

<b>Article details: 2015-0130</b>	
Title	The current and future burden of heart failure hospitalization costs in Canada
Authors	
<b>Reviewer 1</b>	Dr. Julie Polisen
Institution	Canadian Agency for Drugs and Technologies in Health
General comments (author response in bold)	<p>1. P4 Line 23: Did the authors attempt to search for hospital prevalence rates in Quebec? Response: We have found no comparable data from the province of Quebec. As mentioned in our response to the editor's comments, the province of Quebec submits hospitalization data to CIHI in a separate format and is regularly excluded from Canada-wide studies, even those conducted by the Canadian Institutes of Health Information.</p> <p>2. P5 Line25-26: What is the applicability of the OCCI to the other jurisdictions? Response: In this study, we used common Canadian CIHI patient cost estimates (PCE) to estimate HF hospitalization costs for all provinces and territories. The OCCI/Cost Analysis Tool was used to estimate costs for a very small (2%) of hospitalizations for which PCE data were not available. It also appears that the cost estimates from the two sources (CIHI PCE and OCCI) are similar. For example, the cost estimate for CMG 195 (HF with coronary angiogram) was \$11,456 from CIHI PCE and \$10,441 from OCCI. Thus, we believe that the use of OCCI for missing CIHI PCE did not significantly affect our overall cost estimates.</p> <p>3. P9 Line 3: How are low and medium population growths defined? Response: Population growth scenarios are defined by Canadian fertility rate, life expectancy, and immigration and emigration rates. In the manuscript, we referenced the CANSIM-052-0005 table on Statistics Canada website, where there are footnotes on each of the scenario's assumptions.</p> <p>- "The low-growth scenario is defined by the following assumptions: a Canadian total fertility rate that reaches 1.53 births per woman in 2021/2022 and remains constant thereafter; a Canadian life expectancy that reaches 85.9 years for males and 87.1 years for females in 2062/2063; interprovincial migration based on the trends observed between 1991/1992 and 2010/2011; a national immigration rate that reaches 0.5% in 2022/2023 and remains constant thereafter; an annual number of non-permanent residents (Canada) that reaches 733,600 in 2014 and remains constant thereafter; a national net emigration rate of 0.16%". [1]</p> <p>- "The high-growth scenario is defined by the following assumptions: a Canadian total fertility rate that reaches 1.88 births per woman in 2021/2022 and remains constant thereafter; a Canadian life expectancy that reaches 89.9 years for males and 91.9 years for females in 2062/2063; interprovincial migration based on the trends observed between 1991/1992 and 2010/2011; a national immigration rate that reaches 0.9% in 2022/2023 and remains constant thereafter; an annual number of non-permanent residents (Canada) that reaches 1,144,300 in 2031 and remains constant thereafter; a national net emigration rate of 0.21%" [1].</p> <p>- In response to the reviewer's comment, we have added an additional reference for the Statistics Canada technical report entitled "Population Projections for Canada (2013 to 2063), Provinces and Territories (2013 to 2038): Technical Report on Methodology and Assumptions" that describes detailed methodology and assumptions for all population growth scenarios (Page 6, line 121 and Page 7, line 131).</p> <p>4. P10 Line: What are the main cost drivers for HF as the primary versus secondary diagnosis? Response: This is an interesting research question. However, as we used CIHI PCE, which provides an average cost based on CMG grouper and age group to assign costs for each hospitalization, we were not able to study main cost drivers for HF as the primary versus secondary diagnosis. We think that this question can be resolved by examining micro-costing data for HF patients, which we did not have for this manuscript.</p> <p>5. P10 Line 34: Can the authors provide a brief explanation on the declining trend in the in-patient prevalence rates in both sexes? Response: We think that improved HF management in outpatient settings might be the reason for declining trends in the in-patient prevalence rates [2]. In response to the reviewer's comment, we have revised the following sentences in the manuscript "The in-patient prevalence rates are declining in both sexes. This might be due to improved HF management in outpatient clinics". (Page 11, lines 213- 214)</p> <p>6. P11 Lines 44-48: What are some of the emerging new therapies or changes in HF management strategies? How will they impact future costs?  Response: There are several emerging HF management strategies, such as use of devices (CRT, ICD, and LAVD) and a shift to HF management in outpatient clinics. New drugs and devices are expensive but can reduce hospitalizations and thereby can be a cost saving strategy. Furthermore, we should expect better HF management in the future thanks to technology and innovation, such as HF management at home (for example using digital monitoring devices to detect symptoms earlier and adjusting therapy to</p>

	<p>prevent hospitalizations or ER visits early).</p> <p>P10-12 Interpretation:  7. What does this study add to the literature?  Response: There are limited data on the economic burden of HF in Canada. The last study that examined this issue (Johansen et al [3]) was based on data from one fiscal year (1996/1997) and estimated prevalence only. Our study is based on more contemporary data (fiscal years 2004 – 2013) and estimates both HF hospitalization prevalence and costs. As populations age, the prevalence of HF is expected to increase significantly. Estimating the economic impact of these trends is therefore becoming a major focus of national and provincial agencies. We believe our study will be of interest to practitioners and policy-makers.</p> <p>8. How can the results of this analysis be used in future research, including economic evaluations, and in clinical practice?  Response: Our study results provide estimates of HF hospitalization costs in Canada and can serve as useful benchmarks to examine the impact of future innovations on health care costs. In response to the reviewer's comment (Q7 &amp; Q8), we added the following sentence to the manuscript "While long-term HF prevalence and costs in Canada may change as a result of new therapies or changes in HF management strategies, forecasts based on current trends can serve as useful benchmarks to examine the impact of future innovations on health care costs" (Page 3, lines 51-54)</p> <p>9. I suggest that the author indicate that hospitalization costs are one component of HF costs. Other direct costs also include home health care costs, other health costs (e.g., family physician visits, specialist output appointments, emergency department visits, diagnostic tests, and medications), and patient-borne costs (i.e., potential financial impact on patients and their families).  Response: We acknowledged other costs in limitation section (Page 12, lines 230-232). In response to reviewer's comment, we have revised the sentence to make it clearer. "Finally, this study only included HF hospitalization costs and does not include other costs, such as physician, outpatient and drug costs, which are of increasing importance as HF management shifts from the inpatient to the outpatient setting" (Page 13, lines 250- 253)</p>
<b>Reviewer 2</b>	Maria Bennell
Institution	Epidemiologist, Sunnybrook Health Sciences Centre
General comments (author response in bold)	<p>This is an interesting paper of the trends of HF hospitalizations and costs in Canada. Such national studies are important to inform health services research of trends in hospitalization and the future outlook for this disease.</p> <p>Major comments:  1) Objective too broad and doesn't take into consideration prevalence rates and number of hospitalizations. Needs to be clearer. Would appear to me that the paper's focus is on trends in prevalence, total hospitalizations, and costs, then extrapolation. The focus of the results should be on these trends, rather than highlighting certain years numbers in particular. For example, pg. 9 line 3 highlights years 2020 and 2030 only, page 8 line 40 highlights year 2013 only, table 2 shows years 2004, 2007, 2010, and 2013 only. The first paragraph of the discussion should mention ranges rather than just 2004 and 2013.  Response: The objectives of our study were to examine HF hospitalization costs between fiscal years (FY) 2004 and 2013 in Canada, and based on these, model the future prevalence and hospitalization costs until 2030. We examined the change of hospitalization prevalence rates as a way to estimate number of HF patients hospitalized every year and subsequently corresponding hospitalization costs. We did provide some changes in percentage in the results section to reflect changes over time. For example "Hospitalization costs for a HF patient increased by 1.4% annually" (Page 9, lines 168-169). In addition, we provided 95% CI for all point estimates. We think that both annual changes and year-specific data would be more useful to capture the overall picture of HF hospitalization costs in Canada. However, we added the following statement "equal to a 1.7% annual increase during this period" to the manuscript (Page 9, lines 175- 176) to highlight the annual increased trends of total HF costs during FY 2004- 2013.</p> <p>2) These statistical methods confuse me. CIHI-DAD was used to ID hospitalizations for HF as the primary diagnosis. These would be incident cases then? So that's why prevalence rates were estimated using MLR? Can you give a line or two about what the reader should notice about the MLR results in the appendices? What is important about whether there are significant interactions or significant knots or significant age groups? Are the trends significant if the p-values for those variables are significant, and not significant if they aren't?  Response: The reviewer is correct that we used CIHI DAD to identify patients with hospitalizations with a primary diagnosis of HF. These are not necessarily incident cases, i.e., patients may have been hospitalized with HF in the years prior to our study period (2004 – 2013). We therefore consider these estimates to be prevalence estimates, which</p>

include incident hospitalizations.

To summarize, the MLR model is used for two purposes in our study. The first is to estimate hospitalization prevalence rates from 2004 – 2013 for the entire country, i.e., including Quebec. The second is to estimate future prevalence (from 2014 – 2030) of HF hospitalizations. The parameter estimates associated with the independent variables in the model (e.g. age groups, sex, etc....) are used in calculating prevalence estimates. The parameter estimate associated with only the fiscal year variable (see Table S1.1 in appendix) indicates whether the trend over time is significant (which it is)

3) Large limitation to this paper is how inaccurate the estimates are for the data from 2004-2013. All the data, are estimates. CIHI-DAD data is not all that granular either. Much more accurate data could be obtained from provincial registries, or if a national database were developed. Clearly, this is out of the scope of the researchers intentions for this paper, but these estimates are a huge limitation, especially the lack of Quebec data.

Response: Our study is based on empirical data from 2004 – 2013 from 9 provinces and all territories. Administrative data, such as the CIHI DAD, offer perhaps the most comprehensive capture of all patients with HF hospitalizations. We acknowledge the limitation of not having Quebec data (Page 12, lines 228-230). However, in order to provide national estimates we extended our estimation of HF hospitalization prevalence and costs to include Quebec.

4) I don't understand the explanation of how annual costs were estimated. Page 5, line 29 "Annual in-patient costs for a HF patient were derived by summing up costs of individual hospital admissions of the same patient in the same year." I got lost at "same patient in the same year." Does this estimate consider an average length of stay for patients, and an estimate of what hospital tests and procedures were done on each patient? This leads me to also wonder what these hospitalization costs are supposed to cover. Diagnostic tests? Surgery? Rehab? etc.

Response: A patient may have more than one HF hospitalization (HF readmissions) in a year and each hospitalization had an associated cost, provided by CIHI PCE. We summed costs of individual hospital admissions of a patient in a year to have total hospitalization costs for that patient in a year. In response to reviewer's comment, we have revised the sentence as following "Annual in-patient costs for a HF patient were derived by summing up costs of all hospital admissions of that patient in a year" (Page 6, lines 104-105).

The CIHI PCE uses an algorithm, taking case mix groups (CMG), resource intensity weight, cost per weighted case, and length of stay into consideration [4]. It includes all direct acute inpatient care costs including inpatient nursing, diagnostic and therapeutic costs. In response to the reviewer's comment, we have added the following sentence and provided an additional reference in the manuscript "It provides average costs incurred through the direct care of hospital inpatients (for example inpatient nursing, diagnostic and therapeutic costs)" (Page 5, lines 97-100)

Minor comments:

1) CIHI-DAD = Canadian Institute for Health Information Hospital Discharge Abstract Database. Need to correct. Authors wrote "dataset".

Response: It has been corrected in the revised version (Page 3, line 58)

2) Paper needs some editing. Some grammatical errors when it comes to when something should be plural vs. singular. For example, page 7 line 18 "The numbers of hospitalizations and patients..." should be "The number of hospitalizations and patients." There are a lot of similar examples throughout the paper and appendices.

Response: Thank you. We have made a significant editing effort to improve the manuscript.

3) Tables need to include N (of the total population of Canada), especially for your tables on total number of hospitalizations, both for 2004-2013 data, and the extrapolated data. Also, 95% CIs should be in brackets in the same cells as the estimates. It would make the tables less bulky and easier to read.

Response: We have added Canadian population estimates and projection to tables S1.3, S2.2, and S3.3 in appendices. However, we would like to keep the parameter estimates and 95% CI separate in the appendices as we think it will make the tables more readable.

4) I'm confused as to when Quebec is included in the estimates and when Quebec is not included. Is it only table 1 where Quebec is not included?

Response: The reviewer is correct. Table 1 is based on empirical data and does not include data from Quebec. All other estimates are for the whole of Canada, Quebec inclusive.

5) I think there should be some figures for total hospitalizations and projected

	<p>prevalence, total hospitalizations, and costs. The tables have a lot of numbers. Trends are easier to see with figures. Response: In response to this and previous reviewers' comments, we have revised Figure 2 to add a sub-figure describing the trends of HF patients hospitalized over time (Page 16, line 340-341).</p> <p>6) Can you make any kind of prediction in the discussion as to whether the health care system would be able to handle such large increases in cost in the future? Response: Unfortunately whether the Canadian healthcare system will be able to sustain the future burden of HF depends on a lot of external factors including the state of the economy, costs associated with other diseases/conditions, etc. We are therefore unable to speculate whether HF will account for a larger proportion of the healthcare budget or account for the same proportion of a larger health care budget in the future.</p>
<b>Reviewer 3</b>	Dr. Narendra Singh
Institution	
General comments (author response in bold)	<p>1. This paper looks at heart failure hospitalization trends over the past decade in an attempt to predict future trends. That is always a difficult task and I'm not convinced the authors have focused enough on possible scenarios that may disrupt future trends. e.g. as pts take more control of monitoring their own health through digital technology one may see a shift due to early recognition and outpatient treatment. Response: We agree that future trends may be influenced by several factors, such as technology and innovations. As responded to a reviewer previously, our study results provide estimates of HF hospitalization costs in Canada and can serve as useful benchmarks to examine the impact of future innovations on health care costs.</p> <p>2. Do we have any data on regional variation in hospitalizations? If there is not much then the methodology to estimate Quebec admission is more sound. Response: We thank the reviewer for his/her comment. In response, we examined variation across provinces and found no statistically significant difference in hospitalization prevalence rates between Canadian provinces, strengthening our assumption of HF hospitalization prevalence rates in Quebec to be the average of the country. We have added this to the limitations section "However, we examined variation across provinces and found no statistically significant difference in hospitalization prevalence rates between Canadian provinces, where we have data. This result strengthened our assumption." (Page 12, lines 247-250)</p> <p>3. Patients with a secondary diagnosis of HF significantly impact length of stay and therefore can have an important cost contribution to health care. Do we know how many pts annually have a secondary diagnosis of HF? Response: The reviewer is correct that HF as a secondary diagnosis has an important cost contribution in health care. We did a sensitivity analysis where we included all hospitalizations with HF as either primary or secondary diagnosis to examine the escalation of HF associated hospitalization costs. Extending the analyses to include hospitalizations with HF in a secondary diagnosis field more than tripled (n=175,000 (95% CI: 164,000 to 187,000)) the estimate of patients hospitalized with HF in 2030. Consequently, total HF associated hospitalization costs were projected to be \$2,800 (95% CI: \$2,600 to \$3,000) million in 2030. (Page 10 lines 198-203 in the manuscript. Detailed results are presented in Appendix 3).</p> <p>4. There are far too many tables and a figure would often be better to visualize the trends easier Response: As mentioned above, we revised Figure 2 to add a sub-figure describing the trend of increased number of HF patient hospitalized (Page 16, line 340-341). In addition, we would prefer to provide detailed results in table format in appendices.</p> <p>5. Do we know device utilization trends for ICD's and LVAD's as they will also impact hospitalizations? Response: It is possible to identify the utilization trends for ICD and LVAD from the CIHI DAD. In our study, the costs of these devices are incorporated into the CIHI PCE estimates.</p> <p>6. Is there any separation of diastolic vs systolic HF and the underlying pathophysiology of the HF. Response: There is no way to accurately identify diastolic vs systolic HF in administrative data, although this is a field of active research.</p> <p>7. What percentage of hospitalizations are re-hospitalizations? I understand that pts were only counted once but if the number is high then this is important to know from a costing perspective. Response: The reviewer is correct that re-hospitalization is important from a costing perspective. We provide the percentage of patients that had more than one</p>

	<p>hospitalization in a year in Table 1 (the last row). About 17-19% of patients had more than one hospitalization annually.</p>
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We used the patient as the unit of analysis. We used annual hospitalization costs per HF patient to account for the number of HF hospitalizations of a patient in a year.