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Title	Using electronic medical record data to describe the epidemiology and management of dementia in Canadian primary care practices
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Reviewer 1	Dr. Saskia N. Sivananthan
Institution	UBC Centre for Health Services and Policy Research
General comments (author response in bold)	<p>Introduction</p> <p>1. Title should reflect that study focuses on community-dwelling elderly and describes the pharmacological management of dementia.</p> <p><b>Done</b></p> <p>2. P1. Line up limitations with data source.</p> <p><b>Agreed. See p 1 para 4 (and overleaf)</b></p> <p>3. P1. What is meant by large population-based studies?</p> <p><b>We have simplified our argument to propose that differences in reported prevalences for dementia relate to variation in case definition and method of enumeration. It is unnecessary for us to speculate about the specific influences of these variations.</b></p> <p>4. p1 reference outdated.</p> <p><b>We disagree. The reference is from the Lancet in 1997 and its content is still relevant. We have added additional references, but in general the prevalence rate has remained fairly consistent, although the number of cases has increased.</b></p> <p>5. Give more description about use of EMR data for estimating prevalence.</p> <p><b>Agree. See p2 para 4.</b></p> <p>6. Needs more references to existing knowledge.</p> <p><b>We agree and have referenced some high quality recent studies for purposes of comparison (see refs 1-6).</b></p> <p>7. Results do not provide a clinical profile.</p> <p><b>Agreed. We have deleted this phrase as being misleading.</b></p> <p>Method</p> <p>1. provide a brief description of the case definitions and sensitivity /specificity.</p> <p><b>Agreed. See p3 para 2 and Table 1.</b></p> <p>2. Specify the time over which data was collected.</p> <p><b>Agreed. We now identify the period from which the data derives is 1st Jan 2011-31st December 2012.</b></p> <p>3. Provide a brief description of the case definitions for the identified comorbidities.</p> <p><b>We think this will consume many additional words, so instead have made clear reference to our Annals of Fam Med paper where this information is readily available.</b></p> <p>4. Suggest a subheading: "Pharmacological treatment of dementia in primary care".</p> <p><b>Agreed. See p4 para 3.</b></p> <p>5. Include description of dementia specific medications</p> <p><b>Agreed. See p4 para 3 and p 6 para 2.</b></p> <p>6. Give more description of the analysis used.</p> <p><b>We disagree. We think P 4 para 5 gives as clear yet concise a description of our analysis as we could have achieved given the word limit. Is there something specific that the reviewer would like us to clarify?</b></p> <p>Results</p> <p>1. Not clear over what time period clinic visits are being assessed.</p> <p><b>We have clarified that we studied patients aged 65y and older who made at least one clinic visit between 1st Jan 2011 and 31st Dec 2012. (see p3 para 4).</b></p> <p>2. Include missing data in a table.</p> <p><b>We have redrafted Table 2 to indicate the changing denominator values for prevalence estimates in relation to age and sex. And we have revised Table 3 to include missing data relating to location and BMI.</b></p> <p>3. Why was BMI the only variable looked at (apart from comorbidities)?</p> <p><b>We discuss limitations associated with data entry for clinical rather than research purposes on p 7 para 4. We considered age, sex, BMI, comorbidity and location as being a useful starting point in the process of understanding the epidemiology and management of dementia in primary care. Subsequent analyses will go into greater depth of sociodemographic context, for example by including the influence of deprivation categories and by examining antidepressant and antipsychotic prescribing.</b></p> <p>4. Why no mention of the urban and rural differences?</p> <p><b>We have now included discussion of this (p6 para 4), though without more detailed analysis of trends through time our interpretation is speculative. As above, this is an issue for closer examination in a future paper.</b></p>

	<p>5. Were the temporal trends in each province statistically significant?  <b>Age-sex standardized rates are obtained by applying population weights to the corresponding age-specific sample rates and then summing them over all weighted age-specific rates. We do not know of a method for testing the statistically significant difference between age-sex standardized rates.</b>  Discussion  1. Interpretation focuses on specialists without exploring the results in much detail. Why the immediate assumption that prevalence is underestimated and that diagnosis is primarily driven by specialists?  <b>We have elaborated on these issues by observing (p5 para4) that in a sample of people with a condition as insidious as dementia it is certainly the case that estimates of prevalence will be underestimated since many people with the disease will not have been identified as having it. We base our discussion of the relationship between specialists and family physicians in the context of diagnosis on results from previous research (Aminzadeh et al, 2012), though we accept that the precise ratio of family physician to specialist diagnosis is unknown and have attempted to more accurately articulate this in our text.</b>  2. The lower prescription rate could also be attributed to provincial policy.  <b>Agreed. Statement to this effect added (p6 para 2).</b>  3. Generalizability a limitation of the paper?  <b>We disagree. We have included reference to our paper supporting the representativeness of our patient and physician samples. And we have clarified that our focus is on community-dwelling people with dementia rather than all people with dementia, and on the primary care management of their disease. Though we concede that these intentions were not as clearly described in our previous manuscript as they are now.</b></p>
<b>Reviewer 2</b>	Dr. Colleen Maxwell
Institution	University of Waterloo, School of Pharmacy, Kitchener
General comments (author response in bold)	<p>Major issues  1. Introduction and discussion are underdeveloped.  <b>We have supplemented these sections with further information about dementia prevalence, a more explicit rationale for studying the epidemiology and management of dementia in primary care, and more description and interpretation of variation in findings and methods.</b>  2. Add key references on dementia epidemiology and management  <b>We have attempted to do this, focussing on quantitative empirical work. Newer published data on dementia epidemiology appears to be limited to Ontario. We now reference CSHA.</b>  3. Description of CPCSSN is not well articulated  <b>We now include a paragraph describing the background, methods and outputs of the CPCSSN. (p 2 para 3)</b>  4. Why are findings reported up to 31st Dec 2012 and what was the justification for studying cases identified between 2008 and 2012.  <b>We have clarified that this paper is part of a series appearing in CMAJ Open based on analysis of the same dataset (p3 para 2). We have also clarified that cases were eligible if they had made one clinic visit between 1st Jan 2011 and 31st Dec 2012.</b>  5. More details about CPCSSN are needed, including population coverage and likely exclusions, with clear statements about the implications for interpretation of findings  <b>We now describe our samples size (480 sentinels, 600 000 community-dwelling people who had visited their primary care provider at least once in the two year study window, of whom 57 177 were aged 65y and older and met study inclusion criteria and of whom 4552 met case criteria for dementia according to our validated case definition). We have explicitly stated that our community-dwelling sample probably excludes those living in long-term care (p7 para 3), for whom health services are largely provided under different arrangements.</b>  6. Further details about the denominator and the index date for the look-back period are required.  <b>We have clarified that we studied patients aged 65y and older on 31st Dec 2012 who had made at least one clinic visit recorded in their primary care EMR between 1st Jan 2011 and 31st Dec 2012. (see p3 para 4).</b>  7. Need to provide specific details about their case finding algorithm.  <b>The case definition and validation data relating to it are now presented in Table 1 and p3 para 3. The same data is provided in the paper referenced at [17], which also includes all the other CPCSSN case definitions and validation data.</b>  8. No clear rationale was provided to explain the examination of variation on prevalence related to BMI and urban/rural residence.  <b>There are two mutually coherent explanations for our choice of covariates. One is that in attempting to present a coherent set of papers about the epidemiology and management of chronic disease in primary care we have reported the same types of data for the several different diseases: BMI and location have been consistently presented throughout the CMAJ Open series. The second explanation is that BMI and location of residence are important sociodemographic characteristics in their own right, as are age and sex. In employing them to describe the epidemiology and management of dementia in primary care we are simply following well-established epidemiological and clinical practice for primary care. We have briefly described this rational on p3 para 6. We discuss the possibility that missing BMI data may impact the interpretation of our findings on p7 para 4. Nevertheless, in some quarters the presence of BMI values for 70% of a community-dwelling sample of patients is regarded as a very positive feature,</b></p>

	<p><b>and we accordingly have reported it here.</b></p> <p>9. Authors should provide specific details about case definition validity for all comorbid conditions included in their analysis.</p> <p><b>We disagree. It would be nice to be able to include this information in this paper, but given that it appears in full detail in reference 17, and in the context of a very strict word limit for CMAJ Open, we think it would not be reasonable to include such information again here.</b></p> <p>10. Implications related to limitations of using EMR data to estimate variation in prevalence and management have not been well articulated.</p> <p><b>We tend to disagree. We do agree that interpreting the kind of variation that we are reporting is complex. But teasing out these relationships definitively would require a much bigger word allowance than this journal provides, or a larger number of papers, each of smaller scope, than we suspect the editors (and readers) would support. We have identified some variation, interpreted it within reason and attempted to be very clear about potential sources of, and risks for, the misinterpretation of it, including the influence of provincial policy. We have not shirked the inevitable limitations deriving from the use of clinical data for research. The value of this work lies, we believe, in the basic identification of variation in the epidemiology and pharmacological management of dementia using rigorous and consistent methods, which sets the scene for further, detailed investigation of specific aspects of that variation.</b></p> <p>Minor issues</p> <p>1. Table 1. Please provide sample sizes and 95% CIs.</p> <p><b>This is now Table 2. Sample sizes and 95% CIs are now included</b></p> <p>2. Table 2 (now Table 3). Unclear why findings are presented as prevalence ratios. Would be more informative to provide point prevalence estimates with 95% CIs. Also provide the relevant sample sizes for the total sample shown here as well as for the individual characteristics. Also need footnotes to clarify the total number and types of comorbidities and the extent of missing data for selected comorbidity</p> <p><b>We disagree. Although point prevalence and odds ratios are commonly used in health research, we believe that prevalence ratios are more intuitively interpretable measures of association, while simultaneously enabling the assessment of the effect of potential confounders. Prevalence ratios are the natural product of log-binomial regression - a close cousin to logistic regression that is generally regarded as more interpretable. Employing a model based approach accounts for more information than simply providing point prevalences. However, we have also attempted to make the prevalences themselves more obvious in the results section. 95% CIs and sample sizes are provided in the table; missing data were incorporated as one of the categories for each covariate and analyzed to see their impact on the outcome variable, with respect to corresponding reference categories.</b></p> <p>3. Table 3 (now 4). Provide additional information about sample sizes, setting and province, and add columns to show estimates by year.</p> <p><b>Agreed. See Table 4.</b></p> <p>4. Figure 1. Would be informative to provide distribution for a categorical comorbidity variable.</p> <p><b>We have deleted Figure 1 as being neither useful nor interesting</b></p> <p>5. Figure 2 (now Figure 1). Provide relevant sample sizes per province and per year and 95% CI for the point prevalence estimate. It would also be helpful to receive additional footnotes reporting population coverage of CPCSSN across these regions and time periods.</p> <p><b>Sample sizes (ie provincial CPCSSN denominators) and base population figures now included. Prevalences are standardised by age and sex. 95% CIs are now included.</b></p>
<b>Reviewer 3</b>	Dr. Nicola Vanacore
Institution	National Institute of Health, National Center for Epidemiology, Surveillance and Health Promotion Viale Regina Elena, Rome
General comments (author response in bold)	<p>1. Authors should specify the relationship between EMRs and CPCSSN to help readers understand differences between an estimate of prevalence calculated through EMR data and that done by door to door survey.</p> <p><b>Agreed. See p2 paras 2-4.</b></p> <p>2. Authors should deeply report the validation process and specific validation parameters</p> <p><b>Our validation methodology is thoroughly and transparently reported and is readily available elsewhere (reference 17). We include validation data for dementia (p3 para 4) and our validated case definition (Table 1).</b></p> <p>3. Clinical subtypes of dementia should be reported and clinical criteria adopted for each type of dementia.</p> <p><b>That would be nice, but data in primary care EMRs rarely differentiate between type of dementia.</b></p> <p>4. Table 1. Crude and adjusted prevalence of dementia should be reported for each of seven provinces for sex and age class specifying the number of patients and the general population.</p> <p><b>Table 2 now presents crude and age and sex adjusted prevalence rates for dementia in those living in the community aged 65y and older at national level. Figure 1 presents age and sex adjusted data for five provinces through time.</b></p> <p>5. The authors adopt a confused definition of dementia caseness.</p> <p><b>We disagree. Though as further clarification we have included the full case definition in Table 1.</b></p> <p>6. Comparison of prevalence rates through time between provinces should be done with a statistical test or 95% CI.</p> <p><b>We agree. 95% CIs now included.</b></p> <p>7. Clinical and demographic characteristics of the 4552 people with dementia should be deeply</p>

	<p>reported.</p> <p><b>Primary care EMR data rarely includes satisfactory demographic data apart from age, sex and location of residence. We have characterised the sample using the data which is available. We have examined our sample in relation to morbidity and comorbidity and pharmacological treatment. We agree that Figure 1 should be deleted.</b></p> <p>8. Common dementia medications are not defined <b>We agree and have clarified that by dementia medication we mean anticholinesterase and NMDA drugs explicitly.</b></p> <p>9. Authors should be more cautious in the discussion to distinguish the differences between risk factors and comorbidities. <b>We are not aware of any instances in our paper in which we either are, or appear to be, at risk of confusing these types of association.</b></p> <p>10. Anti-dementia drug prescribing may be influenced by recommended treatment for different types of dementia. <b>This is true. But we have no evidence, and no reason to believe that it exists, for significantly different distributions of the different types of dementia within different Canadian provinces at levels of magnitude which would lead to differences in prescription of one AChEi over another, or for any AChEi to be prescribed in favour (or otherwise) of an NMDA agonist.</b></p>
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