Reviewer's report

Title: How Much Are We Really Spending? The Estimation of Research Expenditures on Cardiovascular Disease in Canada

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Reviewer: Jennifer Pohlhaus

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The question posed by the authors is well defined; the methods are appropriate, but could use more description. I am unable to assess whether the data is sound, because it is presented only in the aggregate, and therefore I believe that the work is likely not to adhere to relevant standards for reporting and data deposition. The discussion and conclusion are supported by the data this is presented; however I do not believe it is well-balanced. Limitations of the work are clearly stated, and the title and abstract do accurately convey the findings (although I would suggest removal of the word “really” from the title). The writing is acceptable, but note some required editorial fixes listed below.

Discretionary Revisions

• Inclusion of the final sentence in the abstract is superfluous and mostly outside the scope of this work.

• On p.5, An estimate of the amount of funding provided by MRCC since its establishment until its replacement by the CIHR would make a nice addition to this work, especially in that it would help the reader place in context that CIHR provided 12% of research funding in Canada, making it the largest funder. Was its predecessor also the largest funder?

• In the statement on p.14, “From 1994 and 2004,” do the authors mean “Between 1994 and 2004?”

Minor Essential Revisions

• Punctuation errors scattered throughout document, including:
  o Extra space before the period in the Abstract: Results
  o Commas missing from the second paragraph of the introduction

• There should be a reference for the “Reference Lists” on p. 7

• The statement on page 9 that the private non-pharmaceutical health care sector represents a small portion of total expenditures needs a citation. Otherwise the reader is led to believe that this statement is supported only by the current publication. That circular assumption is problematic because it allows the results to prove the assumption, when, if the assumption changed, the results would likely be different. See also concerns listed elsewhere about the definition of each sector and the choice of inclusion of various sectors in this report.

• The qualifier “in economics” should be removed from the definition of constant
dollars.

- It is unclear what is the reference or the meaning of “a significant portion of research expenditures is allotted to research infrastructure…” on p. 11
- Several of the public funders mentioned on p. 11 are not included in figure 1
- A reference is required for the statement on p. 13 “H&SFC started funding research chairs in cardiovascular and stroke research providing additional funding for researchers”
- A reference is required for the statement on p. 13 “the Canadian economy doubled in size over the same period”
- The statement that the UK has a “larger number” of research funding organizations is provided with no data for reference, and “larger number” is very vague.
- On page 14, $17 is referred to as close to half of $30; this statement should be corrected to indicate that $17 is more than half of $30.
- In Figure 2, it is misleading to label the total line as “total expenditures” when it is clear from the text that the private funding was unknown at earlier timepoints. One solution would be to rename the blue line as “total known expenditures”

Major Compulsory Revisions

- The authors treat charitable funding in the same category as public funding throughout the text. However, the figure shows charitable funding in the industry category. This discrepancy must be addressed and clarified.
- The authors state that various methods were used to determine the funding sources; however, the internet searching method should be described as a “snowball” method, and the qualification should not be stated “like Google.” Preferably, the full list of internet search engines should be provided. Exclusion of this information leads the reader to assume that Google was the only search engine used. If Google was the only search engine that was used, it calls into question the robustness of this approach.
- Supplementary Table 1 should be the focus of this work; however it is lacking in data. First, it includes only a subset of the funding sources identified within the text. Second, it does not provide any funding amounts, for any of the years discussed. In addition, the categorization of the funding sources should be defined as categorized in Figure 1, and the source of determining the funding source (known organization, internet search, or References Lists) as described in the text should be included in this table.
- A percentage of how many organizations provided data directly, versus how many did not should be included on p. 7 after the statement “Information was provided directly by the organization or through its annual reports.”
- The method for determining the amount of cardiovascular research funding from each public source is unclear. The authors state “we scanned” – but provide no additional information. For example, how many people read each report? What controls were employed to ensure that different people came to the same conclusion on each grant? In addition, the authors state, “we applied the same
criteria” but they do not describe the criteria.

o It is unclear why the authors mention the CVD terms from the Ontario IMPACT study. If the authors excluded studies which did not use the same terms as the Ontario IMPACT study, then this should be clarified in the text. If the authors instead included all CVD terms, not just the IMPACT subset, then inclusion of the IMPACT terms is irrelevant. Alternatively, if the authors feel this is relevant information, then it should be presented somewhere in the text about how much research is from this subset of CVD research.

o Finally, the authors state that they employed linear interpolations in a few cases, but they give no context of how often is a “few” – the rigor of this study is impossible to assess without this information.

• The method for determining the amount of cardiovascular research funding from each private source is unclear.

o There is no discussion in the article about R&D is defined. For example, some might disagree that pharmaceutical and medicine research and development includes pharmaceutical and medicine manufacturing, pharmaceutical wholesale trade and pharmaceutical scientific R&D services. Furthermore, upon investigating source #10, Statistics Canada, I am unable to discover a reason for why the authors focused on “testing laboratories” and “health care and social assistance industries” when it appears that “testing laboratories” is not in the list of industries for which data is provided (http://www.statcan.gc.ca/pub/88-202-x/2011000/t006-eng.htm), and there are many other industries in the same table with a greater amount of R&D funds than the “health care and social assistance” industry.

o The authors state that they were required to make “some assumptions” but do not list what the assumptions are. This lack of information makes it impossible to assess the rigor of their methods. The authors state “Disaggregated data by individual therapeutic area were not available” – it is unclear whether this means CVD from other research, or subtypes of CVD research.

• It is unclear whether the “private non-pharmaceutical health care sector” is the same or different from the “private, non-pharmaceutical R&D sector” as described in two adjoining paragraphs on page 9. Again, the paper would benefit from a more concise organization and ensuring that the figure matches the discussion in the text, as well as movement of sup1 into table 1 and providing more details here as described above.

• It appears that the authors have used 15% as an estimate for how much of any R&D is likely to be CVD R&D, for all the private funding sources. However, this is not as clear as it should be from the methods section. If this is the case, then I would prefer to have had more discussion about how the 15% was arrived at, and perhaps a case study of several firms, and use of an average value, instead of using a percentage derived from other countries.

• It is unclear which data is referred to in the statement on page 10 “These data are openly available and can be found on Statistics Canada’s website”. Does this mean the prior sentence which refers to medical devices? I think instead, it means all of the private nonpharmaceutical funding. If so, then it brings into
question the utility of including this data in the current study. Is this current study merely a meta-report of other sources? See also comment immediately above that brings up the issue of estimating CVD research values in private industry.

- On page 11, the authors state that there is some missing data for some years and some organizations. Without the appropriate level of detail in Sup Table 1 (see other comments), I feel that this statement is out of place. There is no quantification about the level of underestimation, and the reader cannot assess for him/herself because of the lack of data.

- The meaning of “our estimates” and “does not change substantially” in the results section on page 12 is unclear. Does this mean the total data presented in this paper? Also, what does “not change substantially” mean in this context?

- The discussion misses the opportunity to summarize findings at a high level. For example, the authors could place total private funding in context of total public funding.

- The utility of including Figures 3, 4, and 5 is unclear. These figures appear to be repeats of various subsets of data already shown in Fig 2, and do not add to the discussion. A better approach would be to reconfigure sup table 1 (as described in other comments), reconfigure figure 2 so that it shows 1995-2005 only, and ensure that table 1, figure 1, and figure 2 use the same organizational structure. An additional figure could cover public funding history from 1975-1995.

- The discussion on p.13-15 about whether funding is “enough or not enough” should be reframed. What is “enough?” Even if Canada were spending the most of all the countries, does that mean it is “enough?” Some would argue yes, others no. This discussion is better framed in the context of asking, “How does Canada’s per capita spending compare to other countries?” This question more accurately frames the discussion that is had in this section.

- The discussion that compares Canada’s spending to other countries should be careful to define what is being compared. The statement “Canada has spent far less on CVD related research over the past 30 years” implies that comparisons are being made about total funding; however, the figures cited in the following sentences refer to public funding only, not total funding. Furthermore, it is unclear if the quoted statement refers to per capita spending or total spending.

- It is unclear what the authors mean on p. 15 by “linked, clinical, research and expenditure data” – linked to what? What is the reason for highlighting clinical data?

- The assumption in the discussion that increased spending on CVD research would automatically translate into improved CVD health outcomes is unsupported and should be left to another publication. For example, it assumes that Canadians only benefit from research spending in their own country, when in fact, research results are often broadly shared in scientific journals and cross between countries.
Level of interest: An article of limited interest

Quality of written English: Acceptable

Statistical review: No, the manuscript does not need to be seen by a statistician.

Declaration of competing interests:
I declare that I have no competing interests