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Title	**Family medicine-directed hepatitis C care and barriers to treatment: a mixed method study**
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Reviewer 1	Carla Ginn
Institution	Biostatistician Research Office, Faculty of Nursing, University of Calgary
General comments and author response	1. The title is slightly misleading, is it possible to eliminate HCV? However, this may have been a quote from one of the physicians interviewed. If so, please add it to the qualitative findings table and clarify. If it is not a quote, the title might be improved by including the terms mixed methods, chart review, antiviral use, and avoid the word eliminate. This is a direct quote from a participant [*"HepC" changed to "hepatitis C" for the title]. We felt it was engaging and captured the ultimate aim of our work. However, we are not wedded to this title. It could certainly be modified. 2. The abstract is clear, indicating a sample size of 542 patient charts, and 8 physician interviews. However, please change the wording, "40,381 active patients" (page 7 line 6), to "40,381 chart reviews" for clarity, as the active patients wording implies active infection when compared with the wording in the abstract. Thank you for pointing this out. Changed to "40 381 chart reviews". 6 (3) 3. In the methods section of the abstract, please specify the qualitative method, and that it is a mixed methods study; later it is clear that thematic analysis will be used. Within the abstract "mixed method" and "conventional content analysis" were added. 2 (2) 4. The background is clear, with the prevalence clearly indicated. It would be helpful if the Canadian prevalence of cirrhosis and liver was also provided. Unfortunately, there is no population-based data on the prevalence of cirrhosis amongst HCV infected persons in Canada. 5. Please clarify how active HCV infection was measured. To calculate "active HCV" in a conservative manner the "HCV cleared" and "HCV status unknown" categories were removed from the total sum of HCV subjects. For clarity, we have changed the term "active HCV" to "HCV requiring treatment". 5 (3) 2 (3) 6. In the quantitative section, page 5, line 6, it is not clear why charts from 2011 were included in the review, but eligible patients were those between March 1, 2015 to March 1, 2017. We hoped to capture the metrics of the "current" HCV population within our

	practice (i.e. patients who had been active in our family medicine practice from 2015-2017). For these patients we wanted to go as far back as possible to understand their full treatment history (2011 marks the start of our EMR). We did not wish to include patients who had left our practice (i.e. a patient who was seeing our group from 2012-2014) as the information would not be "current" nor likely complete. 7. Did the qualitative themes integrate/corroborate with the quantitative results overall, or were there additional themes requiring consideration that contrasted/challenged the quantitative results? A bit more integration of the qualitative themes with the quantitative results would enhance this manuscript. Thank you. The following was added: "When considering the quantitative and qualitative study components in unison, stable housing and intravenous drug use stand out as common themes. Our quantitative results highlight that those able to engage in treatment tended to have stable housing and no history of IVDU. Qualitative participants echoed that unstable housing and IVDU led to difficulty retaining patients in HCV treatment, and many participants suggested that strong social work and addictions programs may ameliorate the situation. Observations such as these underline the urgency of addressing these greater societal issues when aiming to comprehensively address hepatitis C" 8 (4) 8. Please insert the words "ever treated" on Page 7, line 16, in brackets behind the words, "patients who had ever received treatment" for consistency, with the use of "ever-treated" on Page 8, line 23. Similarly, the term "treatment facilitator" could mirror "treatment barrier" on Page 7, line 37. Alternatively, "treatment enabler" could be used. "(ever treated)" and "treatment facilitators" were added 6 (4) 7 (1) 9. Page 8, line 32, please include references to this previous research. The various studies are described and referenced in the phrases following the line to which you refer ("A number of common barriers to HCV care have been identified by previous research."). To help emphasize this we have added "For example…" to the next line. 8 (3) 10. Page 8, line 33, please change "oft" to "often," or "frequently." Page 8, line 40, please reword "notion," could use "idea," or "concept". The terms "frequently" and "idea" were added 8 (3) 11. The table on page 15 has no heading, and appears to be Table 1, demographics (please break this table down to include more detail such as HCV infected, HCV inactive, and total infected). Table 1 has been edited significantly to include more detail. Table 1 12. The table on page 16 appears to be Table 3, but has no heading.

	Apologies, headings have been corrected. Tables 13. The table on page 17 has no heading and appears to be Table 2. This table has been removed from the manuscript 14. Please assign headings to tables for clarity. Apologies, headings have been corrected. Tables
Reviewer 2	Dena Schanzer
Institution	Public Health Agency of Canada, Infectious Disease and Emergency Preparedness Branch
General comments and author response	Does the background accurately represent current knowledge in this field? o No, the authors seem to assume that in Ontario that second-generation DAAs were publicly funded for all chronically infected persons regardless of disease stage. I believe that full funding was instituted in 2018. The first-generation of DAAs were available in 2012, though were not well tolerated. Many patients not at risk for progression to cirrhosis would have waited for the second generation DAAs. This background information on first and second generation DAAs should be included in the introduction. o As 2nd generation DAAs were a considerable improvement over the 1st generation DAAs, the time lines of changes in treatment options and their effectiveness should be included in the introduction. o The Public Health Agency of Canada published a summary of the impact of the availability of 1st and 2nd generation DAAs for hepatitis C on Canadian hospitalization rates for liver disease from 2012 to 2016. Some discussion of benefits, both in terms of a reduction in individual risks as well as evidence of population level benefits should be provided. We have added this information to the Background section. 4 (1) Do the authors explain why they conducted the study? o Yes. There is little information currently available on the cascade of care related to HCV treatment and cure. The authors quote a study published in 2016 that showed very low HCV treatment rates as of 2012 (first year of 1st generation of DAA therapies). As treating physicians found low levels of tolerance and were aware of trials for promising 2nd generation DAA therapies, these issues should be included in the rationale for the study. More information regarding first line agents has been

	added. “First generation direct-acting antiviral agents had a multitude of tolerability issues, yet, fortunately pharmacological advances have now resulted in the availability of safe, effective and well-tolerated second generation direct-acting antivirals agents”. A more up-to-date reference (from 2019) has also been added. 4 (1 & 2) Is there a clear research question? o The authors wanted to report on current treatment rates for HCV and outline barriers to treatment. o The authors also state that their study results support a “one-time screening of those born between 1945-1975”. This objective is out of scope, as such a study would have to demonstrate a substantial burden (hospitalization, or death) among the general population for which this one-time test would be targeted. This study only includes persons who have already been diagnosed with chronic HCV infection, and documents that nearly half of the population has not yet engaged in treatment. We agree with your assertion. The phrase “and one-time screening of those born between 1945-1975 (22)” has been removed. 8 (1) Is the study design appropriate? o Given that treatment was publicly funded only for persons with advanced liver disease during the study period, the main study result (approx. 50% treated) is difficult to interpret without information of the disease stage/eligibility for treatment for each participant. o The study design does not support the authors’ claim that their results support the recommendation for a “one-time screening of those born between 1945-1975”. o Treatment rates (proportion who have engaged in treatment) should be provided by major age group (<45, 45-64, and 65+). We agree with your assertion. The phrase “and one-time screening of those born between 1945-1975 (22)” has been removed. We added the following statement to the limitations section: “Another limitation is that our data did not include an overlay of “outside” administrative changes – such as the introduction of second generation direct-acting antivirals (DAAs) and public drug coverage (and the disease stage requirements for such public coverage).” We have added treatment rates by major age group. Please see Table 1. 8 (1)
Reviewer 3	Camilla Graham
Institution	Beth Israel Deaconess Medical Center, Viral Hepatitis, Infectious Disease
General comments and author response	Reviewer 3: Limitations include:

	1. A single care entity - it is unclear how representative this health system is to other systems in Canada; We agree, hence the highlighted limitation: “One major limitation to this analysis was the single center, urban, academic setting.” 7 (3) 2. A small number of physicians were interviewed for the qualitative portion of the study – it was unclear how representative these physicians were to other PCPs in Canada. We have added demographic data to the Results section. 7 (1) Minor concerns: 3. Page 4: “In Canada, all jurisdictions provide publicly funded therapy to infected persons regardless of the state or severity of infection…” In the Table of issues and common themes, systems barriers included having to come back to a pharmacy every seven days to pick up supply, and patients not meeting treatment criteria. Are these barriers true? If not, is there a suggestion for how to address misconceptions that may pose barriers? Thank you, we have emphasized that indeed this is a new drug coverage change (2018 decision). “In Canada, since 2018, all jurisdictions provide publicly-funded therapy to infected persons regardless of the state or severity of infection (e.g. level of fibrosis). “ 4 (1) 4. Page 4: Reference 9 includes patients with HCV up to 2012, before the approval of all-oral DAA regimens, so percent of patients treated for HCV during that treatment era is not relevant to today’s rates. A more up-to-date (2018 cohort) reference has been added (the 2012 reference has been removed). 4 (2) 5. Page 6: I suspect “lactate dehydrogenase” should be ALT Thank you. The content of Table 2 has been removed entirely. 6. Page 6: What percent of the 40,381 patients had been tested for HCV infection? There was evidence of HCV testing in the electronic medical records for 1408 (3.5%) patients. The following statement has been added: “1408 charts (3.5%) had indication of HCV testing (collected from our automated search)” 6 (3) 7. Page 6: What percent of the patients who had been treated for HCV received treatment through a specialist versus primary care physician? We unfortunately did not collect this information. 8. Page 6: Were there data associated with lack of receiving specialist care? I think that of the 287 treatment naïve patients, 234 were not in specialist care, so

	was it clear why 53 patients in specialist care were not treated? I am trying to figure out the relationship between being treatment naïve and receiving specialist care or not. We have reviewed the specialist data for our study and are confident that it is correct. Our sample of individuals consisted of a large number of individuals with social issues (e.g. history of IVDU, and/or homelessness). HCV treatment practices in Toronto, Canada are sometimes prejudiced (structurally or morally) against these individuals, and even though they have received specialist care their medical/social history may preclude them from ever being treated (i.e. put on pharmacological interventions). Without access to full specialist charts (i.e. only consult notes sent to the family doctor) it is difficult to be certain of the specialist's rationale and process. 9. Page 6: Not everyone with HCV needs an ultrasound. Were the authors able to determine what percent of these treatment naïve patients who were not receiving specialist care met criteria for U/S testing? 116/234 patients had platelets checked in the last year. 23 of these results were "abnormal". This table (Table 2) has however been removed from the manuscript. 10. Page 6: Was the definition of at least ten HCV positive patients in a PCP's panel an arbitrary definition of "significant hepatitis C experience" or was this based on data? Did any of these physicians actually treat any HCV patients with antiviral medications? This value was based upon a review of the distribution of patients within our practice. The bulk of physicians had <10 HCV patients in their practice. While approximately 20 physicians had >10 patients. This "ten" cut off was therefore based on our practice data and clinical gestalt regarding threshold for some degree of expertise. This statement was added: "Ten was chosen as the threshold for "expertise" based upon the review of our department's practice data (number of HCV patients per provider) and our collective clinical experience. " We unfortunately do not have data regarding proportion of family physicians prescribing HCV medications. 6 (2)