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Title	Acceptability and yield of birth cohort screening for hepatitis c in a Canadian colorectal cancer screening population: a cross-sectional study
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Reviewer 1	Jee-Fu Huang
Institution	Kaohsiung Municipal Hsiao-Kang Hospital, Kaohsiung Medical University, Internal Medicine
General comments	The Authors conducted a cross-sectional study aiming to assess the acceptability and yield of HCV screening among patients undergoing colorectal cancer (CRC) screening. A total of 903 subjects participated the screening. Among 483 patients screened for CRC, the prevalence of anti-HCV positive was 0.6%. The figure was lower than expected from previous epidemiological data in Canada. They concluded that the relatively low HCV prevalence suggests further evaluation of the cost-effectiveness of birth cohort screening in this population. The strengths: 1. A novel screening method to raise the detectability of HCV infecction since it's an underestimated infectious disease. 2. The lower than expected prevalence of HCV suggests that birth-cohort screening in this patient population (>50 years of age) may not be the optimal means of improving case identification in Canada. The Weaknesses: 1. Somewhat negative results 2. The results from a regional study might not be applied to other regions. A brief description of the study demographic features will be more comprehensive. Minor Comments: 1. The Authors should list a flowchart including the number of subjects for a better clarification. 2. What is saliva-based testing for HCV testing? It was not depicted in detail in the methods section. 3. May be the study cohort is a well-educated cohort engaged in their health care. A validation test from other regions may be informative.
Reviewer 2	Tom Wong
Institution	PHAC, Community Acquired Infections Division
General comments	The authors may wish to consider the following to strengthen their manuscripts: For the abstract, specify that the baby boomer hepC screening recommendation is a US recommendation. In the Methods section, please specify that the stored blood specimens were from Feb 2011 to Aug 2012. For the Introduction section, please note that the 70% unaware is based on less than 50 anti-HCV seropositive individuals from the CHMS study (confidence interval for the unaware estimate is wide). Should put the range of unaware in Canada as 21% (Remis 2007) to 70% (Rottermann 2013). Similarly, add the range for the US. For the Methodology section, perhaps elaborate on how 496 blood samples in the bio-repository were randomly selected. How did the authors decide on 496 individuals and not a larger sample size? Please include sample size calculations. Please state which REB approved the study. For the logistic regression, the authors may wish to include variables if they are significant at P<0.1 in univariate analysis. For limitations, the authors may wish to discuss the bias with selecting the 496 samples from the biorepository of blood samples from colonoscopy patients for HCV testing. Would the authors consider using a larger sample size in a future study
Author response	**Response to Dr. Huang's Comments:** 1. The Authors should list a flowchart including the number of subjects for a better clarification. **We have now included a Figure 1 describing the flow of study participants.** 2. What is saliva-based testing for HCV testing? It was not depicted in detail in the methods section. **Novel assays now allow one to test for HCV antibodies in saliva (not blood as per usual). Importantly, we did not conduct these assays; we just asked about them in our survey, and hence, they are not described in the Methods. We wanted to determine whether the type of testing would influence screen willingness, and not surprisingly, patients were slightly more accepting of**

	saliva-based HCV testing versus blood testing, presumably due to its less invasive nature. These saliva-based assays should be available for clinical use in the near future and will have a dramatic impact on our ability to do outreach screening for HCV in diverse populations. 3. Maybe the study cohort is a well-educated cohort engaged in their health care. A validation test from other regions may be informative. **This is a potential limitation of the study. We mentioned this on page 11 ("...ours was a highly educated cohort engaged in their health care. Therefore, the generalizability of our findings may be questioned.") We have also included the following sentences on page 12 under "Limitations" to read:** **"As mentioned, the ability to draw inferences regarding the prevalence of HCV in Canada is limited by the specific nature of our study population and small sample size... Validation of our findings in other regions and with a larger sample size would be informative."** **Response to Dr. Tom Wong's Comments**: 1. For the abstract, specify that the baby boomer hepC screening recommendation is a US recommendation. In the Methods section, please specify that the stored blood specimens were from Feb 2011 to Aug 2012. **We have added the requested dates to the Abstract and modified it to read: "Hepatitis C virus (HCV) screening is recommended in patients born between 1945 and 1965 ('baby boomers') in the United States."** 2. For the Introduction section, please note that the 70% unaware is based on less than 50 anti-HCV seropositive individuals from the CHMS study (confidence interval for the unaware estimate is wide). Should put the range of unaware in Canada as 21% (Remis 2007) to 70% (Rottermann 2013). Similarly, add the range for the US. **Regarding the proportion of undiagnosed individuals, we have added the following to the Introduction:** **"Second, most patients are asymptomatic until advanced liver disease has developed; thus, many HCV cases are unaware of their infection (21% to 70% in Canada and 25% to 50% in the U.S.)."** 3. For the Methodology section, perhaps elaborate on how 496 blood samples in the bio-repository were randomly selected. How did the authors decide on 496 individuals and not a larger sample size? Please include sample size calculations. Please state which REB approved the study. For the logistic regression, the authors may wish to include variables if they are significant at P<0.1 in univariate analysis. **As described above, the sample size was based on budgetary constraints, predominantly due to the cost of HCV testing. Therefore, a formal sample size calculation was not conducted. We had sufficient funding to test approximately 500 specimens and 496 were pulled from the freezer.** **We prefer to use a priori a cut-off for variable selection of P<0.05. Nevertheless, none of the 'unselected variables' (e.g. university education or marital status) had a P<0.10, and hence, our model would be unchanged with this less stringent cut-off.** **The study was approved by the Conjoint Health Research Ethics Board at the University of Calgary. This has been added to the Methods.** 4. For limitations, the authors may wish to discuss the bias with selecting the 496 samples from the biorepository of blood samples from colonoscopy patients for HCV testing. Would the authors consider using a larger sample size in a future study. **The limited generalizability of our findings to the general population of individuals within this age group is limited as described on page 11 and in the Limitations section (page 12). We have added the following sentence regarding our small sample size as a limitation (page 12):** **"Validation of our findings in other regions and with a larger sample size would be informative."**