

PEER REVIEW HISTORY

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ARTICLE DETAILS

TITLE (PROVISIONAL)	Examining the immediate and on-going impact of the COVID-19 pandemic on population-based estimates of dementia: a population-based time series analysis in Ontario, Canada
AUTHORS	Jones, Aaron; Bronskill, Susan; Maclagan, Laura; Jaakkimainen, R. Liisa; Kirkwood, David; Mayhew, Alexandra; Costa, Andrew P; Griffith, Lauren

VERSION 1 – REVIEW

REVIEWER	Festa, Natalia Yale School of Medicine, Internal Medicine
REVIEW RETURNED	05-Sep-2022

GENERAL COMMENTS	<p>This is a well-written and timely manuscript that describes the effects of the COVID-19 pandemic on the recording of dementia diagnoses within administrative claims. I have outlined a series of comments, questions, and suggestions. If addressed, these may strengthen the final manuscript. Thank you for the opportunity to review this work.</p> <p>Major Comments</p> <p>Introduction</p> <p>1. It would be helpful to orient readers as to pertinent society guidelines and health services incentives that inform dementia screening practices within Ontario (and perhaps within Canada, more broadly).</p> <p>Methods</p> <p>2. I am less familiar with cognitive screening practices within Ontario's congregate care settings. Do cognitive screening patterns/regulatory requirements differ from those applicable to community-dwellers? For example, United States Long Term Care residents undergo routine cognitive screening (as opposed to nonrandom screening in the community). If there are similar differences in Ontario, this might impact performance of the chosen claims-based dementia definition for different residential groups. Therefore, it could be important to stratify or adjust for residential status within the main analysis.</p> <p>3. It's notable that the Canadian CDSS algorithm has more stringent requirements for claims derived from outpatient encounters. As described by the authors, there is preliminary evidence to suggest that dementia-related claims from inpatient settings are the least accurate. It may be helpful to conduct a sensitivity analysis in which the claims-based definition is modified</p>
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	<p>to require >1 qualifying inpatient claim and <3 qualifying outpatient claims.</p> <p>4. It would be helpful for the authors to clarify the rules that they applied to qualifying claims. For example, did they allow for >1 qualifying claim per healthcare encounter per day?</p> <p>5. It may be helpful to reorient the sensitivity analysis around modified approaches to claims-based dementia ascertainment (as described above), rather than replicating the analysis for diabetes. Using these modified definitions (adjusting # of claims per healthcare setting, # of allowable claims per encounter, etc.), the authors could provide a range of plausible scenarios for changes in dementia ascertainment over the observation period, under different assumptions.</p> <p>6. If feasible, the main models should be risk-adjusted due to a nonrandom distribution of COVID-19 mortality. If this is not feasible, an age-stratified summary of the risk composition of the population for each observation year could help to disentangle the extent to which selection contributed to the reported trends. This could be achieved using a composite claims-based indicator of risk, perhaps an analog to the United States Centers for Medicare & Medicaid Services Hierarchical Condition Categories risk-adjustment score.</p> <p>Results</p> <p>7. Because the authors have posited that changes in health services utilization explain observed trends, it would be helpful to provide a summary of the total number of healthcare encounters, by healthcare setting, for the study population. It would also be additive to disaggregate this information by age group and, potentially, residential setting.</p> <p>Discussion</p> <p>8. I have concerns regarding the assertion that the reported trends are primarily attributable to changes in health services utilization (page 11, lines 51-56). The authors note that possible differential mortality among persons most prone to dementia is, at best, a partial explanation of their findings. Without evaluating age-stratified changes to population composition (dementia risk factors and medical complexity, as described above), it seems premature to conclude that one explanation should be favored. In addition to the above, there are alternative explanations that should be considered. Exposure to social isolation (established dementia risk factor) may have accelerated dementia onset in susceptible older persons, potentially increasing incidence among pandemic survivors and hastening their evaluation once healthcare utilization recovered. Within multigenerational households, pandemic-related remote work could have afforded informal caregivers additional opportunities to observe cognitive or behavioral changes, prompting them to seek formal evaluation on behalf of their family member. Additional considerations relate to the distribution of qualifying claims across healthcare settings as healthcare utilization recovered. If the rebound in qualifying claims were concentrated within inpatient encounters (as opposed to outpatient or prescription drug claims), this might suggest distinct explanatory mechanisms. Outlining multiple plausible explanations for the observed trends, and steps that could be taken to disentangle their relative contributions, should strengthen the discussion.</p>
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	<p>9. It would be helpful to expound upon the limitations of claims-based dementia ascertainment for readers who are less familiar with the literature in this area.</p> <p>10. Because changes in health services utilization are an explanatory mechanism of primary interest, additional context regarding the effects of missed or delayed dementia should reinforce the salience and timeliness of the findings.</p> <p>Minor Comments</p> <p>1. Page 3, Lines 46-50: One could interpret this statement as setting-up the manuscript to evaluate changes in the performance characteristics of validated claims-based algorithms over time (due to changing population composition, etc.). While this provides important framing regarding the clinical and policy relevance of the manuscript, it may help to distinguish the aims of this analysis from descriptions of how this work should be situated within the literature.</p> <p>2. Page 4, Lines 32-35: It would be helpful to include additional detail regarding how the authors defined the population at risk. For example, was there a minimum lookback period (i.e., no dementia-related claims for five-years preceding the observation window)?</p> <p>3. Supplemental Table S1: I would suggest bracketing the name of the diagnosis corresponding to each ICD-10 diagnostic code. It may also enhance clarity to summarize the drug classes subsumed by the listed DINs. I looked up a few of the DINs, which corresponded to different cholinesterase inhibitor formulations. Were NMDA antagonists also included? Were there other included drug classes sometimes used in palliation or symptom management for dementia and other diseases (and how might this affect interpretation of the results)?</p> <p>4. Page 12, Lines 10-11: Comorbid sensory impairment is also an important consideration when determining the clinical appropriateness of virtual cognitive screening and monitoring; this is worth mentioning.</p>
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REVIEWER	Hansen, Jens
REVIEW RETURNED	21-Sep-2022

GENERAL COMMENTS	<p>The article "Examining the immediate and on-going impact of the COVID-19 pandemic on population-based estimates of dementia" is almost ready for publication.</p> <p>The background, methods, findings and discussion is stated clearly and of relevance.</p> <p>However two minor informations are suggested:</p> <p>Add informations on references regarding the the statistical methods (autoregressive linear regression and how the model was controlled).</p> <p>Add some implications e.g. how to handle the patient group during new pandemics in the future.</p>
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VERSION 1 – AUTHOR RESPONSE

Reviewer: 1
 Dr. Natalia Festa, Yale School of Medicine
 Comments to the Author:

To Authors

This is a well-written and timely manuscript that describes the effects of the COVID-19 pandemic on the recording of dementia diagnoses within administrative claims. I have outlined a series of comments, questions, and suggestions. If addressed, these may strengthen the final manuscript. Thank you for the opportunity to review this work.

Response

Thank you for your comments.

Major Comments

Introduction

1. It would be helpful to orient readers as to pertinent society guidelines and health services incentives that inform dementia screening practices within Ontario (and perhaps within Canada, more broadly).

Response

Thank you for this suggestion. We have included the following text under “Methods -> Setting” as we believe it is the most appropriate section: “According to Canadian guidelines, routine cognitive screening of asymptomatic individuals for mild cognitive impairment or dementia is not recommended but that assessment of cognition, activities of daily living, and neuropsychiatric symptoms is indicated when there are clinically significant concerns for a cognitive disorder. In Ontario there are no incentives for clinicians to screen for dementia such as exist for certain other chronic diseases” (p.4)

Methods

2. I am less familiar with cognitive screening practices within Ontario’s congregate care settings. Do cognitive screening patterns/regulatory requirements differ from those applicable to community-dwellers? For example, United States Long Term Care residents undergo routine cognitive screening (as opposed to nonrandom screening in the community). If there are similar differences in Ontario, this might impact performance of the chosen claims-based dementia definition for different residential groups. Therefore, it could be important to stratify or adjust for residential status within the main analysis.

Response

Residents of long-term care homes in Ontario do receive regular clinical assessments that include cognitive screening (typically performed by nurses) but the results of the screening would not directly translate into diagnosis recorded in the administrative record. Dementia in long-term care home residents would be ascertained in the same way as community-dwelling individuals (physician claims, hospital claims, pharmacy claims). However, we recognize that residents of long-term care home population are a distinct population with different care patterns and were differentially affected by the COVID-19 pandemic, therefore we have implemented a sensitivity analysis that removes the long-term care home population from the analysis. (p.6-7)

3. It's notable that the Canadian CDSS algorithm has more stringent requirements for claims derived from outpatient encounters. As described by the authors, there is preliminary evidence to suggest that dementia-related claims from inpatient settings are the least accurate. It may be helpful to conduct a

sensitivity analysis in which the claims-based definition is modified to require >1 qualifying inpatient claim and <3 qualifying outpatient claims.

Response

The dementia algorithm used in this study was developed and validated on Canadian administrative records and is widely used in research and public health surveillance. In the validation paper, multiple formulations of the claims requirements were examined and the present formulation was chosen as the best way to achieve high positive predictive value and high sensitivity. Results of the testing of multiple formulations can be found in the paper[1]. We have further described the algorithm in the methods section of the paper (p.4-5) A number of case ascertainment algorithms using Canadian administrative data require 2+ physician claims but only 1 hospital claim[2]. This reflects differences in data quality across the sources.

4. It would be helpful for the authors to clarify the rules that they applied to qualifying claims. For example, did they allow for >1 qualifying claim per healthcare encounter per day?

Response

Typically claims are restricted to one per patient per physician per day for counting persons. In the case of the dementia algorithm, it is non-consequential since the hospital admission and medication criteria require only 1 claim and the physician billing criteria requires each of the 3 claims to be separated by 30 days, so multiple claims on a single day would have no impact. We have clarified the 30-day separation between physician encounters in the methods section. (p 4)

5. It may be helpful to reorient the sensitivity analysis around modified approaches to claims-based dementia ascertainment (as described above), rather than replicating the analysis for diabetes. Using these modified definitions (adjusting # of claims per healthcare setting, # of allowable claims per encounter, etc.), the authors could provide a range of plausible scenarios for changes in dementia ascertainment over the observation period, under different assumptions.

Response

We agree that there is value in keeping the focus on the dementia population. Based on the reviewer's overall set of comments, our sensitivity analysis section now includes analysis of the community-dwelling population (no long-term care homes residents) and analysis using age-sex standardized rates (Supplemental Table 2 and 3). We would prefer not to examine the impact of altering the case ascertainment definition as we believe there is value in using the validated, standard algorithm that is frequently employed for both research and public health surveillance. Variations on the case ascertainment algorithm have been previously explored.[1]

6. If feasible, the main models should be risk-adjusted due to a nonrandom distribution of COVID-19 mortality. If this is not feasible, an age-stratified summary of the risk composition of the population for each observation year could help to disentangle the extent to which selection contributed to the reported trends. This could be achieved using a composite claims-based indicator of risk, perhaps an analog to the United States Centers for Medicare & Medicaid Services Hierarchical Condition Categories risk-adjustment score.

Response

We agree that additional work on this point is warranted and now include two additional analyses.

First, we have added strata defined by the number of health conditions that have detected via administrative data (0-5, 6-10, 11+).(Table 2, Figure 2) This is based on 226 total possible conditions included in the Canadian Institute for Health Information Population Risk Grouper[3] which is fairly analogous to the CMS-HCC. Second, we have calculated incidence rates standardized to the age-sex distribution of the population as of January 2015. We reported the differences between the standardized and unstandardized rates and repeated the main analysis with the standardized rates (Supplemental Table 2-3).

Results

7. Because the authors have posited that changes in health services utilization explain observed trends, it would be helpful to provide a summary of the total number of healthcare encounters, by healthcare setting, for the study population. It would also be additive to disaggregate this information by age group and, potentially, residential setting.

Response

A full description of the changes in the health service use of the older adults in Ontario during the pandemic is beyond the scope of the paper but has been explored previously in other studies[4,5]. We more fully cite this literature in our discussion now. (p12).

Discussion

8. I have concerns regarding the assertion that the reported trends are primarily attributable to changes in health services utilization (page 11, lines 51-56). The authors note that possible differential mortality among persons most prone to dementia is, at best, a partial explanation of their findings. Without evaluating age-stratified changes to population composition (dementia risk factors and medical complexity, as described above), it seems premature to conclude that one explanation should be favored. In addition to the above, there are alternative explanations that should be considered. Exposure to social isolation (established dementia risk factor) may have accelerated dementia onset in susceptible older persons, potentially increasing incidence among pandemic survivors and hastening their evaluation once healthcare utilization recovered. Within multigenerational households, pandemic-related remote work could have afforded informal caregivers additional opportunities to observe cognitive or behavioral changes, prompting them to seek formal evaluation on behalf of their family member. Additional considerations relate to the distribution of qualifying claims across healthcare settings as healthcare utilization recovered. If the rebound in qualifying claims were concentrated within inpatient encounters (as opposed to outpatient or prescription drug claims), this might suggest distinct explanatory mechanisms. Outlining multiple plausible explanations for the observed trends, and steps that could be taken to disentangle their relative contributions, should strengthen the discussion.

Response

Thank you for this suggestion. We now discuss further potential explanations of our results and have removed language preferring one potential cause. We now additionally mention social isolation, observation by informal caregivers, and specifically mention the increase in hospital admissions (p12-14).

9. It would be helpful to expound upon the limitations of claims-based dementia ascertainment for readers who are less familiar with the literature in this area.

Response

We have added additional text to the limitations section on the limitations of using administrative data for dementia ascertainment (p15).

10. Because changes in health services utilization are an explanatory mechanism of primary interest, additional context regarding the effects of missed or delayed dementia should reinforce the salience and timeliness of the findings.

Response

We now mention refer to consequences of missed or delayed dementia diagnosis at the end of the discussion (p15).

Minor Comments

1. Page 3, Lines 46-50: One could interpret this statement as setting-up the manuscript to evaluate changes in the performance characteristics of validated claims-based algorithms over time (due to changing population composition, etc.). While this provides important framing regarding the clinical and policy relevance of the manuscript, it may help to distinguish the aims of this analysis from descriptions of how this work should be situated within the literature.

Response

We have removed these sentences from the introduction and incorporated them into the discussion. (p13).

2. Page 4, Lines 32-35: It would be helpful to include additional detail regarding how the authors defined the population at risk. For example, was there a minimum lookback period (i.e., no dementia-related claims for five-years preceding the observation window)?

Response

Thank for this suggestion. We have updated the text to include that the lookback goes back to 1996. (p5)

3. Supplemental Table S1: I would suggest bracketing the name of the diagnosis corresponding to each ICD-10 diagnostic code. It may also enhance clarity to summarize the drug classes subsumed by the listed DINs. I looked up a few of the DINs, which corresponded to different cholinesterase inhibitor formulations. Were NMDA antagonists also included? Were there other included drug

classes sometimes used in palliation or symptom management for dementia and other diseases (and how might this affect interpretation of the results)?

Response

We have now included the diagnosis names next to the ICD-10 codes. We have switched our list of DINs to ATC codes to simplify the presentation. Effectively, the drugs included were cholinesterase inhibitors (donepezil, galantamine, rivastigmine). The NMDA antagonist memantine is technically included in the CCDSS definition, as it is approved by Health Canada, but inconsequential for our study as it is not covered by the Ontario Drug Benefit formulary (or any public formulary in Canada). These drugs were selected in the original algorithm as being specific to dementia. Inclusion of other drugs would require a re-validation of the algorithm. (Supplemental Table 1).

4. Page 12, Lines 10-11: Comorbid sensory impairment is also an important consideration when determining the clinical appropriateness of virtual cognitive screening and monitoring; this is worth mentioning.

Response

Thank you for this suggestion we have now included this in the discussion of virtual cognitive screening. (p13).

Reviewer: 2

Jens Hansen

Comments to the Author:

The article "Examining the immediate and on-going impact of the COVID-19 pandemic on population-based estimates of dementia" is almost ready for publication.

The background, methods, findings and discussion is stated clearly and of relevance.

However two minor informations are suggested:

Add informations on references regarding the the statistical methods (autoregressive linear regression and how the model was controlled).

Response

Thank you for your comments. We have added references related to how the analysis were conducted. (p5)

Add some implications e.g. how to handle the patient group during new pandemics in the future.

Response

We have added some implications, including the importance of ensuring on-going access to healthcare, in the discussion. (p15)

References

- 1 Jaakkimainen RL, Bronskill SE, Tierney MC, *et al.* Identification of Physician-Diagnosed Alzheimer’s Disease and Related Dementias in Population-Based Administrative Data: A Validation Study Using Family Physicians’ Electronic Medical Records. *J Alzheimers Dis JAD* 2016;**54**:337–49. doi:10.3233/JAD-160105
- 2 Public Health Agency of Canada. Public Health Infobase, Canadian Chronic Disease Surveillance System (CCDSS) Disease-Specific Case Definitions. https://health-infobase.canada.ca/ccdss/publication/CCDSS_Case_Definitions_v2019.xlsx
- 3 CIHI’s Population Grouping Methodology 1.3 — Overview and Outputs, 2021. ;:28.
- 4 Bronskill SE, Maclagan LC, Maxwell CJ, *et al.* Trends in Health Service Use for Canadian Adults With Dementia and Parkinson Disease During the First Wave of the COVID-19 Pandemic. In: *JAMA Health Forum*. American Medical Association 2022. e214599–e214599.
- 5 Impact of COVID-19 on Canada’s health care systems | CIHI. <https://www.cihi.ca/en/covid-19-resources/impact-of-covid-19-on-canadas-health-care-systems> (accessed 15 Apr 2021).

VERSION 2 – REVIEW

REVIEWER	Festa, Natalia Yale School of Medicine, Internal Medicine
REVIEW RETURNED	30-Nov-2022

GENERAL COMMENTS	<p>Reviewer Comments</p> <p>To Editors</p> <p>This timely manuscript characterizes changes in patterns of dementia ascertainment during the COVID-19 pandemic. In their revisions and stratified analyses, the authors have provided valuable insights into potential explanatory mechanisms for these changes. I believe that the manuscript would be relevant and informative to the readership of BMJ Open.</p> <p>To Authors</p> <p>This is a well-written and timely manuscript that describes the effects of the COVID-19 pandemic on the recording of dementia diagnoses within administrative claims. I appreciate the authors’ thorough response to the suggested revisions, which have substantially strengthened the manuscript. Specifically, the additional analyses across age-groups, residential cohorts, and clinical risk profiles, provide rich information regarding potential explanatory mechanisms for changes in ascertainment. I have offered one final suggestion, below. I appreciated the opportunity to review this interesting and valuable work.</p> <p>Additional Comment</p>
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	In the limitations section, I suggest additional discussion of the potential for delirium to be conflated with dementia during hospital encounters, as well as the disproportionate susceptibility of persons with multimorbidity to delirium. Considering the differential rebound in ascertainment in hospital settings and among persons with 11+ comorbidities, this is worth highlighting as a potential limitation to accurate dementia ascertainment in these subgroups.
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REVIEWER	Hansen, Jens
REVIEW RETURNED	13-Dec-2022

GENERAL COMMENTS	The authors have edited the document according to my previous comments. Thus, I find the article ready for publication
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VERSION 2 – AUTHOR RESPONSE

Reviewer: 1

Dr. Natalia Festa, Yale School of Medicine

Comments to the Author:

To Authors

In the limitations section, I suggest additional discussion of the potential for delirium to be conflated with dementia during hospital encounters, as well as the disproportionate susceptibility of persons with multimorbidity to delirium. Considering the differential rebound in ascertainment in hospital settings and among persons with 11+ comorbidities, this is worth highlighting as a potential limitation to accurate dementia ascertainment in these subgroups.

Response

Thank you for this comment. We have noted the potential conflation of delirium and dementia, particularly in acute care settings and highly comorbid populations, and its potential to result in higher ascertainment, in the limitations section.