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Article title:
The 9th Canadian Symposium on Hepatitis C Virus: Advances in HCV research and treatment towards elimination

Running title:
The 9th Canadian Symposium on HCV

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Abstract:
Hepatitis C virus (HCV) elimination has evolved into a coordinated global effort. Canada, with over 250,000 individuals chronically infected, is among the countries leading this effort. The 9th Canadian Symposium on HCV held in February 2020 thus established and addressed its theme, "Advances in HCV research and treatment towards elimination", by gathering together basic scientists, clinicians, epidemiologists, social scientists and community members interested in HCV research in Canada. Plenary sessions showcased topical research from prominent international and national researchers, complemented by select abstract presentations. This event was hosted by the Canadian Network on Hepatitis C (CanHepC), with its support from the Public Health Agency of Canada and the Canadian Institutes of Health Research, and in partnership with the Canadian Liver Meeting. CanHepC has an established record in HCV research by its members and its advocacy activities to address the care, treatment, diagnosis, and immediate and long-term needs of those affected by HCV infection. Many challenges remain in tackling chronic HCV infection, such as the need for a vaccine, difficult to treat populations or unknown aspects of patient subgroups including pregnant women and children, vulnerable people, and issues distinct to our Indigenous peoples. There is also increasing concern about long-term clinical outcomes after successful treatment, with the rise in co-morbidities such as diabetes, cardiovascular disease, fatty liver disease and remaining risk for hepatocellular carcinoma in cirrhotic individuals. This symposium addressed these topics in highlighting research advances that will collectively play an important role in eliminating HCV and minimizing subsequent health challenges.

Keywords:
biomedical; CanHepC; clinical; epidemiological; hepatitis C virus; people who inject drugs; public health; social sciences

INTRODUCTION

The hepatitis C virus (HCV) affects an estimated 250,000 individuals in Canada (1, 2). The current goal of the World Health Organization (WHO) is to eliminate viral hepatitis as a major global public health threat by 2030 (3). Nowadays, direct-acting antiviral (DAA) therapies make treating HCV cases highly safe, well-tolerated and efficient. Sustained virologic response (SVR) can be achieved within 8-24 weeks using the latest available DAAs in over 95% of cases, an impressive advance compared to traditional interferon-based therapies (4, 5). However, many challenges still linger regarding prevention, diagnosis, and treatment across the country. Improving HCV diagnosis and prevention strategies and vaccine development thus remain primary goals in the effort towards elimination.

This article consolidates the highlights of the 9th Canadian Symposium on HCV (CSHCV), a conference co-chaired by Drs Curtis L. Cooper and Angela M. Crawley (Ottawa Hospital Research Institute, Ottawa, Canada). This event highlighted recent accomplishments and challenges in HCV vaccine development and related studies, presented population health studies aiming to inform strategies, shed light on HCV infection and treatment in pregnancy and children, and considered health services studies which included an update on the *Blueprint to inform hepatitis C elimination efforts in Canada* (referred to herein as "the *Blueprint"*).

THE CANADIAN NETWORK ON HEPATITIS C (CANHEPC)

Having evolved in 2015 from the National Canadian Institutes of Health Research (CIHR) Research Training Program in Hepatitis C (NCRTP-HepC, established in 2003), CanHepC expanded its training mandate to become a national collaborative HCV research network. It is a recipient of ongoing support from the CIHR, the Public Health Agency of Canada (PHAC), and non-governmental (e.g. the Canadian Liver Foundation), industry, community and private organizations. Collectively, the NCRTP-HepC and CanHepC have supported 120 graduate and postdoctoral fellowships and 90 summer studentships since 2003.

THE 9TH CSHCV

The NCRTP-HepC and subsequently CanHepC brought together HCV researchers and community members via the past eight annual symposia (6-11). The 9th CSHCV was held on the 28th of February 2020 in Montréal, Québec as a joint conference with the annual Canadian Liver Meeting. This iteration of the CSHCV hosted over 224 attendees and featured speakers from across Canada and the globe, spanning the four CIHR pillars of health research: (a) biomedical, (b) social, cultural, environmental, and population health, (c) clinical, and (d) health services. The symposium also featured a video premiering and panel discussion session of the *Connecting With Care* film project on low-threshold models of HCV care across Canada. Recordings of all presentations from this and prior symposia can be accessed through the CanHepC YouTube channel (https://www.youtube.com/channel/UCUgCySYhpXIUuqiaQS_rGJw/playlists).

Biomedical research: HCV vaccine development and related studies

Although HCV infection can be cleared through DAA therapy, chronic infection remains a major cause of liver fibrosis, cirrhosis and end-stage liver disease with increased risks of hepatocellular carcinoma. The development of HCV vaccines and related studies remain thus a major theme of HCV research and is the focus of the biomedical sciences session. Recently, a phase I/II human clinical trial with Okairos/GSK tested an adenoviral vector and Modified Vaccinia boost approach to HCV vaccine development, but it was ultimately unsuccessful in preventing chronic HCV infection (NCT01436357).

Dr Ellie Barnes (University of Oxford, Oxford, UK) presented her group's work on adenovirus (Ad)-based T cell vaccines using chimpanzee AdCh3 and human AdHu6 adenoviral strain vectors. Non-structural proteins from HCV genotype 1b were engineered into AdCh3 and AdHu6 vectors and used to immunize rhesus macaques. The priming injections yielded strong responses, while poorly responsive boosts were replaced by Modified Vaccinia Ankara vectors, a switch inspired by the malaria vaccine field. Phenotyping confirmed strong functional and proliferative T cell responses to immunization (12). However, initial human trials vaccinating for HCV 1b induced weaker responses against genotypes 1a, 3a, and 4a, while vaccination with T cell epitope KLSGLGINAV yielded no significant cross-reactivity with other common KLVxxGxNAV

epitopes (13). To overcome this challenge, vectors using conserved sequences were tested in mice with promising results (14). Dr Barnes expects this approach to greatly improve vaccine cross-reactivity in future animal studies and human trials. Dr Barnes also highlighted the potential use of class-II invariant chain as an adjuvant to promote antigen presentation and improve T cell response.

Generating strong cross-reactive responses is also a challenge for antibody vaccine development, as outlined by Dr John Law (University of Alberta, Edmonton, Canada), who continued the session by presenting his work with Dr Michael Houghton on a recombinant gpE1/gpE2 vaccine. Neutralizing antibodies from chimpanzees vaccinated against HCV genotype 1a also conferred protection against HCV genotypes 2a, 3a, 4a, 5a and 6a. This was confirmed in human trials, albeit with higher variation between individuals (15). To combat HCV genotype differences and epitope variations, Dr Law highlighted the importance of generating polyclonal responses and targeting conserved viral mechanisms such as binding and entry. He also noted that the goal is not necessarily to prevent acute infection but rather to reduce chronicity, which is a viable strategy due to the mild consequences of acute infections. Immunizing chimpanzees with gpE1/E2 reduced rates of chronicity from 63% to 16% (16). Dr Law finally emphasized the importance of proper antigen purification and preserving antigen conformation in vaccine production. He also highlighted the potential of using combined vaccination methods (e.g. combining T cell-mediating vaccines) to enhance protective immune responses.

Effective vaccine responses rely on a healthy host immune response. However, mounting evidence suggests there is a multifaceted impairment of the immune system induced by chronic infection. Dr Angela M. Crawley (Ottawa Hospital Research Institute, Ottawa, Canada) continued the session by emphasizing the effect of liver fibrosis severity on the immune response, as studies to-date are mostly performed in T cells from infected individuals with minimal liver fibrosis or are focused on existing virus-specific memory responses. Dr Crawley has shown that bulk circulating and liver-derived CD8+ T cells from HCV-infected individuals with advanced liver fibrosis express less anti-apoptotic Bcl-2 protein upon stimulation with cytokine interleukin-7 compared to those with minimal fibrosis (17). In addition, activated circulating CD8+ T cells express more lytic proteins such as perforin in advanced fibrosis compared to individuals with minimal fibrosis and healthy controls (18). This hyperfunction was coupled with a sustained systemic inflammation that persists long after DAA-mediated HCV clearance (18). RNA sequencing of these study groups revealed 444 differentially expressed genes, many of which are involved in T cell activity, including T cell receptor signalling, actin mobilization, nuclear division, cell cycle, and cytotoxicity (Crawley AM, unpublished). This suggests the involvement of cell cycle anomalies, metabolism, and overall non-specific T cell activation in promoting CD8+ T cell dysfunction, all of which will be investigated in ongoing studies.

The residual effects of HCV infection may also extend beyond immune dysfunction, as introduced by graduate student Hannah L. Wallace (Dr R. Russell lab, Memorial University, St. John's, Canada) in the final presentation of the session. In HCV-infected hepatocytes in vitro, cell death was mediated by apoptosis through caspase-3 activation, or by inflammasome-mediated pyroptosis through NOD-, LRR- and pyrin domain-containing protein 3 (NLRP3) and its downstream activation of caspase-1 and gasdermin D (GSDM-D) (Russell R, unpublished). In addition, approximately 5% of hepatocytes express caspase-1 and caspase-3 simultaneously, suggesting the involvement of both apoptosis and pyroptosis. To investigate this phenomenon, NLRP3, GSDM-D and caspase-3 knock-out hepatocytes were infected with HCV. GSDM-D knock-outs yielded an increase in caspase-3 expression while caspase-3 knock-outs yielded a decrease in caspase-1 expression, suggesting cross-talk between the apoptotic and pyroptotic pathways. In addition, both HCV core protein levels and focus-forming titres were significantly lower in the cultures of knock-out cells compared to wild-type (WT) cells. While extracellular titres were higher than intracellular titres in cultures of HCV-infected WT cells, the reverse was observed in knock-out cells, suggesting cell death promotes HCV pathogenesis. The concept that HCV is, on occasion of cell death, a cytopathic virus, is in contrast with current consensus that HCV is a non-cytopathic virus. Interestingly, Wallace also noted that many uninfected hepatocytes surrounding cells undergoing death were also apoptotic and pyroptotic (i.e. increased caspase-1 and caspase-3 activity), further supporting evidence of bystander effects from HCV-infected cells (19).

Understanding the cellular and mechanistic consequences of HCV infection on hepatocytes and immune cells, as well as their interplay through various stages of infection and liver disease progression, is vital for developing a potent and reliable HCV vaccine, and restoring liver and immune health of affected individuals.

Social, cultural, environmental, and population health research: HCV in underserved populations – modelling and real-life data to inform strategies

The social, cultural, environmental and population health research session focused on modelling and real-life data to inform strategies for reaching HCV elimination among underserved populations, including people who inject drugs (PWID) and those with experience in the prison system.

Dr Natasha Martin (University of California San Diego, San Diego, USA) provided insights from her HCV infection modelling research, highlighting how scaling up harm reduction efforts in parallel with HCV treatment intervention is the most efficient and cost-effective strategy for achieving HCV elimination (20-22). Unfortunately, despite its far-reaching benefits, global coverage of harm reduction services remains poor. Less than 1% of all PWID reside in countries with available harm reduction interventions such as a high-coverage of needle syringe programs (NSP) and opioid agonist therapy (OAT) (23, 24). In addition, addressing stimulant usage is a growing priority as stimulant injection among PWID is associated with a two- to three-fold increased risk in HIV incidence and HCV prevalence compared to people who do not primarily inject stimulants (25). However, unlike with opiates, effective harm reduction interventions for stimulants are still lacking.

Emerging evidence indicates that SVR from DAA therapy reduces mortality risk (26-28). Indeed, since the introduction of DAA therapies in British Columbia, Canada in 2014, liver-related mortality rates among HCV-infected individuals have decreased. However, trends in drug-related mortality rates have increased, suggesting that additional interventions post-SVR are required (29). Dr Prince Adu (University of British Columbia, Vancouver, Canada) presented work from the *British Columbia Hepatitis Tester's Cohort*, using data collected from 1990-2017 to explore whether OAT provides additional benefits for HCV+ individuals with ongoing substance use post-SVR. Relative to individuals without SVR and not on OAT, the effect of SVR coupled with OAT compared to SVR alone was associated with major reductions in all-cause mortality (88% vs 95%), liver-related mortality (94% vs 98%) and drug-related mortality (75% vs 85%). This key finding that OAT is associated with further mortality risk reductions among those who achieve SVR supports the urgent need for more extensive implementation of integrated health services offering harm reduction such as OAT alongside HCV care.

Approximately 25% of people with experience in the prison system have been infected with HCV, and 20% of Canadian inmates report a history of injection drug use prior to incarceration (1, 30). Dr Nadine Kronfli (McGill University, Montréal, Canada) provided a national overview of the delivery of HCV care in Canadian correctional facilities, highlighting the major disparities in the provision of HCV care in federal prisons compared to their provincial and territorial counterparts. She advocated for an evidence-based approach to HCV micro-elimination in correctional facilities, including: (a) adopting systematic opt-out screening, (b) providing universal access to DAA therapies and improved linkage to care programs, and (c) expanding prison-based NSP, OAT and other harm reduction services in correctional facilities. Forrest Gallagher (Dalhousie University, Halifax, Canada) then presented how community- and corrections-based point-of-care testing is being integrated into the Nova Scotia provincial HCV elimination framework. To overcome gaps in HCV care at a provincial level, point-of-care testing will be integrated into existing harm reduction service points and the correctional system. These integrations will consist of simplified diagnostic algorithms, increased patient engagement processes, and HCV capacity building in the community. At the community-level, point-of-care testing was successfully implemented with 163 tests offered to date. Further engagement will be required to conduct implementation studies of point-of-care testing in correctional facilities where testing data is not systematically collected.

Community session: Connecting with care – Canadian models of hepatitis C care, a film preview and panel discussion

This highly impactful iteration of the CSHCV featured the premiering of three films from the *Connecting With Care* project launched by the International Network of Hepatitis C and Substance Users in collaboration with the Community AIDS Treatment Information Exchange (CATIE), CanHepC, and various partners from participating communities. The three films, directed by Australian filmmaker, storyteller and communications strategist, Conor Ashleigh, focused on providing insight into community-based models of HCV care and treatment in three distinct regions across the country: the Ahtahkakoop Cree Nation, in collaboration with the *Know Your Status* hepatitis C program; the city of Montréal, with programs at Dopamine and Centre Sida Amitié; and the city of Toronto, with the *Toronto Community Hepatitis C Program*. The accompanying panel discussion was organized and moderated by CATIE's Hepatitis C Knowledge Exchange Director, Melisa Dickie. The session allowed the community members featured in the films to share their experiences in-person on the presented models of care.

The films and ensuing discussion highlighted that the successful implementation of the care models depends highly on understanding local challenges. In the remotely located Ahtahkakoop Nation, for example, there was a need to improve access to care, which was achieved by bringing care providers on-site instead of expecting clients to travel to urban care centres. In Montréal and Toronto, there was a need to reinstate client trust in the health care system, as many PWID and infected individuals seeking care were often shunned by society and the systems currently in place. This was achieved by developing personalised care at local community centres and facilities that often have pre-established relations with the affected individuals. In all cases, there was a need to implement a model of care that is flexible and adaptive. After completing a treatment and/or rehabilitation program, many individuals have in turn become hired as peer-to-peer community workers at these sites, helping new clients, further refining the models and tailoring future care with their gained experience. This ensures that those seeking care feel adequately included into a program, reduces program abandonment, and improves overall participation and outcomes.

The session emphasized that further improvement of front-line responses to HCV and drug user health heavily relies on the active involvement of individuals and communities with lived experiences.

Clinical research: Hepatitis C infection in pregnancy and children

The clinical research session focused on HCV infection in pregnancy and children. These populations are often neglected in clinical trials due to added safety considerations and ethical concerns. It is acknowledged that both mother and child should be duly considered when testing drugs in a pregnant population and paediatric trials should ensure informed consent is acquired given the more vulnerable nature of this population.

Dr Jonathan R. Honegger (Nationwide Children's Hospital, Columbus, USA) discussed rationales regarding the use of DAA therapy to treat HCV infection during pregnancy. The estimated prevalence of HCV among pregnant woman in Canada is 0.5-0.9% and is expected to increase as rates of HCV infection in young adults rise (31-33). The rate of vertical transmission was estimated at approximately 5.8%, and HCV infection has been related to increased risks of intrahepatic cholestasis and gestational diabetes mellitus in pregnant women, as well as low birth weight and prematurity in infants (34-38). Treatment during pregnancy may improve these outcomes in addition to preventing mother-to-child transmission (MTCT), development of chronic HCV infection in the mother, and horizontal transmission. Studies demonstrated that mothers tend to prioritize the prevention of vertical transmission by favouring treatment during pregnancy despite current limited data on safety and efficacy (39). Phase I trial of ledipasvir/sofosbuvir (LDV/SOF) during pregnancy showed a 12-week SVR (SVR12) achievement in all mothers (n=9), with mild side effects (40). None of the infants were infected and all demonstrated normal birth exams. An additional study administering DAA during pregnancy also demonstrated 100% SVR with only mild maternal adverse effects and no teratogenic signals in children (41). Dr Honegger highlighted the need for additional trials to understand the effects of DAAs on umbilical cord blood and breast milk, as well as the need for larger sample sizes to analyse MTCT and pregnancy outcomes, including the long-term health of the child. There is also a need for more extensive randomized controlled trials to control for other factors including opioid use.

Dr Simon Ling (The Hospital for Sick Children, Toronto, Canada) presented data on the use of DAA therapy in pediatric settings. The prevalence of HCV infection among children is relatively low but still affects

3.5 million children worldwide (42). The consequences of chronic HCV infection in children include liver fibrosis, extrahepatic manifestations, social stigmatization and impaired quality of life, all of which can be improved with curative HCV treatment for both children and their caregivers (43, 44). SVR12 rates are very high in clinical trials involving children, including real world studies for children infected with HCV genotype 4 (45-55). The few cases where children failed to achieve SVR12 were explained by treatment discontinuation or loss to follow-up, except for a single patient with cirrhosis who relapsed despite a 12-week treatment with LDV/SOF (46). When comparing treatment of children aged 6 to 18 years, treating younger was more cost-effective and reduces the risk of end stage liver disease and death (56). Further rationale in favour of treating children include prevention of transmission before children begin engaging in high-risk activities. Dr Ling highlighted the remaining challenges in this field, which include improving methods of identifying infected children and ensuring access and coverage to medication for children of all ages regardless of HCV genotype.

Additional works were presented by Dr Brian Conway (Vancouver Infectious Disease Centre, Vancouver, Canada) and postdoctoral fellow Dr Evan Cunningham (The Kirby Institute of the University of New South Wales, Sydney, Australia). Dr Conway discussed the impact of treatment regimen adherence on the efficacy of sofosbuvir/velpatasvir (SOF/VEL) therapy. Data were extracted from the database of the Canadian Network Undertaking Against Hepatitis (CANUHC). Within the CANUHC cohort, self-reported adherence was high, as was the rate of achieving SVR at 12 weeks post-treatment initiation (SVR12) (98.7%) with the use of SOF/VEL. Suboptimal adherence (<90%) was rare (10/152) and was not associated with treatment failure nor with any specific demographic profile. Nevertheless, all ten non-adherent individuals, including three who demonstrated less than 75% adherence, achieved SVR12. These data validate use of this drug regimen in populations facing obstacles to treatment adherence. Dr Cunningham presented data on HCV reinfection incidence and associated factors among people with recent injection drug use or people currently receiving OAT. Eight cases of reinfection were confirmed via viral sequencing of 177 individuals post-SVR, for an incidence of 3.1/100 person-years (95% CI 1.6-6.3) overall. Younger age and needle/syringe sharing were associated as potential risk factors for HCV reinfection. Dr Cunningham concluded that DAA treatment has the potential to be coupled with safe injection practices and uptake of harm reduction measures.

Health services research: Blueprint update and implementation

The health services research section began with an update on the *Blueprint* delivered by the Chairman of the *Blueprint* writing committee, Dr Jordan J. Feld (University of Toronto, Toronto, Canada). As a policy tool, the *Blueprint* is intended to complement the PHAC framework for the elimination of sexually-transmitted blood borne infections (1, 57). It provides guidance, but more specifically is meant to sketch out measurable objectives and tangible goals for achieving WHO HCV elimination targets (3). It suggests activities and good practices that should be adopted, advocates for a research agenda, and uses an equity lens for representing and respecting priority populations living with HCV in Canada. The publication of the *Blueprint* was not the end goal of this effort, but rather a means to stimulate and guide Canadian provinces and territories to develop their own specific elimination plans. Recent modelling studies profiled the progress of high-income countries towards meeting the WHO HCV elimination targets and found that Canada has made significant effective changes over the past few years (58, 59). For example, it was found that Canada's elimination trajectory prior to the *Blueprint* update was beyond 2050 but recent findings demonstrate that Canada is now on track to meet the WHO's 2030 target. Some of this change is due to increased public health and clinical practice actions, including increased testing and intensified efforts for linkage to care. But most of this change is likely due to the availability of better data to measure and estimate stages of the HCV cascade of care, since previous estimates were fraught with uncertainty. Increased treatment rates could be due to a readily available patient population to put on treatment, yet it was mentioned that this will be hard to maintain in subsequent years as the disease becomes more concentrated among harder to reach groups. To maintain performance, intensified efforts are needed throughout the entire cascade from diagnosis and linkage to care, to post-SVR surveillance. Expanded preventative strategies should be employed, including harm reduction and education to keep incidence low, and post-SVR surveillance should be incorporated for continual monitoring of advanced liver diseases and to minimize risk of re-infection. The next steps for the *Blueprint* are to encourage the incorporation

of these recommendations with an intensified focus on local and regional health care institutions and communities across the country. A sustained push for increased knowledge transfer and exchange at regional meetings is needed to not only identify barriers and challenges, but also to find local solutions. The upcoming national *Blueprint* elimination summit in 2021 will evaluate and report these efforts and update the WHO on Canada's progress towards HCV elimination.

As an example of regional application of *Blueprint* recommendations, Dr Lisa Barrett (Dalhousie University, Halifax, Canada) presented the HCV elimination efforts in Canada's smallest province, Prince Edward Island (PEI). The province initially adopted a model of care paradigm at the treater level based on consorted efforts from health care practitioners, but then transitioned and integrated their focus to be more in line with the *Blueprint* (60). Dr Barrett emphasized that uncoordinated care delivery by clinicians and public health officials does not work and advocated for greater connectivity between PEI and other provinces alongside industry partners. The lack of access to curative therapies was an initial barrier in the province, where industry played a crucial role before treatment funding was switched over to provincial support (61). Provincial coordinating points now facilitate care delivery and triage to appropriate providers, demonstrating the importance of having dedicated staff to facilitate clinical and public health partnerships. The ability to access medication in a comfortable and conducive space where it is wanted and needed by clients underscores the importance of community engagement via peer support and the sharing of personal testimonies. The need for more inclusive prescription guidelines such as unrestricted treatment regardless of fibrosis staging, and sobriety requirements was also highlighted as an important factor that helps in elimination efforts, which includes expanded medication stewardship to opioid substitution therapy clinics, psychiatry, and long-term care facilities (62). Improvements to elimination efforts implemented after 2016 includes the involvement of the justice system in screening and harm reduction activities. More recent changes include enhanced models of care facilitated by self-referral mechanisms for HCV programs. In small communities, these initiatives are important for mitigating the stigma faced by marginalized groups. Dr Barrett ended her presentation by stating that PEI has made great strides towards HCV elimination over the past few years but warns that the remaining 20% of infected individuals will be the most difficult to reach yet necessary to attain elimination goals.

To address the *Blueprint*'s call for information on at-risk populations, presentations by CanHepC trainees concluded the session by reporting on data and research activities among two of the five at-risk pillar groups (i.e. immigrants and immigrant subgroups, and Indigenous populations). Dr Abdool Yasseen (University of Toronto, Toronto, Canada) presented preliminary comparisons of linked laboratory and health administrative data on HBV and HCV mono- and co-infected individuals tested at a centralized public health testing facility in Ontario. By stratifying these infection groups across demographic and clinical factors such as immigration status and place of birth, he showed that immigrants were widely heterogeneous with respect to HCV prevalence. He thus emphasized that the use of culturally distinct, appropriate, and non-stigmatizing approaches to elimination efforts is crucial for effective interventions. He also emphasized the importance of considering possible intersectionality of immigrant populations with other at-risk groups such as PWID or men who have sex with men. Andrew Mendlowitz (University of Toronto, Toronto, Canada) then discussed the process of creating a collaborative partnership between First Nations representatives and academic researchers. The aim of his work is to provide information to inform an assessment of the health and economic burden of HCV infection facing First Nations populations in Ontario. He explained that through partnership between researchers and the Ontario First Nations HIV/AIDs Education Circle (OFNHAEC), local knowledge and cultural understandings are being incorporated into study conception, design, and results interpretation. He reflected on the collaborative research process and how First Nations principles of data governance is engrained in OFNHAEC. This partnership will serve as starting point towards understanding the impact of HCV infection among the First Nations on a provincial scale.

OUTCOMES OF THE 9TH CSHCV

As the overarching theme of the 9th CSHCV, "Advances in HCV research and treatment towards elimination" was discussed. The symposium highlighted recent work on HCV vaccine development and related research, models and strategies of care in underserved populations, insights into HCV treatment in pregnancy

and children, and recent achievements towards HCV elimination. A status update on the *Blueprint* was also provided. This year's symposium emphasized the necessity of maintaining HCV vaccine-related research while concurrently bolstering care and services to be more effective in reaching at-risk populations, with the ultimate goal of reaching national and international HCV elimination targets.

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