Expanding treatment for hepatitis C in Canada

James F. Crismale MD, Jawad Ahmad MD

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Over the past few years, there have been major shifts in the treatment of hepatitis C virus (HCV) infection. Highly effective direct-acting antiviral agents have enabled treatment of patients with all stages of liver disease and with a variety of comorbidities; in the past, these patients would not have tolerated interferon-based therapy. Sustained virologic response, which is equivalent to a virologic cure, can now be attained at a rate of 95% with most treatment regimens.[1] The rapid evolution of HCV treatment has necessitated an equally rapid updating of HCV treatment guidelines. The Canadian Association for the Study of the Liver has just published an updated set of recommendations for the treatment of HCV,[2] focusing on advances in therapy since the publication of the last guideline in 2015. This updated guideline is very similar to those published by the American Association for the Study of Liver Diseases and the Infectious Diseases Society of America, and the European Association for the Study of the Liver.[3,4] Importantly, the updated Canadian guideline also addresses critical issues regarding screening, linkage to care and timing of treatment initiation. The expense of direct-acting antiviral agents, however, poses a dilemma: effective use now of resources to cure HCV in potentially huge numbers of patients to prevent the costs of disease progression in the future.

It is estimated that up to 70% of patients with chronic HCV infection are unaware of their diagnosis, which may be partially attributable to a failure of screening methods for HCV infection that are based on risk factors.[5] Birth cohort screening has been proposed in addition to screening based on risk factors, to increase rates of HCV diagnosis. Screening of the baby boomer cohort (i.e., those born between 1945 and 1965) has been adopted in the United States, where mathematical modelling has suggested its cost-effectiveness, using data from both the eras of interferon and direct-acting antiviral agents.[5,6] This may be the case even with screening extended to the entire adult population in the US.[6]

The Canadian Task Force on Preventive Health Care guideline on screening for HCV, published in April 2017, did not endorse any form of birth cohort or population-based screening.[7] Although the overall prevalence of HCV infection in Canada is four times lower than in the US, at 0.8% compared with 3.25%, Wong and colleagues showed similar cost-effectiveness using birth cohort screening in the Canadian population, with up to $44 034 per quality-adjusted life-year gained.[8] Given its cost-effectiveness and the relative ease of implementation compared with screening based on risk factors, the updated Canadian Association for the Study of the Liver guideline recommends birth cohort screening, modified to include patients born between 1945 and 1975, in addition to screening based on risk factors.[2]

KEY POINTS

- Treatment of chronic hepatitis C virus (HCV) infection has been revolutionized by the development of direct-acting antiviral drugs, which can attain cure of HCV in more than 95% of patients.
- Birth cohort–based screening for HCV is necessary to identify patients who may be infected with HCV but who do not have traditional risk factors for infection.
- Treating HCV with direct-acting antiviral drugs appears to be cost-effective, regardless of fibrosis stage.
- Data on long-term outcomes in patients cured of HCV with direct-acting antivirals are not yet available, but outcomes appear to be favourable and similar to those seen in patients cured with interferon-based therapies.

Increased diagnosis via screening based on birth cohort will likely increase the demand for treatment. Indeed, the World Health Organization has set a goal to eliminate all viral hepatitis by the year 2030 (http://www.who.int/hepatitis/en/). One of the greatest barriers to attaining this goal, however, remains the cost of direct-acting antiviral therapy. In Canada, prescription drug spending increased by 9.2% in 2015 and by 5.5% in 2016, largely because of the cost of these medications (www.cihi.ca/sites/default/files/document/pdex2017-report-en.pdf). In part owing to this expense, initial guidelines published in the era of direct-acting antiviral drugs limited treatment to patients with advanced fibrosis or cirrhosis. However, current guidelines, including the updated guideline published by the Canadian Association for the Study of the Liver, recommend that all patients with chronic HCV receive curative treatment regardless of fibrosis level or other comorbidities.

Several recent cost-effectiveness analyses support this recommendation. Modelling data using a European cohort suggest that a "universal" treatment strategy compared with treating "prioritized" patients (i.e., those with more severe levels of fibrosis or extrahepatic manifestations of HCV) is more cost-effective, especially when drug prices are discounted.[9] A modelling study using a Canadian population also showed similar results.[10] In February

2017, the pan-Canadian Pharmaceutical Alliance negotiated an undisclosed reduction in the prices of ledipasvir/sofosbuvir, daclatasvir, sofosbuvir/velpatasvir, asunaprevir, and elbasvir/grazoprevir. Despite concerns regarding a lack of transparency with respect to the final prices negotiated, this is an important step in allowing all Canadians access to these essential therapies.

Current recommendations for a universal treatment strategy have been countered by a Cochrane review that casts doubt on the effectiveness of direct-acting antiviral agents and the achievement of sustained virologic response to improve outcomes.[11] The methodology and results of this review have been strongly criticized by the American Association for the Study of Liver Diseases and the Infectious Diseases Society of America and European Association for the Study of the Liver, as the study relied on mortality data from registration trials for direct-acting antiviral agents and did not assess the impact of sustained virologic response on long-term liver-related outcomes.[12] Data extrapolated from studies carried out in the interferon era suggest that sustained virologic response improves both liver-related and all-cause mortality.[13] We therefore agree with the response letter published by the European Association for the Study of the Liver, which states that this review should not "affect policy-making, [nor] constrain the gathering momentum for diagnosis, testing and linkage to care for individuals with hepatitis C."[12] The updated Canadian Association for the Study of the Liver guideline takes an important step in continuing the fight against HCV in Canada, expanding screening indications to the baby boomer cohort and recommending curative therapy to all individuals affected by HCV.

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Affiliation: Division of Liver Diseases, Department of Medicine, Icahn School of Medicine at Mount Sinai, New York, NY

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Correspondence to: Jawad Ahmad, jawad.ahmad@mountsinai.org