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Title	Identifying heart failure in patients with chronic obstructive lung disease through the Canadian Primary Care Sentinel Surveillance Network in British Columbia: a case derivation study
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Reviewer 1	Mohamad Hussain
Institution	Surgery, University of Toronto, Toronto, Ont.
General comments (author response in bold)	Comment 19: What is the accuracy of COPD case definition in CPCSSN? **We thank the reviewer for this comment and have added the following accuracy parameters in our Methods:** **CPCSSN data (page 4)** **"The COPD case definition has been found to have a sensitivity of 82.1 (95%CI: 76.0–88.2); specificity of 97.3 (95%CI: 96.5–98.0); positive predictive value (PPV) of 72.1 (95%CI: 65.4–78.8); and negative predictive value (NPV) of 98.4 (95%CI: 97.9–99.0).(15)"** Comment 20: Were the chart abstractors blinded to the diagnosis of HF as per coding in CPCSSN? **Yes, the chart abstractor was blinded to the diagnosis of HF as per coding in CPSSN. We have added the following statement in our Methods:** **Sampling (page 5)** **"RV was blinded to the diagnosis of HF as per coding in CPCSSN."** Comment 21: It would be helpful for the readers if the authors can explain the clinical significance of HF among COPD patients, and why this valediction study was required specifically in a COPD cohort as opposed to HF among the general population. In other words, what is unique about HF in the COPD population that mandated this study? **We have addressed this concern in comments 5 and 6 above from the Editor.**
Reviewer 2	Muhammad Siddiqui
Institution	Department of Research, Saskatchewan Health Authority, Saskatoon, Sask.
General comments (author response in bold)	Comment 22: Abstract Authors may wish to add specific study design in the methods section **We agree and have added this in our Abstract Methods Section:** **"We conducted a cross-sectional retrospective chart review of a cohort of patients from primary care practices in BC recruited through the BC Canadian Primary Care Sentinel Surveillance Network (CPCSSN)."** Comment 23: Methods section written very well. However, when authors introduce an abbreviation in the text for the first time write it in full followed by the abbreviation in parenthesis. This applies to AG and RV. **Thank you for comment on the readability of our methods section. We have now clarified these sections by indicating that these are author initials throughout the methods.**
Reviewer 3	Jonathan Howlett
Institution	Medicine, Calgary Foothills Hospital, Calgary, Alta.
General comments	Comment 24: The authors should better describe the methods by which diagnosis

	adjudication was made. In particular, the gold standard definition is not described. I am left with the impression that one or two cardiologists reviewed the clinical record and made a general assessment as to the presence or absence of heart failure, as opposed to the use of a clinical scoring tool (such as Framingham, Carlson or Boston Criteria). In addition, there is no description of contingencies relating to possible disagreement between adjudicators. **We thank the reviewer for their comment. We defined HF according to the current national (CCS: Reference 18) and international guidelines recommendations (ESC: Reference 19, ACCF/AHA: Reference 20) which require a clinical syndrome (symptoms and signs) combined with objective evidence of cardiac dysfunction. Additional details can be found in our response to comment 9d.** **We designed our standardized abstraction tool to collect all pertinent variables using a systematic approach. While we appreciate the strengths of clinical scoring tools, they also have several limitations in their use. First, they only define the clinical syndrome of HF, and do not include objective measures such as imaging or natriuretic peptide lab results. Second, by focusing only on clinical presentation, they do not define HF in accordance with current national guidelines. Finally, they require complete data on a large range of symptoms and signs, which may not be recorded routinely in primary care- and therefore challenging when using primary care EMR data. For these reasons we utilized the former approach as opposed to the latter. We have amended our Methods: Chart Review and 'Gold standard' (page 5), to better clarify our approach:** **"The presence of HF was defined by national (18) and international guidelines (19,20) which require symptoms and/or signs of reduced cardiac output and/or pulmonary or systemic congestion, supported by objective evidence of structural and/or functional cardiac abnormality, including left ventricular systolic (defined by reduced left ventricular ejection fraction using any imaging modality), diastolic dysfunction (typically by echocardiography), elevated natriuretic peptides, or structural disease (such as severe valve disease."** **We have also further clarified the methods for diagnosis adjudication in our Methods: Chart Review and 'Gold Standard' (page 5):** **"The abstracted data was then reviewed by initially by the abstractor (RV) and then subsequently a cardiologist (author NH), who ultimately determined classification of HF status."** Comment 25: The authors report a Derivation study as opposed to a Validation study. While the authors do mention the limitations involved in the use of a small number of selected primary care practices, the need for validation of the case definition in other populations is not emphasized. In particular, a proper validation study should be performed, preferably in practice settings outside of the CPCSSN. **We completely agree and thank the reviewer for this excellent observation. We have amended our title to state that it is a Case Derivation and not a Case Validation Study. We are currently in the process of validating this case definition in an unselected population. We have added the following clarifications in three parts of the manuscript:** **Interpretation, paragraph 2 (page 9): Our findings are comparable to other studies looking at HF case definitions in EMR database/networks, although**

future validations in practice settings outside of CPCSSN would further bolster external validity.

Interpretation, paragraph 5 (page 10): The case definition may perform differently in other provinces or practice settings.

We have adjusted our conclusion (page 11): "With further external validation of this algorithm, the findings of this study will support ongoing research activities, chronic disease surveillance, and quality improvement initiatives in primary care for HF amongst people with COPD across Canada."

Comment 26: It is not apparent why a population of patients with COPD has been identified as the best cohort for this study. Why not a less highly selected population? As the authors state (but do not emphasize in either the abstract or in the text), these findings only apply to a highly selected patients group with COPD who are followed in a specific Network of clinical practices. This is a far cry from a National patient cohort

We completely agree and apologize that this limitation was not sufficiently emphasized. In response to this and other comments we have extensively rewritten the introduction to highlight the relevance of the population with COPD (please kindly see the response to comments 5 and 6).

We have further emphasized that our work derives from a single network in the abstract, methods section, and interpretation as follows:

Abstract (page 2):

Introduction: "The objective of this study was to validate an EMR-based definition of HF in those with COPD in primary care in British Columbia (BC), Canada."

Methods: "We conducted a cross-sectional retrospective chart review of a cohort of patients from primary care practices in BC recruited through the BC Canadian Primary Care Sentinel Surveillance Network (CPCSSN)."

Introduction (page 3-4): "The objective of this study was to derive and validate an EMR-based definition of HF amongst those with COPD in primary care in British Columbia (BC), Canada."

Methods

Study Design (page 4): "The study was a cross-sectional retrospective chart review of a cohort of patients from primary care practices in BC recruited through the BC Canadian Primary Care Sentinel Surveillance Network (CPCSSN)."

CPSCCSN (page 4): "This project used BC CPCSSN data extracted early 2019 and processed to remove records with dates after December 31, 2018 (2018-Q4)."

Interpretation

Paragraph 1 (pages 8-9): "For this context, definition 1.1 would be the recommended case definition for HF among patients with COPD within the BC-CPCSSN database."

Paragraph 5 (pages 9-10): "Lastly, generalizability of our case definition outside of this selected COPD is not warranted."

Finally, this work is being performed in collaboration with colleagues in Nova Scotia who are examining case definitions in a general population. We initially considered presenting the two studies in a single manuscript, but this was discouraged by the editorial team due to limitations in word count, along with some methodological differences. In response to your previous

| | comment we have added the following statement in our interpretation, paragraph 5 (pages 9-10): "Further validation of our preferred case definition in the unselected HF population in CPCSSN is underway" and in the following statement in our conclusion (page 10): ". With further external validation of this algorithm, the findings of this study will support ongoing research activities, chronic disease surveillance, and quality improvement initiatives in primary care for HF amongst people with COPD across Canada." |