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ORIGINAL ARTICLE

Impact of COVID-19-related public health measures on HCV testing in British Columbia, Canada: An interrupted time series analysis

Mawuena Binka[1] | Sofia Bartlett[1,2] | Héctor A. Velásquez García[1] | Maryam Darvishian[3] | Dahn Jeong[1,4] | Prince Adu[1,4] | Maria Alvarez[1] | Stanley Wong[1] | Amanda Yu[1] | Hasina Samji[1,5] | Mel Krajden[1,2] | Jason Wong[1,4] | Naveed Z. Janjua[1,4]

[1]British Columbia Centre for Disease Control, Vancouver, British Columbia, Canada

[2]Department of Pathology and Laboratory Medicine, University of British Columbia, Vancouver, Canada

[3]British Columbia Cancer Research Centre, Vancouver, British Columbia, Canada

[4]School of Population and Public Health, University of British Columbia, Vancouver, Canada

[5]Faculty of Health Sciences, Simon Fraser University, Burnaby, Canada

Correspondence
Mawuena Binka, PhD, MPH, Epidemiologist, BC Centre for Disease Control, 655 West 12th Avenue, Vancouver, BC V5Z 4R4, Canada.
Email: mawuena.binka@bccdc.ca

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Abstract

Background & Aims: Public health measures introduced to limit transmission of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), which causes coronavirus disease 2019 (COVID-19), also disrupted various healthcare services in many regions worldwide, including British Columbia (BC), Canada. We assessed the impact of these measures, first introduced in BC in March 2020, on hepatitis C (HCV) testing and first-time HCV-positive diagnoses within the province.

Methods: De-identified HCV testing data for BC residents were obtained from the provincial Public Health Laboratory. Weekly changes in anti-HCV, HCV RNA and genotype testing episodes and first-time HCV-positive (anti-HCV/RNA/genotype) diagnoses from January 2018 to December 2020 were assessed and associations were determined using segmented regression models examining rates before vs after calendar week 12 of 2020, when measures were introduced.

Results: Average weekly HCV testing and first-time HCV-positive diagnosis rates fell immediately following the imposition of public health measures by 62.3 per 100 000 population and 2.9 episodes per 1 000 000 population, respectively ($P < .0001$ for both), and recovered in subsequent weeks to near pre-March 2020 levels. Average weekly anti-HCV positivity rates decreased steadily pre-restrictions and this trend remained unchanged afterwards.

Conclusions: Reductions in HCV testing and first-time HCV-positive diagnosis rates, key drivers of progression along the HCV care cascade, occurred following the introduction of COVID-19-related public health measures. Further assessment will be required to better understand the full impact of these service disruptions on the HCV care cascade and to inform strategies for the re-engagement of people who may have been lost to care because of these measures.

Abbreviations: BC, British Columbia; BCCDC, British Columbia Centre for Disease Control; COVID-19, coronavirus disease 2019; HCV, hepatitis C virus; PHL, Public Health Laboratory; RNA, ribonucleic acid; SARS-CoV-2, severe acute respiratory syndrome coronavirus 2; SVR, sustained virologic response; WHO, World Health Organization.

KEYWORDS
COVID-19, HCV elimination, HCV testing, public health measures, SARS-CoV-2

1 | INTRODUCTION

In 2016, Canada, alongside other World Health Organization (WHO) member states, committed to eliminating the threat that hepatitis C virus (HCV) poses to public health worldwide by 2030.[1] To that end, many member states have implemented policies and strategies to facilitate the attainment of the disease prevention, healthcare provision and mortality-reduction goals that form the cornerstone of this Global Health Sector Strategy.[1-3] Canada is making significant progress towards meeting the 2030 elimination goals, with the provision of unrestricted access to publicly funded therapy for persons with chronic HCV infection and elimination efforts being initiated in many provinces, including British Columbia (BC).[4-6] Testing is a key component of these efforts, and is the first step to engaging people living with HCV into care.[7]

The emergence of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) in late 2019 led to the implementation of broad public health measures to prevent and control transmission of the virus and to preserve healthcare resources in many countries across the world, including Canada.[8-14] These measures have had sweeping economic, social and health-related impacts globally, including the disruption of healthcare services such as HCV prevention, testing, treatment and post-treatment follow-up.[15-17] Many people living with HCV have concurrent substance use or mental health challenges, are socially and materially deprived, and living with HIV or HBV co-infection.[18,19] Thus, given the syndemic nature of HCV infection, these service disruptions may have more profound short- and long-term impacts within these groups. Furthermore, HCV-related service disruptions could delay Canada's progression towards the achievement of the viral hepatitis elimination goals. In this study, the impact of COVID-19-related public health measures on HCV testing and first-time HCV-positive diagnoses within the province were assessed using population-level laboratory data as a first step towards understanding the potential impact of healthcare service disruptions on BC's HCV elimination efforts.

Lay Summary

Testing is essential for progression along the HCV care cascade. In this interrupted time series analysis, the introduction of COVID-19-related public health measures in March 2020 was associated with large declines in mean weekly HCV testing and diagnosis rates in British Columbia. Persons living with HCV who may have been lost to care after public health measures were introduced should be re-engaged with care for improved health outcomes and to support progression towards HCV elimination within the province.

2 | METHODS

2.1 | COVID-19-related public health measures in BC

On March 17, 2020, the Provincial Health Officer of BC declared a public health emergency because of COVID-19, ushering in Phase 1 of COVID-19-related public health measures within the province (beginning on March 18, 2020).[20,21] Measures imposed during Phase 1 included the banning of mass gatherings (>50 people) and the closing of establishments that provided non-essential services (e.g. hair salons and barbershops, dine-in services at restaurants and bars), as well as recommendations for physical distancing.[22] Phase 2 of restrictions, beginning on May 19, 2020 and Phase 3, starting on June 24, 2020, saw the gradual loosening of restrictions on travel and gatherings and the reopening of non-essential services.[22] Following a resurgence of COVID-19 cases during Phase 3, all social gatherings and events province-wide were again suspended beginning on November 19, 2020 and remained in place by the end of 2020. Between Phase 1 and Phase 2 (April 1-May 28, 2020), the provincial Public Health Laboratory (PHL) located at the BC Centre for Disease Control (BCCDC) temporarily suspended non-urgent HCV testing to reallocate resources for COVID-19 testing.[23,24] However, urgent HCV testing for hospitalized patients, emergency situations and organ donations continued during this period. This study examines changes in HCV testing patterns following the introduction of restrictions during Phase 1 in March 2020.

2.2 | Variable definitions

De-identified HCV testing data for BC residents were obtained from the BCCDC PHL, which performs over 95% of anti-HCV (antibody) screening and all confirmatory anti-HCV, RNA testing and genotyping in BC. All positive, negative and indeterminate testing episodes were included in this analysis, and testing outcomes were comprised of the integrated test results for each test type (i.e. Anti-HCV: screening/confirmatory; RNA: qualitative/quantitative; genotyping). Testing episodes will be referred to as tests moving forward. First-time HCV-positive rate was defined as the first positive test result for HCV (anti-HCV, RNA, and/or genotype) on record at the BCCDC PHL per 1 000 000 BC population. First-time anti-HCV-positivity rate was defined as the proportion of anti-HCV tests that resulted in first-time anti-HCV-positive diagnoses. The proportion of HCV RNA tests that were negative for the first time following a HCV-positive test was used to assess

progression towards clearing the virus, although differentiating between spontaneous clearance and sustained virologic response (SVR) was not possible, as we did not have access to treatment data. The study period began on January 1, 2018 and ended on December 31, 2020.

2.3 | Statistical analysis

An interrupted time series study design was adopted, using segmented regression models[25-27] to assess the weekly impact of BC's COVID-19-related public health measures on HCV testing within the province, initiated during calendar week 12 of 2020 (week of March 18, 2020). Thus, the pre-restriction period was defined as calendar week 1 of 2018 to calendar week 11 of 2020, and the post-restriction was defined as calendar week 13 of 2020 to calendar week 53 of 2020. Outcomes assessed on a weekly basis were: (i) HCV testing (anti-HCV, RNA and genotyping), (ii) first-time HCV-positive test result, and (iii) first-time RNA-negative test result following a first-time HCV-positive test result. Autoregressive error segmented regression models were run to assess the change in mean weekly rates (slope) pre-restrictions, the change in level of mean weekly rates when restrictions were introduced, and the difference between slopes (change in mean weekly rates) post- vs pre-restrictions, correcting for autocorrelation.

The general model Equations[25,26,28] was:

$$Y_t = \beta_0 + \beta_1 T_t + \beta_2 X_t + \beta_3 Z_t + \nu_t,$$

where Y_t represents the outcome of interest (HCV testing, first-time HCV-positive and first-time HCV RNA-negative rates) in week t; β_0, the baseline mean weekly outcome rate before public health measures (restrictions) were imposed; β_1, the mean weekly change in outcome rates (slope) before public health measures were imposed; T, the time in calendar weeks beginning on January 1, 2018; β_2, the change in the level of outcome rates once public health measures were imposed; X, the dummy variable marking the period before (0) and after (1) restrictions were imposed; β_3, the difference in slope (change in mean weekly outcome rates) after vs before public health measures were imposed; Z, the time (in weeks) post-restrictions; and ν, random variability in

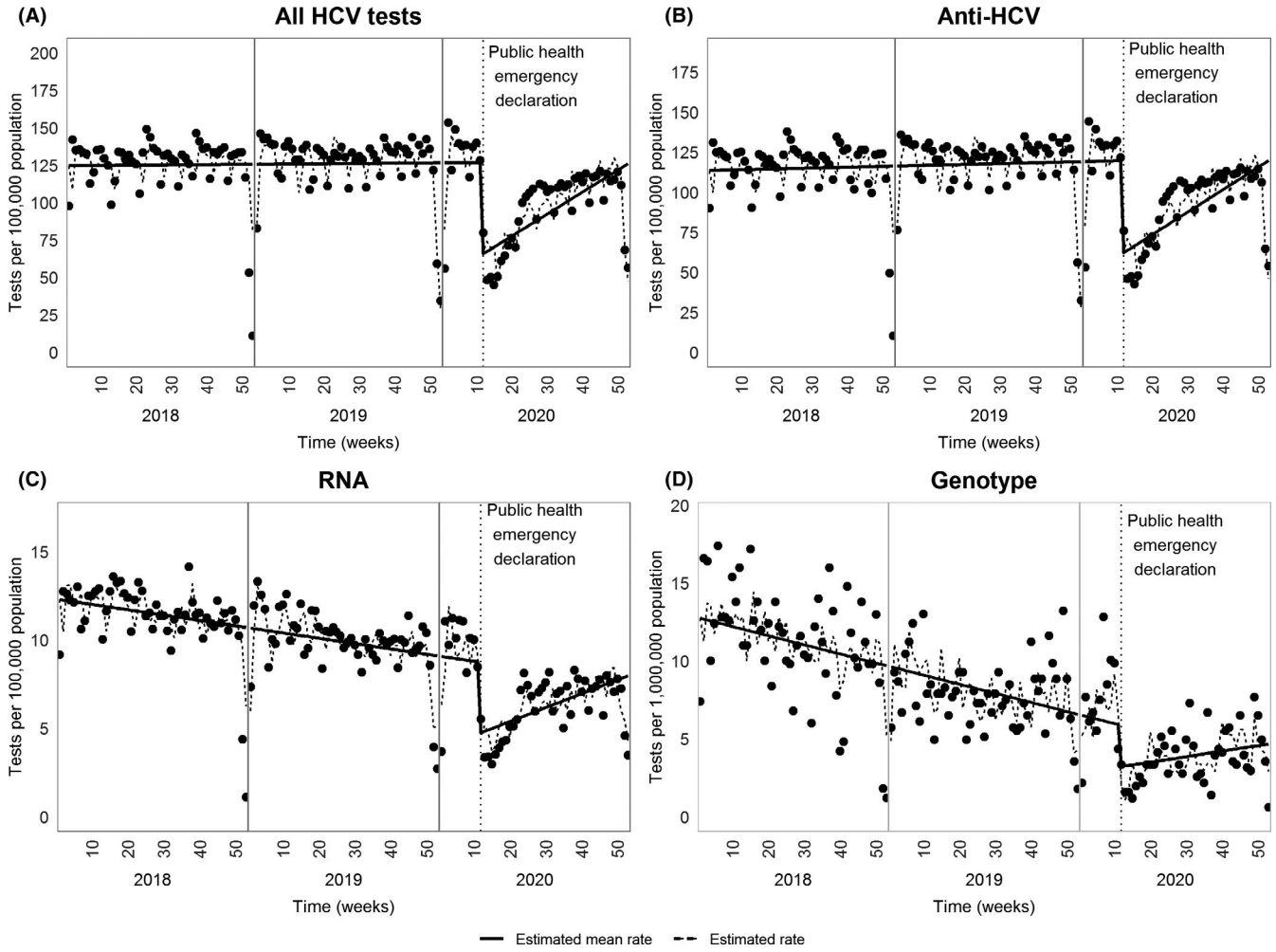

FIGURE 1 Weekly HCV testing rates in British Columbia, 2018-2020. A, All HCV tests, (B) anti-HCV tests, (C) HCV RNA tests, (D) HCV genotyping tests. HCV, hepatitis C virus; RNA, ribonucleic acid

the model adjusted for autocorrelation with the maximum likelihood method. Estimated rate and estimated mean rate (trend) values from the autocorrelation-corrected regression models were also generated with the AUTOREG procedure in SAS 9.4.28,29 The final parameters for inclusion in the model were determined using a stepwise backward elimination approach.[25,28] Autocorrelation was assessed with Durbin-Watson tests. Data preparation and visualization was done using R statistical software (version 3.5.2),[30] while data analysis was done with SAS (version 9.4).29 Statistical significance was defined as $P < .05$.

This study was performed under the public health surveillance mandate of the BCCDC and did not require approval from an ethical review board.

3 | RESULTS

3.1 | HCV testing rates

Estimated mean weekly HCV testing rates in BC were stable at approximately 124.6 HCV tests per 100 000 population per week prior to the introduction of COVID-19-related public health measures in calendar week 12 of 2020 (Figure 1A, Table 1). This overall trend was driven by anti-HCV testing, which formed the majority of HCV testing done in BC (Figure 1B). In contrast, estimated mean weekly HCV RNA testing and HCV genotyping rates fell steadily within this timeframe ($P < .0001$ for both) (Figure 1C,D, Table 1). The overall mean weekly HCV testing rate fell by 62.3 tests per 100 000 population ($P < .0001$) following the announcement of the public health measures during calendar week 12 of 2020. This statistically significant decline in mean weekly testing rates with the introduction of COVID-19-related public health measures was observed across the test types (Anti-HCV: −58.7 tests per 100 000 population, $P < .0001$; RNA: −4.1 tests per 100 000 population, $P < .0001$; genotyping: −2.7 tests per 1 000 000 population, $P < .01$) (Figure 1B-D, Table 1). Estimated mean weekly anti-HCV, RNA and genotyping testing rates increased in the weeks afterwards, recovering to near pre-restriction levels by the end of the year. The difference in rate of change in mean weekly anti-HCV, RNA and genotype testing rates (slope of the curve) post- vs pre-restrictions was also statistically significant (anti-HCV: +1.35 tests per 100 000 population, $P < .0001$; RNA: +0.11 tests per 100 000 population, $P < .001$; genotyping: +0.09 tests per 1 000 000 population, $P < .05$) (Table 1). There was a slight shift in HCV testing towards females and persons aged 30 to 39 years once COVID-19-related restrictions were implemented (Supplementary Table S1).

3.2 | First-time HCV-positive diagnosis rates

Estimated mean weekly first-time HCV-positive diagnosis rates per 1 000 000 population followed a pattern matching that of average weekly HCV RNA and genotype testing rates: declining gradually prior to 2020, falling rapidly after COVID-19 related

TABLE 1 Segmented regression analysis of changes in HCV testing following the introduction of COVID-19-related public health measures in British Columbia in March, 2020

Test type	Unit	Baseline mean weekly rate pre-restrictions[a]		Change in mean weekly rates (slope) pre-restrictions[a]		Change in level of mean weekly rates when restrictions were introduced[a]		Difference between slopes (change in mean weekly rates) post- vs pre-restrictions[a]	
		Estimate		Estimate	*P*-value	Estimate	*P*-value	Estimate	*P*-value
All HCV tests	Tests per 100 000 population	124.6		0.02	.64	−62.3	<.0001	1.45	<.0001
Anti-HCV tests	Tests per 100 000 population	113.4		0.05	.17	−58.7	<.0001	1.35	<.0001
HCV RNA tests	Tests per 100 000 population	12.3		−0.03	<.0001	−4.1	<.0001	0.11	<.0001
HCV genotyping	Tests per 1 000 000 population	12.8		−0.06	<.0001	−2.7	<.01	0.09	.02

Abbreviations: COVID-19, coronavirus disease 2019; HCV, hepatitis C virus; RNA, ribonucleic acid.

[a]Pre-restrictions: calendar week 1 of 2018 to calendar week 11 of 2020; Restrictions imposed during calendar week 12 of 2020; Post-restrictions: calendar week 13 to calendar week 53 of 2020.

public health measures were put in place and then recovering to near pre-restriction levels by the end of the year (Figure 2A). The majority of first-time HCV-positive diagnoses within the BCCDC PHL system were made with anti-HCV tests. As anti-HCV testing rates were changing alongside first-time HCV-positive diagnoses, we also assessed the trend in proportion of weekly first-time anti-HCV-positive diagnoses per weekly anti-HCV tests (first-time anti-HCV positivity rate). Estimated mean weekly first-time anti-HCV-positivity rates declined steadily between calendar week 1 of 2018 and calendar week 11 of 2020 ($P < .0001$) and fell by 2.7 first-time anti-HCV-positive tests per 10 000 anti-HCV tests in calendar week 12 of 2020 ($P = .53$) (Figure 2B, Table 2). The difference in rate of change in mean weekly first-time anti-HCV positivity rates (slope of the curve) post- vs pre-restrictions was not statistically significant ($P = .78$). No major changes were observed in the characteristics of individuals testing HCV-positive for the first time postrestrictions (Supplementary Table S2).

3.3 | First-time HCV RNA-negative testing rates following first-time HCV-positive diagnoses

To estimate trends in progression towards clearing the virus, either spontaneously or following treatment, we assessed the proportion of mean weekly first-time HCV RNA-negative tests following a first-time HCV-positive diagnosis as a percentage of mean weekly HCV RNA tests. Prior to calendar week 12 of 2020, there was a gradual but statistically non-significant increase in the mean weekly percentage of first-time HCV RNA-negative tests following a first-time HCV-positive diagnosis ($P = .12$) (Figure 3, Table 2). These average weekly testing rates dropped slightly as public health measures came into effect in calendar week 12 of 2020 ($P = .68$) and continued to decline steadily until the end of 2020. Despite the reversal in trend following week 12 of 2020, the difference in the rate of change in mean weekly percentage of first-time HCV RNA-negative tests (slope of the curve) post- vs pre-restrictions was not statistically significant ($P = .21$) (Figure 3, Table 2).

4 | DISCUSSION

In this study, we describe the impact of public health measures to control COVID-19 on HCV testing and first-time HCV-positive diagnoses in BC. First-time RNA-negative testing following the first HCV-positive test was assessed as a percentage of all RNA testing episodes as a measure of progression towards clearing the virus. Before COVID-19-related public health measures came into effect, mean weekly anti-HCV testing rates remained relatively stable, contrasting with mean weekly HCV RNA and genotype testing rates which declined steadily. Mean weekly HCV testing rates dropped rapidly across the test types with the implementation of COVID-19-related measures, recovering at varying rates to near pre-restriction levels by the end of the year. Mean weekly first-time HCV-positive diagnosis rates followed an identical pattern, although the fall in HCV positivity rates observed with the imposition of COVID-19-related public health measures was not statistically significant. In contrast, the mean weekly percentage of first-time HCV RNA-negative tests, which were increasing steadily prior to the introduction of public health measures in calendar week 12 of 2020, fell slightly soon afterwards and then maintained a gradual downward trajectory until the end of the year.

Our findings support those of others showing large reductions in HCV testing as a result of measures put in place to control the spread of SARS-CoV-2 worldwide.[15-17] In a survey conducted by the World Hepatitis Alliance (WHA), which included 132 respondents representing hepatitis service providers and civil society organizations from 32 countries across the globe, 64% of respondents reported disrupted access to viral hepatitis testing among HCV-positive

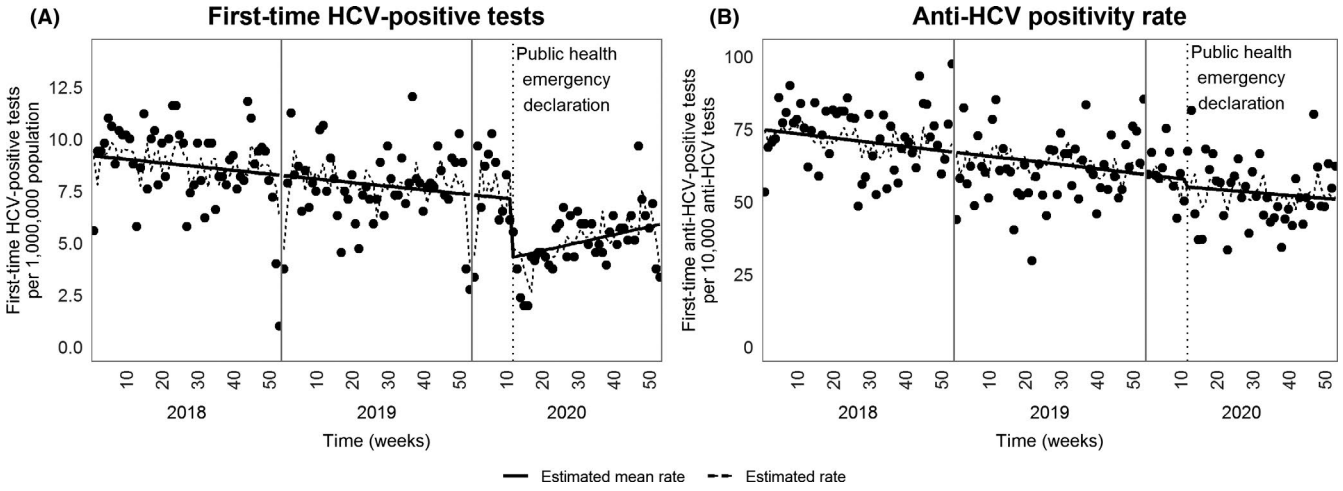

FIGURE 2 Weekly first-time HCV-positive rates in British Columbia, 2018-2020. A, First-time HCV-positive testing rates per 1 000 000 population. This includes first-time HCV-positive diagnoses by anti-HCV, RNA and genotype testing. The majority of first-time HCV-positive diagnoses in BC public health laboratory system are made through anti-HCV testing. B, Anti-HCV positivity rates. This represents the proportion of anti-HCV tests that involved a first-time anti-HCV-positive diagnosis. HCV, hepatitis C virus

TABLE 2 Segmented regression analysis of changes in HCV testing outcomes following the introduction of COVID-19-related public health measures in British Columbia in March, 2020

		Baseline mean weekly rate pre-restrictions[a]	Change in mean weekly rates (slope) pre-restrictions[a]		Change in level of mean weekly rates when restrictions were introduced[a]		Difference between slopes (change in mean weekly rates) post- vs pre-restrictions[a]	
Outcomes	Unit	Estimate	Estimate	*P*-value	Estimate	*P*-value	Estimate	*P*-value
First-time HCV-positive tests	First-time HCV-positive tests per 1 000 000 population	9.2	−0.02	<.01	−2.9	<.001	0.06	.05
First-time anti-HCV positivity rates	First-time anti-HCV-positive tests per 10 000 anti-HCV tests	74.9	−0.15	<.0001	−2.7	.53	0.04	.78
Percentage of first-time RNA-negative tests after a first-time HCV-positive diagnosis	First-time RNA-negative tests per 100 RNA tests	14.3	0.01	.12	−0.5	.68	−0.06	.21

Abbreviations: COVID-19, coronavirus disease 2019; HCV, hepatitis C virus; RNA, ribonucleic acid.

[a]Pre-restrictions: calendar week 1 of 2018 to calendar week 11 of 2020; Restrictions imposed during calendar week 12 of 2020; Postrestrictions: calendar week 13 to calendar week 53 of 2020.

patients during the COVID-19 pandemic.[16] Major reasons for lack of testing included avoidance because of COVID-19-related concerns (65%) and testing facility closures (46%). At the Boston Medical Center in the United States, resource reallocation to accommodate COVID-19 patients resulted in a 50% decrease in HCV testing and a 42% decline in new HCV diagnoses, with larger reductions in testing (−72%) and new diagnoses (−63%) at ambulatory clinics within the Center.[15] In our population-based study, similar decreases in HCV testing and new HCV diagnosis rates were observed immediately following the introduction of province-wide public health measures in BC, although these rates rebounded to near pre-restriction levels by December 2020. This recovery in testing rates is encouraging as it suggests some re-engagement with healthcare despite ongoing restrictions on non-essential travel and gatherings. Interestingly, although first-time HCV-positive diagnoses declined substantially soon after the imposition of public health measures in BC, minimal impact on the trajectory of anti-HCV positivity rates was observed, suggesting that a similar pool of at-risk individuals was being tested post- vs pre-restrictions despite the decreased rate of anti-HCV testing beginning in calendar week 12 of 2020. Further evaluation is needed to understand the impact of these reductions in HCV testing and diagnosis rates on health outcomes within the province.

Some reports of restricted access to HCV therapies and delayed HCV treatment initiation because of COVID-19 were made by WHA survey respondents from various parts of the world.[16] Although treatment initiation was not assessed in this study, the observed decline in HCV RNA testing could have affected HCV treatment initiation and SVR assessment within the province, as was observed in England.[17] Thus, some HCV-positive individuals may have delayed treatment initiation and could potentially be lost to follow-up during this interval. Furthermore, the reversal of the steadily increasing trend in first-time RNA-negative testing episodes after the first recorded HCV-positive test, an indicator of spontaneous clearance or progression towards SVR, in the weeks following the introduction of COVID-19-related public health measures despite the rebound in RNA testing during this time period may be indicative of reduced detection of spontaneous clearance, decreased on-treatment RNA testing and/or decreased SVR rates, amongst others. Additional assessment is required to better characterize the affected steps of the care cascade and to better understand the implications for BC's HCV elimination efforts.

The use of population-level testing data was a major strength of this study. This study was also strengthened by the adjustment for autocorrelation in this interrupted time series study design. However, we were unable to assess HCV treatment initiation, spontaneous clearance and SVR, which are key steps of the cascade of care. As treatment data becomes available, we will be able to construct an HCV care cascade to better describe the scope of the impact of COVID-19-related public health measures on HCV care in BC. Data on key at-risk groups, including people who inject drugs, people experiencing homelessness, and people with low socioeconomic status, were not available for this study. Future studies should address the impact of service disruptions within these groups,

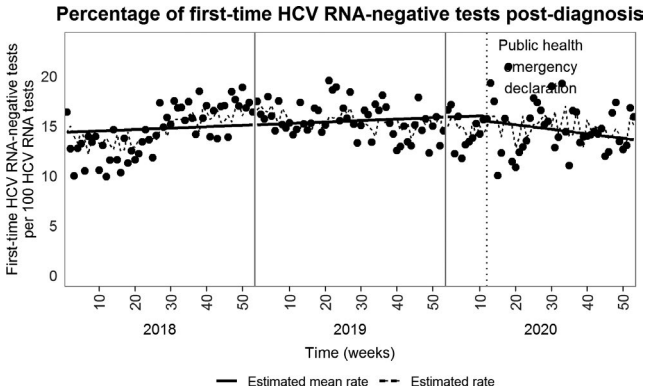

FIGURE 3 Weekly proportions of first-time HCV RNA-negative testing episodes following a first-time HCV-positive diagnosis in British Columbia, 2018-2020. This shows the proportion of HCV RNA tests that represented the first RNA-negative test result following a first-time HCV-positive diagnosis within the BC Public Health Laboratory system. HCV, hepatitis C virus; RNA, ribonucleic acid

given the broader implications for risk of HCV infection and/or re-infection.

Our findings depict major disruptions in HCV testing, new diagnoses and first-time RNA-negative testing episodes within BC after restrictions on travel and mass gatherings came into effect in March, 2020. The increased perception of personal risk of SARS-CoV-2 infection among British Columbians, both among care providers and care seekers, coupled with the systemic barriers generated by these restrictions were among the likely causes of these large declines in testing and diagnosis.[15,16] Without intervention, these service disruptions may serve to broaden existing gaps in the HCV care cascade in the province and potentially increase the rates of advanced liver disease and liver-related mortality among persons living with HCV within the province in the long-term.[31] It is therefore imperative that persons lost to follow-up following restrictions, many of whom are likely marginalized individuals, are re-engaged into the healthcare system without compromising their safety. Leveraging the rapid advancements in healthcare that emerged as a result of the COVID-19 pandemic, such as the widespread adoption and acceptance of telemedicine, could provide avenues for linkage with HCV care as efforts to control the spread of SARS-CoV-2 continue.[32] Failure to do so may undermine the progress that has been made in HCV care provincially and prevent BC from eliminating HCV as a threat to public health by 2030.

ETHICS APPROVAL STATEMENT

This study was performed under the public health surveillance mandate of the BCCDC and did not require approval from an ethical review board.

DISCLAIMER

All inferences, opinions and conclusions drawn in this publication are those of the authors, and do not necessarily reflect the opinions or policies of the Data Steward(s).

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CONFLICT OF INTEREST

MK has received grant/research support from Roche, Merck, Siemens, Boeringer Ingelheim and Hologic, Inc. SB has spoken and consulted for Gilead Sciences Canada Inc and AbbVie Canada. The remaining authors have no conflicts of interest to declare.

DATA AVAILABILITY STATEMENT

The data that support the findings are from the British Columbia provincial surveillance system and are not publicly available. Access to the data may be provided through the British Columbia Centre for Disease Control Institutional Data Access process to researchers who meet the criteria for accessing the confidential data.

ORCID

Mawuena Binka https://orcid.org/0000-0002-9370-1708
Sofia Bartlett https://orcid.org/0000-0003-0699-2250
Héctor A. Velásquez García https://orcid.org/0000-0002-0764-4664

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SUPPORTING INFORMATION

Additional supporting information may be found in the online version of the article at the publisher's website.

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