PEER REVIEW HISTORY

ARTICLE DETAILS

TITLE (PROVISIONAL)	Cardiovascular risk factor documentation and management in primary care electronic medical records among people with schizophrenia in Ontario, Canada: retrospective cohort study
AUTHORS	O'Neill, Braden; Kalia, Sumeet; Aliarzadeh, Babak; Sullivan, Frank; Moineddin, Rahim; Kelly, Martina; Greiver, Michelle

VERSION 1 - REVIEW

REVIEWER	Dr Emanuele F Osimo Imperial College London and University of Cambridge
REVIEW RETURNED	31-Mar-2020

GENERAL COMMENTS	Thanks for sending this paper for peer review. The paper is clearly written and pleasant to read. The question is of limited scope but relevant and timely. The authors set out to analyse the extent to which CVD risk factors were documented in primary care electronic medical records, and compared their documentation by diagnosis (scz or not), patient and provider characteristics. The over-arching question is why the authors have not decided to also present the contents of these measures, for example comparing them between cases and controls. As it stands, this is a good study with a very limited question (rate of completion of documentation). This, however, is not a pertinent question for a peer reviewer as it sits with the Editorial board. In terms of specific comments, they are all quite minor: - title: it should stress even more strongly that this is just about documentation rates, so it could read like this: "retrospective cohort study of risk factor documentation and management in primary care electronic medical records", removing the previous general part - methods: I am unsure why the authors have decided not to correct p values for multiple testing, and I think this should be done - discussion: the authors should address what's happened to the actual content of these measures: are they being drafted for publication elsewhere? Are they not available? - discussion: further work. What has this study prompted and what are the next steps for the team?

REVIEWER	Francesco Rotella Careggi Teaching Hospital, Psychiatry Unit. Florence, Italy.
REVIEW RETURNED	24-Apr-2020

GENERAL COMMENTS	Authors performed an observational, retrospective study on a cohort of 572,311 subject obtained from a primary care electronic medical records (EMR) contained in the UTOPIAN Data Safe Heaven (University of Toronto). The objectives of the study were to describe (and evaluate?) the documentation of cardiovascular disease risk factors in subjects with or without schizophrenia. The main results of the study are that patients with schizophrenia display a more complete documentation and that the overall documentation of cardiovascular risk factors is not considered "adequate" by the authors. However, as stated in the discussion section, there are no Canadian national standards for necessary elements of EMR documentation in primary care, and the fact that a clinical datum is not reported in EMR does not necessarily mean that it is not taken into consideration from a clinical standpoint. In my opinion this represent the major issue of the paper, as it weakens the relevance of data reported. Minor points 1. Results 2nd par.: The number of patients without schizophrenia is 192,427. The quantification of the risk should be reported, not only significance. 2. Results 3rd par.: The first sentence of the par. sounds like a comment. In this section authors should only describe data reported in Figure 2. Furthermore, if an OR is not significant, is NOT significant. It does not "appear" anything else than this. 3. Results 3rd par.: The OR reported in the text are summarized in Tables included in the supplementary material and not in Table 2 and 3. 4. introduction section 2nd par.: To date, little is known about the real effects in terms of long-term cardiovascular and metabolic effects of antipsychotic medication. Authors should better discuss this point with adequate and more recent references.

VERSION 1 – AUTHOR RESPONSE

Reviewer: 1
Reviewer Name: Dr Emanuele F Osimo
Institution and Country: Imperial College London and University of Cambridge Please state any competing interests or state 'None declared': None declared

Please leave your comments for the authors below Thanks for sending this paper for peer review.
The paper is clearly written and pleasant to read. The question is of limited scope but relevant and timely.
The authors set out to analyse the extent to which CVD risk factors were documented in primary care electronic medical records, and compared their documentation by diagnosis (scz or not), patient and provider characteristics.
The over-arching question is why the authors have not decided to also present the contents of these measures, for example comparing them between cases and controls. As it stands, this is a good study with a very limited question (rate of completion of documentation). This, however, is not a pertinent question for a peer reviewer as it sits with the Editorial board.

Authors' response: Since this was a retrospective cohort study with 4882 patients with schizophrenia and 192427 patients without schizophrenia, we chose to use the data for the entire eligible cohort rather than a matched case-control set. Although we do acknowledge that the statistical efficiency of logistic estimators tend to plateau (level off) as the ratio of case-control pair is increased to more than 1:4, we felt that the use of the entire eligible cohort was more sensible because it allowed us to directly estimate the adjusted proportion of patients with calculable Framingham score with respect to patient characteristics (e.g. age, sex) which may otherwise be part of the design aspect of statistical methods (i.e. adjusting for matched characteristics in regression model does not yield interpretable estimators).

Regarding the question about the scope of the study: There is a substantial body of literature already identifying that patients with schizophrenia are identified to be at higher cardiovascular risk, including higher Framingham risk score. There are also studies attempting to improve upon the quantification of risk among this population by developing novel risk assessments, none of which are to our knowledge in widespread use in clinical practice. Guidelines across several countries recommend yearly risk factor assessment among people with schizophrenia (with the intent that this assessment will improve management) but it is unknown how well those guidelines are adhered to; that is the question addressed in this manuscript.

In terms of specific comments, they are all quite minor:
- title: it should stress even more strongly that this is just about documentation rates, so it could read like this: "retrospective cohort study of risk factor documentation and management in primary care electronic medical records", removing the previous general part

Authors response: We would be pleased to change the title to ensure it more accurately reflects the content of the manuscript and to consider any suggestions from the reviewers or editors about this. We have an alternate suggestion that we think is more specific and addresses the reviewer's comment: "Cardiovascular risk factor documentation and management in primary care electronic medical records among people with schizophrenia: retrospective cohort study"

- methods: I am unsure why the authors have decided not to correct p values for multiple testing, and I think this should be done

Authors' response: We revised the reported P-values and adjusted for the possibility of inflated type I error rate due to multiple hypothesis testing using false discovery rate.

- discussion: the authors should address what's happened to the actual content of these measures: are they being drafted for publication elsewhere? Are they not available?

Authors' response: We do not currently intend to publish the 'content' of the Framingham score results. (We have interpreted that this comment refers to the 'low, medium, high' risk assessment category that can be calculated using the Framingham score; please accept our apologies if we are in error in this assumption.) There is an extensive literature on this already and we do not believe presenting this would provide substantive additional information. The present manuscript attempts to unpack why people with schizophrenia continue to have markedly higher risk of developing cardiovascular disease than people without, and to identify possible solutions.

- discussion: further work. What has this study prompted and what are the next steps for the team?

Authors' response: This is to our knowledge the first study addressing 'real world' cardiovascular disease risk assessment among people with schizophrenia. We anticipated finding poorer risk factor

documentation among people with schizophrenia and thought this would lead to an intervention specifically in that population. It is apparent from this study that overall, cardiovascular risk factor assessment could be improved for everyone, not just those with schizophrenia. This then raises the question of what else is contributing to the markedly higher rates of cardiovascular disease among people with schizophrenia and in particular what could be done about this in primary care. We have concurrent studies on diabetes management and cancer screening among people with schizophrenia as well. Once these are completed, we intend to convene a group of people with schizophrenia and their caregivers and explore these results together in order to try to identify what could be done in primary care to address their concerns.

Reviewer: 2
Reviewer Name: Francesco Rotella
Institution and Country: Careggi Teaching Hospital, Psychiatry Unit. Florence, Italy.
Please state any competing interests or state 'None declared': None declared

Please leave your comments for the authors below

Authors performed an observational, retrospective study on a cohort of 572,311 subject obtained from a primary care electronic medical records (EMR) contained in the UTOPIAN Data Safe Heaven (University of Toronto). The objectives of the study were to describe (and evaluate?) the documentation of cardiovascular disease risk factors in subjects with or without schizophrenia.
The main results of the study are that patients with schizophrenia display a more complete documentation and that the overall documentation of cardiovascular risk factors is not considered "adequate" by the authors. However, as stated in the discussion section, there are no Canadian national standards for necessary elements of EMR documentation in primary care, and the fact that a clinical datum is not reported in EMR does not necessarily mean that it is not taken into consideration from a clinical standpoint.
In my opinion this represent the major issue of the paper, as it weakens the relevance of data reported.

Authors' comments: Although there are no Canadian national standards for necessary elements of EMR documentation in primary care, there are Canadian guidelines that state that people with schizophrenia should have cardiovascular disease risk screening yearly. That is the question addressed in the manuscript. The reviewer points out that because something is not reported does not mean that it is considered; but it is impossible to consider a blood pressure reading that has not been taken or a cholesterol level that has not been measured. We believe it is unlikely that people are receiving adequate cardiovascular disease risk screening that is then not being documented; either it is being done and being documented, or it is inadequate and therefore inadequately documented. We believe documentation in this case is an appropriate proxy for the conduct of risk assessment.

Minor points
1. Results 2nd par.: The number of patients without schizophrenia is 192,427. The quantification of the risk should be reported, not only significance.

Authors' response: We quantified the proportion of patients with recorded Framingham elements in second sentence of paragraph 2 as

"Framingham elements were documented more completely among those with schizophrenia: 25.5% of those with schizophrenia and 32.7% of those without had no documented blood pressure readings over the last two years ($p < 0.0001$)."

2. Results 3rd par.: The first sentence of the par. sounds like a comment. In this section authors should only describe data reported in Figure 2. Furthermore, if an OR is not significant, is NOT significant. It does not “appear” anything else than this.

Authors’ response: This sentence has been modified as

“Patients with schizophrenia did not have statistically significant decreased adjusted odds for the complete documentation of Framingham score as compared to patients without schizophrenia, (OR = 0.90, 95% CI 0.79 – 1.01, p-value=0.10).”

This paragraph only reports the results corresponding to Figure 2 in the revised draft.

3. Results 3rd par.: The OR reported in the text are summarized in Tables included in the supplementary material and not in Table 2 and 3.

Authors’ response: We apologize for this confusion. Table 2 and 3 are meant to provide descriptive information regarding the EMR cohort (i.e. proportion of patients with calculate Framingham with respect to Framingham components (Table 2) and other patient/provider/geographic characteristics (Table 3)). We chose to report the unadjusted ORs in supplementary Table S1 because it can be directly computed from the information provided in Table 1 and 2. The adjusted odds ratios are summarized in Figure 2 and also provided in supplementary Table S2.

4. introduction section 2nd par.: To date, little is known about the real effects in terms of long-term cardiovascular and metabolic effects of antipsychotic medication. Authors should better discuss this point with adequate and more recent references.

Authors’ response: We thank the reviewer for encouraging clarification on this point and have added two more recent references as well as amending the statement which now reads: “While the long-term metabolic effects of antipsychotic medications used to treat schizophrenia are unclear, their use is associated with increased weight and blood glucose.(8,9) Patients may also face challenges with self-care or accessing appropriate medical care.(10)”

VERSION 2 – REVIEW

REVIEWER	Emanuele Osimo Imperial College London, UK
REVIEW RETURNED	09-Jun-2020

GENERAL COMMENTS	The authors have responded to my comments adequately

REVIEWER	Francesco Rotella Careggi Teaching Hospital, Firenze, Italy
REVIEW RETURNED	07-Jul-2020

GENERAL COMMENTS	Authors adequately amended the minor point raised. I still believe that authors consider a documentation "adequate" on the basis of arbitrary evaluations. The fact that the main point raised in my review has not even added in the discussion section, suggests that authors are very still in their position. I therefore do not have any further comment.

VERSION 2 – AUTHOR RESPONSE

Reviewer: 1

Reviewer Name: Emanuele Osimo

Institution and Country: Imperial College London, UK

Please state any competing interests or state ‘None declared’: None declared

Please leave your comments for the authors below

The authors have responded to my comments adequately

Reviewer: 2

Reviewer Name: Francesco Rotella

Institution and Country: Careggi Teaching Hospital, Firenze, Italy

Please state any competing interests or state ‘None declared’: None declared

Please leave your comments for the authors below

Authors adequately amended the minor point raised.

I still believe that authors consider a documentation "adequate" on the basis of arbitrary evaluations. The fact that the main point raised in my review has not even added in the discussion section, suggests that authors are very still in their position. I therefore do not have any further comment.

Response: Thank you for this clarification of your previous comment and for the opportunity to respond and modify the manuscript accordingly. We agree that you have raised an important point and that we previously inadequately responded. We hope this response is sufficient to address your concern; we believe by modifying the manuscript it is substantially strengthened.

‘Adequacy of documentation in health records’ as a proxy for quality of care is a frequently used approach in the primary care literature. We believe the use of electronic medical record for these data is a valid approach on the basis that it has been used in other studies. Rreferences in the manuscript supporting the use of this approach include:

1. Greiver M, Aliarzadeh B, Meaney C, Moineddin R, Southgate CA, Barber DT, White DG, Martin KB, Ikhtiar T, Williamson T. Are we asking patients if they smoke? Missing information on tobacco use in Canadian electronic medical records. Am J Prevent Med. 2015 Aug 31;49(2):264-8

2. Singer A, Yakubovich S, Kroeker AL, Dufault B, Duarte R, Katz A. Data quality of electronic medical records in Manitoba: do problem lists accurately reflect chronic disease billing diagnoses? J

Am Med Inform Assoc. 2016 Apr 23;23(6):1107-12" .and also that it is the only way to be able to conduct a study with such broad scope (a 'chart review' for example would be prohibitively resource intensive to conduct on this scale).

3. Weiskopf NG, Weng C. Methods and dimensions of electronic health record data quality assessment: enabling reuse for clinical research. J Am Inform Assoc. 2013 Jan 1;20(1):144-51.

4. Birtwhistle R, Williamson T. Primary care electronic medical records: a new data source for research in Canada. CMAJ. 2015 Mar 3;187(4):239-40.

In terms of whether the approach is "arbitrary" or not, we would respectfully disagree with this assertion and provide additional clarification here and in modifications to the manuscript to address this. As outlined in the background of the manuscript, Canadian guidelines recommend cardiovascular risk screening for all patients with schizophrenia at least yearly (Pringsheim T, Kelly M, Urness D, Teehan M, Ismail Z, Gardner D. Physical Health and Drug Safety in individuals with schizophrenia. Can J Psych. 2017 Sep;62(9):673-83.) We have investigated the extent to which the tests (e.g. lipid measurement) and aspects of physical examination (e.g. blood pressure readings) and clinical history (e.g. smoking status) that would be necessary to conduct standardized cardiovascular risk screening have been conducted. It is likely there is some degree of 'overestimate' using this approach (for example, all the 'correct' tests could have been ordered but not brought together to do formalized cardiovascular risk screening). We have modified the manuscript to specifically address this issue (see addition in p 11 line 306: "We acknowledge that this approach may result in 'overestimation' of the extent to which cardiovascular disease risk screening is occurring for patients with schizophrenia. It is possible to have all of the Framingham items documented in the medical record but not to have brought them together to estimate overall cardiovascular risk. However, given the primary conclusion that cardiovascular risk screening is inadequate in this sample, the study methods biasing towards 'overestimation', if anything, support this main finding"). But even if this is an 'overestimate', the primary conclusion of the manuscript, that overall these tests are inadequately completed despite guidelines recommending their conduct, remains.

Another aspect related to this may have been inadequately described in the manuscript. In Ontario, Canada, primary care providers receive copies of all tests conducted by everyone involved in a patient's care. We thought that we had adequately described this in the previous version but appreciate the opportunity to further clarify in the manuscript (see addition in p 10 line 301: "Primary care providers therefore receive test results from all other providers involved in a patient's care, making primary care records an appropriate location to assess these parameters") Therefore even if these tests are being conducted by another provider (a cardiologist or a psychiatrist, these data would be available for analysis in our present study.