Barriers to hepatitis C diagnosis and treatment in the DAA era: Preliminary results of a community-based survey of primary care practitioners

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ABSTRACT
Notwithstanding the groundbreaking achievement of hepatitis C curative treatment with direct-acting antiviral therapies, Canada faces an uphill battle in reaching the 2030 goal of viral elimination set forth by the World Health Organization, a goal made more difficult by the COVID-19 pandemic. There is limited understanding of the diagnostic and treatment barriers, and challenges in linkage to care in Canada, especially as it pertains to primary care providers in a community context. Therefore, in this article, the authors conducted a survey study to evaluate the following factors: primary care providers’ knowledge of specialist treatment options and the importance of screening and treatment; and patient factors, including transportation, linguistic barriers, and other socio-economic status indicators that impact the screening and management of hepatitis C. The results suggest that public health campaigns that protocolize and/or incentivize screening and referrals may provide solutions to addressing such barriers.

KEYWORDS: barriers; DAA; diagnosis; hepatitis C; treatment

BACKGROUND
Hepatitis C virus (HCV) carries a significant burden in Canada and internationally, with recent estimates from the World Health Organization (WHO) placing it as a burgeoning public health threat accounting for nearly 400,000 deaths in 2016 alone (1). Despite HCV being a curable disease, it is estimated that more than 11,000 Canadians contract acute HCV on an annual basis, and it is widely believed that just under half of patients are undiagnosed (2). In Canada, where the
The seroprevalence of HCV is approximately 0.8 to 1.0%, a dichotomous screening and linkage to treatment gap problem curtails efforts to expeditiously reach HCV elimination goals set by the WHO. Furthermore, the complex epidemiology of HCV in Canada (current and former IVDU population, immigrant populations, and regional/provincial heterogeneity characteristics) muddle a uniform nation-wide screening and management strategy. Notwithstanding these variables, the onset of oral direct-acting antiviral (DAA) therapy regimens affords highly efficacious, cost-effective, and safe treatment options (3,4).

As of January 2021, first- and second-line DAAs (inhibitors of the NS3/4A protease, the NS5A protein, and the NS5B polymerase; eg, sofosbuvir/velpatasvir, glecaprevir/pibrentasvir, and voxilaprevir) are now listed on public formularies. However, it is the identification of patients with hepatitis C, and the linkage of these patients to specialty care, which present complex and poorly characterized challenges. A noteworthy added hurdle to HCV management is the current COVID-19 pandemic. The impact of the COVID-19 pandemic on hepatitis C screening and linkage to care since March 2020 is an area of active study, though current data suggests the ability to meet WHO targets will be negatively impacted (5). However, there may be opportunities for improved access in the era of telemedicine, and virtual care may provide better access of care to certain populations of patients where in-person visits prove difficult (6,7).

The actual treatment of chronic HCV is thankfully no longer a barrier as it was in the interferon era. Indeed, since 2014, the availability of the first DAAs dramatically transformed the HCV treatment landscape forever. Current DAA treatment strategies, all pangenotypic and requiring minimal monitoring, have shown favourable patient tolerability and efficacy profiles in clinical trials as well as in data from real-world cohorts, including historically difficult-to-treat populations (8–10). Furthermore, physicians in the fields of gastroenterology, hepatology, and infectious diseases, are comfortable prescribing such regimens resulting in burgeoning prescription rates (11,12). Several studies have shown that a primary care setting is well poised for the delivery of DAA therapy, owing to a ‘medical home’ structure that incentivizes patient engagement and the favourable side-effect profile of DAA treatment (13). Notwithstanding the groundbreaking achievement in HCV curative treatment strategies, there is a gap in the literature on the treatment barriers in the DAA era and linkage to care in Canada, especially as it pertains to primary care providers in a community context. In addition, community health centres and addiction centres have proven to be effective treatment sites, providing credence to the notion that trained general practitioners are apt care providers in a medical home conceptualization of HCV management.

Brampton is Canada’s ninth most populous municipality with over 600,000 people, with a significant proportion of residents identifiable as ethnic minorities (>55% based on 2016 Census data) (14). As a consequence of a large immigrant population, the seroprevalence in Brampton is three times higher than in less diverse populations such as London, Ontario, or Ottawa (2).

**METHODS**

The authors sought to study the barriers to linkage to care and access to care using a survey-based study. Specifically, the authors evaluated the following factors: primary care providers’ (PCP) knowledge of specialist treatment options and the importance of screening and treatment; and patient factors, including transportation, linguistic barriers, and other socio-economic status indicators. REB approval was obtained from the Research and Ethics Board of the William Osler Health System.

The survey was distributed to PCPs in Brampton, Ontario, offering a unique multi-ethnic community deployment. The largest ethnic group in Brampton are South Asians, comprising 45% of the population (14). Further particularities of the municipality include lower socio-economic status and English language fluency. A list of PCPs was obtained from William Osler Health System which operates two hospitals in the city of Brampton, and with whom the vast majority of PCPs have an affiliation. PCPs were contacted via letter, fax, or e-mail and invited to complete the survey.

Survey results were analysed using descriptive statistics.

**RESULTS**

Twenty-three of 75 (31% response rate) PCPs responded voluntarily. Non-responding PCPs were contacted twice for reminders or repeated invitations to participate. 52% of respondents were male, and 48% were female. The majority of physician
respondents had several years of practice experience—83% had more than 20 years of practice experience, 4% had between 15–20 years of experience, and 13% has less than 5 years of experience. The majority of respondents (83%) hold a medical degree from Canada. 48% of physician respondents had comprehensive screening strategies, and years of practice was not a significant predictor of comprehensiveness of screening approach. Among limitations to screening identified by PCPs, 39% of respondents reported an uncertainty insofar as the appropriate lab tests to order for screening purposes, 13% reported lack of patient compliance, 9% reported lack of physician time, and another 9% attributed incomplete screening practices with forgetfulness to screen. The majority (87%) of physician respondents have a routine practice to refer patients to a specialist (gastroenterologist, infectious disease specialist, or hepatologist) upon diagnosis of hepatitis C for treatment and other aspects of management. Among identified barriers to referral, 43% of respondents alluded to a perceived or actual problem of wait time in accessibility to specialists. 13% of respondents identified a problem of patient compliance as a barrier to specialist referral. Interestingly, the majority of respondents self-assessed their screening practice as fair or poor (65%), with 52% self-evaluated as ‘fair’ and 13% as ‘poor’). Only 30% of respondents assessed their screening practice as ‘good.’ In terms of self-assessment of knowledge pertaining to HCV treatment guidelines, 70% of respondents identified a need for improvement and only 26% identified their knowledge as ‘adequate.’

**DISCUSSION**

The survey presented in this study, albeit based on a small sample size, does suggest several interesting findings on the suboptimal screening and linkage to care gaps experienced in a large multi-ethnic urban population in Canada for HCV patients. Barriers can be broadly classified as physician-level and patient-level. Physician-level deficits include lack of knowledge and familiarity with hepatitis C blood tests (HCV antibody versus polymerase chain reaction), limited knowledge around DAA regimens, and lack of collaborative PCP-specialist treatment models. Patient-level obstacles include health illiteracy, transportation and financial challenges to attending appointments, and other socio-cultural factors.

The authors postulate that an incentivized or protocolized screening and referral program may provide a solution to addressing such barriers. It is our perception and observation in working closely with PCPs in our community that they are overworked, have tremendous patient loads, and lack the time to implement recent updated HCV screening recommendations as set forth by the CASL (16). Better understanding of the complex epidemiology of viral hepatitis by family medicine practitioners will indubitably translate to improved screening rates. For instance, anecdotally, our experience at the Viral Hepatitis Clinic at William Osler, under whom over 2000 patients have received hepatitis C treatment, shows that in a 4–8 week period following the institution of a curriculum of a hepatitis C continuing medical education geared towards PCPs, there was a 5–10% increase in specialist referrals. Notwithstanding that most Ontario PCPs use EMR technology, physician and patient reminders for screening are seldom used. Public health campaigns should, therefore, aim to improve targeted screening. Linkage to care in our municipality seems less of an issue of finding a specialist than convincing some patients to see a specialist.

In the context of the current COVID-19 pandemic, hepatitis C screening and treatment has proven to face an uphill battle, particularly in communities such as Brampton which has been a national hotspot for COVID-19 during the first 3 phases of the pandemic (17). Further studies to understand how the pandemic has impacted the care of chronic diseases, including hepatitis C, is an important area for future research, and will hopefully generate strategies involving virtual care and specialty-PCP integrated care models to improve HCV detection and treatment rates.

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REFERENCES

1. WHO, 2020.
2. Public Health Agency of Canada, Report on Hepatitis B and C, 2017.
3. Gutkind S, Schackman BR, Morgan JR, Leff JA, Agymang L, Murphy SM, Akiyama MJ, Norton BL, Litwin AH & Linas BP. (2020). Cost-effectiveness of hepatitis C virus treatment models for people who inject drugs in opioid agonist treatment programs. *Clinical Infectious Diseases, 70*(7), 1397–1405. https://doi.org/10.1093/cid/ciz384 Medline:31095683
4. Chhatwal J, Kanwal F, Roberts MS & Dunn MA (2015). Cost-effectiveness and budget impact of hepatitis C virus treatment with sofosbuvir and ledipasvir in the United States. *Annals of internal medicine, 162*(6), 397–406. https://doi.org/10.7326/M14-1336 Medline:25775312
5. Blach S, Kondili LA, Aghemo A, Cai Z, Dugan E, Estes C, Gamkrelidze I, Ma S, Pawlotsky JM, Razavi-Shearer D & Razavi H. (2021). Impact of COVID-19 on global HCV elimination efforts. *Journal of hepatology, 74*(1), 31–36. https://doi.org/10.1016/j.jhep.2020.07.042 Medline:32777322
6. Arora S, & Thornton K. (2020). Novel models of hepatitis C virus care delivery: Telemedicine, project ECHO, and integrative care. *Clinical Liver Disease, 16*(1), 5. https://doi.org/10.1002/clld.912 Medline:32714515
7. Arrase M. (2020). Telemedicine, COVID-19 and liver diseases: Revamping remote care initiatives in hepatology. *Annals of Hepatology, 19*(4), 339. https://doi.org/10.1016/j.aohep.2020.05.002 Medline:32482463
8. Asselah T, Marcellin P, & Schinazi RF. (2018). Treatment of hepatitis C virus infection with direct-acting antiviral agents: 100% cure?. *Liver International, 38*, 7–13. https://doi.org/10.1111/liv.13673 Medline:29427484
9. CheemaSUR, RehmanMS, HussainI, Cheema SS, & Gilani N. (2019). Efficacy and tolerability of sofosbuvir and daclatasvir for treatment of hepatitis C genotype 1 & 3 in patients undergoing hemodialysis—a prospective interventional clinical trial. *BMC nephrology, 20*(1), 1–8. https://doi.org/10.1186/s12882-019-1631-4 Medline:31779583
10. Beig J, Orr D, Harrison B, & Gane E. (2018). Hepatitis C virus eradication with new interferon-free treatment improves metabolic profile in hepatitis C virus-related liver transplant recipients. *Liver Transplantation, 24*(8), 1031–1039. https://doi.org/10.1002/lt.25060 Medline:29577581
11. Kattakuzhy S, Gross C, Emmanuel B, Teferi G, Jenkins V, Silk R, Akoth E, Thomas A, Ahmed C, Espinosa M & Price A. (2017). Expansion of treatment for hepatitis C virus infection by task shifting to community-based nonspecialist providers: A nonrandomized clinical trial. *Annals of internal medicine, 167*(5), 311–318. https://doi.org/10.7326/M17-0118 Medline:28785771
12. Wade AJ, McCormack A, Roder C, McDonald K, Davies M, Scott N, Wardrop M, Athan E & Hellard ME. (2018). Aiming for elimination: Outcomes of a consultation pathway supporting regional general practitioners to prescribe direct-acting antiviral therapy for hepatitis C. *Journal of viral hepatitis, 25*(9), 1089–1098. https://doi.org/10.1111/jvh.12910 Medline:29660212
13. Lazarus JV, Pericàs JM, Picchio C, Cernosa J, Hoekstra M, Luhmann N, Maticic M, Read P, Robinson EM & Dillon JF. (2019). We know DAAs work, so now what? Simplifying models of care to enhance the hepatitis C cascade. *Journal of internal medicine, 286*(5), 503–525. https://doi.org/10.1111/joim.12972 Medline:31472002
14. Statistics Canada. 2017. Brampton, CY [Census subdivision], Ontario and Ontario.
[Province] (table). Census Profile. 2016 Census. Statistics Canada Catalogue no. 98-316-X2016001. Ottawa. Released November 29, 2017. https://www12.statcan.gc.ca/census-recensement/2016/dp-pd/prof/index.cfm?Lang=E (accessed September 6, 2021).

15. Ontario Agency for Health Protection and Promotion (Public Health Ontario). Diseases of public health significance cases for January to June 2021. Toronto, ON: Queen’s Printer for Ontario; 2021.

16. Shah H, Bilodeau M, Burak KW, Cooper C, Klein M, Ramji A, Smyth D & Feld JJ. (2018). The management of chronic hepatitis C: 2018 guideline update from the Canadian Association for the Study of the Liver. Cmaj, 190(22), E677–E687. https://doi.org/10.1503/cmaj.170453 Medline:29866893

17. Amberber N, Iveniuk J, & McKenzie K. (2021). Inequities over time in COVID-19 infection and COVID-19-related hospitalizations/deaths. Wellesley Institute.