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Title	A review of restrictions for reimbursement of direct-acting antiviral treatment for hepatitis C virus infection in Canada
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Reviewer 1	Dan Smyth MD
Institution	Department of Medicine, Horizon Health, Moncton, NB
General comments (author response in bold)	This is a well prepared manuscript summarizing the criteria for reimbursement of currently available DAA regimens for HCV treatment in Canada. This information is currently not available in a compiled document and is often not easily accessible. The inclusion of reimbursement criteria for First Nations and incarcerated persons is notable. The article illustrates very well the diversity of approaches to HCV treatment in Canada, from a progressive access plan in Quebec to a non-fibrosis restricted strategy in PEI. The need for a more uniform and evidence based approach to care, particularly in higher risk persons, is an important conclusion. Minor comments: 1. The authors may wish to consider an expanded discussion regarding the best mechanisms by which a national strategy could begin to address criteria heterogeneity, taking into account the existence of strategies in countries like Australia and Scotland. **Thank you for this suggestion. We have provided additional detail in the Interpretation section to more clearly state the benefits of a national strategy: "the development and adoption of a national HCV strategy in Canada… will facilitate volume-based discounting, reduce provincial- territorial heterogeneity, direct treatment to at-risk populations, and broaden equitable access to enable the elimination of HCV infection in Canada."** 2. The appropriateness of a one size fits all HCV strategy in Canada might also be discussed, recognizing that clinical, epidemiologic, and cost effectiveness are dependent on variables which may be very different in Vancouver, Saskatoon, or Saint John. **Thank you for your comment. We agree and have added a brief statement about this drawback in the Interpretation section.** 3. While a national strategy should indeed promote evidence based practice, criteria heterogeneity exists at least in part due to the lack of prospective and long term data, particularly in certain patient populations or in regards to models of care which were not well represented in registration trials. I would suggest this be emphasized. This is particularly relevant in PWID populations, where the authors rightfully advocate for expanded treatment access, yet where many important questions remain regarding an optimal care model. The ongoing prospective measurement of such patients will provide important insights into some of these areas of uncertainty, with evidence that can then be used as a tool to inform and promote best clinical practice and further streamline care models nationally, and have maximal health policy impact. **Thank you to the reviewer for this comment. We respectfully disagree with the reviewer. The simplification of interferon-free HCV therapies has drastically changed the HCV treatment landscape and it could be argued, the need for multiple models of care. Thus far, preliminary results have shown that universal access to HCV therapies in Australia has enabled rapid scale-up of therapies across various population groups, including people who inject drugs via different models of care. Although the evidence is limited, this suggests that various models of care will be possible rather than one optimal model of care.**
Reviewer 2	Lauren Canary
Institution	Division of Viral Hepatitis, National Foundation for the Centers for Disease Control and Prevention, Atlanta, GA
General comments (author response in bold)	The manuscript is a well-written, straight-forward descriptive analysis that compares criteria for new HCV treatments across Canadian provinces/territories. It would be of interest to policy makers, payers, and the HCV community in Canada and beyond. 1- Page 9, line 3: It would be helpful for the author to clarify whether all provinces allowing general practitioners to treat HCV require that the GP have experience treating HCV or if that requirement is only specific to certain provinces allowing GPs to treat. Further, a definition of 'experience treating HCV' as defined by provinces, if available, may be of interest to readers. **We understand the reviewer's comment. Unfortunately, the limited information provided online does not make it entirely clear how much 'experience' is required for general practitioners to become a designated prescriber. For example, a jurisdiction might say: "experience in treating HCV" while another jurisdiction (e.g. Quebec) instead states: "experience with hepatitis infections and substance abuse." The definition of designated prescriber seems to vary by province-territory so it is difficult to confirm this by the limited information available online. The lack of information transparency is certainly a challenge.**

	2- Page 11, line 19: It may be helpful for the author to expand upon the statement "In practice, there are no fibrosis stage restrictions." **Thank you for this comment. This sentence has been made clearer to state: "Quebec does not list this information; however, in clinical practice there are no known fibrosis stage restrictions."** 3- Page 12, line 20: It may be unclear to the reader whether the DOT program in Saskatchewan and the multidisciplinary health team requirement in NIHB are specific to those with high risk for noncompliance or rather pertain to all patients. **We have made this sentence clearer by stating all criteria are at the prescriber's discretion: "There were no drug and alcohol use restrictions although at the prescriber's discretion, British Columbia criteria stated that 'patients who are at high risk for non-compliance' were ineligible and Saskatchewan provided a Directly Observed Therapy option for prescribers." We removed the sentence related to the Non-Insured Health Benefits program to be clearer because even though the Non-Insured Health Benefits program is a national plan, contact information for a multi-disciplinary team was not a requirement for all jurisdictions. For example, British Columbia required this information while other jurisdictions did not.** 4- Page 13, line 14: Some readers might consider required abstinence from injecting drug use to be a 'drug use restriction'. Suggest including in table footnote at the least. **Thank you for this comment. All of the restrictions in Prince Edward Island are at the discretion of the prescriber and hence, are not 'definite'. We did have a footnote in the Table about methadone use but instead changed it to include injecting drug use.** 5- Page 15, line 32: Sentence needs revising. It is not reasonable to extrapolate Medicaid reimbursement findings specific to 3 states and 2 pharmacies to the entire US. **Thank you for this suggestion. The wording has been revised to be clearer: "Two US studies [41-43] that investigated <7 state plans found that type of insurance was associated with HCV treatment initiation and approval of reimbursement claims."**
Reviewer 3	Dr. Camilla Graham
Institution	Beth Israel Deaconess Medical Center, Viral Hepatitis, Infectious Disease, Boston, Mass.
General comments (author response in bold)	This study analyzed restrictions on reimbursement for direct acting antiviral-containing regimens among publicly funded programs in Canada, and compared them to one specific public payer in the United States. The comparable study of US Medicaid reimbursement restrictions has been helpful in terms of advancing public policy around access to HCV treatment and I assume the same would be true for this study in Canada. I have a few comments and questions: 1. Page 4: Are the HCV-associated health care costs annual costs? **Thank you for bringing this to our attention. The sentence has been made clearer.** 2. Page 4: Canadian readers may not be familiar with the US Medicaid program. The cited study by Barua was limited to state fee-for-service Medicaid programs, in distinction to managed care Medicaid programs. It may be worth mentioning that each state Medicaid establishes its own reimbursement criteria, although 23 state Medicaids used a common Pharmacy Benefits Manager organization (PBM) to negotiate drug prices with manufacturers. These criteria are distinct from federal and state corrections plans, the >600 private plans, and other payer sources in the US. Perhaps it is sufficient to make clear that only one type of publicly funded payer plan in the US was used as a reference for restriction criteria. **We agree with the reviewer's recommendation. The introduction has been corrected to include a sentence about the limitation of the Barua et al. 2015 study.** 3. Page 6: State the last date in which data were extracted. The descriptions of restrictions should be stated in the past tense since criteria could change between the last date of extraction and publication of this study. **Thank you for this comment. The last date in which the data was extracted has been made clearer and all findings have been put into past tense.** 4. Page 7: It is unclear which prisoners are covered by CSC. It was hard to understand who was covered by what plan on page 12. **Thank you for this suggestion. For clarification, we added "Criteria for prisoners in federal penitentiaries (sentences ≥ 2 years) are covered by Correctional Service Canada and were also reviewed."** 5. Page 7: Did any jurisdiction require liver biopsy, or did all regions allow non-invasive tests to determine fibrosis stage? **Thank you for your comment. The information provided by each reimbursement form varies. For example, a form could state: "Fibrosis stage F2 or greater (Metavir scale or equivalent)". However, it did not always state what method should be utilized. The authors did not come across a situation by which "liver biopsy" was stated as being the only requirement. However, given this vagueness we also couldn't definitively confirm that (in practice) a liver biopsy report was not specifically required on occasion. It would be challenging to report how often this occurred.**

	6. Page 11: The progressive inclusion of lower fibrosis stages over time in Quebec was obviously different from other jurisdictions. In the discussion, can the authors add any insight into how this came about? Does it hold any insight into how other provinces could expand treatment criteria? **Thank you for this suggestion. A brief statement about Quebec was included in the Interpretation section.** 7. Page 12: In the US, the problem with requiring a specialist is that for many areas of the US, this can introduce a substantial barrier to access. Is there any issue with difficulty accessing specialists in Canada? I am specifically wondering about those people living with HIV/HCV coinfection in Prince Edward Island, but the question is general. **This is a good point. We added a sentence in the Interpretation section on how additional training and education to general practitioners to allow prescribing would improve therapy access.** 8. Page 12: As above, the corrections restrictions were unclear. **The First Nations People and Inuit and Federal Prisoners section has been reworded to help increase clarity.** 9. Page 13: 74% of state fee for service Medicaid plans in the US limit reimbursement.... **Thank you to the reviewer for this suggestion. This change has been made.** 10. Page 14: Medicaid can negotiate drug prices (discounts and rebates) on top of the ACA-mandated 23.1% rebate - it is Medicare (the program for older people) that is prohibited from negotiating drug prices. The problem is that each state lacks the negotiating power that a central agency such as pCPA has. **Thank you to the reviewer for this clarification. The sentence has been reworded to more clearly emphasize the US lacks an equivalent committee.** 11. Page 15: The policy conclusions could be stronger. If Canada develops a national strategy for the elimination of hepatitis C, it would facilitate volume-based discounting, decrease regional variation, direct treatment to vulnerable populations, and provide equitable access. **Thank you to the reviewer for this suggestion. The above sentence has been paraphrased and added to the manuscript in the Interpretation section.**