals with dementia over time, opioid prescribing remained lower among those with dementia compared to those without (16.3% vs. 26.0% in 2016/17; **Figure 2a**). Opioid prevalence was higher among frail residents, and increased 38.3% over the study period. Therefore, the gap in opioid prevalence between frail and non-frail residents widened over time (**Figure 2b**). Across the study period, the prevalence of opioids decreased by 3.8% among residents newly entering LTC compared to a 42.1% increase among on-going residents (p-value <0.001 for interaction).

INTERPRETATION

Opioid prescribing patterns in Ontario LTC residents have changed significantly over the eight year study period, with the most notable change being a shift towards the use of hydromorphone, and an increase over time in the prevalence of opioid dispensations in older, more frail, more cognitively impaired residents, and in those who are assessed as having no pain.. These changes remained significant even after adjustment for the changing demographics of LTC residents over time. Overall, there was an increase in the prescribing of opioid therapy in LTC with a point prevalence of 19.6% of LTC residents in 2016/17. This increase in opioid prevalence was not attributable to opioid users in the community being newly admitted into LTC facilities and is in line with recent point prevalence estimates of opioid use in LTC in Finland (22%; (30)) and Norway (23%; (31)).

In keeping with guideline-recommended practices for safer prescribing, prescriptions exceeding dose guidelines and the co-prescribing of benzodiazepines with opioids decreased significantly over the study period. Another observed change over time was a decrease in the use of codeine. Guidelines caution against codeine for several reasons, including the potential for reduced effectiveness due to genetic polymorphisms or drug interactions in the CYP2D6 pathway. Hydromorphone and oxycodone have been specifically named in Canadian prescribing guidelines as preferred agents for managing pain in older adults.(16) The observed increasing preference for hydromorphone, and the decrease in oxycodone prescribing in LTC, are also both in keeping with trends across Ontario more broadly after drug reimbursement changes were put in place in 2012 to address the misuse of controlled release oxycodone.(24) At present, it is difficult to estimate the

impact of policy changes designed to address the wider crisis of non-medical opioid use and opioid-related adverse events in the community on LTC opioid prescribing. However, it is important to note that concerns regarding opioid misuse may be less relevant in the LTC setting, in which medication administration is medically supervised.

A majority of residents of LTC in Ontario have cognitive impairment, and there is a lack of evidence-based guidance for appropriate pain management in this population.(32) Our findings are consistent with previous studies, finding a gap in opioid prescribing between those with and without dementia.(33, 34) Challenges in the management of pain in dementia arise out of changes in pain processing, perception and communication in dementia, and difficulties in assessing pain by observation, with misinterpretation of pain-related behaviours.(33) For example, poorly managed pain may manifest as agitation or depression. There is evidence of benefit for the empiric step-wise treatment of pain in LTC residents with dementia and agitation, starting with acetaminophen and proceeding to low-dose opioids.(35) However, a recent clinical trial found poor tolerability and lack of efficacy of buprenorphine for the treatment of depression in dementia.(36, 37)

Although Canadian guidelines address the issue of age in opioid prescribing, they do not specifically address frailty as a prescribing consideration. Frail older adults are at increased risk of adverse events such as falls, fractures, delirium, and cognitive impairment,(26, 27, 38) but these risks need to be balanced with appropriate pain management. Unfortunately there is a paucity of evidence to guide the safe and effective prescribing of opioid therapies for pain in frail older adults. There remains a difficult balance between advocating for caution in the use and dosing of these therapies, and advocating for appropriate pain management. From our results, we are unable to determine if the higher rates of prescribing in frail LTC residents is related to the degree of comorbidity and medical complexity of this population, or is an indicator of potentially inappropriate prescribing.

Limitations

In our analysis, we were unable to examine trends in possible under- or over-treatment of pain given the clinical and methodological challenges of measuring pain in this setting,(3, 39, 40) and without assessing any alternative non-opioid drug and non-drug pain management strategies that may be available to LTC residents. These factors, and the fact that pain is modified by opiate use, also contribute to difficulty in the interpretation of the pain-stratified analysis. Another limitation of this study is that there are a small number of opioid drugs and formulations which are not covered by the ODB program, namely buprenorphine and tramadol. From clinical experience, we know that

these are rarely prescribed as the uninsured drug costs are prohibitive to families, and their use is unlikely to have an impact on our results.

Conclusion

While the prevalence of opioid prescribing is increasing in LTC in Ontario with a large shift towards using hydromorphone, the declining use of high-dose opioids and benzodiazepine co-prescription is in line with Canadian guidelines for older adults. There remains an opportunity to address the prescribing gap among those with and without dementia and to better understand the appropriateness of treatment patterns among frail residents. Future studies should examine the impact of increased opioid prescribing on pain-related outcomes and on adverse events in the LTC population.

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TABLES

Table 1 – Summary of opioid prescribing to Ontario LTC residents at start and end of the study period, study years 2009/10 and 2016/17

	Percentage (%) of LTC residents		Unadjusted results		Adjusted[a] results	
Opioid prescription on assessment date	2009/10	2016/17	Percent change[b]	P-value	Percent change[b]	P-value
Any opioid	15.8	19.6	+23.8	<0.001	+30.3	<0.001
Opioid agent						
Codeine	5.8	4.1	-29.1	<0.001	-26.1	<0.001
Hydromorphone	3.7	11.8	+220.8	<0.001	+235.6	<0.001
Morphine	1.6	1.2	-21.9	<0.001	-16.6	<0.001
Fentanyl	3.4	1.9	-44.9	<0.001	-39.8	<0.001
Oxycodone	2.9	1.7	-41.0	<0.001	-36.8	<0.001
Opioid formulation						
Long-acting	7.1	7.3	+3.4	0.065	+13.1	<0.001
Short-acting	10.7	14.6	+37.2	<0.001	+42.4	<0.001
Opioid dose over 90 MMEs	4.8	3.6	-25.3	<0.001	-17.4	<0.001
Opioids co-prescribed with benzodiazepines	4.8	3.4	-29.8	<0.001	-23.6	<0.001

Abbreviations: LTC = Long-Term Care; MME = Milligrams of Morphine Equivalents
a – Adjusted for age, sex, frailty, dementia diagnosis, and LTC assessment type
b – Percentage change from study year 2009/10 to study year 2016/17

Table 2 – Proportion of Ontario LTC residents receiving any opioids at start and end of the study period stratified by resident characteristics, study years 2009/10 and 2016/17

	Percentage (%) of LTC residents		Unadjusted results			Adjusted[a] results		
Resident characteristic	2009/10	2016/17	Percent change[b]	P-value	P-value (interaction)	Percent change[b]	P-value	P-value (interaction)
Age					0.017			0.003
≤ 85 years	16.6	20.2	+22.4	<0.001		+27.3	<0.001	
> 85 years	15.1	19.1	+26.2	<0.001		+33.6	<0.001	
Sex					0.915			0.903
Female	17.2	21.3	+24.2	<0.001		+30.4	<0.001	
Male	12.2	15.4	+25.8	<0.001		+30.0	<0.001	
Dementia					<0.001			<0.001
No	21.3	26.0	+21.8	<0.001		+21.9	<0.001	
Yes	11.8	16.3	+38.5	<0.001		+39.2	<0.001	
Frail resident					<0.001			<0.001
No	15.0	16.7	+11.5	<0.001		+18.9	<0.001	
Yes	16.6	21.7	+30.6	<0.001		+38.3	<0.001	
Pain frequency					<0.001			<0.001
No pain	6.9	12.4	+80.0	<0.001		+87.1	<0.001	
Any pain	28.1	35.3	+25.6	<0.001		+31.6	<0.001	
LTC assessment type					<0.001			<0.001
Entry assessments	16.6	15.4	-7.3	0.001		-3.8	0.091	
On-going assessments	15.6	21.3	+36.8	<0.001		+42.1	<0.001	

Abbreviations: LTC = Long-Term Care

a – Adjusted for age, sex, frailty, dementia diagnosis, and LTC assessment type but excluding the stratifying variable

b – Percentage change from study year 2009/10 to study year 2016/17

FIGURES

Figure 1 – Proportion of Ontario LTC residents receiving any opioid and specific opioid agents in each study year between 2009/10 and 2016/17

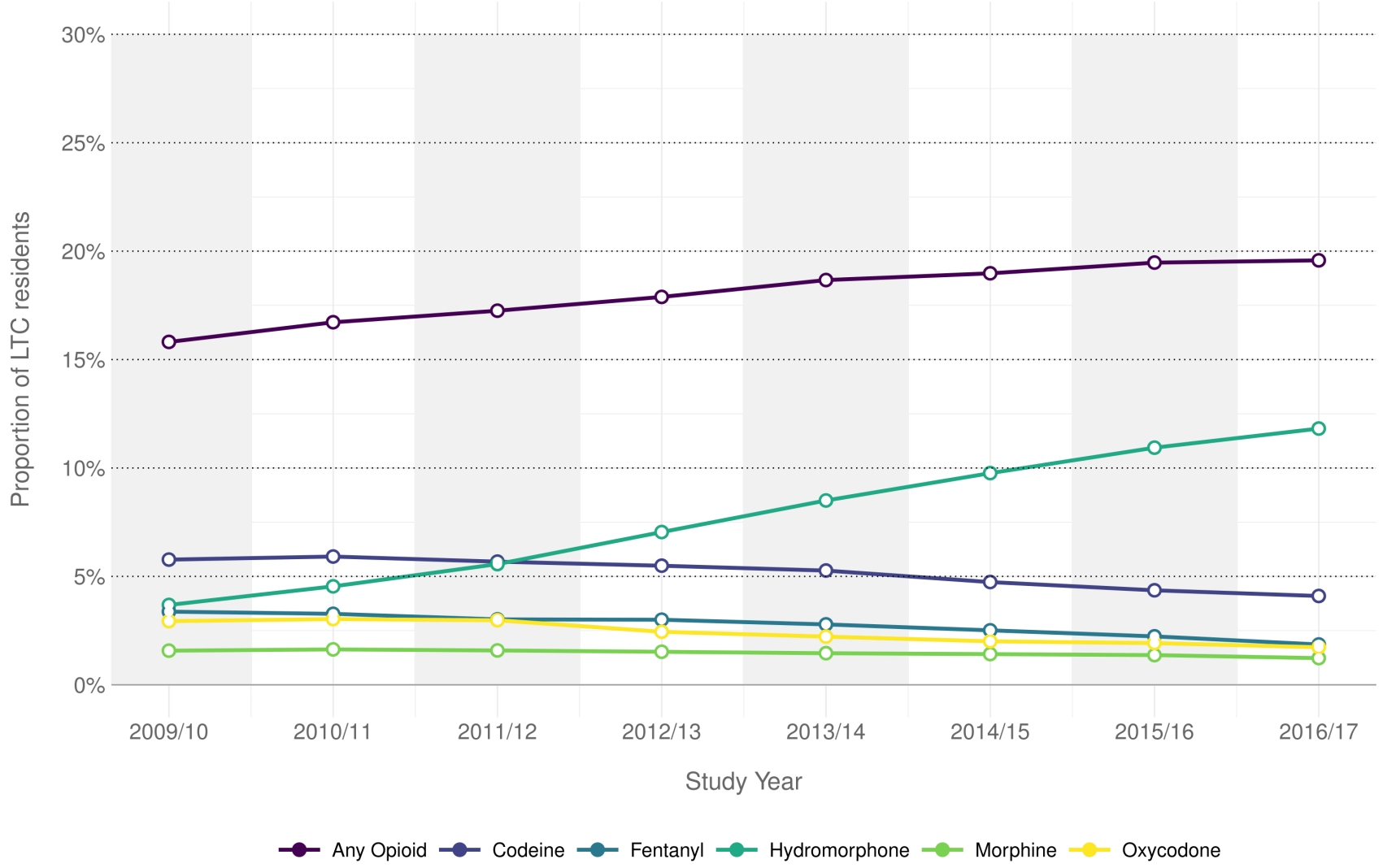
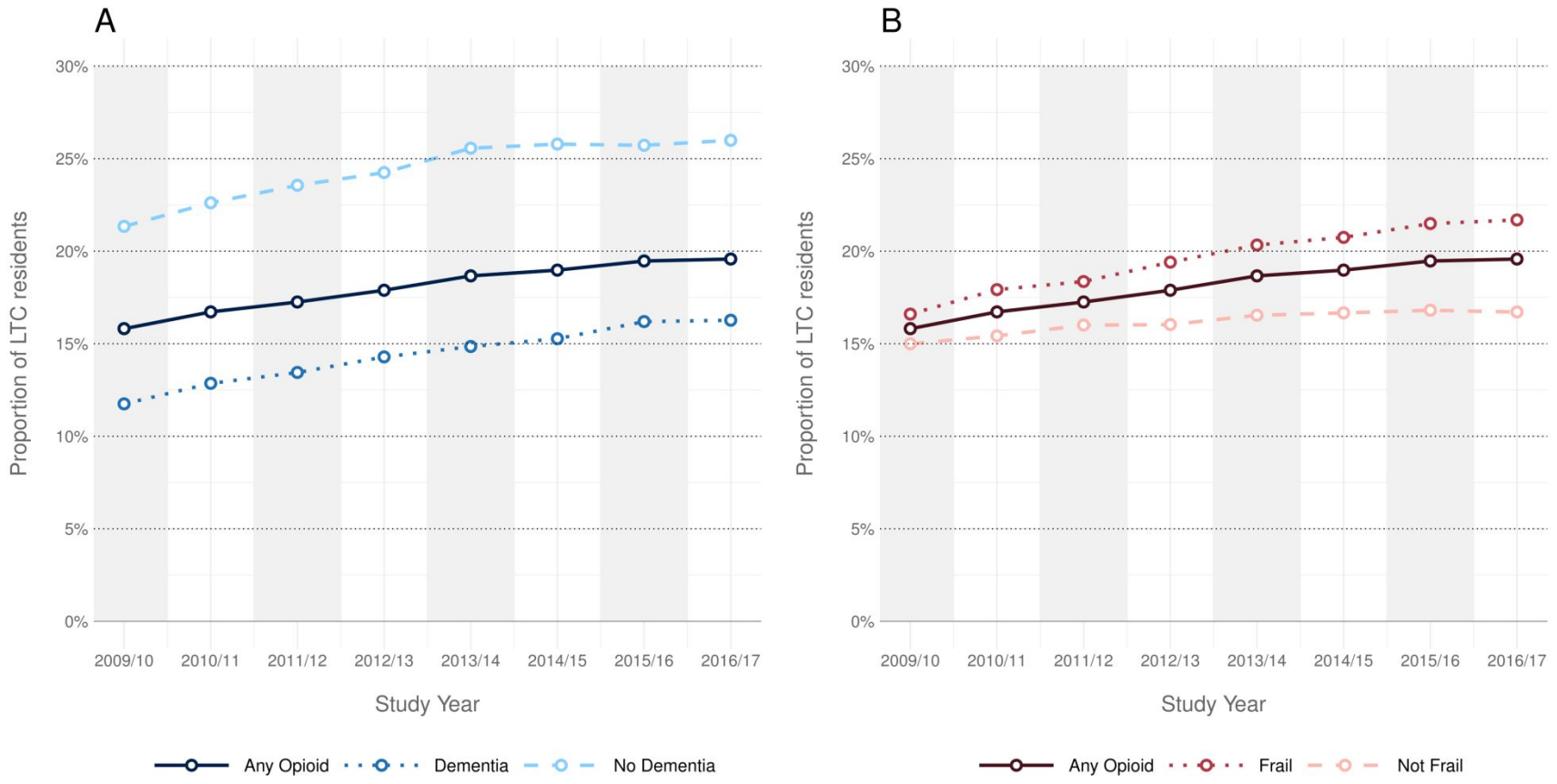


Figure 2 – Proportion of Ontario LTC residents, stratified by dementia diagnosis (A) and frailty (B), receiving any opioid in each study year between 2009/10 and 2016/17



ONLINE SUPPLEMENT

eTable 1. Description of Ontario health administrative data sources included in this study

Database	Description
Continuing Care Reporting System Long-Term Care (CCRS-LTC) database	The CCRS-LTC database is comprised of mandatory, clinical assessments performed on all nursing home residents in Ontario. Nursing home assessments are made using the Resident Assessment Instrument Minimum Data Set (RAI-MDS) version 2.0, a previously validated tool.[1;2] Full assessments are completed on admission, annually, and following a significant health status change by trained medical personnel.
Ontario Drug Benefit (ODB) program database	The ODB database contains prescription medication claims for those covered under the provincial drug program, mainly those aged 65 years and older, nursing home residents, and those receiving social assistance. Each medication claim has an associated prescriber identifier which indicates the health practitioner who wrote the prescription. A special flag in the ODB database indicates whether the prescription was dispensed in the community or nursing home setting. An audit of 5,155 randomly selected prescriptions dispensed from 50 Ontario pharmacies determined that the ODB had an error rate of 0.7% and none of the pharmacy characteristics examined (locations, owner affiliation, productivity) were associated with coding errors.[3]
Registered Persons Database (RPDB)	The RPDB provides basic demographic information (age, sex, area of residence, date of birth, and date of death for deceased individuals) about anyone who has ever received an Ontario health card number (e.g., been enrolled in the province's publicly funded health insurance system).

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eTable 2. Opioid medications dispensed under Ontario's Drug Benefit program between April 1, 2009 and March 31, 2017

Opioid Medication	Formulation	Dosages
Codeine		
Codeine Phosphate	Short-acting	5mg
		15mg
		25mg
		30mg
		60mg
Codeine Phosphate + Acetaminophen	Short-acting combination	15mg
		30mg
		60mg
Codeine Phosphate + Acetylsalicylic Acid	Short-acting combination	15mg
		30mg
		60mg
Codeine Sulfate	Long-acting	50mg
		100mg
		150mg
		200mg
Fentanyl		
Fentanyl Citrate	Long-acting	25mcg/hr
		50mcg/hr
		75mcg/hr
		100mcg/hr
Hydromorphone		
Hydromorphone HCL	Short-acting	1mg
		2mg
		4mg
		8mg
		10mg
		20mg
		50mg
Hydromorphone HCL	Long-acting	3mg
		4.5mg
		6mg
		9mg
		12mg
		18mg
		24mg
		30mg
Morphine		
Morphine HCL	Short-acting	1mg
		5mg
		10mg
		20mg
		40mg
		50mg
		60mg
Morphine Sulfate	Short-acting	1mg
		2mg
		5mg
		10mg
		15mg
		20mg
		25mg

		30mg
		50mg
Morphine Sulfate	Long-acting	10mg
		15mg
		20mg
		30mg
		50mg
		60mg
		100mg
		200mg
Oxycodone		
Oxycodone HCL	Short-acting	5mg
		10mg
		20mg
Oxycodone HCL + Acetaminophen	Short-acting combination	5mg
Oxycodone HCL + Acetylsalicylic Acid	Short-acting combination	5mg
Oxycodone HCL	Long-acting	10mg
		15mg
		20mg
		30mg
		40mg
		60mg
		80mg
Other		
Meperidine HCL	Short-acting	50mg
		75mg
		100mg
Methadone HCL[a]		1mg
		5mg
		10mg
		25mg

Abbreviations: mg = milligrams; mcg/hr = micrograms per hour
a - Prescribed for pain purposes

eTable 3. Baseline characteristics of study population at each study year between 2009/10 and 2016/17

Resident Characteristic	Study Year							
	2009/10 (N=74,371)	2010/11 (N=76,084)	2011/12 (N=76,080)	2012/13 (N=76,320)	2013/14 (N=76,252)	2014/15 (N=77,304)	2015/16 (N=76,512)	2016/17 (N=76,254)
Age								
≤ 85 years	38,276 (51.5%)	38,263 (50.3%)	37,754 (49.6%)	37,095 (48.6%)	36,543 (47.9%)	36,610 (47.4%)	36,034 (47.1%)	35,409 (46.4%)
> 85 years	36,095 (48.5%)	37,821 (49.7%)	38,326 (50.4%)	39,225 (51.4%)	39,709 (52.1%)	40,694 (52.6%)	40,478 (52.9%)	40,845 (53.6%)
Sex								
Female	53,994 (72.6%)	54,974 (72.3%)	54,785 (72.0%)	54,657 (71.6%)	54,407 (71.4%)	54,887 (71.0%)	54,153 (70.8%)	53,838 (70.6%)
Male	20,377 (27.4%)	21,110 (27.7%)	21,295 (28.0%)	21,663 (28.4%)	21,845 (28.6%)	22,417 (29.0%)	22,359 (29.2%)	22,416 (29.4%)
Dementia								
No	31,515 (42.4%)	30,105 (39.6%)	28,647 (37.7%)	27,602 (36.2%)	27,165 (35.6%)	27,242 (35.2%)	26,307 (34.4%)	25,915 (34.0%)
Yes	42,856 (57.6%)	45,979 (60.4%)	47,433 (62.3%)	48,718 (63.8%)	49,087 (64.4%)	50,062 (64.8%)	50,205 (65.6%)	50,339 (66.0%)
Frail resident								
No	36,524 (49.1%)	36,650 (48.2%)	35,833 (47.1%)	34,335 (45.0%)	33,506 (43.9%)	33,534 (43.4%)	33,021 (43.2%)	32,405 (42.5%)
Yes	37,847 (50.9%)	39,434 (51.8%)	40,247 (52.9%)	41,985 (55.0%)	42,746 (56.1%)	43,770 (56.6%)	43,491 (56.8%)	43,849 (57.5%)
Pain Frequency								
No pain	43,151 (58.0%)	44,803 (58.9%)	46,210 (60.7%)	48,069 (63.0%)	48,954 (64.2%)	50,770 (65.7%)	51,418 (67.2%)	52,485 (68.8%)
Any pain	31,220 (42.0%)	31,281 (41.1%)	29,870 (39.3%)	28,251 (37.0%)	27,298 (35.8%)	26,534 (34.3%)	25,094 (32.8%)	23,769 (31.2%)
LTC assessment type								
Entry	17,041 (22.9%)	21,723 (28.6%)	21,741 (28.6%)	21,325 (27.9%)	22,148 (29.0%)	23,480 (30.4%)	22,556 (29.5%)	22,359 (29.3%)
Follow-up	57,330 (77.1%)	54,361 (71.4%)	54,339 (71.4%)	54,995 (72.1%)	54,104 (71.0%)	53,824 (69.6%)	53,956 (70.5%)	53,895 (70.7%)

Abbreviations: LTC = Long-Term Care