CanHepC
Canadian Network on Hepatitis C
Réseau Canadien sur l'Hépatite C

7th Canadian Symposium on Hepatitis C Virus

7ème Symposium canadien sur le virus de l'hépatite C

February 9, 2018 – 9 février 2018

The Intercontinental Toronto Centre, Toronto, ON

Program and Abstracts
Programme et résumés

Table of contents - Table des matières

Welcome Message - Message d'accueil

Dear Colleagues,

We are pleased to welcome you to the 7th Canadian Symposium on the Hepatitis C Virus (HCV).

The advent of highly effective HCV treatments, and their widespread use, has led to great advances in the care of many Canadians afflicted by hepatitis C. However, many individuals living with this viral disease lack access to care. We believe that strengthening communication and supporting interactions between Canadian scientists, clinicians, the affected communities, and policy makers are essential to effectively respond to the challenges of preventing and treating all hepatitis C patients.

The Canadian HCV Symposia have provided an ideal forum for such an exchange. The Canadian Network on Hepatitis C (CanHepC) has contributed to research training and knowledge translation of hepatitis C findings to benefit patients. Importantly, CanHepC has developed a network of motivated and collaborative investigators whose work encompasses the social, behavioural, clinical, and basic sciences. This multidisciplinary collaboration is crucial for the development of programs to eradicate HCV.

We would like to welcome you to the beautiful town of Toronto! We look forward to learning about your exciting research and work in the field of hepatitis C, and discussing how we can shape the future of hepatitis C research and policy in Canada.

Chers Collègues,

Nous vous souhaitons la bienvenue au 7e Symposium canadien sur le virus de l'hépatite C (VHC). L'instauration de traitements hautement efficaces contre le VHC, ainsi que leur utilisation étendue représente un avancement significatif pour plusieurs Canadiens souffrant de l'hépatite C. Cependant, un grand nombre d'individus infectés par ce virus n'ont pas facilement accès au soin de santé. Nous croyons qu'il est primordial de renforcer la communication et les interactions entre les scientifiques, les médecins, les communautés affectées et les responsables politiques afin de répondre aux défis rencontrés pour prévenir et traiter l'hépatite C partout au Canada.

Le symposium canadien sur le VHC représente un forum idéal pour ce type d'échanges. Le Réseau Canadien sur l'Hépatite C (CanHepC) a contribué à la formation en recherche et au transfert de connaissances sur l'hépatite C pour le bénéfice des patients. De manière importante, le CanHepC a développé un réseau de chercheurs motivés collaborant sur des travaux englobant les sciences sociales, comportementales, cliniques et fondamentales. Ces collaborations interdisciplinaires sont cruciales pour le développement des programmes requis pour éradiquer le VHC.

Nous vous souhaitons la bienvenue dans la magnifique ville de Toronto!

Nous avons hâte d'en apprendre plus sur vos recherches et travaux concernant l'hépatite C. Nous discuterons des orientations possibles pour la recherche et les politiques sur l'hépatite C au Canada.
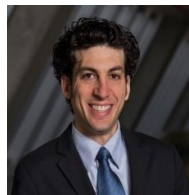
Jordan Feld, MD, MPH   Sonya MacParland, PhD

Biographies of Co-Chairs

Jordan Feld, University of Toronto, Toronto, Canada – Chair

Biography

Jordan Feld, MD, Associate Professor of Medicine, University of Toronto, Ontario, Canada, graduated from medical school at the University of Toronto in 1997 and then completed residency programs in Internal Medicine and Gastroenterology. Following his clinical training, Dr. Feld focused on developing skills in clinical and laboratory research in liver disease, with a particular interest in viral hepatitis. He completed a clinical research fellowship in hepatology and then spent 4 years doing clinical and laboratory research in the Liver Diseases Branch of the National Institutes of Health. He received a Masters of Public Health with a focus on Infectious Diseases as a Sommer Scholar from Johns Hopkins University and has worked extensively abroad, maintaining a strong interest in International Health. Currently, Dr. Feld is clinician-scientist based at the Toronto General Hospital, Toronto Centre for Liver Disease and the McLaughlin-Rotman Centre for Global Health.

Sonya MacParland, University of Toronto, Toronto, Canada – Co-Chair

Biography

Sonya MacParland, Ph.D., Assistant Professor of Immunology, University of Toronto, Ontario, Canada, received her doctoral degree from the Memorial University of Newfoundland in 2010 under the supervision of Dr. Thomas Michalak and then completed her postdoctoral studies in the laboratory of Dr. Mario Ostrowski at the University of Toronto in 2016. Dr. MacParland was an NCRTP HepC/CanHepC trainee from 2006-2013. Dr. MacParland is currently an Assistant Scientist at Toronto General Hospital Research Institute. Her biomedical science research group investigates how liver immune dysregulation drives liver disease development and how the hepatic immune microenvironment can be therapeutically manipulated by nanoparticle-mediated targeted drug delivery in order to slow or reverse ongoing damage and promote liver regeneration.

Program – Programme

Toward Elimination of HCV: How to Get There

07h15 - 08h00	Registration, breakfast Inscription, petit déjeuner
08h00 - 08h15	Welcome and Introductions – Mot de bienvenue **Naglaa Shoukry, Université de Montréal, Montréal, Canada**

Biomedical Research
Co-Chairs: Sonya MacParland & Mohamed Abdel-Hakeem

08h15 - 08h35	Reinfection with Hepatitis C Virus – T Cells to the Rescue? **Georg Lauer, Harvard University, Boston, USA**
08h35 - 08h55	DAA-induced Reversal of Immune Senescence **Lisa Barrett, Dalhousie University, Halifax, Canada**
08h55 - 09h15	Questions/Panel Discussion
09h15 - 09h27	miR-122 does not impact recognition of the HCV genome by innate sensors of RNA but rather protects the 5' end from the cellular triphosphatases, DOM3Z and DUSP11 **Annie Bernier, McGill University, Montréal, Canada**
09h27 - 09h39	Increased usage of a public CD8 T cell clonotype in spontaneously resolved HCV infection **Sabrina Mazouz, CRCHUM, Montréal, Canada**
09h39 - 09h51	Impaired CD8+ T-cell function is associated with liver disease severity in chronic HCV infection and remains unresolved after HCV cure **Angela Crawley, Ottawa Hospital Research Institute, Ottawa, Canada**
09h51 - 10h10	Coffee Break – Pause café

Social, Cultural, Environmental, and Population Health Research
Co-Chairs: Didier Jutras-Aswad & Alexandra King

10h10 - 10h30	Health Systems and HCV Elimination: Overcoming Challenges through a Micro-Elimination Approach **Jeffrey Lazarus, ISGlobal, Hospital Clínic, University of Barcelona**
10h30 - 10h50	Indigenous Data Sovereignty on the Path to HCV Elimination **Jennifer Walker, Laurentian University, Sudbury, Canada**
10h50 - 11h02	Nothing About Us Without Us: The Value of Engaging People With Lived Experience of HCV in all Areas of the HCV Response **Lindsay Jennings, Shujaat Hussain, Suzanne Fish, CATIE**
11h02 - 11h22	Questions/Panel Discussion
11h22 - 11h34	HCV: Bringing care to patients in rural and remote settings **Dustin Dapp, Simon Fraser University, Vancouver, Canada** **Lucy Newman-Hogan, University of Guelph, Guelph, Canada**
11h34 - 11h46	Ontario Hepatitis C education and outreach program with immigrants and newcomers **Fozia Tanveer, CATIE, Canada**
11h46 - 13h30	Lunch and poster session – Diner et présentation des affiches

Clinical Research
Co-Chairs: Valérie Martel-Laferrière & Giada Sebastiani

13h30 - 13h50	NK Cell and T Cell Function During and After HCV **Heiner Wedemeyer, Hannover Medical School, Hannover, Germany**
13h50 - 14h10	Optimal Screening Strategies: It's all About the Local Situation **Jordan Feld, Toronto General Hospital Research Institute, Toronto, Canada**
14h10 - 14h30	Questions/Panel Discussion
14h30 - 14h42	Real-world effectiveness of interferon-free, all-oral direct-acting antivirals in the setting of hepatitis C and HIV co-infection **Carmine Rossi, Research Institute of the McGill University Health Centre, Montreal, Canada**
14h42 - 14h54	All-Oral Anti-HCV Therapy in Injection Drug Users: Updated Real World Data **Arshia Alimohammadi, Vancouver Infectious Diseases Centre, Vancouver, Canada**
14h54 - 15h06	Decreased hepatitis C (HCV) treatment uptake among HIV-HCV co-infected patients with a history of incarceration: Missed opportunities for care **Nadine Kronfli, McGill University Health Centre, Montreal, Canada**
15h06 - 15h20	Coffee Break – Pause café

Health Services Research
Co-Chairs: Brian Conway & Maryam Darvishian

15h20 - 15h40	Use of Data to Drive Global Policy to Eliminate HCV **Homie Razavi, Center for Disease Analysis, Colorado, USA**
15h40 - 16h00	What is needed to eliminate Hepatitis C in Canada? **Naveed Janjua, University of British Columbia, Vancouver, Canada**
16h00 - 16h20	Questions/Panel Discussion
16h20 - 16h32	Decreased confirmation of chronic hepatitis C infections in correctional institutions compared to the community in Ontario **Nagma Grewal, Queen's University, Toronto, Canada**
16h32 - 16h44	Estimation of hepatitis C prevalence in Canada via a two-stage back-calculation algorithm **Abdullah Hamadeh, University of Waterloo, Toronto, Canada**
16h44 - 16h56	Population-level cascade of care for hepatitis C in British Columbia: Differences over time, by gender and birth cohort **Nuria Chapinal, BC Centre for Disease Control, Vancouver, Canada**
16h56 – 17h16	A Framework of a National Hepatitis C Elimination Strategy in Canada **Alison Marshall, University of New South Wales, Australia, CanHepC trainee, Canada**
17h16 – 17h30	Questions & Answers
17h30 – 17h45	CanHepC trainee Awards Ceremony
17h45 – 17h50	**CanHepC Symposium Closing Remarks** Jordan Feld, Sonya MacParland, University of Toronto
17h50 – 18h00	**Canadian Liver Meeting Opening Remarks** Rick Schreiber, University of British Columbia
18h00 – 18h20	HCV Policy in Action: Lessons learned from Portugal **Ricardo Baptista Leite, Member of Parliament, Lisbon, Portugal**
18h20 – 18h30	Questions & Answers
18h30– 19h30	**Canadian Liver Meeting Opening Reception**

Posters can be hung up before lunch time and taken down after mixer

Committees – Comités

Organizing Committee - Comité organisateur

Jordan Feld, University of Toronto, Chair
Sonya MacParland, University of Toronto, Co-Chair

Dan Allman, University of Toronto
Lisa Barrett, Dalhousie University
Suzanne Fish, CATIE
Jason Grebely, University of New South Wales
Naveed Janjua, University of British Columbia
Alexandra King, University of Saskatchewan
Selena Sagan, McGill University
Naglaa Shoukry, Université de Montréal

Mohamed Abdel Hakeem, University of Pennsylvania, Trainee representative

Norma Choucha, CRCHUM, Symposium Coordinator

Session Chairs - Modérateurs de sessions

Biomedical Research
Sonya MacParland, University Health Network
Mohamed Abdel Hakeem, University of Pennsylvania

Clinical Research
Giada Sebastiani, McGill University
Valerie Martel-Laferrière, Centre de recherche du CHUM

Health Services Research
Maryam Darvishian, University of British Columbia
Brian Conway, Vancouver Infectious Diseases Centre

Social, Cultural, Environmental, and Population Health Research
Alexandra King, University of Saskatchewan
Didier Jutras-Aswad, Université de Montréal

Abstract Reviewers - Réviseurs des résumés

Biomedical Research
Angela Crawley, University of Ottawa
Sonya MacParland, University of Toronto
Joyce Wilson, University of Saskatchewan
Che Colpitts, University College London
John Pezacki, University of Ottawa
Amador-Canizares, Yalena University of Saskatchewan
Mohamed Abdel Hakeem: University of Pennsylvania

Clinical Research
Brian Conway, VIDC
Curtis Cooper, University of Ottawa
Valerie Martel-Laferriere, Centre de recherche du CHUM
Marc Bilodeau, Université de Montréal
Alexandra King, University of Saskatchewan
Nazia Selzner, University Health Network
Giada Sebastiani, McGill University
Thomas Michalak, Memorial University

Health Service Research
Naveed Janjua, University of British Columbia
Jason Grebely, University of New South Wales
Rosie Thein, University of Toronto
Alison Marshall, University of New South Wales
Maryam Darvishian, University of British Columbia
Alexandra King, Simon Fraser University

**Social, Cultural, Environmental, and Population Health Research**
Julie Bruneau, Université de Montréal
Gerry Mugford, Memorial University
Sahar Saeed, McGill University
Christina Greenaway, McGill University
Carrielynn Lund, CAAN

Speaker Biographies and Abstracts – Biographies des conférenciers et résumés

Biomedical Research

Georg Lauer, Harvard University, Boston, USA

Biography
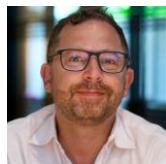
Georg Lauer studied medicine at the universities of Tübingen, Hamburg and Bochum in Germany. He practiced at the university hospital in Bochum for several years in internal medicine, focusing on viral hepatitis, before joining what was then the Partners AIDS Research Center at Massachusetts General Hospital and Harvard Medical School (now the Ragon Institute) for a post doctoral fellowship on HCV immunology with Dr. Bruce Walker. He later became a faculty member at MGH and HMS, where he is now Associate Professor of Medicine in the Gastrointestinal Unit. His research focuses on adaptive immunity in acute and chronic HCV and HBV infection, with a special focus on CD4 and CD8 T cells. Beyond their direct relevance for HBV and HCV disease he is mostly interested in what constitutes protective immunity in humans and in the mechanisms employed by viruses to circumvent the host immune response and establish chronic infection.

Abstract

Reinfection with Hepatitis C Virus – T Cells to the Rescue?

A major challenge for our goal to eliminate hepatitis C virus infection through antiviral therapy is the risk for re-infection in major HCV infected populations, most notably people who inject drugs. In these persons the ability to induce protective immunity that can reliably prevent chronic re-infection would be a critical breakthrough. However, we already know that vaccinating people during chronic infection has limited effects on the HCV-specific T cell response, indicating the challenge we face for inducing immunity in people who already have developed chronic infection. Currently, there is some controversy in the field whether DAA therapies and viral resolution on their own can lead to recovered immunity that might be able to sustain viral control and to protect from chronic reinfection. I will discuss these issues in the context of our own studies that suggest only partial recovery of CD8 and almost no recovery for CD4 responses targeting HCV when treatment is initiated in the chronic phase of infection. Nevertheless, there might be a window of opportunity after successful DAA treatment to further boost or modulate these partially recovered anti-HCV immune response in order to achieve protection from re-infection. At the end of the talk I hope the audience will be familiar with our current understanding of protective HCV immunity, the immunologic state after DAA therapy and potential options for immunologic prevention of re-infection after DAA cure.

Lisa Barrett, Dalhousie University, Halifax, Canada

Biography
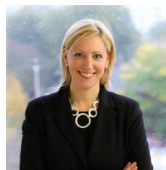
Dr. Lisa Barrett is Assistant Professor in the Division of Infectious Diseases at Dalhousie University in Halifax. She is Royal College certified in Internal Medicine and Infectious Disease and is also a viral immunologist studying chronic viral infection in humans. She was involved in hepatitis C studies at the National Institutes of Health, and is currently doing trials assessing both the clinical and pathogenesis aspects of HCV to expand the body of knowledge in treatment and prevention.

Social, Cultural, Environmental, and Population Health Research

Jeffrey Lazarus, ISGlobal, Hospital Clínic, University of Barcelona, Barcelona, Spain

Biography

Prof Jeffrey V. Lazarus is on the faculty of the Barcelona Institute for Global Health (ISGlobal), Hospital Clínic, University of Barcelona, and CHIP, the WHO Collaborating Centre on HIV and Viral Hepatitis at Rigshospitalet, the University of Copenhagen. His decade-long career as a health systems and communicable diseases expert at WHO's Regional Office for Europe was followed by three years at the Global Fund. He now serves as the Board Chair of AFEW International, a Board member of the EASL International Liver Foundation, a steering committee member of the ACHIEVE European Hepatitis Elimination coalition and of the European Commission's two joint actions on HIV, hepatitis and TB. He is a member of the INHSU International Education Committee and the BMC Editorial Advisory Group.

Abstract

Health Systems and HCV Elimination: Overcoming Challenges through a Micro-Elimination Approach

Achieving the World Health Organization (WHO) goal of eliminating hepatitis C virus as a public health threat is feasible, but only with greater attention to the role of health systems. This presentation will review the main components of a people-centred health systems approach to viral hepatitis elimination with a focus on micro-elimination efforts.

Only about 20% of people with chronic HCV are thought to be aware of their disease, and only a small fraction of those diagnosed are receiving treatment. Estimates are characterised by great uncertainty, and governments need to do much more to meet their HCV monitoring responsibilities. Without reliable information about the extent of the problem, and about the impact of interventions to mitigate the problem, it is difficult for health systems to determine how to best allocate resources.

Given the scale, complexity and cost of identifying and treating very large numbers of chronically HCV-infected people, one pragmatic approach would be to break down national elimination goals into smaller goals for individual population segments, for which treatment and prevention interventions can be delivered and monitored more efficiently and effectively using targeted methods. This concept is known as ''micro-elimination''. Pursuing the micro-elimination of HCV means working to achieve WHO elimination targets in specific sub-populations (e.g., people living with HIV, prisoners, people with haemophilia, children), settings (hospitals, addiction centres), generational cohorts (baby-boomers) or geographic areas (cities, regions).

Micro-elimination "wins" can provide important political capital by showing policy-makers that when adequate health system resources are invested, HCV becomes a conquerable disease.

Jennifer Walker, Laurentian University, Sudbury, Canada

Biography

Jennifer Walker is a health services researcher and epidemiologist. She has Indigenous (Haudenosaunee) family roots and is a member of the Six Nations of the Grand River. She has a PhD in Community Health Sciences (Epidemiology specialization) from the University of Calgary. Her work focuses on Indigenous use of Indigenous health and health services data across the life course, with a focus on older adults. She collaborates closely with Indigenous organizations and communities to address health information needs.

Jennifer holds a Canada Research Chair in Indigenous Health at Laurentian University in the School of Rural and Northern Health. She is a Core Scientist and Indigenous Health Lead at the Institute for Clinical Evaluative Sciences. She also holds appointments at the Centre for Rural and Northern Health Research, the Northern Ontario School of Medicine and the Dalla Lana School of Public Health.

Abstract

Indigenous Data Sovereignty on the Path to HCV Elimination

There is increased interest in principles of Indigenous data sovereignty, as established by Indigenous peoples in Canada and internationally. Understanding these principles and their practical application in health care, research and surveillance is important for CanHepC researchers to ensure that international and Canadian standards for Indigenous rights and ethical research are upheld. This presentation will provide participants with an overview of the Indigenous data sovereignty movement and the key principles, exploring both the diverse and common perspectives of Indigenous peoples. Practical examples of effective and collaborative implementation of Indigenous data governance models will be provided and the relevance to CanHepC and HCV elimination will be explored.

Clinical Research

Heiner Wedemeyer, Hannover Medical School, Hannover, Germany

Biography

Heiner Wedemeyer is Professor and Chairmen of the Department of Gastroenterology and Hepatology at the University Clinic Essen since February 2018.

He received his medical degree from the University of Göttingen in 1996 and subsequently started his training in Internal Medicine at Hannover Medical School in Germany. From 1998 to 2000, he was a research fellow in immunology at the Liver Diseases Branch, National Institutes of Health, Bethesda, USA. Since 2001, he completed his training in Internal Medicine and Gastroenterology at Hannover Medical School, where he became Professor of Medicine in 2011.

Professor Wedemeyer has been involved in the scientific coordination of the German Network of Competence on Viral Hepatitis (Hep-Net) and the German Liver Foundation for more than 15 years. Currently, he serves as the Managing Director of the German Hepatitis C-Registry. Heiner Wedemeyer is member of several scientific organizations and was Secretary General of the European Association for the Study of the Liver from 2009 to 2011.

Professor Wedemeyer has a long-term research interest in liver diseases with a main focus on viral hepatitis, liver transplantation and hepatocellular carcinoma. He has been principal investigator in numerous clinical trials, focusing on antiviral therapy and immunotherapy of viral hepatitis B, C, D and E. He has authored over 325 original articles; his current Hirsch-Index is 80 (google scholar; January 2018) and his work has been quoted more than 28.000 times.

Heiner Wedemeyer has received numerous awards including the Hans Popper Award of the International Association of the Study of the Liver in 2002, the Innovation Award of the German Medical Faculties (2011) and the Rudolph-Schoen-Awards (2011). His research has been funded by the Deutsche Forschungsgemeinschaft, the German Ministry of Research and Education, the European Union, the European Association for the Study of the Liver and the Bill and Melinda Gates Foundation.

Abstract

NK and T cell Function During and After Hepatitis C

Chronic viral infections lead to exhaustion of immune responses which may not only affect virus-specific T cell responses but also other immune cell populations and immunity to unrelated pathogens or even tumor antigens. Hepatitis C virus (HCV) infection can be regarded as a model infection to study the effects of persistent viremia and viral elimination on the immune system as HCV can be cured in almost all patients with novel direct acting antivirals (DAA). There has been some evidence that both NK cell function as well as HCV-specific T cells may partially recover when HCV is cleared by DAAs. However, conflicting data has been published. We showed in recent years that (i) that HCV influences immune responses to other common pathogens such as CMV, EBV either by T cell cross-reactivity or the HCV-altered cytokine milieu (ii) that restoration of HCV-specific T cell function can be achieved in-vitro by blocking co-regulatory receptors such as PD-1, 2B4, CTLA-4; however, response patterns were highly variable between patients; and (iii) that cure of chronic hepatitis C was associated with a partial restoration of immune responses but systemic cytokine and chemokine profiles as well as T cell responses did not normalize 12-24 weeks after the end of DAA therapy. Based on these findings we hypothesize that a longer follow-up after HCV clearance may be needed to achieve full restoration of virus-specific and heterologous immunity, which is of major clinical relevance in case of HCV-re-exposure, for surveillance of hepatocellular carcinoma and for resolution of extrahepatic morbidity.

Jordan Feld, University of Toronto, Toronto, Canada – Chair

Biography

Jordan Feld, MD, Associate Professor of Medicine, University of Toronto, Ontario, Canada, graduated from medical school at the University of Toronto in 1997 and then completed residency programs in Internal Medicine and Gastroenterology. Following his clinical training, Dr. Feld focused on developing skills in clinical and laboratory research in liver disease, with a particular interest in viral hepatitis. He completed a clinical research fellowship in hepatology and then spent 4 years doing clinical and laboratory research in the Liver Diseases Branch of the National Institutes of Health. He received a Masters of Public Health with a focus on Infectious Diseases as a Sommer Scholar from Johns Hopkins University and has worked extensively abroad, maintaining a strong interest in International Health. Currently, Dr. Feld is clinician-scientist based at the Toronto General Hospital, Toronto Centre for Liver Disease and the McLaughlin-Rotman Centre for Global Health.

Abstract

Optimal Screening Strategies: It's all about the local situation

With few exceptions, diagnosis rates for hepatitis C virus (HCV) remain very low, greatly limiting the ability to achieve the WHO elimination targets. To identify the undiagnosed population, major efforts will be required to enhance screening. Many different screening strategies have been implemented in different settings with varying success. Both population-based and risk-factor targeted screening can be successful but both also have important limitations. The optimal approach to screening very much depends on the local epidemiology of the region with consideration of the demographics of the infected population, the degree of engagement with the healthcare system and the screening tools available. Different screening strategies will be discussed with a focus on specific examples from Canada in which screening has been more and less successful.

Health Services Research

Homie Razavi, Center for Disease Analysis, Colorado, USA

Biography
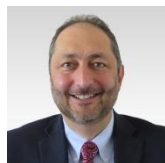
Homie Razavi, PhD, MBA, is the managing director at the Center for Disease Analysis (CDA) and the CDA Foundation. His team has analyzed and published the hepatitis epidemiology in over 100 countries and has worked with individual countries to develop national hepatitis strategies. He also leads the Polaris Observatory, which provides up to date estimates for HCV, HBV and HDV disease burden and the impact of strategies that meet national targets. Finally, he is the founder of the Global Procurement Fund (GPRO), which provides affordable quality treatment and diagnostics to low and middle-income countries. He has a broad background, which includes basic research, business development, commercial development, portfolio management, and decision analysis. He is a fellow in the Society of Decision Professionals and an overseas fellow in the Royal Society of Medicine.

Abstract

Use of data to drive global policy to eliminate HCV

As scientists, we seek data to better understand the epidemiology of hepatitis at the national and global level. However, the policy-makers don't have the time or the desire to review all available data and rely on panel of national experts to provide them with key insights to develop a national policy. Over the last three years, the Polaris Observatory has worked with panels of experts to help collect data and use mathematical models to create insights that can result in national hepatitis strategies. The global/national estimates of HCV and HBV prevalence will be reviewed as well as the requirements to achieve the hepatitis elimination targets.

The global prevalence of HCV is now declining by more than 1 million cases annually as treatment increased to 1.6 million patients in 2016. The overall prevalence of HBV is also declining due to the impact of current vaccination programs as well as vaccination programs 20 years ago. We are observing the secondary impact of HBV vaccination that has resulted in woman of childbearing age having a lower HBV due to childhood vaccination. However, the current interventions are not sufficient to achieve the elimination targets and national strategies are needed to reduce disease burden and incidence by 2030.

Naveed Janjua, University of British Columbia, Vancouver, Canada

Biography

Dr. Naveed Zafar Janjua is a Senior Scientist at the BC Centre for Disease Control and Clinical Associate Professor at School of Population and Public Health, University of British Columbia. Dr. Janjua is a Medical Doctor (MBBS) with a Master of Science (MSc) degree in Epidemiology & Biostatistics and Doctorate in Public Health (DrPH). At BCCDC, his work involves surveillance, research and policy advice and programing related to hepatitis B and C in British Columbia.

His research interest includes hepatitis B and C epidemiology, syndemics of substance use, mental illness and blood-borne and sexually transmitted infections, intervention effectiveness, disparities in treatment access and disease outcomes, HCV care access and strategies to enhance access to care. He is also involved in work on hepatitis epidemiology, transmission through medical practices and treatment in South Asia.

Most of his work is based on the **BC Hepatitis Testers Cohort,** a longitudinal cohort of about 1.7 million individuals tested for HCV or HIV or diagnosed with HBV or TB in British Columbia linked with their medical visits, hospitalization, cancer, prescription drugs and mortality. **(http://bchtc.med.ubc.ca/)**.

Abstract

What is Needed to Eliminate Hepatitis C in Canada?

HCV is a significant health concern in Canada. Two thirds of chronic HCV infections are among those born in 1945–1965 and, having acquired the virus decades ago, are now increasingly presenting with serious liver-related illnesses. Advent of highly effective and well tolerated direct acting antiviral agents (DAAs) have herald a new era in the management of hepatitis C infection which could potentially reverse the rising tide of HCV-related morbidity and mortality. Treatment optimism promoted World Health Organization to set ambitious goals for hepatitis elimination. In this presentation, I will present data on what level of scale up will be needed to achieve World Health Organization hepatitis elimination goals in Canada.

Alison Marshall, University of New South Wales, Australia, CanHepC Trainee, Canada

Biography

Alison is currently a PhD student in the CanHepC Network. Alison's research is primarily focused on hepatitis C virus (HCV) and drug use with particular attention to reducing barriers to HCV assessment and care for people who inject drugs. Prior to joining the Kirby Institute, UNSW, Sydney, Australia, Alison's work in Canada involved collaborations with international and national public health agencies to facilitate the uptake of evidence-based research in the development of HCV policy, programs, and practices in global health settings.

Abstract

A Framework for a National Hepatitis C Elimination Strategy in Canada

An estimated 220,000 persons in Canada have chronic HCV infection. To this end, it is projected that annual cases of hepatocellular carcinoma, decompensated cirrhosis, and other liver-related deaths will peak in 2031-2035. While the development of HCV direct-acting antivirals (DAAs) with sustained virologic responses (SVR) of >95% has spurred global momentum for the elimination of HCV as a public health threat, there are several remaining challenges in Canada that will need to be addressed to meet the WHO targets by 2030, which are: an 80% reduction in HCV infections, 65% reduction in HCV-related mortality, and 80% of persons with HCV infection treated.

Unlike countries with comparable HCV burdens, Canada has yet to develop a national HCV elimination strategy. This presentation will outline the main research priorities in HCV prevention, testing, and treatment in Canada in the context of the 2030 targets set by the WHO viral hepatitis elimination strategy. Through this collective initiative with multiple stakeholders – researchers, healthcare practitioners, community groups, and policy officers and decision-makers – it is hoped that a national HCV elimination strategy will help thrust Canada's current global status as 'working towards elimination' to being 'on track for WHO elimination targets'.

Opening Canadian Liver Meeting

Ricardo Baptista Leite, *Member of Parliament | Head of Public Health | Medical Doctor | University Professor | Public Health Advocate*

Biography

Ricardo Baptista Leite, MP, MD, PhD(c) Born 31st May 1980 | Portuguese-Canadian Citizenship (Born TO, Canada)

Member of the Portuguese Parliament, **Medical Doctor** trained in infectious diseases and **Head of Public Health** at *Católica University of Portugal.*

Under the auspices of **UNAIDS**, Ricardo is the **Founder and President of** *'UNITE – Parliamentarians Network to End HIV/AIDS, Viral Hepatitis and Tuberculosis'*, **a global platform of policy makers**.

Awarded by **'The Economist Intelligence Unit'** as a **'HCV Change Maker'** (2016). This acknowledgment, attributed to solely six people globally, came in due recognition of Ricardo's academic work and policy leadership in the field of hepatitis c.

Member of the Portuguese Parliament, currently on a 2nd term (2011-Present), serving as a permanent member of the *Parliamentary Health Committee* and of the *Parliamentary Foreign Affairs Committee* and having served as Vice-President of the Foreign Affairs Committee, permanent member of the *Parliamentary group on Population and Development*, Chair of the *all-party Parliamentary HIV/AIDS workgroup* and President of the *Portuguese-Canadian Parliamentary Friendship Group*.

Head of Public Health at the *Institute of Health Sciences* of *Católica University of Portugal.* **Guest Lecturer** at *NOVA Medical School* (Infectious Diseases and Microbiology) *and* at *NOVA Information Management School* (Coordinator of Sustainable Healthcare Unit), both at *NOVA University*. **Senior Fellow** at *New Westminster College* (BC, Canada) and **PhD candidate** in Public Health and Health Systems at *Maastricht University* (The Netherlands). Elected member of the supervisory board of the *National Genetic Database Protection Agency*. A decade of experience in **health technology** as a medical consultant at *Glintt Healthcare Solutions* (2009-2016), a multinational software house.

From 2015 to 2017, **Deputy Mayor** and **City Councilor of Cascais**, responsible for local health policy, academic partnerships, international relations (including economic diplomacy), youth (including Cascais European Youth Capital 2018) and employment policies.

In the past, **practicing physician** during 7 years, including a 5-year **Infectious Diseases** residency program at the Western Lisbon Hospital Center. Intern in public health (HIV, Hepatitis and STI's) as a formal collaborator of the *World Health Organization Regional Office for Europe*, based in Copenhagen (2011).

Post-graduate studies in many universities in Europe and abroad, among which are **Johns Hopkins University** (MD, USA), **Harvard Medical School** (MA, USA), **Harvard Kennedy School of Government/IESE** (Madrid, Spain), **Albert Einstein College of Medicine** (NY, USA), **Universitat Autònoma de Barcelona** (Spain) and **AESE Business School** (Lisbon, Portugal).

Volunteer work related with health and development organizations, such as being member of the *Center for Health and Development* **International Advisory Board (Mangalore, India)**, member of the *Hepatitis B and C Public Policy Association* (Brussels, Belgium), among many other affiliations with **Patient Associations**. Fellow of the **Millennium Fellowship** at **The Atlantic Council** and of the **Marshall Memorial Fellowship** at the **German Marshall Fund**. Member of the *European Leadership Network* (www.europeanleadershipnetwork.org), *European Young Leaders* (Friends of Europe | Europanova), *European Young Leaders Forum* (BMW Foundation), *Emerging Leaders in Environmental and Energy Policy Network* (ELEEP | The Atlantic Council), *Chatham House* (The Royal Institute of International Affairs). Fellow at the *ZEIT Stiftung - Fundação Gertúlio Vargas* 2015 *Latin American Forum on Global Governance* and member of the ZEIT Stiftung alumni. Member of the Antigua Forum alumni at Universidad Francisco Marroquín (Guatemala).

Founder of *CREATING HEALTH – Research and Innovation funding*, a sustainable nonprofit which has been set up within the Catholic University of Portugal to help capture funding for health innovation and research projects (http://creatinghealth.ics.lisboa.ucp.pt).

Co-founder of the *Estoril Conferences*, which are focused on the issue of globalization under the motto *Global Challenges, Local Answers* (www.estorilconferences.com).

Main author of the book "*Citizenship for Health***"** (PT, 2015), which is focused on the role of Citizens in health promotion and disease prevention, and of the book **"***Strategic Consensus on Integrated Management of Hepatitis C in Portugal***"** (PT, 2014), among other publications.

Oral Abstracts – résumés oraux

Biomedical Research

Oral presentation at 09h15

miR-122 does not impact recognition of the HCV genome by innate sensors of RNA but rather protects the 5' end from the cellular triphosphatases, DOM3Z and DUSP11

Annie Bernier, McGill University; Joyce Wilson, University of Saskatchewan; Selena Sagan, McGill University; Yalena Amador-Canizares, University of Saskatchewan

Background: Hepatitis C virus (HCV) recruits two molecules of the liver-specific microRNA-122 (miR-122) to the 5' end of its genome. In contrast to the canonical activity of miRNAs, the interaction of miR-122 with the viral genome promotes viral RNA accumulation in cultured cells and animal models of HCV infection. Although this interaction has been the subject of several studies, the precise mechanism of miR-122-mediated viral RNA accumulation remains incomplete. Previous studies suggest that miR-122 is able to protect the HCV genome from 5' exonucleases (Xrn1/2), but this protection is not sufficient to account for the effect of miR-122 on HCV RNA accumulation.

Purpose: We investigated a protective role for miR-122 in preventing recognition of the viral 5' triphosphate by innate sensors of RNA or cellular triphosphatases.

Methods: We made use of our previously established luciferase-based systems to investigate miR-122 activity. Briefly, a full-length (FL) wild-type (WT) Japanese fulminant hepatitis 1 (JFH-1) HCV construct containing a Renilla luciferase reporter was used to investigate viral replication during knockdown of cellular sensors or triphosphatases in Huh-7 or Huh-7.5 cells, where endogenous miR-122 can interact with the WT 5' terminus of the viral genome. Alternatively, we used a bicistronic subgenomic replicon (SGR) construct with mutations in both miR-122 binding sites (S1+S2:p3) expressing a firefly luciferase reporter gene, which can replicate to low levels without exogenous addition of miR-122 molecules containing a compensatory mutation that restores binding, miR-122p3. Using this SGR system, if protection of the 5' terminus from the gene of interest is the primary role for miR-122, then knockdown will restore miR-122-independent replication to levels similar to miR-122-dependent replication. Finally, we further investigated the contribution of cellular triphosphatases to HCV RNA accumulation in the absence of miR-122 using miR-122 knockout cells.

Results: We found that miR-122 does not play a protective role against recognition by protein kinase R (PKR), Retinoic acid inducible I (RIG-I)-like receptors, or IFN-induced protein with tetratricopeptide repeats (IFITs) 1 and 5. However, we found that knockdown of both cellular triphosphatases, DOM3Z and DUSP11, was able to restore viral RNA accumulation of subgenomic replicons in the absence of miR-122. However, triphosphatase knockdown was not able to rescue viral RNA replication in miR-122 knockout cells.

Conclusions: We have further elucidated the role of miR-122 in the HCV life cycle and demonstrated that miR-122 protects the viral 5' terminus from cellular triphosphatase activity and subsequent turnover by Xrn1/2, mediating viral genome stability. However, knockdown of the triphosphatases was not sufficient to rescue viral RNA replication in miR-122 KO cells, and as such, miR-122 is likely to play an additional role(s) in the viral life cycle beyond genome stability.

Oral presentation at 09h27

Increased usage of a public CD8 T cell clonotype in spontaneously resolved HCV infection

Sabrina Mazouz, CRCHUM; Maude Boisvert, CRCHUM; Julie Bruneau, CRCHUM; Naglaa Shoukry, CRCHUM

Expansion of polyfunctional (producing multiple cytokines) HCV-specific CD8 T cells was associated with viral clearance during primary infection and reinfection. Factors governing expansion of such polyfunctional T cells remain elusive. Here, we sought to determine if this response is associated with a common set of HCV-specific T cells. Diversity in the T-cell receptor (TCR) repertoire is achieved through germline V(D)J rearrangements, resulting in a specific clonotype. An identical clonotype "public" detected in several individuals was associated with better control of other viral infections like HIV while a more diverse or "private" repertoire was not. We hypothesize that spontaneous resolution will be associated with preferential expansion of a narrow but public TCR repertoire comprised of highly functional clonotypes. We analyzed the TCR repertoire of CD8 T cells specific to the dominant HCV epitope (HLA-A2/NS3-1073) during HCV in 9 resolver and 9 chronic subjects in relation to autologous viral sequence. We observed comparable TCR repertoire diversity (i.e. number of clonotypes) in the two groups and a tendency towards enrichment of the TRBV04 family in resolvers. Furthermore, a single TCR clonotype (TRBV4-02/TRBJ02-02) was among dominant (frequency >1%) clonotypes in 4/10 resolvers but only detectable within the sub-dominant (frequency < 1 %) clonotypes in chronics. This unique public clonotype persisted at a frequency of 0.3-1.6% within the memory population at 1 -2 years post resolution. Expansion of this public clonotype was not associated with a specific viral mutation or variant within this epitope. Our results suggest that spontaneous clearance of HCV is associated with an increased of one public clonotype. Further work is needed to characterize the functional implications of this public clonotype.

Oral presentation at 09h39

Impaired CD8+ T-cell function is associated with liver disease severity in chronic HCV infection and remains unresolved after HCV cure

Angela Crawley, Ottawa Hospital Research Institute; Agatha Vranjkovic, Ottawa Hospital Research Institue; Felicia Deonarine, University of Ottawa; Curtis Cooper, U Ottawa

Background
The relationship of immune dysfunction to advanced liver fibrosis is not well understood. In chronic HCV infection, we previously observed impaired CD8+ T-cell survival and signaling in the liver and in circulating CD8+ T-cells, particularly in advanced fibrosis, unrestricted to HCV-specific cells. Such systemic impairment would affect the important roles CD8+ T-cells play in host-pathogen defense and cancer cell surveillance which are clinically relevant in advanced liver fibrosis. It is unknown whether CD8+ T-cell functions, irrespective of their specificity, are influenced by the degree of liver fibrosis in HCV infection or resolved with direct-acting antiviral (DAA) treatment.

Purpose
To determine if progressive liver fibrosis is associated with generalized CD8+ T-cell dysfunction in HCV infection and whether this is resolved following HCV cure.

Methods
Cell subset determination of isolated CD8+ T-cells was determined by flow cytometry based on CD28, CD45RA and CCR7 expression. Cells were stimulated in vitro with anti-CD3/-CD28 antibodies and expression of immunomodulating IFN-g, cytolytic perforin or degranulation marker CD107 was assessed by flow cytometry. Study groups included healthy HCV- controls and treatment-naïve HCV-infected individuals with either minimal (F0-F1, 13.6 kPa), using the Metavir fibrosis scoring system. T-cell responses of DAA-treated HCV+ individuals with minimal or advanced fibrosis at treatment initiation (wk 0) and 48 weeks post treatment initiation (48 wk p.t.i.) were also evaluated.

Results
In HCV+ individuals with advanced fibrosis, the proportion of naïve CD8+ T-cells was significantly reduced, while effector memory CD8+ T-cells increased compared to controls or HCV+ individuals with minimal fibrosis. This was unchanged after viral cure. The proportion of CD107+ bulk central memory CD8+ T-cells was reduced in HCV infection, irrespective of fibrosis stage. In HCV+ individuals with advanced fibrosis, there were more IFN-g+ late effector and central memory CD8+ T-cells and fewer perforin+ cells (particularly central memory cells) compared to controls. Curing HCV infection with DAA did not resolve impaired CTL responses in naïve, effector and central memory cells (48 wk p.t.i. vs. wk 0) which was most pronounced in advanced fibrosis. While few individuals experienced liver fibrosis reversal after 48 wk p.t.i. (i.e. F4 à F1, n = 2), they demonstrated an improvement in the induction of perforin production in naïve and central memory cells. In those without a change in liver fibrosis stage following HCV cure, CD8+ T-cell functions remained the same.

Conclusions
These data indicate that generalized CTL dysfunction is a feature of advanced liver fibrosis. This fibrosis-related dysfunction was well modelled in its persistence after HCV cure, thereby broadening the potential relevance of these findings to liver disease of non-infectious origin. The contribution of such immune impairment to exacerbated co-morbidities and liver cancer risk in advanced liver disease requires investigation.

Social, Cultural, Environmental, and Population Health Research

Oral presentation at 10h50

Nothing About Us Without Us: The Value of Engaging People With Lived Experience of HCV in all areas of the HCV response

Lindsay Jennings, Shujaat Hussain, Suzanne Fish

Background
Transformative health movements have always been led by and for those with lived experience of the health issue. The principle of 'Nothing About Us Without Us' is about engaging people with lived experience in every aspect of programming, policy and research. The principle of 'Nothing About Us Without Us' has its roots in disability activism and the HIV movement where this principle has been popularized as GIPA/MIPA – Greater Involvement of People with AIDS/ Meaningful Involvement of People with AIDS.

Purpose
HCV programs, policies and research can be out of touch with real world realities unless people with lived experience of HCV are meaningfully engaged and leading in these areas. Since stigma and discrimination are key drivers of the HCV epidemic, engaging people with lived experience of HCV at every stage of the response is also a critical way of addressing a root driver of the epidemic – exclusion, discrimination and stigma towards people who use drugs, people who are in prison, newcomers and other priority populations.

Methods
Frontline programs are leading the way in terms of operationalizing the 'Nothing About Us Without Us' within the HCV response. PASAN provides an excellent example of how to engage people with lived experience in program design and organizational structure. At PASAN, lived experience is a key asset in hiring. There is not a specific peer program, but instead people with lived experience are embedded within the organization at every level. Within the newcomer community, Shujeet Husein is a leader who is engaging and informing research, programming and policy.

Results
When people inside prison and newcomers lead HCV programming, policy and research the result is more relevant programs, policies and research. When people with lived experience of HCV are meaningfully involved in the response, the root causes of the epidemic including stigma and discrimination are also addressed.

Conclusions
It is critical for all stakeholders engaged in the HCV response to examine how they currently incorporate the 'Nothing About Us Without Us' principle and explore how they might engage people with lived experience of HCV more fully into programming, policy, research and strategies for elimination.

Oral presentation at 11h22

HCV: Bringing care to patients in rural and remote settings

Dustin Dapp, Simon Fraser University ; Lucy Newman-Hogan, University of Guelph; Kehinde Ametepee, Simon Fraser University; Alexandra King, University of British Columbia; Wendy Wobeser, Queen's University

Background
The biomedical methods of treating HCV have evolved substantially in under a decade. This evolution of treatment options has reduced the necessity of inpatient care and complex multidisciplinary teams. Effective in situ treatment is now a tangible goal for patients in previously unserved rural and remote (R&R) communities, which are predominantly composed of Indigenous people, where prevalence and incidence rates are accepted to be double the national average. As part of its mandate to address inequity, the Knowledge, Translation and Exchange Core (KTE Core) supported two undergraduate students (the first two authors) through a summer student scholarship scheme to investigate the nuances of HCV screening and linkage to care in R&R Canada.

Purpose
The study aims to describe current methods/models for R&R HCV screening and linkage to care in Canada with a particular focus on Indigenous peoples. Specific goals set for this project included determining the screening methods and treatment models currently employed in Canada.

Methods
This study, largely an environmental scan of CanHepC members, employs a mixed methods research design involving the use of online surveys and key informant semi-structured interviews. The survey, composed of 28 questions, was forwarded to all members of the network and purposive sampling technique was used to identify interview participants. Telephone interviews are currently being conducted, with the completed ones already transcribed and coded using a grounded theory approach.

Preliminary Results
Results from 11 surveys were discounted for an incompletion. Survey responses (n=34) provided 15 potential interviewees. Despite a targeted effort to enlist individuals who practice in R&R settings, less than 30% of the respondents engage in R&R care. R&R survey respondents overwhelmingly indicated HCV prevalence in excess of 3%. The largest proportion of R&R healthcare providers (44%) participate in a shared care model; further, qualitative analysis of responses indicates this model promotes patient engagement and retention, professional satisfaction, local capacity building and cost efficiencies. Respondents preferred population-wide screening to targeted screening by a margin of 2:1. Practitioners who choose to practice in R&R communities often devote significant amounts of time overcoming obstacles to access funds for administration, services offered and travel cost. These themes will be further explored in the currently ongoing interviews.

Conclusion
As this study aims to explore the nuances involved in HCV R&R care in addition to discerning the obstacles to clinician recruitment, engagement, and retention from the perspectives of healthcare providers and researchers, further work needs to be done to examine the viewpoints of the patients and the community. To develop a national plan that can be contextualized across diverse communities, a needs assessment describing patient experiences in accessing care should also be prioritized.

Oral presentation at 11h34

Ontario Hepatitis C education and outreach program with immigrants and newcomers

Fozia Tanveer CATIE; Melisa Dickie, CATIE; Laurel Challacombe, CATIE; Erica Lee, CATIE; Tim Rogers, CATIE; Laurie Edmiston, CATIE

Background
Canadians from countries where HCV is endemic carry a significant proportion of the hepatitis C epidemic in Canada. Of all the past and present HCV infections in Canada, an estimated 35% are in Canada's foreign-born population[1].

Purpose
In 2011, Canada had a foreign-born population of about 6,775,800[2], about 20.6% of its total population. Of this, about 3,611,400 immigrants or 53.3% lived in Ontario. Due to the large burden of hepatitis C in Canada's foreign-born population and the abundance of immigrants living in Ontario, CATIE started its Ontario multi-lingual HCV education and outreach program in 2010 with funding support from the Ontario Ministry of Health and Long-Term Care. The aim of the program has been to increase the knowledge and awareness of HCV in the four largest immigrant communities in Ontario - Chinese, Filipino, Punjabi and Pakistani. After five years of the community focused work, CATIE conducted a program evaluation and a provincial needs assessment to inform program expansion.

Method
CATIE carried out an internal five-year Program Evaluation of Hepatitis C Ethnocultural Education, Outreach and Social Marketing Program (2011-2016) and commissioned an external Environmental Scan and Situational Analysis of Health Services and Networks in Ontario to Address Hepatitis Screening and Treatment Needs in Recent Immigrants in order to identify gaps and priority directions for future work.

Result(s)
The program evaluation and the needs assessment informed recommendations for future expansion, including expanding the program focus beyond community education to include front-line workers working in immigrant health, public health and other community settings serving this priority population

There were five core recommendations made to inform CATIE's hepatitis C work with ethnocultural communities:
 Continue to provide basic, up-to-date HCV prevention, testing and treatment information to immigrant communities in their own languages through online and print resources.
 Expand community education and outreach work beyond the Greater Toronto Area.
 Use effective and tailored strategies to ensure continuous coverage of hepatitis C content in ethnic media outlets.
 Provide education, capacity building and knowledge exchange for frontline workers and service providers.
 Develop resources for frontline workers and service providers.

Conclusion(s)
CATIE's Ontario Hepatitis C Ethno-cultural Education and Outreach Program has been successfully reaching out to immigrant and newcomer communities with culturally and linguistically tailored hepatitis C information. The program is well situated to work more closely with service providers to increase testing and linkage to care in this population group.

Clinical Research

Oral presentation at 14h30

Real-world effectiveness of interferon-free, all-oral direct-acting antivirals in the setting of hepatitis C and HIV co-infection

Carmine Rossi, Research Institute of the McGill University Health Centre; Sahar Saeed, McGill University ; Marina Klein, McGill University

Background: Sustained virologic response (SVR) is associated with reductions in liver-related morbidity and mortality among hepatitis C virus (HCV) and HIV co-infected individuals. Clinical trials have demonstrated that all-oral direct-acting antiviral (DAA) therapy nears 100% efficacy, however trial results may have limited generalizability to "real-world" co-infected populations.

Purpose: To assess clinical and socio-demographic characteristics associated with HCV treatment failure among HCV-HIV co-infected Canadians initiating therapy with all-oral DAA regimens in a real-world clinical setting.

Method: Data was obtained from the Canadian Co-Infection Cohort Study which prospectively follows 1,785 HIV/HCV co-infected participants from 18 centers in six Canadian provinces. Both treatment-naive and treatment-experienced participants who initiated therapy with an interferon-free, all-oral DAA regimen between November 2013 and July 2017 were included. Participants who i) initiated DAAs through a clinical trial, ii) were missing a treatment response, or iii) had no pre-treatment CCC study visits were excluded from the analysis. Treatment failure was defined by treatment non-response or discontinuation due to side-effects, as well as, relapse or death prior to achieving a sustained virologic response (SVR-12). Demographic and pre-treatment clinical characteristics were compared between treatment failures and those achieving SVR-12, using χ2 or Fischer's exact test, as appropriate.

Results: 259 co-infected participants initiated all-oral DAA therapy. Most participants were male (76%), median age 52 years (interquartile range [IQR]: 48, 56), and had history of injection drug use (72%). All participants were on combination antiretroviral therapy with a median CD4+ count of 490 cells/μL (IQR: 300, 710). HCV genotype (GT) distribution was GT1 80%, GT2 5%, GT3 12% and GT4 3%. Overall, the SVR-12 rate was 92% (237/259), with 22 participants experiencing treatment failure. Non-response was reported in most treatment failures (n=17), while 3 deaths, 1 discontinuation and 1 relapse were also observed. SVR-12 rates were significantly higher in women than men (98% vs. 89%), but did not differ by age (≥50: 92%, 60: 93%). SVR-12 rates were marginally lower among cirrhotic than non-cirrhotic patients (88% vs. 93%) and those who were interferon treatment-experienced, as compared to treatment-naïve (89% vs. 93%). Rates did not differ by self-reported income, active injection drug use, recent hazardous alcohol drinking, or history of depression.

Conclusion(s): HCV-HIV co-infected patients treated with all-oral DAA regimens experienced low rates of treatment failure, including those who engage in substance use. Patients with comorbid conditions, including inadequately controlled HIV infection, renal impairment and liver disease demonstrated lower rates of SVR-12. As treatment failure rates remain low, DAA therapy has brought renewed optimism for HCV elimination in this population.

Oral presentation at 14h42

ALL-ORAL ANTI-HCV THERAPY IN INJECTION DRUG USERS: UPDATED REAL WORLD DATA

Arshia Alimohammadi , Vancouver Infectious Diseases Centre , Amandeep Bassi, Vancouver Infectious Diseases Canada; Julie Holeksa, Vancouver Infectious Diseases Centre; Yashna Bhutani, Vancouver Infectious Diseases Canada; Rossitta Yung, Vancouver Infectious Diseases Canada; Astou Thiam , Vancouver Infectious Diseases Canada; Brian Conway, Vancouver Infectious Diseases Centre

Introduction
Recent clinical trials of all-oral HCV therapies among people who use drugs (PWUD) have confirmed SVR rates >90% in this group (D3FEAT, SIMPLIFY). There is a need to confirm these results in clinical practice and institute post-SVR monitoring to document recurrent viremia.

Purpose
To document occurrence and maintenance of SVR in a cohort of active PWUD receiving all-oral HCV therapy delivered in a multidisciplinary health care setting.

Methods
A retrospective analysis was performed on all HCV-infected patients (with current/recent drug use, as documented by urine drug screen) who were treated at the Vancouver Infectious Diseases Centre, including all treatment starts from May 2014-Sept 2017. All subjects were enrolled in a multidisciplinary model of care, addressing medical, psychologic, social and addiction-related needs. The primary outcome was achievement of SVR 12 (undetectable HCV RNA 12 or more weeks after the completion of HCV therapy). A secondary outcome was maintenance of SVR in long-term follow-up in subjects with ongoing risk behaviors for recurrent viremia.

Results
Since 2014, 238 individuals have initiated treatment with all-oral DAAs (160 treatment naïve, 48 cirrhotic, 46 HIV co-infected, 162 GT1, 38 GT3). All patients had a recent/current history of drug use (68% / 58% injected opiates/cocaine, with 16 individuals experiencing opiate overdoses, 1 fatal). Specific HCV treatment regimens (as clinically indicated) were: 135 including sofosbuvir [SOF] (63 with ledipasvir [LDV], 45 with velpatasvir [VPV]), 66 with PrOD, 39 with grazoprevir/elbasvir [GZV/EBV]. To date, 180 patients are evaluable for SVR, with 153 achieving SVR, 10 cases of virologic relapse, 11 lost to follow-up, 1 death unrelated to medication, and 5 treatment discontinuations (mITT SVR rate 93.8%). Of patients on SOF/VEL or GZV/EBV, 9/9 (mITT) and 20/20 (mITT) achieved SVR, with no replaces. There were no cases of recurrent viremia (mean follow-up of 1.5 years)

Conclusion
Within a multidisciplinary model of care, the treatment of HCV-infected PWUD with all-oral regimens is safe and highly effective, with no cases of recurrent viremia to data. These data justify targeted efforts to enhance access to HCV treatment in this vulnerable and often marginalized population.

Oral presentation at 14h54

Decreased hepatitis C (HCV) treatment uptake among HIV-HCV co-infected patients with a history of incarceration: Missed opportunities for care

Nadine Kronfli, McGill University Health Centre; Roy Nitulescu, McGill University; Joseph Cox, McGill University; Sharon Walmsley, University Health Network ; Curtis Cooper, U Ottawa; John Gill, Southern Alberta Clinic; Marie-Louise Vachon, Centre Hospitalier de l'Universite Laval; Valerie Martel-Laferriere, Centre de Recherche du Centre hospitalier de l'Université de Montréal; Marina Klein, McGill University; Brian Conway, Vancouver Infectious Diseases Centre; CTN 222 Canadian HIV/HCV Co-Infection Cohort Study , McGill University Research Institute

Background: Rates of HIV and HCV are far higher in prison settings than in the general population. Incarceration may destabilize care and lead to worse health outcomes, but may also represent an opportunity to intervene especially with new short course direct-acting antivirals (DAAs).

Purpose: We aimed to describe the incarceration patterns among HIV-HCV co-infected patients in Canada and to determine whether incarceration impacts HCV treatment uptake.

Methods: We analysed data from the Canadian Co-infection Cohort (CCC), a prospective multicentre cohort of 1783 co-infected patients from 18 sites. All patients with at least two study visits who completed information on incarceration were included. Self-reported incarceration history at baseline, and rates of first re-incarceration (or incarceration) among patients with (or without) a history of incarceration were described. Time to first re-incarceration (or incarceration) was analyzed using the Kaplan-Meier method. To assess the effect of time-updated incarceration status on HCV treatment uptake (among patients eligible for treatment), an adjusted Cox proportional hazards model was used. Hazard ratios (HR) and 95% confidence intervals (CI) are reported.

Results: Overall, 67% (951/1429) of patients reported a history of incarceration at baseline. Among patients with a history of incarceration, the rate of first re-incarceration was 11.4/100 person-years over a median of 3.9 years, with an estimated median time to re-incarceration of 7.5 years. Among patients without a history of incarceration, the rate of first incarceration was 1.6/100 person-years over a median of 4.0 years. At baseline, previously incarcerated patients had worse HIV clinical outcomes (less likely to be virally suppressed (61% vs. 70%, p-value 1.5 or end-stage liver disease). Incarcerated patients also reported a higher mean number of emergency room visits (1.25 vs. 0.69, p-value 0.004) and overnight hospitalizations (1.53 vs. 0.58, p-value 0.029) in the previous six months. Both incarceration (HR 0.69, 95% CI: 0.54,0.88) and active injection drug use at baseline (HR 0.68, 95% CI: 0.48, 0.95) were associated with lower HCV treatment uptake (see Table).

Conclusions: A history of incarceration was very common in HIV-HCV co-infected individuals, many of whom experienced repeat incarceration. People who experience incarceration are at a high risk for poor HIV and HCV care and subsequently experience negative health outcomes. Interactions with the health care system may represent missed opportunities for linkage to both HIV and HCV care.

Table: Risk factors associated with HCV treatment uptake

Variable	Adjusted HR (95% CI)
Incarceration status	0.69 (0.54,0.88)
Age	0.99 (0.98,1.01)

Female
  0.62 (0.47,0.81)
Indigenous
  0.71 (0.49,1.01)
High school education or less
  0.82 (0.64,1.07)
  History of IDU
  0.81 (0.59,1.12)
 Active IDU
  0.68 (0.48,0.95)
  Binge drinking
  0.82 (0.63,1.06)
APRI>1.5
  1.76 (1.38,2.25)
HCV G3
  1.67 (1.16,2.39)
 Psychiatric comorbidities
  0.83(0.67,1.03)
 Saskatchewan
  0.20(0.08,0.52)
 Quebec
  0.82(0.55,1.22)
  Other province (ON,AB,NS)
  1.39(0.92,2.08)
 DAA era
  2.31(1.52,3.50)
 DAA era*G3
  0.38(0.21,0.70)
DAA era*Quebec
  1.98(1.20,3.28)
 DAA era*Other province
  0.78(0.46,1.33)

Health Services Research

Oral presentation at 16h20

Decreased Confirmation of Chronic Hepatitis C Infections in Correctional Institutions Compared to the Community in Ontario

Nagma Grewal, Queen's University ; Jennifer Flemming, Queen's University; Wendy Wobeser, Queen's University; Anna Majury, Queen's University

Background: The prevalence of hepatitis C (HCV) in Canadian federal correctional facilities ranges between 18-40%, compared to < 1 % in the general population. No studies have investigated the proportion of individuals with a positive HCV antibody (HCV-Ab) test who subsequently failed to have HCV-RNA confirmation testing in routine clinical practise in Ontario.

Purpose: To describe incarcerated individuals with positive HCV-Ab tests and evaluate the association between the locations (correctional facilities or the community) of HCV-Ab testing and HCV-RNA testing.

Methods: Longitudinal retrospective cohort study using Public Health Ontario (PHO) data collected from 1999 to 2014 on all HCV-Ab test results and all subsequent HCV-RNA tests sent to PHO during those years. Individuals with at least one positive HCV-Ab test and known to have been incarcerated as indicated by at least one HCV-Ab test being submitted from a correctional facility were identified. The main exposure variable was the location from where the first positive HCV-Ab was sent. Using the submitter name and postal code in the database, locations were classified as either: i) federal correctional facility ii) provincial correctional facility or iii) outside of correctional facility (community). The primary outcome variable was an HCV-RNA test being ordered after the positive HCV-Ab test. The association between location of the HCV-Ab testing and subsequent HCV-RNA testing was evaluated using multivariate logistic regression.

Results: 7,768 individuals were identified; median age at first positive HCV-Ab test was 35 years (IQR 29-45), 80% male. 70% of the cohort had HCV-RNA testing upon receipt of a positive HCV-Ab test. HCV-RNA testing was highest if the HCV-Ab test was ordered in the community (85%), followed by federal correctional institutions (75%), and then provincial institutions (50%). After adjusting for age, sex, and year of testing, individuals whose first positive HCV-Ab test was sent from a federal institution (OR= 0.66, 95% CI = 0.57-0.76, P < 0 .001) or provincial institution (OR = 0.20, 95% CI = 0.17-0.22; P < 0 .001) were less likely to have HCV-RNA testing compared to those sent from the community. Individuals were also less likely to have HCV-RNA testing if they were older (OR = 0.99; 95% CI = 0.98-1.0 for each one year increase, P=< .001) or if they were female (OR = 0.68; 95% CI = 0.59-0.78, P < 0 .001).

Conclusion: Our results suggest that individuals with a history of incarceration whose HCV-Ab positive test was identified while incarcerated are less likely to be linked to HCV care than if they were tested in the community. The reason for this gap in care requires further investigation.

Oral presentation at 16h32

Estimation of hepatitis C prevalence in Canada via a two-stage back-calculation algorithm

Abdullah Hamadeh, University of Waterloo; Zeny Feng, University of Guelph; Murray Krahn, Toronto Health Economics and Technology Assessment Collaborative (THETA), University of Toronto,; William WL Wong, School of Pharmacy, University of Waterloo

Background
Despite the availability of highly-effective treatments, hepatitis C virus (HCV) screening has remained controversial in Canada. In the U.S, the CDC recommends HCV screening for baby boomers. However, in Canada, the Canadian Task Force and Preventive Health Care (CTFPHC) recently published opposing recommendations. A significant concern cited by CTFPHC was the wide variation in prevalence estimates.

Purpose
The objective of this study is to update the current prevalence estimates based on a widely used Canadian HCV policy model together with recent data.

Methods
A two-stage back-calculation Markov chain Monte Carlo (MCMC) algorithm was developed along with a state-transition model. The model includes health states related to treatment, fibrosis stages (F0 to F4), states representing the presence or absence of a clinical diagnosis, and clinical states (e.g., cirrhosis and hepatocellular carcinoma (HCC)). Model parameters were obtained from the published literature. The main data sources used to calibrate the model were HCC and HCV diagnosis data from Canadian government agencies. To begin the back-calculation, a convex optimization method was first used to obtain initial estimates of prevalence in 1999 and incidence from 1999 until 2013. Global optimization via the Metropolis-Hastings algorithm was then used to refine these estimates, while additionally calibrating the diagnosis rates.

Results
Our results showed that the average prevalence of chronic hepatitis C in Canada among the individuals born before 1945 is 1.42% (0.69-2.70%). For those born between 1945 and 1964, the average prevalence of chronic hepatitis C in Canada is 1.42% (0.94-2.04%). For those born after 1964, the average prevalence of chronic hepatitis C in Canada is 0.41% (0.26-0.57%). After adjustment for the size of each cohort, the average prevalence of chronic hepatitis C in Canada is 0.79% (0.51-1.18%).
In earlier studies used by CTFPHC, prevalence was estimated to be 0.71% in 2011. Our results indicate a HCV prevalence of 0.8% in 2011, higher than the previous estimate and in line with the results of a recently conducted seroprevalence survey.

Conclusions
Prevalence estimates have a significant impact in cost-effectiveness analysis on HCV screening and budget-impact analyses on HCV treatment, and thus have direct influence on screening and treatment decisions regarding HCV. Considering the rapid pace of development of treatments for CHC, updated prevalence estimates will become increasingly necessary. Our study provides a platform for estimating this information in a robust and efficient way.

Oral presentation at 16h44

Population-level cascade of care for hepatitis C in British Columbia: Differences over time, by gender and birth cohort

Nuria Chapinal, BC Centre for Disease Control; Maria Alvarez, BC Centre for Disease Control; Amanda Yu, BC Centre for Disease Control; Stanley Wong, BC Centre for Disease Control; Terri Buller-Taylor, BCCDC; Zahid Butt, University of British Columbia; Maryam Darvishian, University of British Columbia; Carmine Rossi, Research Institute of the McGill University Health Centre; Jason Wong, BC Centre for Disease Control; Mark Tyndall, BC Centre for Disease Control; Mel Krajden, University of British Columbia; Mark Gilbert, BC Centre for Disease Control; Naveed Janjua, BC-CDC

Background: Population-level monitoring of people living with hepatitis C virus (HCV) across the cascade of care helps identify gaps in access and engagement in care and treatment. These data help the design, implementation and evaluation of population-level prevention, care and treatment programs.

Purpose: To characterize changes in the cascade of care in British Columbia (BC) from 2000 to 2016 and identify differences by gender and birth cohorts.

Method: The BC Testers Cohort (BC-HTC) was used for this analysis. It includes all individuals tested for HCV in BC since 1990 who linked to data on prescription drugs, medical visits, hospitalizations and mortality data. We defined the following cascade of care stages: 1) anti-HCV positive (diagnosed); 2) RNA tested; 3) genotyped; 4) initiated treatment; and 5) achieved a post-treatment sustained virologic response (SVR).

Results: The number of anti-HCV positive individuals diagnosed in BC gradually increased from 2000 to 2016. The proportion of anti-HCV positive individuals who were RNA tested also steadily increased over time, particularly from 2000 to 2009. A similar trend was seen in the proportion of RNA positive individuals who were genotyped. Treatment initiation and achievement of SVR after treatment increased very slowly over time until 2013. A marked increase was seen in both stages since 2013, corresponding to the introduction of the first direct-acting antivirals (DAAs) in BC.

In 2016, there were more anti-HCV positive males than females living in BC. Females were more likely than males to be RNA tested (84% vs 80% of those anti-HCV positive) and to clear infection spontaneously (32% vs 23% of those RNA tested). Both males and females with active infection (RNA positive) moved through the continuum of the cascade in a similar fashion.

People born between 1945-64 represented the highest burden of HCV in 2016. Of those anti-HCV positive, 82% were RNA tested, 90% of those who were RNA positive were genotyped, and 52% of those genotyped initiated treatment. The younger birth cohorts (≥ 1965) had larger gaps in genotyping (83%) and treatment initiation (32%).

Conclusions: Although there has been progress across the cascade of care, gaps remain in treatment initiation, especially for younger birth cohorts. Lower treatment initiation in younger birth cohorts is expected given that the current standard for treatment requires fibrosis staging ≥ F2 and fibrosis is less likely in younger individuals.

Posters - Affiches

Poster 1

Characterization of Exosomal MicroRNA Content During HCV Infection
Christopher Ablenas, University of Ottawa; John Pezacki, University of Ottawa; Curtis Cooper, University of Ottawa

Background
Hepatitis C virus (HCV) treatments with high cure rates have reduced but not eliminated the elevated risk in HCV infected patients for developing hepatocellular carcinoma (HCC) (1). In the coming years, HCV-related HCC in the aging population is projected to increase (2). Despite progress in our understanding of viral pathogenesis, the mechanisms of viral-induced HCC remain elusive.
MicroRNAs (miRNAs) are important modulators of physiological processes. Dysregulation of miRNA expression has been documented in both HCV infection and many types of cancer, including HCC. An emerging area of miRNA study is in the context of exosomes.
Exosomes are membrane-enclosed vesicles that are actively packaged with RNAs, proteins, and lipids within cells, and released into the extracellular space. Exosomes participate in cell-to-cell communication, provide an indication of the physiological/pathological state of their cells of origin, and can play important roles in disease progression.

Purpose
To identify miRNAs that are differentially packaged into exosomes during HCV infection that may play a role in the development of HCC.

Methods
Exosomes from cell culture supernatants of HCV JFH1 infected cells were isolated by differential ultracentrifugation and the miRNA content was profiled using Nanostring Technologies nCounter analysis system. The exosomal miRNA profile was compared to that of uninfected cells to identify exosomal miRNAs that are dysregulated during HCV infection. Computational target prediction algorithms were then used to identify putative mRNA targets for the altered miRNAs.

Results
The miRNAs differentially packaged into exosomes in cell culture during HCV infection will be discussed, along with their putative mRNA targets and preliminary target validation.

Conclusions
This study provides a better understanding of the role of exosomal miRNAs in cell-to-cell signaling during HCV infection, and serves as a basis to screen for altered exosomal miRNAs in HCV-infected patient sera before and after treatment. This will provide a better understanding of the biological mechanism through which patients develop HCC.

Poster 2

Identification of Host and Viral Proteins at the 5' Terminus of the HCV Genome by BioID

Alexander Southward, McGill University
Identification of Host and Viral Proteins at the 5' Terminus of the HCV Genome by BioID
Alexander Southward1, Annie Bernier1 and Selena M. Sagan1, 2
1Department of Microbiology & Immunology, McGill University, Montréal, QC, Canada
2Department of Biochemistry, McGill University, Montréal, QC, Canada

Background
Hepatitis C virus (HCV) is a positive-sense, single-stranded RNA virus belonging to the Flaviviridae family. The HCV genome consists of a single ORF that is flanked by highly structured 5' and 3' untranslated regions (UTRs). The 5' UTR promotes several important protein and RNA interactions essential for protein synthesis and viral RNA replication. Among these interactions, the highly-abundant, liver-specific microRNA-122 (miR-122), interacts with two sites within the 5' UTR. This interaction promotes viral RNA accumulation; however, the precise mechanism(s) of miR-122-mediated viral RNA accumulation remain unclear.

Purpose
The purpose of this study is to uncover novel proteins interacting with the 5' UTR of the HCV genome. We hypothesize that host and/or viral proteins localize to the 5' terminus of the HCV genome and play a role in HCV RNA replication, genome circularization, or in complex with miR-122.

Methods
We aim to identify host and viral factors interacting with the 5' terminus of HCV using a proximity-dependent biotin identification method (BioID). An essential component of the BioID strategy revolves around promiscuous biotinylation of nearby proteins by BirA, an E. coli derived biotin ligase. In this study, we exploit the high affinity interaction between the Bacteriophage λ BoxB stem-loop structure and the λN protein to localize a BirA fusion protein to the 5' terminus of the HCV genome. Biotinylated proteins will be affinity purified and analyzed using mass spectrometry. Identified proteins will be further investigated for their role in miR-122 mediated viral RNA accumulation through immunoprecipitation, siRNA knockdowns, and overexpression studies.

Results
To date, we have demonstrated that HCV containing a BoxB stem-loop accumulates appropriately in cell culture and we have developed the λN-BirA fusion protein. We are currently in the process of expressing both the λN-BirA fusion protein and BoxB HCV RNA in cell culture. Subsequently, we will use BioID to identify vicinal proteins by mass spectrometry. Vicinal proteins will be investigated for their role in the HCV life cycle using knockdown or overexpression studies in the presence or absence of miR-122.

Conclusions
The identification of proteins at the 5' terminus of the HCV genome will reveal new host-virus interactions, will help elucidate the mechanisms of miR-122-mediated viral RNA accumulation, and may provide novel targets for antiviral therapy.

Poster 3

Investigating how miR-122 alters the secondary structure of the HCV genome

Jasmin Chahal, McGill University; Selena Sagan, McGill University

Background:
Hepatitis C virus (HCV) is a positive-sense single-stranded RNA virus and thus, its genomic RNA itself must act as a template for viral translation, replication, and packaging. To accommodate this, the 5' and 3' non-coding regions (NCRs) contain cis-acting RNA elements (CREs) that play key roles in the viral life cycle. These CREs are involved in interactions with RNA and proteins, one of which is with the liver-specific microRNA, miR-122. miR-122 binds to two sites on the 5'NCR and promotes HCV RNA accumulation, although the precise role of miR-122 in the HCV life cycle is unclear. Recent studies suggest that miR-122 may modulate the structure of the 5' NCR and/or the viral internal ribosomal entry site (IRES).

Purpose:
We are investigating how miR-122 binding alters the structure of the HCV genome.

Methods:
We have performed Selective 2' Hydroxyl Acylation analyzed by Primer Extension (SHAPE) to analyze the structure of the HCV 5' NCR in the presence and absence of miR-122 in vitro and in vivo, using the in vivo SHAPE reagent, methylnicotinic acid imidazolide azide (NAI-N3). SHAPE analysis was performed by both gel and capillary electrophoresis and data was analyzed using SAFA or QuSHAPE, respectively. The secondary structural alterations of the two miR-122 bindings site on HCV RNA (the first 42 nts of the 5' end) were analyzed using gel electrophoresis while SHAPE analysis of the entire HCV RNA 5'NCR was done by capillary electrophoresis. In addition, to further understand these interactions we are using Electrophoretic Mobility Shift Assays (EMSA) and isothermal titration calorimetry (ITC) to measure dissociation constants of miR-122 binding at site 1, site 2 or both sites.

Results:
Not surprisingly, our in vitro SHAPE results of the 5' terminus (nts 1-42) of the HCV RNA +/- miR-122 suggest that in the single-stranded RNA stretch and SLI of the HCV genome become more constrained upon miR-122 binding. We are currently analyzing the entire 5'NCR (nts 1-370) of HCV RNA +/- miR-122 to determine whether miR-122 induces changes in the secondary structure in the IRES region. Our preliminary analysis suggests that nts at stem-loop IIIa and IV of the IRES are more constrained when miR-122 is bound.

Conclusions:
We observed that miR-122 binding alters the secondary structure of the HCV 5'NCR. In addition to the miR-122 sites, regions in the IRES become more constrained when miR-122 is bound, suggesting that there may be cross-talk between miR-122 and the HCV IRES. We anticipate that these studies will uncover how miR-122 alters the structure of the HCV genome and will help to clarify the role of miR-122 in HCV RNA accumulation. We hope to identify new modes of RNA regulation and may uncover novel RNA-based targets for antiviral intervention.

Poster 4

Exploring Immunological Restoration with Second Generation DAA in HCV-Infected Individuals

Natalia Rosário, Universidade Federal Fluminense; Thalia Medeiros, Universidade Federal Fluminense; Geórgia Saraiva, Universidade Federal Fluminense; Gilmar Lacerda, Universidade Federal Fluminense; Camila Salviato, Universidade Federal Fluminense; Thais Guaraná, Universidade Federal Fluminense; Jorge Reis, Universidade Federal Fluminense; Analúcia Xavier, Universidade Federal Fluminense; Petronela Ancuta, Centre de Recherche du Centre Hospitalier de l'Université de Montréal; Andrea Silva, Universidade Federal Fluminense

Background:
HCV establishes a chronic infection causing liver fibrosis, cirrhosis and hepatocellular carcinoma. Liver macrophages (MF) originating in part from blood monocytes are involved in promoting HCV immunity but also cause tissue damage by their ability to create a pro-inflammatory environment. Although the ability of blood monocytes and liver MF to support productive HCV replication is still on debate, it is well established that their activation can be mediated by HCV RNA and viral proteins, via specific Toll-like receptors engagement. Of note, HCV infection is associated with alterations in monocytes homeostasis, with higher frequency of pro-inflammatory CD16+ monocytes that may differentiate into pathogenic MF. Second generation direct-action antiviral therapy (DAA) is effective in clearing HCV infection; however, whether DAA reverses liver inflammation through the restoration of monocyte homeostasis remains unknown.

Purpose:
This study aims to analyze changes in frequency and activation phenotype of blood monocyte subsets in chronically HCV-infected individuals undergoing DAA treatment.

Methods:
Individuals were enrolled in the Reference Center for Hepatitis Treatment (Brazil). Blood samples were collected before (T0) and 12 weeks after the end of therapy, corresponding to sustained virological response (SVR). Blood from uninfected individuals was used as controls. Peripheral blood mononuclear cells were isolated using Ficoll gradient centrifugation. Monocyte phenotype was analysed by flow cytometry upon staining with CD14, CD16, HLA-DR, and CCR2 Abs. Inflammatory molecules were quantified in serum by Luminex® Multiplex Assay.

Results:
Ninety participants were followed until SVR time. At baseline, this group exhibited a mean age of 59.6±9.3 years, 74.4% presented cirrhosis, and genotype 1 was found in 82.2%. Of note, 60% participants were treatment-experienced. The blood monocytes phenotypic analysis was performed on 20/90 HCV+ and 10 controls. The total monocytes frequency identified as CD14+HLA-DR+ cells, as well as the CD16- monocytes frequency, were significantly reduced in HCV+ individuals at T0 compared to controls, with no significant difference in CD16+ monocytes. DAA therapy resulted in a significant increase in total monocytes as well as CD16- monocytes frequencies that reached values similar to the controls. Regarding CCR2 expression on CD16+/CD16- monocyte subsets, no significant changes were observed between HCV+ and control groups and neither within HCV+ at T0 and SVR. The quantification of inflammatory molecules of 36 HCV+ individuals demonstrated a significant decrease in IP-10, CCL3, CCL4, IL-1β, IL-15, IFN-g and TGF-β levels and a significant increase in IL-1ra levels at SVR time compared to T0.

Conclusions:
These results demonstrate that DAA therapy was successful in mediating SVR in HCV+ individuals included in the study. They also reveal the capacity of DAA to promote the normalisation of CD16- monocyte frequency as well as the plasmatic inflammatory milieu. Future studies should address the capacity of DAA to restore liver function.

Poster 5

Removal of an Immune Masking Domain, Hypervariable Region 1 (HVR1) of HCV Glycoprotein E2, Does Not Enhance the Immunogenicity of a Glycoprotein-Based HCV Vaccine

John Law, University of Alberta; Michael Logan, University of Alberta; Jason Wong, University of Alberta; Darren Hockman, University of Alberta; Amir Landi, University of Alberta; Elzbieta Dudek, University of Alberta; Ana Clementin, University of Alberta; Chao Chen, University of Alberta.ca; Juthika Kundu, University of Alberta; Ninad Mehta, University of Alberta; Kevin Crawford, University of Alberta; Mark Wininger, University of Alberta; Catalina Prince, University of Alberta; Kelly Mottet, University of Alberta; Janelle Johnson, University of Alberta; D. Lorne Tyrrell, University of Alberta; Michael Houghton, University of Alberta

Current evidence points to a protective role for virus neutralizing antibodies and virus-specific cellular immune responses in immunity against HCV infection. Many cross-neutralizing monoclonal antibodies have been identified. These antibodies have been shown to protect or clear infection in animal models. We are developing a recombinant envelope glycoprotein vaccine containing the gpE1/gpE2 heterodimer along with a T cell antigen to broaden HCV-specific cellular immune responses. Previous clinical trials have shown a gpE1/gpE2 vaccine can induce antibodies that neutralize the in vitro infectivity of all the major HCVcc genotypes around the world. However, cross-neutralization appeared to favour certain genotypes with significant but lower neutralization against others. HCV may employ epitope masking to avoid immunoglobulin-mediated control. The HVR1 at the amino-terminus of glycoprotein E2 blocks access to many neutralizing antibodies. Consistent with this, other groups have reported that recombinant viruses lacking the HVR1 are hypersensitive to neutralization. It has been proposed that E1E2 lacking this domain could be a better vaccine antigen to induce broadly neutralizing antibodies. In this study, we examined the immunogenicity of recombinant E1E2 lacking the HVR1 (DHVR1). We found that WT and DHVR1 E1E2 can induce HCV specific antibodies equally well and both antigens induced antibodies targeting many well-characterized cross-genotype neutralizing epitopes. However, while antisera from DHVR1 immunized mice can effectively neutralize HCVpp lacking the HVR1, this antisera showed a reduction in neutralization activity against WT HCVpp. This data suggests DHVR1 E1E2 is not a superior vaccine antigen. Based on chimpanzee protection data reported previously using wt gpE1/gpE2 and our current findings, we are preparing a combination vaccine including a wild type recombinant gpE1/gpE2 for clinical testing in the near future.

Poster 6

The Use of Oncolytic Measles-Based Vectors for Targeted Treatment of HCV-Induced Liver Cancer

Ching-Hsuan Liu, Department of Microbiology & Immunology, Dalhousie University; Liang-Tzung Lin, Taipei Medical University; Christopher Richardson, Dalhousie University; Yu-Chi Pan, Taipei Medical University
Ching-Hsuan Liu1,2,3, Yu-Chi Pan2, Liang-Tzung Lin1,2,3,*, Christopher D. Richardson1,4,*
1 Department of Microbiology & Immunology, Dalhousie University, Halifax, NS, Canada
2 Department of Microbiology and Immunology, Taipei Medical University, Taipei, Taiwan
3 Graduate Institute of Medical Sciences, Taipei Medical University, Taipei, Taiwan
4 Department of Pediatrics and Canadian Center for Vaccinology, Izaak Walton Killam Health Centre, Halifax, NS, Canada

Background:
While novel antiviral agents offer potential cure for hepatitis C, options for the treatment of hepatocellular carcinoma (HCC) resulting from HCV infection remain limited. Current approaches include surgical resection, radiofrequency ablation, embolization, liver transplantation, and chemotherapy, etc.; however, these therapies are ineffective in advanced HCC stage, and situations such as contraindications, lack of donor livers, risk of recurrence, and the varied responses lead to the poor prognosis of such disease. These issues highlight the importance of developing novel therapies for the treatment of HCV-induced HCC. Recently, the tumor marker nectin-4, which is found on many adenocarcinomas including HCC, was identified as one of the receptors for measles virus (MV). This discovery highlighted the potential of using oncolytic MV-based vectors for treating liver cancers, including the context of HCV-induced HCC.

Purpose:
To explore the use of MV-based oncolytic viruses to target the tumor marker nectin-4 on HCV-induced HCC.

Method:
We first examine the level of nectin-4 expression in clinical HCC specimens from the Oncomine online microarray/gene expression database (https://www.oncomine.org). Commercially available HCC cell lines are evaluated for nectin-4 expression in vitro. The targeting and oncolytic abilities of a recombinant wild type (wt) MV (strain IC323) are validated in the HCC cell lines and their derivatives containing HCV subgenomic RNA. The role of HCV NS3/4A protease and cell innate immunity in the scenario of oncolytic virus treatment will also be examined. We will subsequently determine the effect of MV-based vectors on tumor growth in HCC mouse tumor models.

Results:
Oncomine online dataset analysis reveals that nectin-4 is overexpressed in clinical HCC specimens, including those with HCV infection, compared to normal liver tissue. Preliminary results indicate that HCC cell lines including Huh-7, HepG2, and Hep3B, express nectin-4 and are susceptible to oncolytic MV infection. Additionally, Huh-7 cells harboring replicating HCV subgenomes (GT1b and GT2a) exhibit better MV infectivity and spread compared to the HCV-negative parental cells.

Conclusion:
We have shown that nectin-4 is overexpressed in clinical HCC specimens, and that HCC cell lines expressing nectin-4 can be targeted by MV-based oncolytic vector. More importantly, enhanced MV infectivity and spread in the hepatoma cell lines with replicating HCV subgenomes suggest that suppressed cell innate immunity may have influenced the infectivity of oncolytic vector. We expect that oncolytic virus treatment will retard tumor growth, and a functional immune system should further enhance remission in these liver cancer   models.

Poster 7

Exploring treatment adherence to direct acting antivirals among HCV positive individuals who use drugs in Bangladesh

Aslam Anis, Centre for Health Evaluation and Outcome Sciences; Naveed Janjua, BC-CDC; Mustafiz Rahman, International Centre for Diarrhoeal Disease Research, Bangladesh; Taznim Azim, International Centre for Diarrhoeal Disease Research, Bangladesh; Tanveer Shafiq, International Centre for Diarrhoeal Disease Research, Bangladesh; Sharful Khan, International Centre for Diarrhoeal Disease Research, Bangladesh; Safiullah Sarker, International Centre for Diarrhoeal Disease Research, Bangladesh; Omar Faruque, Save the Children (Bangladesh); Ezazul Chowdhury, International Centre for Diarrhoeal Disease Research, Bangladesh

Background:
In Bangladesh, people who use drugs (PWUD) account for the vast majority of hepatitis C virus (HCV) infections (prevalence ~ 40%). While well-tolerated, interferon-free, direct-acting antivirals (DAAs) for HCV have been available since 2013, policy makers are reluctant to treat PWUD due to the perceived risk of non-adherence and reinfection through ongoing drug use. Given this entrenched bias and stigma against treatment, we undertook a feasibility study to assess adherence to treatment with directly acting antivirals (DAA) in Bangladesh.

Purpose:
To assess adherence to DAA treatment and success in terms of achieving sustained virological response at 12 weeks (SVR12). Additionally, we also measured the underlying reasons associated with good adherence.

Methods:
HCV mono-infected and non-cirrhotic adult PWUD receiving harm reduction services (needle/syringe exchange or opioid substitution therapy) at a drop-in center in old Dhaka were screened and if eligible, enrolled into treatment. PWUDs were provided with directly observed therapy or with carries of Sofosbuvir and Daclatasvir for 12 weeks dependant on their housing status. Prior to starting treatment, risk behaviours were ascertained using a semi-structured questionnaire and clinical examination. Regular follow-ups of those on treatment were conducted by outreach workers to determine treatment adherence. In-depth interviews were conducted to identify the reasons for good- or non-adherence to enable immediate modifications, if required, for drug dispensing strategy.

Results:
The study started on 27 March 2017 and is ongoing. As of 30 September 2017, a total of 224 PWUD were brought to the DIC and 55 were eligible for HCV treatment. Among the 55 enrolled, all were male and 93% were >30 years of age. Of the 55 patients on treatment, to date 39 have completed treatment: 36 (92.3%) adhered based on an 80% threshold set for compliance with DAA regimen, 3 non-adhered. SVR12 assessments are expected to be completed by January 2018. In-depth interviews revealed that close family ties, regular follow-ups and influence by peers enabled PWUD to adhere to treatment. However, barriers to adherence identified included lack of knowledge regarding HCV resulting in mistrust among some as to why they were receiving such extra attention.

Conclusion: Our findings suggest that the overall adherence to DAA was good and facilitated by close follow up, support by family members and raising awareness amongst PWUD regarding HCV in the surrounding community. However, most of the PWUDs lead chaotic lifestyles, which were associated with mental and physical health problems, financial difficulties and lack of meaningful social relationships. Regular follow-up by outreach staff attenuated the impact of the preceding factors and contributed to improved adherence. The findings of the pilot study will help with developing strategies for effectively treating PWUD with HCV.

Poster 8

SUBSTITUTION TREATMENT FOR OPIOIDES IS A KEY OF SUCCESS FOR HCV CURE IN INJECTION DRUG USERS

Nima Machouf, Clinique de Médecine Urbaine du Quartier Latin; Emmanuelle Huchet, Clinique de Médecine Urbaine du Quartier Latin; Pierre Coté, Clinique de Médecine Urbaine du Quartier Latin; Sylvie Vézina, Clinique de Médecine Urbaine du Quartier Latin; Marc Poliquin, Clinique de Médecine Urbaine du Quartier Latin; Pierre-Luc Morissette, Clinique de Médecine Urbaine du Quartier Latin; Jean-Guy Baril, Clinique de Médecine Urbaine du Quartier Latin; Benoit Trottier, Clinique Médicale du Quartier Latin

Introduction:
In Canada, despite the universal health care system, access to HCV treatment remains limited for drug users (DU). Many physicians prefer to ensure abstinence before initiating treatment. However, Intravenous DU (IDU) consuming drugs are more at risk of transmission. The aim of this study was to assess our ability to cure HCV infection in IDU regardless of their consumption.

Methods:
All HCV-treated patients followed at Clinique Medicale du Quartier Latin (CMQL) were included in this retrospective study. Information on socio-demographics, medical history and treatment was collected from the electronic medical chart. At CMQL HCV-patients are followed by a multidisciplinary team (nurse, family doctor, hepatologist, social worker, community pharmacist) and have access to a low threshold opioid substitution therapy (OST) if they need so. Sustained virological response rate at 12 weeks after end of treatment (SVR12) was calculated by Intent-to-treat analysis (ITT). Determinants of SVR were analysed by multiple logistical regression using SPSS-24.

Results:
104 HCV patients treated with INF-free-DAA were included in this study. 79% were men, with a mean age of 53 y (IQR: 48y - 59y). 46% were HIV-coinfected, 23% were active-IDU, 14% were on OST, 5% without housing, 46% with ROH-problem, 31% were cirrhotic, 77% were infected with genotype-1and 70% were naïve at the INF-free-DAA treatment initiation. Over all, 85% achieved SVR12 while 2% discontinued treatment. Even if SVR seems higher in non-IDU, the difference was not statistically significant (SVR=90% for non IDU vs. 84% for previous-IDU and 78% for active-IDU; p=0.471). 100% of patients on OST achieved SVR. In multivariate analyses, after controlling for gender, age, drug and alcohol use, housing, depression, diabetes, HIV-coinfection, treatment history and genotype, cirrhosis was the only determinant who impacted SVR (aOR= 0.13; 95%CI= 0.04 - 0.46; p=0.002).

Conclusion: At CMQL, the SVR rate remained high and did not differ by IDU status. The «difficult-to-treat» IDU are manageable if we offer them adequate support. OST is one of the best opportunities for curing active-drug users for their HCV.

Poster 9

Sofosbuvir plus Ribavirine for 24 weeks in an HIV-infected, cirrhotic Patient with Chronic Hepatitis E Virus Infection

Marc Poliquin, Clinique de Médecine Urbaine du Quartier Latin; Nima Machouf, Clinique de Médecine Urbaine du Quartier Latin; Daniel Murphy, Hopital Verdun; Daniel Brainard, Gilead Science; Zahra Mokhtari, Clinique de Médecine Urbaine du Quartier Latin; Emmanuelle Huchet, Clinique de Médecine Urbaine du Quartier Latin; Anton Andonov, National Microbiology Laboratory ; Benoit Trottier, Clinique Médicale du Quartier Latin

Introduction:
Chronic Hepatitis E virus (HEV) infection as a cause of liver disease, including rapid progression to cirrhosis, has been well described in immuno-compromised patients. Treatment of this condition has included reduction of immunosuppression in transplant recipients, peg-interferon therapy, and ribavirin (RBV) monotherapy, all with suboptimal rates of sustained viral eradication. More recently, reports of in vitro activity of sofosbuvir (SOF) against HEV as well as transient suppression of viremia in a single patient have raised the question of whether SOF-based therapy could provide an effective treatment option. Methods: This is a case report of a 51 year old HIV-infected male with a history of AIDS, Kaposi's sarcoma, lymphoma and chronic genotype 3 HEV resulting in cirrhosis had failed to clear HEV with 5 years of RBV monotherapy, despite ALT normalization. He was then treated and cured with sofosbuvir 400 mg daily plus RBV 1000 mg daily for 24 weeks. Results: Pretreatment HEV RNA was 1500 IU/mL for this patient and ALT was within normal limits. Subsequent HEV RNA assessments at monthly intervals during treatment were negative. Six months after completing 24 weeks of treatment, HEV RNA remains negative and ALT and AST stay within normal limits. SOF+RBV was well tolerated with no adverse effects and no new laboratory abnormalities. The patient's CD4 count which had been consistently around 80 cells/ml increased to 150 cells/ml at the end of treatment. Conclusions: This is the first case report of chronic HEV treated with SOF+RBV for 24 weeks. The patient remains HEV negative 6 months after completing treatment. Further studies are needed to investigate the safety and efficacy of SOF+RBV as a treatment for chronic HEV infection.

Poster 10

Proteomics: The Doctor is IN the Tardis

Douglas Laird, HepC BC

Background
The liver biopsy was the golden standard for liver fibrosis diagnosis. Advances in non-invasive techniques started with the Fibrosure, which was based on an algorithm of blood composition done in a laboratory. Then the ultrasound technique Fibroscan was developed and placed into wider practice by technicians and physicians.

The Fibrosure is compact and portable. It is expensive and requires recalibration, which is also very costly. The cost can be justified by quantity of scale, mainly inside of zones of urban populations. Rural populations are not serviced on a routine basis, and travel costs can be significant to do so.

Purpose
While not widely in use in Canada, proteomics offer a method of analytical detail and increase health comprehension enormously. Given the wide range of comorbidities involved in Hepatitis C virus, the technology would increase diagnostics using a sample of blood to give a profile of 210 proteins. The number of diagnostic tests for fibrosis and the potential for hepatic carcinoma would increase, with monitoring results post SVR giving critical information on a range of health concerns that could reduce mortality.

Method
Studies indicate that serum proteomics are useful for HCC diagnostics (Uto et al, 2010) while serum proteomics can predict hepatic fibrosis in HCV (Hannivoort, Hernandez-Gea, & Friedman, 2012).

Result(s)
There is an important need for HCC diagnostics with HCV and HBV clients that is unmet, especially for rural clients where travel costs to major centers take up a considerable proportion of health care budgets in the far north. Post SVR results for cirrhotic patients are critical to reduce cancer mortality. As baby boomer testing remains controversial in Canada, advancing the availability to proteomics would be an alternative request by advocacy groups that would extend protection against other comorbidities such as stroke. Taken together, cost savings to the health care system could be substantial.

Conclusion(s)
Having proteomic technology available would result divergent advantages, especially in the proper diagnostics of TIA or mimics involved in stroke diagnostics. Further studies are warranted to add proteomics to standard medical diagnostics as a benefit to decrease mortality due to HCC.

Sources
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Poster 11

HepCInfo Updates: National Hepatitis C Research Knowledge Synthesis, Evaluation

Suzanne Fish, Laurie Edmiston, CATIE; Laurel Challacombe, CATIE; Scott Anderson, CATIE; Tim Rogers, CATIE; Erica Lee, CATIE; David McLay, CATIE

Authors and Institutions: Scott Anderson, David McLay, Erica Lee, Laurel Challacombe, Tim Rogers, Laurie Edmiston

Background: HepCInfo Updates is CATIE's bi-weekly e-newsletter covering the latest in hepatitis C research and news, including treatment, prevention, harm reduction and epidemiology information relevant to the Canadian context. Each newsletter contains two sections: "New and noteworthy" which summarizes 2-3 new developments in hepatitis C and "Straight to the source for new science" which provides links to recent research of interest.

HepCInfo Updates is available online through CATIE's website and is emailed to subscribers. There are 3062 HepCInfo Updates subscribers – including 2605 English subscribers and 457 French subscribers.

In November 2016, CATIE launched an online survey in FluidSurveys to evaluate HepCInfo Updates.

Purpose: As one of CATIE's key publications, HepCInfo Updates has two primary objectives: Objective 1: Increase knowledge and awareness of the nature of hepatitis C and ways to address them. Objective 2: Enhance individual and organizational capacity to plan and deliver programs and services.

Methods: CATIE launched an online survey in FluidSurveys to evaluate HepCInfo Updates. The survey was promoted through the HepCInfo Updates subscribers list. Notice of the survey was included in the e-mail distribution of two HepCInfo Updates issues and an additional request to complete the survey was e-mailed to subscribers. The survey was available online for nine weeks. Ninety-eight people started the survey with 90 people completing all questions in the survey (completion rate 91.8%). Frequency descriptives were compiled for all respondents.

Results: The evaluation demonstrated that HepCInfo Updates is relevant to our stakeholders and effective at achieving our knowledge exchange objectives.
Is HepCInfo Updates relevant?
 98% reported that at least 'some' of the content of HepCInfo Updates is relevant to them.
 92% were 'satisfied' or 'very satisfied' with the publication.
Is HepCInfo Updates effective?
Objective 1: Increased knowledge and awareness of the nature of hepatitis C and ways to address them.
 95% agreed or strongly agreed that HepCInfo Updates made them aware of information that has increased their knowledge of hepatitis C.
 94% agreed or strongly agreed that HepCInfo Updates made them aware of relevant, up-to-date information on developments in the treatment and prevention of hepatitis C.
 87% have used the information they were made aware of through HepCInfo Updates to educate or inform clients, health professionals, colleagues or members of the public.
Objective 2: Enhanced individual and organizational capacity to plan and deliver programs and services.
 87% agreed or strongly agreed that they can use/apply the information they were made aware of through HepCInfo Updates in their work.
 59% have used the information they were made aware of through HepCInfo Updates to change work practices and/or implement/change programming. Specifically.

Conclusions: Readership evaluation of HepCInfo Updates was overwhelmingly positive. HepCInfo Updates is meeting   its   objectives.

Poster 12

Evaluation of Hepatitis C Knowledge Among Medical and Nursing Students

Lucy Smith, Memorial University of Newfoundland; Rodney Russell, Memorial University of Newfoundland

Background:
Early diagnosis of Hepatitis C and identification of asymptomatic patients is necessary for timely treatment to prevent progression to severe liver disease and death. Past studies have shown that one of the major barriers to early diagnosis is the fact Hepatitis awareness remains low in the general public as well as among healthcare professionals. While most primary healthcare professionals will not receive specialized training in Hepatitis C, they are often the ones involved in the initial diagnosis. The current suboptimal diagnostic rate highlights a need to increase awareness of Hepatitis C among healthcare professionals, and to help them have a better understanding of the disease. Advocacy for more training and education on Hepatitis C knowledge among healthcare trainees could be beneficial in improving the delivery of timely diagnosis and treatment to patients.

Purpose:
The purpose of this study was to perform a knowledge evaluation of Hepatitis C among medical and nursing students at Memorial University to advocate for better Hepatitis C education among healthcare professional trainees.

Method:
An electronic questionnaire containing 10 multiple choice questions assessing knowledge and awareness of Hepatitis C was distributed to all current medical and nursing students at Memorial University of Newfoundland for voluntary response.

Results:
A total of 88 students responded to the questionnaire with a ratio of 64% medical students and 35% nursing students. Results showed that 25% of respondents believe jaundice is the most common symptom of a chronic Hepatitis C infection, with additional 28% respondents answering with either cirrhosis or "I don't know". A shocking 39% of respondents believe that Hepatitis C is a vaccine-preventable disease. A question assessing their knowledge regarding current effective treatment of Hepatitis C infection showed that 24% of the students picked vaccination as the most effective treatment, while another 15% believe Hepatitis C cannot be cured.

Conclusion:
While acknowledging the limited sample size of this study and appreciating the fact that 41% of the respondents were first year medical or nursing students, it is clearly evident that Hepatitis C knowledge and awareness is low among healthcare trainees. Healthcare professional trainees are expected to have a better knowledge base of Hepatitis C than the general population and increasing their awareness of this disease early in their education could have profound impact on improving the diagnostic rate of Hepatitis C later in their established career. This study shows that better educational efforts on this topic is warranted at the undergraduate   level.

Poster 13

The interface between sexual and injecting risk for hepatitis C virus infection among people who inject drugs in Montreal

Brendan Jacka, Centre de Recherche du CHUM; Julie Bruneau, CRCHUM; Stine Hoj, Université de Montréal; Didier Jutras-Aswad, Research Centre of the Centre Hospitalier de l'Université de Montréal; Department of Psychiatry, Université de Montréal; Nanor Minoyan, Université de Montréal / CRCHUM; Élise Roy , Université de Sherbrooke; Institut national de santé publique du Québec ; Geng Zang, CRCHUM

Background
Although hepatitis C virus (HCV) infection is both preventable and curable, acquisition remains high among key affected populations, particularly people who inject drugs and men who have sex with men. Most studies examining HCV infection and acquisition have focused on injecting risk behaviours with few considering the contribution of sexual activity, particularly among sexual minorities. Considering the complex interplay between sexual behaviour and drug consumption, a better understanding of HCV seropositivity and incidence in sexual minorities is necessary and timely.

Purpose
In a cohort of people who inject drugs, this study aimed to examine the association of recent sexual activity with 1) HCV seropositivity at enrolment, and 2) HCV seroconversion among those HCV seronegative at enrolment.

Methods
All participants enrolled in the HEPCO study (Nov 2004-Dec 2016) were eligible for the HCV seropositivity analysis, while those HCV seronegative at enrolment with >1 follow-up visit were eligible for the HCV seroconversion incidence analysis. Comprehensive behavioural and socio-demographic questionnaires and anti-HCV antibody testing was undertaken at enrolment and 3-6 month follow-up intervals. We assessed sexual activity in the past 3-6 months as a time-updating variable as follows: no sexual partner, opposite sex partner only, or same-sex (+/- opposite) partner. Associations between sexual activity and HCV infection at enrolment and time to HCV seroconversion were examined using logistic regression and Cox regression analysis, respectively.

Result
At baseline, of the 1518 participants enrolled (17% female), median age was 38 years (IQR: 29-46), and 65% (n=980) were anti-HCV antibody positive. Most participants recently injected cocaine (63%), 31% recently injected heroin and 34% prescription opioids. In unadjusted logistic regression, participants reporting recent opposite-sex partner only [odds ratio: 0.45, 95% CI: 0.35, 0.58], or same-sex partner (odds ratio: 0.50, 95% CI: 0.34, 0.73) were less likely to be HCV seropositive at baseline, compared to participants that reported no sexual partner. Within the HCV seroconversion incidence analysis, 153 of 432 participants had HCV seroconversion during 1229.29 years follow-up time: an incidence rate of 13.55/100py (11.53-15.82). In unadjusted Cox regression analysis, reporting recent same-sex partner (Hazard ratio: 2.06, 95% CI: 1.20, 3.54), but not opposite-sex partner only (Hazard ratio: 1.33, 95% CI: 0.91, 1.95), was associated with HCV seroconversion relative to reporting no sexual partner.

Conclusion
In this cohort of people who inject drugs, reporting recent same-sex partners was associated with reduced odds of HCV seropositivity at enrolment, but greater risk of HCV acquisition. These results suggest complicated interactions of risk behaviours, and the need for targeted prevention strategies for people who report   same-sex   activity.

Poster 14

Neighbourhood Risk Environments And Hepatitis C Virus Infection Among Persons Who Inject Drugs In Montreal

Nanor Minoyan, Université de Montréal / CRCHUM; Andreea Adelina Artenie, Université de Montréal; Julie Bruneau, CRCHUM

Background
Decades of research have elucidated the primary individual-level determinants of HCV infection among persons who inject drugs (PWID), the primary reservoir for the virus in high-income countries. Nevertheless, in Montreal, Canada, an estimated 72% of PWID will acquire HCV over the course of their lifetimes. The combined challenges of substance use, social vulnerability, and blood-borne-virus infection faced by this population imply a need to diversify harm-reduction strategies. According to the "risk environment" framework (1), harm reduction strategies must address the upstream social circumstances in which risk behaviours take place. Neighbourhoods have previously been used to represent exposures dictated by social vulnerability. However, few studies apply a longitudinal perspective to study the influence of neighbourhoods on HCV and drug related harms among persons who inject drugs (PWID).

Purpose
We aimed to examine the relationship between neighborhood deprivation and HCV transmission among PWID in Montreal.

Methods
We analysed data from the HEPCO prospective cohort study of Montreal PWID. Every 3 months, participants provide details on drug behaviours, sociodemographics, and dwelling postal codes. Blood samples are tested at baseline for presence of HCV RNA and antibody; RNA testing is performed at follow-up visits. Neighborhood deprivation was defined based on the Pampalon deprivation index, an aggregate census measure widely used in Quebec to represent social inequalities in health. Based on population quintiles of the index, participants were classified as residing in deprived (Q4-5) vs non-deprived areas (Q1-2-3). Descriptive analyses compared participant risk behaviours across deprivation categories. Cox proportional hazards regression was performed to estimate the association between neighbourhood deprivation and incident HCV infection (defined as a positive RNA test among RNA-participants).

Results
277 participants contributed 449 person-years of follow-up. 49 cases of incident HCV infection were observed among participants RNA-negative at baseline (IR: 11.0 cases 100 person-years). 543 postal codes were recorded throughout follow-up. Participants living in deprived neighborhoods (n=114, 47.5%) were less likely to report injecting heroin (32% vs 44.4%), sharing syringes (16.0% vs 23.0%), unstable housing (13.3% vs 23.0%) and employment (18% vs 31%) than those living in non-deprived areas. 84.8% of consecutive follow-up visits represented a move into or out of deprived neighborhoods. No association was found between neighborhood deprivation and rate of HCV infection (aHR: 1.1, 95% CI: 0.6-1.9, 76% of observations non-missing for deprivation).

Conclusion
Neighborhood deprivation was not associated with HCV transmission in analyses considering current neighbourhoods. Greater consideration of mobility across levels of deprivation in subsequent analyses may reveal a dynamic relationship between risk environments and HCV transmission, informing harm reduction strategies.

Reference:
1. Rhodes T. Risk environments and drug harms: a social science for harm reduction approach. Int J Drug Policy. 2009 May;20(3):193–201.

Poster 15

Reinfection/Recurrence of hepatitis C virus infection in a prospective cohort study of people who inject drugs in Montreal: does viral clearance mechanism play a role?

Nanor Minoyan, Université de Montréal , Geng Zang, CRCHUM; CRCHUM; Marie-Ève Turcotte, Research Centre of the Centre Hospitalier de l'Université de Montréal; Andreea Adelina Artenie, Université de Montréal; Élise Roy , Université de Sherbrooke; Institut national de santé publique du Québec ; Didier Jutras-Aswad, Research Centre of the Centre Hospitalier de l'Université de Montréal; Department of Psychiatry, Université de Montréal; Stine Hoj, Université de Montréal; Brendan Jacka, Centre de Recherche du CHUM; Naglaa Shoukry, CRCHUM; Julie Bruneau, CRCHUM

Background

Hepatitis C viral transmission among people who inject drugs (PWID) remains high in Montreal, despite availability of harm reduction strategies. The recent introduction of highly efficient, direct-acting antiretroviral therapies may have significant potential in curbing the HCV epidemic in this high-risk group. A portion of the HCV disease burden is attributable to HCV reinfection/recurrence among PWID who have previously cleared the virus, though estimates differ across studies. It further remains unclear whether the rate of reinfection/recurrence following spontaneous resolution differs from the rate following treatment-induced SVR. Estimating rates of reinfection/recurrence among these specific groups could have important implications for treatment guidelines, as well as to inform treatment-as-prevention strategies.

Purpose

We sought to estimate the rate of HCV reinfection/recurrence among PWID in Montreal. We also sought to compare rates observed among PWID who cleared the virus spontaneously (SC) to those who achieved SVR through IFN- or DAA-based treatment (TX).

Methods

We constructed an HCV reinfection/recurrence cohort using data from a prospective cohort study of PWID (Jan.2010-May 2017). Blood samples were tested at baseline for presence of HCV RNA and antibody, followed by tri-monthly follow-up visits to detect HCV RNA. Interviewer-administered questionnaires collected behavioural and sociodemographic data at each visit. Participants were eligible if they tested anti-HCV positive and negative for HCV RNA at baseline or over the course of follow-up. They were classified as SC or TX using a combination of self-report and clinical data. Participants began accruing follow-up time from baseline if they tested RNA-/Ab+. Those with active infection at baseline, as well as those who seroconverted over the course of the study, began contributing follow-up time once they became RNA-negative (SC group: ≥6 months after known infection date; TX group: following end-of-treatment SVR date). We defined HCV reinfection/recurrence as a positive HCV RNA test among individuals having previously cleared the virus, consistent with current clinical definitions. Kaplan-Meier survival curves were plotted, and time-to-event methods were used to calculate recurrence rates (overall and by clearance group).

Result

269 individuals contributed 771.0 person-years of follow-up (median follow-up: 27 months). Overall, 53 participants tested positive for HCV-RNA during follow-up (IR: 6.88/100 person-years, 95% CI: 5.15-8.99). 25 cases were observed in the TX group (IRTX: 6.58/100 p-y); 28 were observed in the SC group (IRSC: 7.16/100 p-y). Reinfection rates did not differ according to viral clearance mechanism (K-M log-rank test p-value: 0.65).

Conclusion

HCV reinfection/recurrence rates did not differ according to viral clearance mechanism within this prospective cohort study with relatively long follow-up and frequent testing intervals. The estimated overall rate of HCV recurrence was comparable to current estimates of primary infection in the cohort. Preventive strategies must therefore be promulgated alongside treatment to reduce drug-related harms among PWID.

Poster 16

Mental Health, Risk Behaviors and Substance Use Profiling of Patients Infected or At-Risk of Acquiring Hepatitis C Seen in Community and Hospital Care Settings in New Brunswick.

Samantha Bland, Dalhousie University; Daniel Smyth, The Moncton Hospital; Alyssa Margeson, The Moncton Hospital ; Stefanie Materniak , The Saint John Regional Hospital/Centre for Research, Education & Clinical Care of At-Risk Populations (RECAP); Meghan O'Brien, Upper River Valley Hospital; Duncan Webster, Saint John Regional Hospital

Background:
In New Brunswick, care for those infected with Hepatitis C Virus (HCV) is provided in both hospital and community-based settings. Limited provincial data currently exists about differences between patients seen in these settings. The Hepatitis C Positive and At-Risk (HEAR) database was created in 2014 to capture information about this population as a way to better understand the social and environmental factors contributing to the burden of HCV in the province. The current study utilized data in the HEAR database to analyze differences of socioeconomic status, high risk behaviors, mental health and psychiatric comorbidities, and patterns of substance abuse.

Purpose:
The aim of this study is to characterize the socioeconomic and environmental factors affecting patients seen in two common care settings in New Brunswick.

Method:
Personal health information was collected once informed consent was obtained both prospectively and retrospectively via self-reported questionnaires, by the patient's clinician or via electronic medical records. Baseline characteristics for all patients enrolled in the database between April 2014 and April 2016 were included in the analysis. Univariate comparisons of hospital-based and community-based patients were conducted using chi-square or Fisher's exact tests for nominal variables. Mann-Whitney or analysis of variance (ANOVA) was used for ordinal or interval data for non-normally and normally distributed data, respectively.

Results:
There were 374 patients included in the analysis. It was demonstrated that the community group had a greater proportion of unemployment (64%), social assistance (82%), past incarceration (70%) and mental illness treatment (72%). These patients also reported engaging in high risk activities including sexual behaviors (45%), tattoos (51%) and shared drug paraphenelia (75%). Notably, the community group demonstrated significantly higher rates of suffering abuse (47%) and positive family histories of addictions (72%) and psychiatric conditions (36%). Current substance use was more prevalent in the community group for all substances analyzed including tobacco (79%), alcohol (59%), cannabis (69%), benzodiazepines (47%), cocaine (40%), opiates (36%) and methamphetamine (10%). Substance abuse profiling of the cohort demonstrated a progression from tobacco, alcohol and cannabis use in early teens (age of first use 13.5, 14, and 14 respectively) to benzodiazepines, cocaine, methamphetamine and opiate use in early 20's (age of first use 20, 20, 21 and 22 respectively).

Conclusions:
The current study provides a comprehensive snapshot on the NB population infected or at-risk of acquiring HCV which was not previously available. Findings confirm that distinct differences exist between the patients seen in each type of setting. Barriers associated with both settings may limit screening and treatment uptake but understanding the fundamental differences between patients treated in each care setting has the potential to aid in facilitating targeted screening practices, reduce barriers associated with the uptake of care and identify key areas of clinical need in the future.

Poster 17

Toward taking account to provide care for Indigenous persons living with Hepatitis C virus (HCV) – identifying areas for future research and engagement

Wendy Wobeser, Queen's University; Alexandra King, University of British Columbia; Renee Masching, Canadian Aboriginal AIDS Network; Carrielyn Lund, Canadian Aboriginal AIDS Network; Daryl Luster, Pacific Hepatitis C Network

Background:
Our existing understanding suggests that there are significant needs and opportunities to care for Indigenous persons living with HCV. Innovative strategies can address challenges related to providing care in remote regions, stigma and competing health and social demand to improve access for all. Work to improve the readiness of both individuals and communities will be foundational to working toward HCV elimination.

Methods:
We conducted a face-to-face interactive workshop at the Wise Practices, Skills Building and Annual General Meeting of the Canadian Aboriginal AIDS Network in Calgary 2017. A sharing circle in which individual safety was emphasized was used.

Results:
A number of themes were identified. These included 1) the need for wise practices for care cascades for Indigenous people in general which promote wholistic health and wellness; 2) the need for after-care again guided by wise practices; 3) the importance of the criminal justice system and the need for the development of improved linkages to care and support between correctional facility and community; 4) the need to support wise practices to reduce and combat stigma, particularly at the local small community level and in a variety of contexts and 5) the need for education and support of health care workers in the evolving field of HCV treatment.

Discussion:
Future research to support the development of a wise practice approach to HCV care for Indigenous people in Canada will need attention to linkage and after-care. A wholistic and two-eyed seeing approach will be the focus of our future work.

Poster 18

Previously-exhausted T cells show enhanced memory properties following elimination of chronic antigen exposure

Mohamed S. Abdel-Hakeem, University of Pennsylvania (U Penn); Pierre Tonnerre, Harvard University; Jean-Christophe Beltra, University of Pennsylvania; Mohammed-Alkhatim Ali, University of Pennsylvania; Georg M. Lauer, Harvard University; E. John Wherry, University of Pennsylvania

T-cell exhaustion is a hallmark of immunological failure to control chronic viral infection and cancer. Blocking inhibitory receptors such as programmed death-1 (PD-1) can re-invigorate exhausted T cells (TEX) in animal models of chronic viral infection and in cancer patients. However, clinically, many patients fail to achieve durable tumor control with checkpoint inhibitors. Thus, a deeper understanding of other molecular pathways and mechanisms underlying reversal of T-cell exhaustion is needed. Human chronic infection by HCV represents a unique model, where treatment with novel DAAs leads to complete virological cure even following years of chronic infection. Whether TEX in these cured subjects convert to recovered T cells (TRECOV) with better functional and durable memory profile remains unknown. Here, we aim to determine the cellular profiles, molecular mechanisms, and population dynamics of TRECOV, and to investigate whether TEX become "reprogrammed" into more functional T cells following non-immunological cure of chronic disease. For these aims, we are examining virus-specific T cells from chronic HCV patients cured by DAA treatment and from mice cured of chronic lymphocytic choriomeningitis virus clone 13 (LCMV-cl13) by adoptive transfer. Using this well-defined tractable mouse model we can dissect the molecular mechanisms underlying changes in TEX following the elimination of chronic antigen stimulation. Additionally, this mouse model enables the investigation of the recall and protective capacities of TRECOV upon re-exposure to the antigen compared to TEX and memory T cells (TMEM). Our data indicate that some markers of exhaustion (including PD-1) are downregulated on TRECOV, while some markers of TMEM may be recovered upon cure of infection. Nevertheless, other aspects of TEX biology do not appear to be corrected simply by eliminating chronic infection. Rechallenge studies indicate that TEX retain some recall capacity. Nevertheless, co-transfer of TEX and TMEM indicate that TEX are highly compromised in this recall capacity when compared to TMEM on a per cell basis. The expansion of TEX was associated with a specific subset of cells identified by intermediate expression of PD-1 and expression of the transcription factor TCF-1+ (PD-1int TCF-1+). TRECOV possess enhanced recall response compared to TEX indicating some improvement in this key memory T cell property. However, we are currently examining the recall capacity of TRECOV compared to Tmem, and the subset dynamics involved. We are also investigating whether the changes in TRECOV are linked to selective recovery of a specific subset of TEX, and/or changes in their transcriptional profiles and epigenetic landscapes. We expect these studies to enhance our understanding of the immunological and epigenetic mechanisms of TEX recovery. These studies could also identify candidate transcriptional circuits differentially regulated in readily-recovered T cells that could represent novel therapeutic targets for reversal of immune exhaustion.

Poster 19

Participation of Argonaute isoforms and the TNRC6 family of proteins in small RNA-dependent promotion of HCV replication.

Yalena Amador-Canizares, University of Saskatchewan; Joyce Wilson, University of Saskatchewan

Background:
A liver-specific microRNA, miR-122, promotes replication of Hepatitis C Virus (HCV) by a poorly understood mechanism. Argonaute (Ago) proteins are host proteins involved in the activity of miRNAs, and are necessary for miR-122 promotion of the HCV life cycle. Humans express four Ago isoforms. Ago 1 and 2 are more widely and highly expressed among different cell lines and Ago2 is considered the primary Ago involved in HCV replication. TNRC6 (GW182 related) family proteins (A, B and C) interact directly with Ago proteins and are required for miRNA-mediated gene silencing in animal cells but their involvement in HCV replication has not been clarified.

Purpose:
Identify the contribution of Ago1 and 2 and the TNRC6 family proteins in the promotion of HCV replication dependent on small RNAs.

Method:
To investigate the specific role of Ago1 and 2 and the impact of other Ago isoforms in the HCV life cycle, we generated Ago2 and Ago1-2 knockout (KO) cells using the CRISPR/Cas9 technology. To determine the contribution of the TNRC6 family proteins we used lentivirus vectors to express a TNRC6B-derived inhibitory peptide that interacts with Ago proteins and represses miRNA pathways. We transfected in vitro transcribed viral RNA into the Ago-KO and TNRC6-inhibitory peptide expressing cells by electroporation, and compared the viral replication in wild type cells.

Results:
Sanger sequencing confirmed biallelic indel mutations consistent with abrogation of the expression of Ago2 and Ago1-2 genes, respectively. The absence of expression of both proteins was confirmed by Western blot. Ago2 KO cells supported relatively robust HCV replication with replication levels only 30-50% lower than in wild-type cells. This indicates that at least one of the other Ago isoforms is able to sustain high levels of HCV replication when Ago2 is not present. Interestingly, in the absence of Ago2's cleavage activity, perfect match small RNAs directed against miR-122 binding site 1 can promote HCV replication as miR-122 mimics. Data on the ability of the Ago1-2 KO cells to support HCV replication will be presented. Although expression of the TNRC6B-derived peptide abrogated the activity of small RNAs in a plasmid-based reporter assay, preliminary results showed no effect on viral replication.

Conclusions:
Our results suggest that miR-122 specific binding pattern is dispensable for HCV replication, in the absence of the slicer activity of Ago2, and that other small RNAs that bind to the 5' end of the genome can substitute for miR-122. Additionally, other Ago isoforms can support miR-122-dependent HCV replication. Interestingly, the TNRC6 family proteins seem to be nonessential for the promotion of viral replication. These data add information on the mechanism by which miR-122 promotes the HCV life cycle and also provide insight into the roles of the different Ago isoforms in miRNA activity.

Poster 20

Dissecting the role of the poly(C)-binding protein 2 KH domains in the hepatitis C virus life cycle

Sophie Cousineau, McGill University; Selena Sagan, McGill University

Background:
The hepatitis C virus (HCV) uses a number of cellular elements - including proteins and microRNAs - to promote its own replication and to protect itself from cellular molecular defenses against viruses. One particular cellular RNA-binding protein, the poly(C)-binding protein 2 (PCBP2), is known to mediate the stability and expression of a number of cellular transcripts, and is also known to be co-opted by several positive-strand RNA viruses to promote their replication. Six PCBP2 binding sites have been identified on the HCV genome, including in areas of the 5' and 3' untranslated regions which are known to play important roles in HCV translation and RNA replication. However, the exact mechanism by which PCBP2 affects HCV replication still remains to be elucidated.

Aims:
We aim to identify the specific step(s) of viral replication that are affected by PCBP2, and the specific PCBP2 RNA binding domains (called K homologous domains, or KH domains) involved in these interactions.

Methods:
We are using the HCV cell culture system (specifically the JFH-1T viral strain and the Huh-7.5 cell line) to assess how viral protein synthesis, viral RNA accumulation, and the production of infectious viral particles is affected by siRNA-mediated knockdown of PCBP2 or the overexpression of a FLAG-tagged PCBP2 construct. We have generated FLAG-tagged constructs with mutations in each PCBP2 KH domain, which we will use to identify the domains whose RNA-binding activity is crucial for PCBP2's role in the viral life cycle. We are also using luciferase assay systems to investigate the effect of PCBP2 on viral IRES-mediated translation independently of HCV RNA accumulation, and a chimeric viral construct where HCV protein expression is driven by a PCBP2-independent EMCV IRES to assess how PCBP2 affects viral RNA replication and accumulation.

Results:
We have found that knocking down endogenous PCBP2 inhibits HCV protein expression, RNA accumulation, and infectious particle production — which can all be partially rescued by the expression of wild type PCBP2-FLAG. Our preliminary results show that while the KH3 domain mutant construct is also able to partially rescue HCV replication, the KH1 and KH2 domain mutants are unable to rescue viral RNA accumulation and infectious particle production. Our luciferase assay results suggest that PCBP2 is important - but not limiting - for HCV IRES-mediated translation. We will present preliminary results that examine if PCBP2 has an effect on viral RNA stability and replication.

Conclusions:
We anticipate that investigating PCBP2-HCV interactions will help clarify the role of this host protein in the viral life cycle, and will provide a model for the regulation of viral RNA accumulation, and/or the switch from translation   to   replication.

Poster 22

Characterisation of the role of cyclophilin A in innate immune responses during HCV infection

Che Colpitts, University College London; Justin Warne, Wolfson Institute for Biomedical Research, University College London; David Selwood, Wolfson Institute for Biomedical Research, University College London; Greg Towers, Division of Infection and Immunity, University College London

Background.
Cyclophilin A (CypA) is a key player in several viral infections. For example, the capsid of HIV-1 binds CypA to help cloak itself from pattern recognition receptors and evade innate immune responses in macrophages (Rasaiyaah et al. 2013 Nature 503:402-5). Treatment of HIV-1-infected macrophages with cyclophilin inhibitors (CypIs) elicits interferon (IFN)-β production and suppresses HIV-1 replication. Interestingly, a CypI (SCY-635) that was evaluated in a phase 1b clinical trial for chronic HCV infection suppressed HCV replication and led to an increase in endogenous IFN levels in patients (Hopkins et al. 2012 J. Hepatol. 57:47-54). CypIs have been shown to disrupt formation of the membranous web (Madan et al. 2014 Gastroenterology 146:1361-72), the virus-induced membrane rearrangements thought to cloak HCV replication intermediates from pattern recognition receptors . Furthermore, CypA was recently shown to regulate the activation of innate antiviral RNA sensing pathways (e.g. RIG-I) (Liu et al. 2017 eLife 6:e24425). These findings suggest a link between CypA and innate immune responses during HCV infection, although the mechanisms are unclear.

Purpose.
To dissect the role of CypA in innate immune responses during HCV infection.

Method.
We are employing chemical biology (using a panel of novel CypIs that are either non-immunosuppressive derivatives of cyclosporin A or unrelated synthetic small molecules) in combination with virological, biochemical and biophysical approaches.

Results.
We screened the novel CypIs for antiviral activity against HCV. Huh7.5 cells were pre-treated with CypIs prior to infection with HCVcc (Luc-J6/JFH1) and then incubated in the presence of CypIs for 72 hours. HCV infection was measured by luciferase reporter activity. Several of the novel CypIs were active at nanomolar or low micromolar concentrations, exhibiting strong antiviral activity against HCV without immunosuppressive effects. Antiviral activity correlated with the binding affinity of the CypI for CypA (i.e., molecules lacking HCV antiviral activity did not bind to CypA), supporting the specific role of CypA in HCV infection. The active CypIs were more potent against full-length HCVcc than subgenomic replicons, consistent with the involvement of innate immune responses (which target multiple steps of the viral life cycle). Furthermore, the active CypIs were 5- to 10-fold more potent in Huh7 cells (where RIG-I is functional) than in Huh7.5 cells (where RIG-I is defective).

Conclusions.
We have identified novel CypIs with potent anti-HCV activity, which we are currently using in mechanistic studies aimed at elucidating the role of CypA in innate immune sensing of HCV. Our findings may contribute to the development of complementary treatment strategies for HCV. Furthermore, they may open perspectives for novel immunomodulatory antiviral approaches against other medically important viruses that rely on CypA as a host factor and for which curative treatment strategies are lacking (e.g., hepatitis B virus, Dengue virus, Zika virus).

Poster 23

Investigation of the Molecular Mechanisms that Determine Isolate Specific Differences in Neutralization Sensitivity of HCV

Janelle Johnson, University of Alberta; Holly Freedman, University of Alberta; jianqu He, University of Alberta; John Law, University of Alberta; Michael Houghton, University of Alberta

Background:
It is estimated that there are about 1.75 million new Hepatitis C Virus (HCV) infections per year worldwide and around 20% will develop liver cirrhosis or liver cancer if left untreated. Direct acting antiviral drugs are available for the treatment of HCV with success rates of over 90%. But these treatments are expensive and cured patients can still be reinfected. To eliminate HCV, a prophylactic vaccine is needed. One of the major challenges in the development of a vaccine is the genetic diversity of the virus. Currently, there are 7 major genotypes and hundreds of subtypes. A global vaccine needs to be effective against all HCV genotypes. Our laboratory is developing an adjuvanted vaccine comprising recombinant E1/E2 viral envelope glycoprotein and non-structural protein components designed to elicit cross-neutralizing antibodies along with broad cross-reactive T cell responses against HCV. Our previous data shows that our E1/E2 glycoprotein component can elicit broad cross-neutralizing antibodies in humans and animals. However, variation is seen in the effectiveness of these antibodies to neutralize different HCV genotypes. Our vaccine-induced antisera showed strong homologous neutralization activity against genotype 1a H77c virus, while exhibiting significant differences in neutralizing activity against two closely related isolates of HCV genotype 2a, the J6 and JFH-1 strains.

Methods:
E1 and E2 glycoprotein domains were swapped between the resistant J6 and sensitive JFH strains to narrow down the location of this differential neutralization sensitivity. Exchanges of variant amino acids in the E2 glycoprotein of these two HCV genotype 2a viruses were then conducted systematically to determine if specific amino acids were important for conferring this differential neutralization sensitivity. In addition, we investigated the role of the N-terminal hypervariable region 1 (HVR1) of the E2 protein in this isolate-specific neutralization by making recombinant virus with the HVR1 deleted or swapped for the JFH-1 version in the J6 virus. We tested these recombinant viruses for neutralization sensitivity against our 1a E1/E2 antisera.

Results:
We have shown that 1) the E2 glycoprotein dictates this differential neutralization sensitivity between these two isolates; 2) isolate specific amino acids within E2 do not affect the differential neutralization sensitivity; but 3) differential neutralization is mediated by the HVR1 and; 4) antibodies in our vaccine antisera are not directly targeting the HVR1 of JFH-1 or J6 2a virus.

Conclusions: While HVR1 can be implicated in mediating this isolate-specific neutralization, interestingly, our vaccine antisera does not appear to target the HVR1 of either of the genotype 2a viruses directly implying that HVR1 has an indirect effect. We are currently investigating the potential mechanisms of HVR1's indirect effect on neutralization sensitivity. Together, our data could help us to design a better vaccine antigen or antigen cocktail capable of expanding and optimizing the breadth of cross-genotype protection.

Poster 24

The annealing location, not the annealing pattern, is important for the mechanism of small-RNA/miR122 promotion of Hepatitis C Virus genome replication

Rasika Kunden, University of Saskatchewan; Yalena Amador-Canizares, University of Saskatchewan; Joyce Wilson, University of Saskatchewan

Background:
Hepatitis C virus infects over 120 million people worldwide and can lead to the development of liver cirrhosis and hepatocellular carcinoma. Replication of HCV is unique in requiring a liver-specific host cellular microRNA, miR-122, but the mechanism by which miR-122 promotes HCV replication is poorly understood.

Purpose:
MiR-122 anneals to two sites in the 5' untranslated region (UTR) of the genomic RNA and the mechanism of replication promotion is thought to rely on the specific annealing pattern between miR-122 and the HCV genome. However, contrary to this notion, we recently identified that synthetic small-RNAs having perfect complementarity with the miR-122 binding region, on HCV genome, can also promote HCV replication. The annealing pattern of the synthetic small-RNAs did not resemble that of miR-122 and suggested that the annealing location rather than the annealing pattern was more important for the mechanism by which small-RNA annealing promotes the HCV life cycle.

Method:
To test this notion, we aimed to map the range of locations to which small-RNA annealing can promote HCV replication. We designed several 19bp small-RNA duplexes to target different locations on the HCV genome; including on and near the miR-122 binding sites; within the HCV Internal ribosome entry sequence (IRES); at other predicted miR122 binding sites; and within the 3'UTR. We assayed HCV replication promotion by the small-RNAs in cells in which endogenous miR-122 activity was blocked using a miR-122 antagonist. Since the 19 bp synthetic small-RNA duplexes were also potential small interfering RNAs (siRNA), we used Ago2 knockout (Ago2KO) cells to abolish siRNA knockdown activity.

Results:
From analysis of an array of small-RNAs, we found that annealing of 19 bp duplexes at or near the miR-122 binding sites promoted HCV replication, and that annealing of small-RNA elsewhere on the HCV genome did not. A small-RNA that anneals to nucleotides 19-37 was the most efficient at promoting HCV replication, and annealing of this RNA to one site promoted HCV replication more potently than miR-122 annealing to two sites. Small-RNAs that anneal between nucleotides 13 and 44 in the 5' UTR were also active, but their potency decreased as they moved away from base-pairs 19-37 in either direction. Finally, HCV replication promotion required annealing of at least 13 nucleotides.

Conclusions:
We have identified nucleotides 13 and 44 as the boundary between which annealing small-RNAs can promote HCV replication, with annealing to nucleotides 19-37 being the most efficient. In future studies, we will identify RNA structures and RNA protein binding modulated by the small-RNAs that promoted HCV replication versus small-RNAs that did not, in order to better understand the mechanism by which miR-122 promotes HCV replication.

Poster 25

Post-treatment liver stiffness measurements predict the development of liver-related complications in patients with HCV cirrhosis who achieve SVR post-DAA therapy

Frederic Nguyen, University of Ottawa; Cynthia Tsien, University of Ottawa; Curtis Cooper, U Ottawa; Chrissi Galanakis, Ottawa Hospital Research Institute

Background

Chronic hepatitis C virus (HCV) infection may lead to cirrhosis and liver-related complications (LRC) such as hepatocellular carcinoma (HCC), ascites, hepatic encephalopathy (HE) and esophageal varices. Transient elastography (TE) is a reproducible, non-invasive measurement of liver fibrosis in HCV, and may predict LRC. HCV therapy with SVR appears to decrease liver stiffness (LS) however, whether this is also associated with fewer LRC is unclear.

Purpose

To evaluate whether a reduction in LS post-HCV treatment with sustained virologic response (SVR) is associated with a lower incidence of LRC in cirrhotic patients within 24 months of therapy.

Methods

We included all cirrhotic patients (LS >12.5 kPa) treated with direct acting antivirals (DAAs) between May 1, 2013 and June 1, 2016 with SVR and pre- and post-treatment TE. We excluded patients with new/worsening events before post-treatment TE. Those with baseline events (HCC, ascites, etc.) were included, and evaluated for worsening events, as defined by progression of post-treatment grading of ascites/varices/HE compared to baseline. The absence of new or worsening events was recorded as 'non-event'. ROC curves and Kaplan-Meir analysis were used. Person-time was calculated from the post-treatment TE date to the last clinic visit up to 24 months post-treatment.

Results

Of 57 patients, we excluded 4 patients with new LRC prior to post-treatment TE. TE was performed a median 32 weeks after end of treatment (IQR 28.5 weeks). 40/53 (75.5%) patients had reduction in LS, with a mean decrease of 10.7 kPa (SD 10.4). There were no differences in baseline characteristics of patients with/without decreased LS. Post-treatment, 4 events occurred during follow-up: 1 new varices, 1 new HCC, and 2 progression known varices. The incidence rate for patients with increased LS was 0.47/100 person-weeks, vs. 0.19/100 person-weeks for patients with decreased LS (RR 2.5, p=0.40, 95% CI: 0.26-24.0), with no significant difference in mean time to event (74 weeks vs. 79 weeks, respectively, p=0.55). All events occurred in individuals with LS >20.75 kPa, while no events occurred in individuals with LS score < 2 0.75 kPa (4/20 vs. 0/33, p=0.02). This LS cutoff also had the best AUC (0.786) with a sensitivity of 100% and specificity of 67%. Post-treatment, 20/53 (37.7%) patients still had a LS above 20.75 kPa.

Conclusions

In our cohort of patients with early cirrhosis (Child-Pugh class A, MELD < 1 5), successful antiviral therapy led to a reduction in LS in most patients. Prior studies have identified a LS cutoff of 20 kPa as associated with clinically significant portal hypertension, and this was confirmed in our post-treatment cohort. Many (37.7%) patients remained above this cut-off and require LRC monitoring post-SVR. The predictive value of long-term, serial LS measurements requires evaluation.

Poster 26

Influence of Ribavirin on Metabolic Measures in Paritaprevir-Ombitasvir-Dasabuvir Hepatitis C Antiviral Treatment Recipients

Curtis Cooper, U Ottawa Chrissi Galanakis, Ottawa Hospital Research Institute; Mary-Anne Doyle, The Ottawa Hospital; Angela Crawley, Ottawa Hospital Research Institute;

Background-
Chronic HCV infection perturbs lipid and glucose metabolism. The influence of HCV cure as well as DAA and ribavirin (RBV) exposure on these measures is unclear.

Methods-
HOMA-IR, glucose and lipid metabolic measures were assessed from baseline at week 4, week 12 and 12 weeks post-treatment. Pre- and post-treatment transient elastography were performed. The measures were compared between RBV-free and RBV-containing regimens using t-tests at a significance level of $p < 0.05$.

Results-
22/24 (92%) patients completed treatment and achieved SVR (PP= 22/23, 96% SVR). Two patients were lost to follow-up at week 12 with one of the latter having detectable virus at the end of treatment. HbA1c decreased during treatment in both groups with a more significant decrease in the RBV-containing group (week 4: mean change ± SD RBV-containing -0.89 ± 0.56 vs -0.21 ± 0.25, p=0.01), (week 12: RBV-containing -1.3 ± 0.41 vs -0.08 ± 0.28, $p < 0.0001$). However, this likely primarily represents a RBV-induced anemia effect and not a true decline in HbA1c. These improvements were not sustained 12 weeks post-treatment where the HbA1c in the RBV-containing group had increased from baseline while RBV-free regimen was associated with a further decrease (mean change ± SD RBV-containing 0.14 ± 2.2 vs -0.18 ± 0.29, p=0.03). No differences were observed in HOMA-IR, glucose and insulin during or 12 weeks post-treatment. LDL-C, non-HDL-C and TC: HDL-C levels increased less during treatment with RBV-containing regimens compared with RBV-free regimens (week 12 mean change ± SD: LDL-C RBV-containing 0.09± 0.59 vs 0.78± 0.93, p=0.04, non-HDL-C 0.09± 0.63 versus 0.89 ±1.0, p=0.03, TC:HDL-C -0.04±0.61 vs 1.2±1.4, p=0.01). There was no difference in mean changes in lipid levels 12 weeks post-treatment compared with baseline in either group. Overall fibrosis scores decreased (mean change ± SD: -0.49 ± 5.9) at 12 weeks post-treatment compared to the screening visit. This did not differ among RBV groups (p=0.84) and cirrhosis status (p=0.85). At 12 weeks post treatment, CAP scores increased (29.2 ± 64.6) compared to screening. CAP scores increased in both RBV-free and containing groups (31 ± 71.1 and 25± 55.1, p=0.90) and in cirrhotic and non-cirrhotic patients (25 ± 84.5 and 31 ± 57.5, p=0.91), though no significant differences were observed among the groups.

Conclusion:
Eradication of HCV with RBV-containing regimens resulted in an earlier and more signficant decrease in HbA1c yet slower and less pronounced increase in cholesterol levels compared with RBV-free regimens during the treatment phase. Further studies are needed to understand the mechanism by which ribavarin impacts glucose and lipid pathways and the long term significance of these differences.

Poster 27

Cirrhosis regression with DAA treatment in early and advanced cirrhosis

Curtis Cooper, U Ottawa; Chrissi Galanakis, Ottawa Hospital Research Institute;

Background:
Fibrosis regresses following direct acting antivirals (DAA) treatment in non-cirrhotic HCV-infected patients. Fibrosis regression has also been noted in cirrhotics, though the extent to which regression occurs in advanced cirrhosis is unclear.

Methods:
We examined fibrosis regression in HCV infected patients with cirrhosis treated with interferon-free DAA. Fibrosis was measured by Fibroscan® Transient Elastography (TE). We compared changes in fibrosis scores pre- and post-treatment in patients with early and advanced cirrhosis. Early cirrhosis was defined as 12.5-19.9 kPa and advanced cirrhosis 20.0 kPa or more. Changes from baseline were measured by chi-square and t-tests at a $p < 0.05$ significance level. Mid-P exact tests were used for cells with less than five patients.

Results:
43 cirrhotic patients were included. Patients were male (72%) with a mean age of 59 years (SD 8.2). The majority were infected with genotype 1 (74%), treatment naïve (51%) and 25 (58%) were defined as advanced cirrhotics. Patients were mainly treated with Sofosbuvir/Ledipasvir ±Ribavirin (RBV) (42%) and Simeprevir + Sofosbuvir ± RBV (26%). 38/43 (88%) achieved SVR. Post-treatment Fibroscans were performed a mean of 33 weeks (SD 24.3) after treatment end. Median pre-treatment fibrosis score was 21.8 kPa (IQR 19.2) and the median change from pre- to post-treatment was -6.0 kPa (IQR 10.2). The overall mean fibrosis score decreased from pre-treatment (mean change -6.7 kPa, SD 10.7, $p < 0.0001$).15/43 (36%) of patients regressed to a non-cirrhotic range by TE following DAA treatment. Patients with early cirrhosis were more likely to regress to a non-cirrhotic TE range compared to those with advanced cirrhosis (56% early vs. 20% advanced, p=0.02). Patients with early cirrhosis were also more likely to have a lower Metavir score post-treatment compared to patients with advanced cirrhosis among HCV genotype 1 infections (60% early vs. 24% advanced, p=0.04) and among treatment naïve patients (60% early vs. 17% advanced, p=0.05). Despite not regressing to non-cirrhotic range, patients with advanced cirrhosis achieved fibrosis regression as well (mean change -10.9kpa, SD 10.7, $p < 0.0001$).

Conclusions:
Patients with early and advanced cirrhosis exhibit fibrosis regression with DAA treatment. Patients with early cirrhosis often regress to non-cirrhotic range fibrosis following treatment, while those with advanced cirrhosis are less likely.

Poster 28

Effects of Direct Acting Antiviral HCV treatment on Lactate and Glucose patterns

Curtis Cooper, U Ottawa; Chrissi Galanakis, Ottawa Hospital Research Institute; Matt Driedger, University of Ottawa

Background:
Metabolic function may be influenced by HCV infection, cirrhosis, Direct Acting Antivirals (DAA) and ribavirin (RBV). We explored patterns of lactate and random glucose in DAA+/-RBV treated patients with chronic HCV infection.

Methods:
All HCV infected patients treated with interferon-free DAAs with available lactate and glucose data were included. Lactate and random glucose were evaluated at baseline, week 4, end of treatment and 12-24 weeks post-treatment. Group-based trajectory modeling was used to identify the number of lactate and glucose trajectories. Model selection was based on the Bayes Information Criterion (BIC). The posterior probability of group membership for each trajectory ranged from 0-1. Factors determining the probability of group membership were assessed by multivariate linear regression analysis.

Results:
442 patients received 457 DAA treatments. Patients were male (65%) with a mean age of 56 (SD9.5). Patients were infected with genotype 1 (72%) and 47% were cirrhotic. Treatments consisted of SOF/LDV ± RBV (55%) and 40% contained RBV. 162 patients had available lactate data. Mean baseline lactate was 2.3mmol/L (SD0.67). The 2-group trajectory model best fit the data (BIC -600.74). 93 patients (57%) were assigned to group 1 (declining lactate over the course of treatment and post-treatment), while 69 (43%) patients were in group 2 (increasing lactate on treatment followed by a post-treatment decline in lactate). Cirrhosis predicted 16% greater probability of membership to the group 1 trajectory (B=0.16, 95%CI 0.06-0.27, p 0.05).

Conclusion:
Distinct lactate and glucose trajectories were identified. Most patients had declining lactate values while those on RBV and with elevated baseline lactate experienced an increase in lactate during treatment. Random glucose is mostly unchanged during DAA treatment and elevated glucose at baseline tends to normalize post-treatment.

Poster 29

A Descriptive Analysis of the Effectiveness of Direct Acting Antiviral Therapies at Achieving SVR-12 in Chronic HCV Patients with Various Co-Morbidities and Characteristics in NB

Matthew Stewart, Dalhousie Medicine New Brunswick; Daniel Smyth, The Moncton Hospital; Stefanie Materniak, The Saint John Regional Hospital/Centre for Research, Education & Clinical Care of At-Risk Populations (RECAP); Alyssa Margeson, The Moncton Hospital ; Meghan O'Brien, Upper River Valley Hospital; Duncan Webster, Saint John Regional Hospital

Background:
Chronic Hepatitis C Virus (HCV) affects approximately 0.7% of Canadians and is associated with significant burden for both patients and the healthcare system. New Direct Acting Antiviral (DAA) treatments have been demonstrated to be up to 99% effective across a variety of genotypes.

Purpose:
There is limited research demonstrating the effectiveness of DAAs in New Brunswick (NB) patients with differing underlying comorbidities. Using data contained within the Hepatitis C Positive and at Risk (HEAR) database, the study aims to describe cure rates amongst patients in NB who presented with various comorbidities at baseline in order to inform physicians, patients and policy makers.

Method:
Data was collected from the HEAR database, an anonymous registry that contains data on roughly 800 New Brunswick patients who are either infected with HCV or at-risk of infection. Patients who received treatment between April 2014 and April 2016 and whom had SVR-12 results available prior to April 30, 2016 were included in the current analysis. Univariate comparisons of those who did and did not achieve SVR-12 on the basis of a number of potential confounders were conducted using Fisher's exact tests, chi-squared tests, p-values and 95% confidence intervals, as appropriate.

Results:
Of the 139 patients in the registry who received DAA containing therapy for their HCV infection, 92.8% (95% CI, 88.5-92.2) achieved SVR-12. No medical or psychiatric comorbidities reported at baseline were found to be a statistically significant predictor for treatment success or failure.

Conclusions:
The findings of the current study demonstrate that patients in NB can be successfully treated with a variety of DAA regimens, regardless of their baseline comorbidities. This study adds valuable local data to the treatment knowledge base with the potential to assist in informing policy makers involved in expanding access and care across the province.

Poster 30

Z-PROFILE: Real-world utilization and effectiveness of elbasvir/grazoprevir in adult patients with chronic hepatitis C in Canada

Keith Tsoi, Janie Trepanier, Merck Canada Inc.; Keith Tsoi, St. Joseph's Healthcare Hamilton; Edward Tam, LAIR Centre; Brian Conway, Vancouver Infectious Diseases Centre; Chris Fraser, The Cool Aid Community Health Centre; Bahe Rajendran, The Peterborough Clinic; Julie Tremblay, Centre Sida Amitié; Kris Stewart, Saskatchewan Infectious Disease Care Network; Benoit Trottier, Clinique Médicale du Quartier Latin; Alnoor Ramji, University of British Columbia; Sergio Borgia, William Osler Health System; Victor Kramer, Merck Canada Inc.

Background:
Elbasvir/grazoprevir (EBR/GZR) is approved in Canada for the treatment of chronic HCV infection with genotypes (GT) 1 and 4, with/without ribavirin, and for GT3 with sofosbuvir (SOF). Broad government and private reimbursement is now available.

Purpose:
The aim of this study is to describe the effectiveness of EBR/GZR and the profile of patients selected for treatment in a Canadian real-world setting.

Method:
A multicenter retrospective chart review of HCV-infected patients treated with EBR/GZR among selected Canadian health care providers was undertaken. In this interim analysis, patients initiating EBR/GZR treatment between 01/2016 and 05/2017 were included.

Results:
A total of 185 patients from 10 sites were included in this interim analysis. The mean age was 53.2 years, 56.8% were male, 80.5% Caucasian and 7.6% Aboriginal. Genotype distribution included patients infected by GT1a (n=116, 62.7%), GT1b (n=30, 16.2%), GT1 subtype unavailable (n=8, 4.3%), GT3 (n=19, 10.3%), GT4 (n=8, 4.3%), GT6 (n=1, 0.5%) or mixed infections (n=3, 1.6%). Pre-treatment fibrosis was evaluated by FibroScan in 86% of cases. Fibrosis score ranged from F0-1 (n=101, 54.6%), F2 (n=34, 18.4%), F3 (n=17, 9.2%), F4 (n=32, 17.3%) and 1 unknown. In this cohort, 7.6% had CKD stages 3-5 and 21.1% had documented injection of illicit drugs within 12 months of EBR/GZR treatment initiation. Baseline NS5A resistance-associated substitutions (RAS) were only detected in 1/17 evaluated patients (H58wt/Y) infected by GT1a or GT1 subtype unavailable. Prescribed regimens included: EBR/GZR x 12 weeks (n=168, 90.8%); or EBR/GZR+RBV x 16 weeks (n=17, 9.2%). Patients receiving longer courses of treatment were most often infected by GT1a (n=12) and/or treatment experienced (n=14, including 3 who previously failed all-oral DAAs). SOF was prescribed with EBR/GZR for all 19 patients with GT3. Per protocol evaluation demonstrated an SVR12 of 99.0% (97/98) and an SVR24 of 98.2% (56/57). The single relapsed patient was F1, GT1A and PegIFN+RBV treatment-experienced who received 16 weeks of EBR/GZR+RBV. One patient also had a confirmed reinfection by genetic testing.

Conclusion:
Following approval of EBR/GZR in Canada, it has been used quite broadly across its entire range of indications. The achievement of SVR in all but one patient to date in the per protocol analysis of this Real-World cohort supports the utility of EBR/GZR as a therapeutic modality for the treatment of chronic HCV infection. This study is collecting Real-World Evidence on 400 patients from 25 sites across Canada.

Poster 31

Paritaprevir/ritonavir/ombitasvir, dasabuvir + ribavirin in people with HCV genotype 1 and recent injecting drug use or receiving OST: The D3FEAT study

Brain Conway, Jason Grebely, Kirby Institute, UNSW Sydney; Brian Conway, Vancouver Infectious Diseases Centre; Chris Fraser, The Cool Aid Community Health Centre; Alberto Moriggia, Fondazione Epatocentro Ticino; Evan Cunningham, UNSW Sydney; Edward Gane, Auckland Clinical Studies; Catherine Stedman, Christchurch Hospital and University of Otago; Curtis Cooper, U Ottawa; Erika Castro, Centre Hospitalier Universitaire Vaudois; Patrick Schmid, Kantonsspital St Gallen; Kathy Petoumenos, Kirby Institute, UNSW Sydney; Behzad Hajarizadeh, The Kirby Institute; Marks Philippa, The Kirby Institute; Amanda Erratt, The Kirby Institute, UNSW Sydney; Sharmila Siriragavan, The Kirby Institute; Olav Dalgard, Akershus University Hospital; Karine Lacombe, Hôpital Saint-Antoine; Jordan Feld, To; Julie Bruneau, CRCHUM; Jean-pierre Daulouede, Csapa Bizia; Jeff Powis, South Riverdale Community Health Centre; Philip Bruggmann, Arud Centres for Addiction Medicine; Gail Matthews, The Kirby Institute, UNSW Sydney; Ian Kronborg, Footscray Hospital; David Shaw, Royal Adelaide Hospital, Adelaide; Adrian Dunlop, Newcastle Pharmacotherapy Service; Tanya Applegate, The Kirby Institute, UNSW Sydney; Sione Crawford, Hepatitis Victoria; Gregory J Dore, The Kirby Institute

Background:
Direct-acting antiviral therapy is safe and effective in people with HCV receiving opioid substitution therapy (OST), but there are little data among people with recent injecting drug use (IDU).

Purpose:
The aim of this study was to evaluate the efficacy, and safety of paritaprevir/ritonavir, ombitasvir, dasabuvir with or without ribavirin for chronic HCV genotype (G) 1 among people with recent IDU and/or receiving OST.

Methods:
D3FEAT is an international open-label study that recruited untreated participants with recent IDU (past 6 months) and chronic HCV G1 infection between June 2016 and February 2017 in seven countries. Participants received paritaprevir/ritonavir, ombitasvir, dasabuvir with (G1a) or without ribavirin (G1b) administered twice daily in a one-week electronic blister pack (records timing of each dose) for 12 weeks. The primary endpoint was undetectable HCV RNA 12 weeks post-treatment (SVR12). Modified intent-to-treat analyses was calculated excluding those lost to follow-up and/or not achieving SVR for reasons unrelated to HCV infection or its treatment.

Results:
Among 87 participants (mean age 48; 26% female; 8% with cirrhosis, 90% G1a), 21% were not receiving OST and had recent IDU, 43% were receiving OST with no recent IDU and 37% were receiving OST and had recent IDU. Overall, 94% (82/87) completed 12 weeks of therapy and 97% (84/87) had undetectable HCV RNA at the end of treatment (ETR), including 96% (75/78) and 100% (9/9) in those with HCV G1a and G1b, respectively. ETR was similar in those with and without recent IDU prior to screening (96% vs. 97%, P = 0.743). SVR was 91% (79/87). In modified intent-to-treat analyses excluding those lost to follow-up between ETR and SVR (n=3), SVR was 94% (79/84). There were no virological failures and two cases of virologic recurrence (phylogenetic analysis pending to confirm reinfection vs. relapse).

Conclusions:
Paritaprevir/ritonavir/ombitasvir, dasabuvir with or without ribavirin for 12 weeks is effective among people with HCV genotype 1 with recent IDU and/or receiving OST.

Poster 32

Global, regional, and country-level estimates of viraemic hepatitis C virus infection among recent people who inject drugs: A systematic review

Jason Grebely, Kirby Institute, UNSW Sydney; Sarah Larney, National Drug and Alcohol Research Centre, UNSW Sydney; Amy Peacock, National Drug and Alcohol Research Centre, UNSW Sydney; Sam Colledge, National Drug and Alcohol Research Centre, UNSW Sydney; Janni Leung, School of Public Health, Faculty of Medicine, University of Queensland, ; Matthew Hickman, University of Bristol; Peter Vickerman, University of Bristol; Sarah Blach, Center for Disease Analysis; Evan Cunningham, UNSW Sydney; Konstantin Dumchev, Ukrainian Institute for Public Health Policy; Michael Lynskey, National Addiction Centre, King's College London; Jack Stone, University of Bristol; Adam Trickey, University of Bristol; Homie Razavi, Center for Disease Analysis; Richard Mattick, National Drug and Alcohol Research Centre, UNSW Sydney; Gregory J Dore, The Kirby Institute; Louisa Degenhardt, National Drug and Alcohol Research Centre, UNSW Sydney

Background:
People who inject drugs (PWID) are a priority population in the response to achieving hepatitis C virus (HCV) elimination. However, recent estimates of viremic HCV among PWID at the global, regional, and county-levels are needed.

Purpose:
We undertook multiple global systematic reviews to estimate the viraemic prevalence and number of recent (within the past 12 months) PWID with HCV infection, and the proportion of all people with HCV infection who are recent PWID. Estimates were produced at global, regional, and country-levels.

Methods:
Data generated from a systematic review of the global HCV prevalence and country-level disease burden models were combined with systemic reviews of global injecting drug use prevalence and HCV prevalence among recent PWID. Viraemic prevalence among recent PWID, the numbers of recent PWID living with HCV infection, and the proportion of total global infections occurring among recent PWID were estimated.

Findings:
There are an estimated 6.1 million recent PWID aged 15-64 years living with HCV globally [39.2% prevalence among recent PWID, uncertainty intervals (UI 31.5-47.0]. People who recently inject drugs comprise an estimated 8.7% (UI 5.2-13.7) of all viraemic HCV infections globally. The number of viraemic HCV infections among recent PWID was greatest in East and Southeast Asia (1.5 million, UI 1.0-2.1), Eastern Europe (1.5 million, UI 0.7-2.4), and North America (1.1 million, UI 0.5-1.8). Half of all viraemic HCV infections among recent PWID are from just four countries: the Russian Federation, the United States, China, and Brazil. The proportion of all viraemic HCV infections among recent PWID was greatest in Latin America (21.7%, UI 16.5-29.1), Eastern Europe (19.0%, UI 9.7-33.2), Australasia (17.8%, UI 13.2-24.6), Caribbean (17.0%, UI 9.1-39.4), and Western Europe (16.7%, UI 9.5-36.6). Countries where it is estimated that at least one-third of people with viraemic HCV are recent PWID include Georgia, Austria, Finland, Germany, Malaysia, Puerto Rico, and Canada. In a further eight countries (Estonia, Slovakia, Denmark, Luxembourg, Iran, Brazil, United States, and New Zealand), at least one-quarter of people with viraemic HCV are estimated to be recent PWID.

Implications: There is considerable variation between countries and regions in HCV viraemia prevalence among recent PWID, and in the proportion of total HCV viraemia that is among recent PWID. This study highlights the need to understand the relative importance of recent PWID in local HCV epidemics, and to tailor prevention and treatment responses to meet global HCV elimination targets.

Poster 33

Eradication Of Chronic Hepatitis C Infection With Direct Acting Antivirals Is Associated With Reduction In Fibrosis By Transient Elastography (Fibroscan).

Apoorva Bollu[1], George Ou[1], Hin Hin Ko[1], Jeanette Feizi[2], Amy Wong[2], Alnoor Ramji[1]

1 Department of Medicine, Division of Gastroenterology, University of British Columbia, Vancouver, BC, Canada, 2 Gastrointestinal Research Institute, Vancouver, BC, Canada

Background: Eradication of chronic hepatitis C infection (CHC) is associated with reduced mortality and morbidity, particularly in those with advanced fibrosis. Histological regression of liver fibrosis has been reported in interferon (IFN)-based therapies, which may be partly attributed to IFN's anti-fibrotic effect. There is evolving data for fibrosis regression post- Direct acting antiviral (DAA) therapy.

Purpose: To determine if liver stiffness, an indirect measure of fibrosis, improves with SVR following DAA therapy.

Methods: This was a retrospective study conducted at a University-affiliated, tertiary referral hepatology clinic in Vancouver, Canada.

Patients with CHC treated with IFN-free, DAA regimens between 03/2013-10/2016, and SVR at 12 weeks post-therapy were assessed for inclusion in the study. Patients with concomitant non-CHC liver disease, and those missing either pre-therapy or post-therapy transient elastography (TE) were excluded. FibroScan was used for all TE measurements.

Results
105 patients met study criteria and were included. Mean age was 58±8.3 years and 71 (68%) were male. 95 (90%) patients had genotype 1 (1a – 57, 1b – 33, unknown – 5). 63 (60%) received LDV/SOF based regimens, while 17 (16%) and 16 (15%) received SOF/VEL and PrOD based regimens, respectively. Remaining 9 (9%) received SOF/SIM or SOF/RBV.

After a median follow-up of 34 (range 12-70) weeks post-therapy, there was significant reduction in TE (p=0.016) (see table 1).

Of 53 patients with F3/4 fibrosis, after a median follow-up of 34 (range 12-58) weeks, the TE scores improved from 21.1±14.0 kPa to 15.0±11.0 kPa (p=0.01). Fibrosis stage was downgraded in 25 (47%) patients.

Of 52 patients with F1/2 fibrosis, after a median follow up of 35 (range 12-70) weeks, the TE scores improved from 6.3±1.8 kPa to 5.2±1.6 kPa (p<0.01). Fibrosis stage was downgraded in 17 of 20 (85%) F2 patients after SVR.

Conclusion: Eradication of CHC with DAAs is associated with improved TE scores. Fibrosis stage reduction was more frequent among those with F3/F4 fibrosis pre-therapy. Further longer-term studies are needed to verify whether the change in TE is due to reduction in inflammation or hepatic fibrosis.

Table 1

	Pre-Treatment	Post-treatment
TE Score, kPa Mean (SD) Median (IQR)	13.8 ± 12.4 9.5 (6.1, 15.6)	10.1 ± 9.2 6.5 (5.1, 11.6)
Fibrosis Stage, n (%) F1 (<7.1kpa) F2 (7.1 – 9.4 kPa) F3 (9.5 – 12.4 kPa) F4 (>12.5 kPa)	32 (30.5%) 20 (19.0%) 22 (21.0%) 31 (29.5%)	61 (58.1%) 11 (10.5%) 9 (8.6%) 24 (22.9%)

Poster 34

REAL WORLD IMPACT OF DIRECT ACTING ANTIVIRAL THERAPY ON PATIENT REPORTED OUTCOMES

Sahar Saeed, McGill University; Erica EM Moodie, McGill Univesity; John Gill, Southern Alberta HIV Clinic; Alexander Wong, Regina Qu'Appelle Health Region; Curtis Cooper, University Ottawa; Sharon Walmsley, University Health Network; Mark Hull, BC Center of Excellence; Valerie Martel-Laferriere, Centre de Recherche du Centre hospitalier de l'Université de Montréal; Erin Strumpf, McGill University; Marina Klein, McGill University; CTN 222 Canadian HIV/HCV Co-Infection Cohort Study , McGill University Research Institute

Background: Clinical trials evaluating direct-acting antivirals (DAA) show substantial improvements in patient-reported outcomes (PROs) in HIV-HCV co-infected patients. However, trials have limited generalizability and patients are seldom followed post treatment response. We therefore investigated the impact of all oral-DAA therapy on health-related quality of life (HR-QOL) in a generalizable HIV-HCV co-infected population.

Methods: The Canadian Co-Infection Cohort Study prospectively follows 1785 HIV/HCV co-infected participants from 18 centers. Data on sociodemographic, clinical, PRO and prescriptions are collected biannually through self-administered questionnaires and chart review. A segmented multivariate linear mixed model compared changes in HR-QOL post-DAA compared to pre-treatment trends. HR-QOL was measured using the EQ-5D© questionnaire in English or French. Current health was scored on a visual analog scale (VAS) from 0 to 100 (worst to best health) and participants reported extent of difficulty (no/some/extreme problems) in five health domains: mobility, self-care, usual activities, pain/ discomfort, anxiety, or depression. Multivariate models included time-updated CD4 cell count, HIV viral load, injection drug use and fixed covariates at DAA initiation; age, sex, Indigenous ethnicity, liver fibrosis and diagnosis of psychiatric disorder.

Results: Between 2014-2016, 318 participants initiated oral DAAs, 200 completed at least 1 visit before and after DAA treatment (total of 1868 visits) with a mean of 3.2 years (SD 2.6) pre- and 0.7 years (SD 0.5) post-DAA follow up time. 70% of DAA regimens consisted of ledipasvir/ sofosbuvir. Median age at DAA initiation was 52 (IQR 48, 56), 76% were male, 90% had HIV viral load <50 copies/mL, median CD4 count was 505 cells/mL (IQR 297, 710) and 27% had evidence of liver fibrosis. Sustained virologic response rates were 92%. Table 1 summarizes changes in VAS and EQ5D utility scores pre- and post- DAA treatment. No changes in HR-QOL were observed before DAA initiation. The immediate effect of DAA therapy resulted in a 2 unit (95% CI, -1.0- 4.9) increase in patient's current health state and continued to increase post-treatment by 1.6 units/year (-1.3, 4.4).

Table 1. Impact of DAA treatment on health-rated quality of life on current health state (VAS) and EQ5D.

	HR-QOL (VAS) ß (95% CI) Adjusted	EQ5D ß (95% CI) Adjusted
Mean score at DAA initiation	65 (60, 69)	0.77 (0.73, 0.81)
Pre-treatment Rate (Secular trend before DAA initiation, per year)	-0.5 (-1.0, 4.9)	-0.004 (-0.009, 0.0004)
Change in Intercept (Immediate effect)	2.0 (-1.0, 4.9)	-0.004 (-0.03, 0.02)
Post-DAA Rate (Compared to pre-treatment rate, per year)	1.6 (-1.3, 4.4)	0.005 (-0.021, 0.031)

Conclusion: Limited data currently exists on real world PROs post DAA treatment. To our knowledge this is the first report to investigate changes in PROs in a real-world setting where we found slight improvements in HR-QOL in the short-term following DAA treatment.

Poster 35

Efficacy and adherence to sofosbuvir and velpatasvir among people with chronic hepatitis C virus infection and recent injection drug use: the SIMPLIFY study

Evan Cunningham, UNSW Sydney; Alan H Litwin, Montefiore Medical Centre; Olav Dalgard, Akershus University Hospital; Janaki Amin, Faculty of Medicine and Health Sciences; Jeff Powis, South Riverdale Community Health Centre; Julie Bruneau, CRCHUM; Jordan Feld, To; Margaret Hellard, The Burnet Institute; Philip Bruggmann, Arud Centres for Addiction Medicine; Phillip Read, Kirketon Road Centre; Curtis Cooper, U Ottawa; Brian Conway, Vancouver Infectious Diseases Centre; Adrian Dunlop, Newcastle Pharmacotherapy Service; Edward Gane, Auckland Clinical Studies; Chris Fraser, The Cool Aid Community Health Centre; Behzad Hajarizadeh, The Kirby Institute; Marks Philippa, The Kirby Institute; Quiene Sophie, The Kirby Institute; Sharmila Siriragavan, The Kirby Institute; Melanie Lacalamita, Poliklinik für Infektiologie; Gregory J Dore, The Kirby Institute; Jason Grebely, Kirby Institute, UNSW Sydney

Background:
Interferon-free direct-acting antiviral therapy (DAA) is safe and effective in people with hepatitis C virus (HCV) receiving stable opioid substitution therapy (OST), but there are little data among recent people who inject drugs (PWID). Improved evidence of DAA outcomes among recent PWID is crucial for elimination efforts, given the potential impact of HCV treatment as prevention.

Purpose:
The aim of this study was to evaluate the efficacy and adherence to sofosbuvir and velpatasvir therapy for chronic HCV among recent PWID.

Methods:
SIMPLIFY is an international open-label study that recruited participants with recent injecting drug use (previous six months) and chronic HCV genotype (G) 1-6 infection between March and October, 2016 in seven countries (19 sites). Participants received sofosbuvir/velpatasvir daily administered in a one-week electronic blister pack (records the time and date of each dose) for 12 weeks. Adherence was calculated by dividing the number of total doses removed from the blister-pack (to a maximum of one per day) by the total number of expected doses (84 doses). The primary endpoints included sustained virological response at 12 weeks (SVR) after the end of therapy and non-adherence (daily in the past month. A total of 96% (n=99) of the population completed treatment with four early discontinuations (loss to follow-up, n=3; overdose death, n=1). End of treatment response (ETR) was 96% (99/103). Two participants with an ETR did not have SVR12 (loss to follow-up, n=1; reinfection, n=1). In intent-to-treat analyses among all participants, SVR12 was 94% (97/103). Median adherence to therapy was 94%, although 88% missed at least one dose of therapy and adherence significantly decreased during therapy. Recent injecting of cocaine/amphetamines at treatment initiation and during treatment was associated with non-adherence. Inconsistent dose timing was also associated with non-adherence to therapy. Non-adherence did not impact sustained virological response.

Conclusion:
This study demonstrated high rates of SVR and high adherence to once-daily sofosbuvir/velpatasvir therapy among a population of people with recent injecting drug use. Despite imperfect adherence to therapy, there was no impact of non-adherence on response to therapy, suggesting that adherence is not barrier to successful DAA therapy in PWID. These data support the inclusion of people with recent injecting drug use in HCV treatment strategies.

Poster 36

Elbasvir, Grazoprevir; with or without Ribavirin and its Effectiveness with Sofosbuvir resulting SVR in chronic hepatitis C genotype 1 prior experienced co-infected individuals. A randomized open label clinical prospective trial: EGRESS – C

Menisa, Zaman, Nimy John, Saint Vincent Hospital; Dr.Patrick Basu, Cornell University Medical Center ,NY; Aanchal Malhotra, Cornell University Medical Center ,NY; Menisa Zaman, Cornell University Medical Center, NY; Aloysius Madhok, JJP VAMC Icahn School of Medicine at Mount Sinai

Objectives: Oral directly acting anti-viral therapy has virtually cured Chronic Hepatitis C. However, for a few sub-groups (genotype 1,3 and 4 with co-infection with HIV) in HCV remain challenging. Also baseline resistance associated variance in genotype 1a and 3 need longer duration of therapy.

Aim: Study evaluates the safety and SVR of Elbasvir, Grazoprevir; with or without Ribavirin and its effectiveness with Sofosbuvir

Methods: Twenty-two patients recruited from 2014-2016 from community with prior experience to HCV therapy

Exclusion: Liver transplant, HCC, HBV, Hemoglobinopathies (Sickle cell), HIV RNA undetectable, CHF, Renal insufficiency, prior allergy to DAA's, cirrhosis of liver with MELD > 12, sepsis, cardiomyopathy, active IVDU, active cocaine, no family support, non-compliant to drug rehab program, Major depression, decompensated affective disease, treatment failure prior because non-compliance, high dose PPI
Prior DAA failure:
n=7 were on Harvoni
n=8 were on Olysio
n= 5 Viekera Pak
n=2: Sofosbuvir plus Ribavirin
All HIV co-infected individuals were on Atripla; while few were also on Raltegravir.
Further subdivided into two groups:
Group A (n= 10): Elbasvir 100 mg + Grazoprevir 50 mg + Sofosbuvir 400 mg for 12 weeks
Group B (n= 12): Elbasvir 100 mg + Grazoprevir 50 mg + Sofosbuvir 400 mg for 12 weeks with RBV 600 mg a day

Patient Characteristics :
Group A (n = 10) Mean age 59, Genotype 1a(n = 5),1b (n = 5),Mean HCV viral load 4.7 million, Mean CD4 count 560,Mean HIV viral load 3699. Out of the total 10, past response unknown in 4/10, 3/10 were partial responders and 3/10 were relapsers.
Group B (n = 12) Mean age 58, Genotype 1a (n =6), 1b (n = 6),Mean HCV viral load 3 million, Mean CD4 count 436,Mean HIV viral load 387. Out of the total 12 , past response rate was unknown in 4/12, 4/12 were relapsers,3/12 were partial responders and 1/12 was non responder.

Results :
In group A HCV RNA load became undetectable in 8/10 by week 4 and 10/10 by week 8,Retention was 100% and ITT was 100%.Mean hemoglobin and ALT remained stable throughout 24 weeks.
In group B HCV RNA load became undetectable in 10/12 by week 4 and 11/12 (91.67%) by week 8. One patient withdrew due to shortness of breath and chest pain. Retention was 91.67% and ITT was 100%.Mean hemoglobin and ALT remained stable throughout 24 weeks.

Side Events:

Fatigue, Nausea ,Vomiting,Headache,Anemia (group B 9/29),Insomnia,Diarrhea

Constipation,UTIAbdominal pain, Hematuria, Renal Stone

Gouty attack ,Hypoglycemia,,Hyperglycemia,URI, Dysgeusia

Pruritus, Pneumonia (Group B,stopped meds and got hospitalised)

Conclusion: Clinical trial reveals promising SVR in a very selective Cohort of Chronic Hepatitis C Co-Infection in Prior experienced population with severe fibrosis and significant morbidities. A larger trial needs to validate.

Poster 37

Hepatitis C core antigen testing from dried blood spots as a diagnostic alternative for difficult to reach populations

Mia Biondi, University Health Network, Analiza Aquino, Mount Sinai Hospital; David Smookler, University Health Network; Marjolein van Tilborg, Toronto Centre for Liver Disease; Tony Mazzulli, Mount Sinai Hospital ; Harry Janssen, Toronto Centre for Liver Disease; Gregory Heymann, Toronto Centre for Liver Disease; Vera Cherepanov, Toronto Centre for Liver Disease; Gavin Cloherty, Abbott Molecular; Robert de Knegt, Erasmus MC University Medical Center Rotterdam; Matthew Kowgier, Toronto Centre for Liver Disease; Jordan Feld, To

BACKGROUND: Dried blood spots (DBS) are a simple and effective way to obtain patient samples for diagnosing blood-borne viruses, and are especially useful when sample processing time and cold storage is a challenge. DBS can be used for the detection of anti-hepatitis C antibodies as well as for reflex testing, bypassing the need for a second patient visit to confirm infection. Typically the confirmatory test has been the detection of viral RNA, however, this method may not be the most cost-effective. An alternative reflex test using HCV core protein is available, but there is relatively little information on core protein stability on DBS. It is also unclear whether variations in temperature affect detectability of core protein.

PURPOSE: To determine the stability of HCV core antigen on DBS cards under several environmental temperatures representative of transportation from rural and remote regions of Canada to public health laboratories.

METHODS: Blood was collected from five healthy controls and 74 confirmed HCV RNA-positive individuals, and spotted onto five DBS cards and allowed to dry overnight. Cards were subsequently stored under the following conditions for one week: -80oC (gold-standard), 4oC, 21oC, 37oC and alternating between 37oC and 4oC. A matched serum sample stored at -80oC served as a reference. DBS cards were eluted and all samples were tested in duplicate for the presence of anti-HCV antibodies and HCV core antigen.

RESULTS: Sensitivity and specificity for anti-HCV antibodies from DBS was 99-100% (depending on the condition) and 100%, respectively. When using a cut-off of 3 fmol/L the sensitivies of HCV core antigen from DBS were: 93% (-80oC), 93% (4oC), 92% (21oC), 90% (37oC), and 91% (37oC/4oC), while all healthy controls tested negative for core antigen. It should be noted that one HCV-positive sample was below a viral load of 500-3500 IU/mL (limit of detection), and therefore our diagnostic sensitivity would slightly improve had we excluded this sample. Interestingly, while we observed excellent concordance between serum and DBS samples for positivity, our data does not support the use of core antigen from DBS for virus quantification. Finally, negligible differences were noted between the storage conditions of DBS cards.

CONCLUSIONS: Our data demonstrates HCV core antigen stored on DBS cards is detectable under a range of temperatures. This suggests that the relatively inexpensive core antigen test could be incorporated into an algorithm where HCV antibody testing of DBS samples would be followed by reflex core testing. We propose the use of this method for large-scale, inexpensive screening programs to identify HCV-infected persons in rural or remote locations, as well as to improve testing rates among street-involved persons.

Poster 38

Pilot Project to Increase HCV Linkage to Care in Ontario's First Nations.

David Smookler, University Health Network; Leroy Quoquat, Lac Seul First Nation; Jordan Feld, To; Hemant Shah, University of Toronto, Toronto Centre for Liver Disease; John Kim, Public Health Agency of Canada

Background:
The government is dedicated to eliminating HCV in Canada by 2030. With SVR rates typically >95%, the challenge for HCV treatment is linkage to care. Multiple studies show First Nations people have especially high exposure to HCV, as well as other blood-borne infections; yet Indigenous Canadians have some of the poorest access to care in the country. How to deliver care to this demographic is essential knowledge for meeting Canada's target. Comprehensive data on incidence and prevalence of HCV in First Nations communities is lacking, due to limited testing. Complicating efforts to study this is a long history of unethical research performed on Aboriginal people in Canada, which has often left communities feeling used and disempowered.

We are developing a model of HCV testing and treatment for remote First Nations in Northwestern Ontario that addresses these challenges. By partnering with community leaders and local healthcare providers, introducing novel techniques for gathering HCV blood samples, and training local community members to obtain samples, we hypothesize that we can dramatically increase regional HCV testing and improving access to care. Here we recount the results of our pilot endeavor to introduce testing in a First Nation community in Northwestern Ontario.

Method:
A pilot community was selected based on the invitation of the local chief, after the proposal was presented to a Chiefs' Committee on Health in Northwestern Ontario. The community's health director
assembled a testing team composed of health staff and members of that community. The team developed a locally relevant approach to informing and incentivizing community members to participate in HCV testing. Team members were trained in Dry Blood Spot (DBS) sample gathering by the Public Health Agency of Canada. Pilot testing drive initiated in January 2017.

Results:
226 people in a community with an adult population of 655 were tested for HCV. 85% of those were also tested for HIV, and >90% for HBV. Testing was conducted over 3.5 days. Costs for the reagents and sample analysis were covered by the federal government; and local government was willing to pay for staff time and rewards for attendance, resulting in minimal financial outlay for the initiative. Qualitative evaluation of satisfaction of team members suggested excellent response to the initiative, with strong encouragement from the local Health Director to continue the initiative in other communities.

Conclusion:
This pilot gathered blood samples using DBS, which is presently unusual in Canada for HCV testing with linkage to care. This tactic of HCV testing, using DBS; with a community-guided, participatory approach; utilizing local community members is a successful method to obtain widespread HCV testing, one which could form the basis for an expanded model to test for infectious disease in First Nations communities throughout Canada.

Poster 39

Viral persistence in an HLA-B*27+ patient with acute hepatitis C virus infection: an evolving virus escapes from the haunting virus-specific CD8+ T cells

[1,2]Janine Kemming, [3]Nathalie Bedard, [1]Katja Nitschke, [1] Robert Thimme, [3,4]Naglaa H. Shoukry, [1]Christoph Neumann-Haefelin

[1]Internal Medicine II, University Hospital Freiburg, Freiburg, Germany; [2]Fakulty of Biology, Albert-Ludwigs University Freiburg, Freiburg, Germany; [3]Centre de Recherche du Centre Hospitalier de l'Université de Montréal (CRCHUM), Montréal, Québec, Canada, [4]Département de médecine, Université de Montréal, Montréal, Québec, Canada

Background and aims: HLA-B*27+ individuals have a great chance to spontaneously clear hepatitis C virus (HCV) genotype 1 infection. This protective effect of HLA-B*27 has been linked to an immunodominant HLA-B*27 restricted HCV-specific CD8+ T-cell epitope that is targeted in virtually all HLA-B*27+ patients with acute HCV genotype 1. Viral escape from this CD8+ T-cell response is hard for the virus to achieve, partially due to viral fitness constraints and partially due to a broad cross-recognition of evolving viral variants. In consequence, the virus is eliminated before it can select for several amino acid mutations that would allow viral escape. This concept, although very attractive, is based on findings from HLA-B*27+ patients with resolved or chronic HCV infection, respectively. Analysis of the CD8+ T-cell response in a patient with acute-persisting HCV genotype 1 infection as well as further phenotypical characterization of the HLA*B27 restricted response in this patient could confirm this concept.

Methods: To characterize the virus-specific CD8+ T-cell response in the acute persistent patient we perform longitudinal analysis of the CD8+ T-cell phenotype by flow cytometry, ultra deep sequencing and CD8+ T cell cross-recognition assessment of evolving variants via antigen-specific expansion.

Results: Next generation sequencing analysis demonstrated that the HCV genotype 1 infected acute-persisting patient displays gradual viral evolution over time: at the first available date after infection (calculated day 37 post infection), the main viral quasispecies contains the wild-type HLA-B*27 epitope, however, until day 465 post infection a total of 4 amino acid mutations develop within the 9-mer epitope sequence. Interestingly, HLA-B*27+ patients with chronic infection and detectable epitope-specific CD8+ T-cells are able to control viremia at low levels and display an PD1+/CD127+/TCF1+ phenotype, indicating that these cells still cross-recognized the variant virus despite the presence of several viral escape mutations in these patients. First data derived from the HLA-B*27+ patient with acute-persistent infection shows that the patient's virus-specific CD8+ T-cell phenotype shifts towards a CD127+/PD1+ phenotype coinciding with the establishment of viral mutations. These results support the link between cross-recognition of epitope variants, CD8+ T-cell phenotype and viral control. A deeper immunological analysis of this patient will be performed during Janine Kemming's visit to the group of Naglaa Shoukry and will be presented at the meeting.

Conclusion: Here we directly demonstrate the importance of broad cross-recognition of evolving viral variants for HCV clearance by HLA-B*27 restricted CD8+ T-cells and also describe the establishment of a unique phenotype of these cells that mediate viral control even in chronic infection.

Poster 40

FIBROSIS REVERSAL IN HCV/HIV CO-INFECTED PEOPLE WHO INJECT DRUGS (PWID) AFTER SUCCESSFUL HCV TREATMENT

Julie Holeksa, Vancouver Infectious Diseases Centre; Arshia Alimohammadi , Vancouver Infectious Diseases Centre; Brian Conway, Vancouver Infectious Diseases Centre; Amandeep Bassi, Vancouver Infectious Diseases Canada; Leo Wong, MUHC; Roy Nitulescu, McGill University; Marina Klein, McGill University; Astou Thiam , Vancouver Infectious Diseases Canada

Background:
Hepatitis C (HCV) is a virus that, if left untreated, will cause 5-25% of those infected to develop cirrhosis, hepatic failure or hepatocellular carcinoma, over 20 years or more. Individuals co-infected with HIV have been shown to progress more rapidly, with cirrhosis often developing within 10 years. Recent data suggest that an additional benefit of curing HCV infection may be reversal of fibrosis, but this has not been well documented in the setting of HIV co-infection and active intravenous drug use.

Purpose:
To document reversal of fibrosis after successful HCV treatment in HCV/HIV co-infected people who inject drugs (PWID), to provide additional rationale to expand access to HCV treatment in this population.

Methods:
Data were generated within the Canadian HIV/HCV Co-infection cohort, an ongoing national observational study. Demographic, behavioural, and clinical information were collected at 6-month intervals. Active PWID (drug use < 6 mo prior to HCV treatment), documented cure of HCV infection, and available liver staging data pre-HCV treatment and 24-48 weeks post-treatment were identified. Liver fibrosis was assessed by APRI scoring.

Results:
There are 91 participants: mean age 48 ± 8.8 years, 74% male, 89% Caucasian, 10% Aboriginal, with documentation of HCV and HIV infection 14 ± 6.7 and 15 ± 8.6 years prior to HCV treatment. Post hoc analysis using the Bonferroni correction revealed significant differences between APRI at baseline, (1.54 ± 1.62, n = 91) and 24 (0.56 ± 0.45, n = 73) and 48 (0.54 ± 0.37, n = 64) weeks post-treatment (p = 0.00). There was no difference between the two latter time points. For patients with baseline cirrhosis pre- and post-treatment APRI scores were baseline (3.65 ± 1.72 n = 19), 24 (1.02 ± 0.58, n = 16) and 48 (0.94 ± 0.48, n = 13) weeks post-treatment, while for patients with genotype 3 infection, these were baseline (1.91 ± 2.07, n = 14), 24 (0.73 ± 0.63, n = 11) and 48 (0.52 ± 0.43, n = 11) weeks post-treatment.

Conclusion:
Among HIV co-infected PWID successfully treated for HCV infection, a very significant reversal of fibrosis is measured. This correlation can also be seen amongst patients with advanced disease at baseline as well as those with genotype 3 infection (where fatty liver disease may be more prevalent), though sample size did not allow for power calculation. This documents another benefit of HCV therapy in a population at higher risk of long-term disease complications.

Poster 41

Type I Interferon-Associated Impairment of the Humoral Immune Response against HCV

Armstrong Murira, Institut Armand Frappier; Alain Lamarre, Institut Armand Frappier

Type I interferon (IFN-I) has been characterized to enhance cell-mediated immune responses against acute viral infections whilst impair immune activation in chronic viral settings as would be in the case of HCV and HIV. Here, we show that in addition to its effect on T cells, IFN-I drives impairment of effective humoral immune responses through direct interaction with B cells upon chronic viral infection. Using the classic LCMV murine infection model, we co-administered 4-hydroxy-3-nitrophenyl (NP) at the time of infection whereby flow cytometry analysis of B cell proportions and ELISPOT data revealed that compared to a normal humoral immune response in the VSV (acute) infection, LCMV-infected mice developed non-specific hypergammaglobulinemia along with diminished NP-specific responses shortly after infection. Notably, during persistent viral infections, infected hosts also exhibit aberrancies to the humoral response such as polyclonal activation and hypergammaglobulinemia. Accompanying this dysregulation, the emergence of neutralizing antibodies (nAbs) is delayed and bears negligible impact on the progression of the disease by the time they are successfully elicited. Altogether, these perturbations result in a diminished antigen-specific Ab response and an enhanced non-specific polyclonal response. These are hallmarks of disruption in the humoral immune response during a chronic infection. Our results also demonstrated that this impairment was limited to the T-cell dependent B-cell response and function was restored by ablation of IFN signaling through antibody-dependent IFN receptor blockade as well as B-cell specific IFN receptor knockouts. In addition, disrupted lymphoid architecture observed following immunofluorescent microscopy was also restored upon elimination of B-cell specific IFN signaling. Importantly, restoration of effective B-cell responses in transgenic mice also featured increased neutralizing antibody titers in ELISA assays, which were absent in the wildtype model with functional IFN signaling. Our findings illustrate the role played by IFN in limiting effective antibody responses by action on B-cells. Whereas complete blockade of IFN signaling would be deleterious, targeted B-cell specific restriction could improve humoral responses towards effective therapeutic and prophylactic measures against chronic infections such as HCV.

Poster 42

Reduced risk of HCV seroconversion among individuals undergoing psychotherapy: A population-based retrospective cohort of multi-testers 1992-2013

Abdool Yasseen, University of Toronto; Carmine Rossi, Research Institute of the McGill University Health Centre; Nazrul Islam, Harvard University; Stanley Wong, BC Centre for Disease Control; Zahid Butt, University of British Columbia; Nuria Chapinal, BC Centre for Disease Control; Maria Alvarez, BC Centre for Disease Control; Maryam Darvishian, University of British Columbia; Mel Krajden, University of British Columbia; Naveed Janjua, BC-CDC

Background:
Most new hepatitis C Virus (HCV) infections in developed countries occur among people who inject drugs (PWID); many of whom have concurrent mental illnesses. Although intervention strategies are recommended including psychotherapy, there is limited data on the effectiveness of psychotherapy.

Purpose:
To examine the effectiveness of psychotherapy counseling for reducing the risk of HCV seroconversion, and to compare this association across various at-risk subgroups.

Population:
Individuals tested for HCV between 1992 and 2013 in British Columbia, Canada.

Study design:
Population-based retrospective cohort, with time to event analysis.

Method:
Incidence rates of HCV seroconversion was calculated using an intercept only Poisson regression model and reported per 1,000 person-years. Univariable and multivariable Cox proportional hazards model was used to examine the associations between psychotherapy counseling and HCV seroconversion, and this analysis was repeated on stratified subgroups.

Results:
A total of 364,774 individuals were included in the study cohort, of which 7,669 (2.1%) experienced a HCV seroconversion event, and 14,560 (4.0%) underwent at least one psychotherapy session. Incidence of HCV seroconversion were highest among persons who inject drugs (14.9 (95%CI: 14.4, 15.4)), individuals living with HIV 11.3 (95%CI: 9.8, 13.1), problematic alcohol use (9.5 (95CI: 9.2, 4.1)), and those with missing or no fixed address (7.9 (95%CI: 6.8, 9.2). Overall psychotherapy was protective against HCV serconversion (aHR: 0.68 (95%CI: 0.62, 0.74)), with consistent effect estimates among PWID (aHR: 0.64 (95%CI: 0.58, 0.70)), problematic alcohol use (aHR: 0.73 (95%CI: 0.65, 0.81)), and psychotherapy session types (family - aHR: 0.59 (95%CI: 0.50, 0.70), small group - aHR: 0.72 (95%CI: 0.57, 0.91), large group - aHR: 0.41 (95%CI: 0.17, 0.99)). Individuals with 140 visits (aHR: 0.35 (95%CI: 0.30, 0.40)) showed protective effects indicative of a dose response relationship.

Conclusion:
Psychotherapy is effective at reducing the risk of HCV seroconversion among individuals with substance use issues, and the number of counseling visits was shown to be influential. Psychotherapy could be part of a package of services targeted to prevent HCV incidence to achieve World Health Organization elimination goals.

Poster 43

Patterns of practice and barriers to care for hepatitis C in the direct-acting antiviral (DAA) era: a cross-sectional national survey of Canadian physicians

Justin Chan, NYC Health + Hospitals; Marina Klein, McGill University; Joseph Cox, McGill University; Roy Nitulescu, McGill University; Jim Young, University Hospital Basel

Background:
DAA therapy for hepatitis C virus (HCV) infection provides an opportunity to decrease the burden of liver disease in Canada. However, of the 250,000 Canadians with chronic HCV, few have been treated (1). Several health system-related, patient-related, and physician-related barriers to care impede treatment scale up. Physician-related barriers include suboptimal training (2-3), negative attitudes towards treating high risk populations (4), and uneven application of clinical practice guidelines (5).

Infectious diseases (ID) physicians, having experience treating other chronic viral infections such as HIV, represent a physician group important to HCV care delivery in Canada. However, little is known regarding their HCV-related practices. Many may feel unprepared to treat HCV (2). Therefore, improving ID physician engagement in HCV care will be important for treating more HCV-infected patients in Canada.

Purpose:
To better identify areas in need of physician support or education, and to identify challenges that physicians are facing in the current era, our study aims to investigate the current patterns of practice and perceived barriers to HCV care that Canadian physicians face. We plan to survey general internists, ID physicians, hepatologists, gastroenterologists, and addiction medicine specialists to identify current practice patterns, interest in engaging in care, and factors associated with barriers to care. Herein, we describe our survey of ID physicians.

Method:
The study population includes ID physicians who are members of the Association of Medical Microbiology and Infectious Disease (AMMI) Canada, the national association representing medical microbiology and infectious diseases physicians. We selected a simple random sample of 30 members within each province. For provinces with fewer than 30 members, we included all members. This resulted in a total sample size of 167 potential respondents. We will deliver a one-time, web-based, response-guided survey. Questions relate to demographics, practice patterns, knowledge, attitudes toward treatment, and barriers to care. To encourage response, we will provide two weekly reminders after the initial invitation, and monetary compensation to each respondent.

Results:
Our primary outcome of interest is current level of HCV care provided, ranging to include no care, testing, evaluating, referring, and treating. The secondary outcome is respondent interest in starting to treat HCV in the upcoming year. We will report these findings along with barriers to care identified by respondents, such as suboptimal training or poor access to specialist support.

Conclusions:
HCV therapies have improved dramatically, but treatment rates are low. Our study provides data on the status of HCV care provided by ID physicians, their interest in scaling up treatment, and barriers to doing so. This will help us develop ways to support Canadian ID physicians, and improve the quality of HCV care.

Poster 44

Mobile Technology Access and Patient Preferences for HCV Care in the new Era of DAAs

Julie Beaulac, The Ottawa Hospital; Curtis Cooper, U Ottawa; Kim Corace, The Royal; Louise Balfour, The Ottawa Hospital; Mark Kaluzienski, The Ottawa Hospital

Background:
In this era of emerging, well tolerated, highly curative but costly HCV DAA treatments, gaps in engaging individuals in HCV care results in harm to infected individuals as well as contributing to ongoing risks of HCV transmission. Alternatives to traditional models of care are needed to reach and engage more individuals. Mobile technology interventions present opportunities for enhancing patient engagement, retention, satisfaction, and outcomes.

Purpose:
To assess the feasibility and patient attitudes toward using mobile technology in HCV care.

Method:
Cross-sectional survey data were collected from HCV patients (N=115) across two sites of The Ottawa Hospital Viral Hepatitis Program, a hospital-based outpatient clinic and a community program. Participants completed measures of demographics, HCV disease status and risk factors, and mobile technology access and preferences. Medical chart review supplemented survey data. Mann-Whitney and chi-square tests assessed for differences in mobile technology access, use, and preferences by treatment experience, ethnicity, site, gender, education level, or income level.

Results:
77.6% indicated that they owned a mobile device and of these, the majority also reported having access to the Internet (69.4%) and unlimited text plans on their devices (71.6%). Although most indicated that they had never used mobile technology to communicate with a health care provider, the majority (65.5%) reported comfort in sending/receiving texts. Half of respondents liked the idea of using a cell phone for HCV clinical care and follow-up; others expressed dislike or uncertainty. Poorer access to mobile technology was reported by treatment naïve, community site, and non-White participants (p values ranging from .02 to .003). Respondents from the community site, as compared to the hospital site, also rated significantly lower levels of comfort in sending/receiving texts (p = .008). A similar trend was found for respondents with incomes below $30,000 as compared to higher income (p = .085).Yet, groups equally liked the idea of using mobile technology in HCV care.

Conclusion:
Mobile technology may be an attractive and feasible alternative model to augment existing HCV care. The majority of participants have access to this technology and expressed favourable attitudes toward using this innovative method in their care. Variability in acceptability and accessibility of this approach was highlighted for specific sub-populations, so it will be critical to tailor care delivery to patient needs in order to effectively engage all individuals with HCV and ultimately increase successful HCV treatment delivery.

Poster 45

Strategies to improve the Cascade of Hepatitis C (HCV) Care at CUPS – an inner city clinic in Calgary.

Gisela Macphail , CUPS & University of Calgary; Andrew Lafreniere, CUPS; Lynda Watson-Waddington, CUPS; Rachael Edwards, CUPS; Kate Newcombe, CUPS

Background:
Calgary Urban Project Society (CUPS) serves those living in poverty in Calgary, Alberta. It integrates health, education, and housing supports together in one building. People with hepatitis C (HCV) are assessed in the primary care clinic and referred to the on-site HCV clinic for counselling, assessment, treatment, and peer support. Our cascade of care was recently defined.

Purpose:
To develop strategies to improve our cascade of care by suiting patients' and clinicians' needs better in terms of screening, testing, and supporting those with HCV.

Methods:
After determining our cascade of care data, electronic medical records were reviewed to assess reasons why people did not progress through from testing to treatment. Ensuing discussions with primary care providers and the multi-disciplinary HCV team elicited potential strategies to improve the cascade.

Results:
The cascade of care for CUPS showed 13 % of antibody tests (119/873) were positive over a 2 ½ year period. Only 67% of antibody positive people had a PCR. Of the people with HCV viremia, 39% followed through with the HCV clinic. Loss to follow up is the primary issue why people did not progress through the cascade of care. Additionally, competing issues such as insecure housing, mental health, and addictions are often preventing people from progressing. Breakdown of communication and documentation also accounts for some people failing to progress. 13% (15/119) of antibody positive people had no documentation of being informed of their results. 10 of these people were lost to follow up, making them unable to be informed, but 5 of them had repeat clinic visits. Through discussions with primary care providers and the HCV team, challenges regarding inconsistent charting and variable screening policies were identified. The HCV clinic is open half of the week, limiting options for care, as well as for support to the primary clinic. During the study time-frame, a fibrosis score F2 or greater was required for HCV medication coverage, thus 50% of patients were treatment ineligible.

Conclusions:
With the changing landscape of HCV care, new avenues for engagement are available. Patients no longer require a stage 2 fibrosis score or higher if certain symptoms are present, making more patients eligible for treatment coverage. Point of care (POC) antibody testing was recently implemented by the HCV team to help accelerate the testing process and allow for outreach testing in the future. Standardized documentation is being explored. The HCV clinic is designing a screening tool to assist health care providers in identifying and screening at-risk individuals. These supports should streamline care and provide structure when the HCV team is not available. To help support these changes, education sessions will be held and electronic medical record reminders will be used to help engage staff.

Poster 46

Identifying Patients Subgroups Who Benefit Most from Immediate vs. Delayed Treatment for Chronic Hepatitis C

Aysegul Erman, University of Toronto; William WL Wong, School of Pharmacy, University of Waterloo; Jordan Feld, To; Paul Grootendorst, Leslie Dan Faculty of Pharmacy, University of Toronto; Murray Krahn, Toronto Health Economics and Technology Assessment Collaborative (THETA), University of Toronto,

Background:
Recently introduced direct-acting antivirals (DAA) are highly effective but costly treatments for chronic hepatitis (CHC). Because of their cost, drug plans have restricted access to DAA therapy based on fibrosis level.

Purpose:
To identify patient subgroups most likely to benefit from immediate treatment vs. delaying treatment by 1 year.

Method:
A decision-analytic state-transition model with a weekly cycle length was developed to quantify the effects of a 1-year delay in DAA therapy on quality-adjusted life years (QALY) of CHC patient subgroups stratified by age, fibrosis level and viral genotype over their lifetime. The model assumed that patients would receive a Sofosbuvir-based DAA regimen depending on their fibrosis level and genotype as recommended by Canadian guidelines. Stage-specific fibrosis progression rates were estimated for each subgroup using a meta-regression model considering mean age, sex, duration of infection, genotype, alcohol and injection drug use behavior. All other clinical parameters were obtained from published literature. QALY gains associated with immediate vs. delayed treatment for each subgroup was determined and stratified into four levels of benefit. Results are displayed using a look-up table.

Results:
On average, 30-year-old patients infected with genotypes 2 or 3 with significant fibrosis (F3) obtained the greatest benefit from immediate vs. delayed DAA therapy (>1.00 QALYs). This was followed by cirrhotic patients younger than 60 years, who also displayed a large benefit (0.50-0.97 QALYs). All other groups had only a small or questionable benefit. More specifically, 40-50 year old genotype-1 patients with significant fibrosis, as well as 60 year-olds with at least significant fibrosis, displayed only a small benefit (0.20-0.45 QALYs) from immediate vs. delayed therapy. Individuals with no or mild fibrosis (F0 or F1) and those 70+ years of age with any level of fibrosis experienced no material gains from immediate treatment (0.05-0.18 QALYs). The relatively greater benefit of immediate treatment for certain groups with significant fibrosis are likely driven by a faster progression from F3 to F4 in younger patients and in those with non-genotype-1 infections, as well as by the higher sustained viral response rates for non-cirrhotic vs. cirrhotic patient.

Conclusion:
The current study presents estimates of benefit of immediate vs. 1- year delay in DAA therapy for various patient subgroups considering the effects of patient's age, disease severity and genotype on the natural history of CHC and on DAA treatment choice and outcomes. Results suggest that younger patients with more advanced fibrosis (≥F3) will benefit the most from earlier access to treatment while those with F0-F1 and older patients realize smaller benefit. Results are congruent with current reimbursement criteria focusing on prioritizing more advanced patients.

Poster 47

Restrictions for reimbursement of interferon-free direct-acting antiviral drugs for HCV infection in Europe

Alison Marshall, The Kirby Institute, University of New South Wales, Sydney; Stine Nielsen, INHSU; Alessio Aghemo, Department of Biomedical Sciences and Humanitas Clinical and Research Center, Humanitas University; Hannu Alho, Abdominal Center, Helsinki University Hospital, Helsinki University,; Markus Backmund, Ludwig-Maximilians- University; Philip Bruggmann, Arud Centres for Addiction Medicine; Olav Dalgard, Akershus University Hospital; Carole Seguin-Devaux, Department of Infection and Immunity, Luxembourg Institute of Health; Graham R Foster, Queen Mary University of London; Robert Flisiak, Department of Infectious Diseases a Hepatology, Medical University of Bialystok; Patrick Hoffmann, Ministry of Health; Liana Gheorghe, Gastroenterology and Hepatology, Fundeni Clinical Institute; David Goldberg, Health Protection Scotland; Ioannis Goulis, Department of Internal Medicine, Aristotle University of Thessaloniki; Matthew Hickman, University of Bristol; Ligita Jancoriené, Centre of Infectious Diseases, Vilnius University Hospital Santaros Klinikos, Vilnius University; Peter Jarcuska, First Department of Internal Medicine, University Hospital, University of Pavol Jozef Safarik; Martin Kåberg, Department of Infectious Diseases, Karolinska University Hospital,; Leondios G Kostrikis, University of Cyprus; Mihály Makara, Hepatology Center, St István and St László Hospital; Matti Maimets, Department of Internal Medicine, University of Tartu; Rui Tato Marinho, Department of Gastroenterology and Hepatology, Hospital Santa Maria, Medical School Lisbon, University of Lisbon; Mojca Matičič, Clinic for Infectious Diseases and Febrile Illnesses, University Medical Centre; Suzanne Norris, National Hepatitis C Treatment Programme, Health Service Executive, Dr Steevens' Hospital; Sigurður Ólafsson, Division of Gastroenterology, Department of Medicine, Landspitali University Hospital; Anne Øvrehus, Department of Infectious Diseases, Odense University Hospital, University of Southern Denmark; Jean-Michel Pawlotsky, Hopital Henri Mondor, Universite Paris Est; James Pocock, Gastroenterology Department, Mater Dei Hospital; Geert Robaeys, Department of Gastroenterology and Hepatology, Ziekenhuis Oost Limburg; Carlos Roncero, Addiction and Dual Diagnosis Unit, Psychiatric Department, Hospital Universitario Vall d'Hebron, Universidad Autónoma de Barcelona; Marieta Simonova, Department of Gastroenterology, Hepato-Pancreato-Biliary Surgery and Transplantology, Military Medical Academy; Jan Sperl, Department of Hepatogastroenterology, Institute for Clinical and Experimental Medicine; Michele Tait, National Hepatitis C Treatment Programme, Health Service Executive, Dr Steevens' Hospital; Ieva Tolmane, Department of Hepatology, Infectology Center of Latvia, Riga East University Hospital; Stefan Tomaselli, Office of Public Health; Marc van der Valk, Department of Infectious Diseases, Academic Medical Center; Adriana Vince, University Hospital for Infectious Diseases, University of Zagreb; Gregory J Dore, The Kirby Institute; Jeffrey V Lazarus, Barcelona Institute for Global Health (ISGlobal), Hospital Clínic, Univeristy of Barcelona; CHIP, Rigshospitalet, University of Copenhagen ; Jason Grebely, Kirby Institute, UNSW Sydney; Evan Cunningham, UNSW Sydney

All-oral direct-acting antiviral drugs (DAAs) for hepatitis C virus, which have response rates of 95% or more, represent a major clinical advance. However, the high list price of DAAs has led many governments to restrict their reimbursement. We reviewed the availability of, and national criteria for, interferon-free DAA reimbursement among countries in the European Union and European Economic Area, and Switzerland. Reimbursement documentation was reviewed between Nov 18, 2016, and Aug 1, 2017. Primary outcomes were fibrosis stage, drug or alcohol use, prescriber type, and HIV co-infection restrictions. Among the 35 European countries and jurisdictions included, the most commonly reimbursed DAA was ombitasvir, paritaprevir, and ritonavir, with dasabuvir, and with or without ribavirin (33 [94%] countries and jurisdictions). 16 (46%) countries and jurisdictions required patients to have fibrosis at stage F2 or higher, 29 (83%) had no listed restrictions based on drug or alcohol use, 33 (94%) required a specialist prescriber, and 34 (97%) had no additional restrictions for people co-infected with HIV and hepatitis C virus.

These findings have implications for meeting WHO targets, with evidence of some countries not following the 2016 hepatitis C virus treatment guidelines by the European Association for the Study of Liver.

Poster 48

A Meta-analysis of Health Utilities (Preference-Based Quality of Life) in Chronic Hepatitis C Patients

Yasmin Saeed, Leslie Dan Faculty of Pharmacy, University of Toronto; Joanna Bielecki, Toronto Health Economics and Technology Assessment (THETA) Collaborative; Lusine Abrahamyan, Toronto Health Economics and Technology Assessment (THETA) Collaborative; Petros Pechlivanoglou, Child Health Evaluative Sciences, The Hospital for Sick Children; Murray Krahn, Toronto Health Economics and Technology Assessment Collaborative (THETA), University of Toronto,; William WL Wong, School of Pharmacy, University of Waterloo

Background:
Chronic hepatitis C (CHC) has been shown to negatively impact patients' quality of life. Health utility is a measure of quality of life that incorporates a patient's preference for their current health state, and can be used to quantify the burden of a disease in terms of quality-adjusted life years lost. There has been an explosion of new research on health utilities in CHC patients since the advent of new antiviral therapies, yet no meta-analysis has been published in this area since 2008.

Purpose:
To synthesize the health utilities of patients with CHC in order to understand the burden of CHC; and for use in economic evaluations of CHC treatments and screening programs to guide funding decisions.

Method:
We searched MEDLINE, EMBASE, and the Cochrane Library for studies measuring health utilities in CHC patients using any instrument. The search was limited to English-language papers published from 1989 onward. Results were pooled by disease severity, treatment status, and utility instrument using meta-analysis. A meta-regression was used to examine patient and study design factors that impact utility scores.

Results:
Forty records met inclusion criteria and were included in the analysis. Results for studies using the EQ-5D-3L instrument are presented here. Sixteen clinical studies with a total of 6,012 CHC patients measured utilities using the EQ-5D-3L instrument. The mean age of patients was 45 years, and 64% were male.

Mild/moderate CHC was associated with a mild impairment in health utility (pooled utility score 0.79; 95% CI 0.75,0.82). Compensated cirrhosis (0.73; 0.63,0.83) and hepatocellular carcinoma (HCC) (0.75; 0.68,0.81) utilities were slightly lower, and decompensated cirrhosis utilities were substantially lower (0.65; 0.58,0.71). Being on treatment also lowered utilities (0.74; 0.71,0.78), but sustained virologic response (SVR) (0.82; 0.76,0.87) resulted in higher utilities than mild/moderate CHC.
There was a large degree of heterogeneity between studies in terms of study and patient characteristics. A meta-regression found that randomized controlled trials had higher mean utilities than observational studies ($p < 0.05$).
Limited utility data exist for certain subpopulations of CHC patients, including: decompensated cirrhosis, HCC, and post-transplant patients; patients with comorbidities such as HIV and haemophilia; and socioeconomically marginalized patients.

Conclusions:
CHC is associated with a significant impairment in quality of life, particularly in advanced disease. Curative therapy can alleviate this burden.
The large degree of heterogeneity between studies highlights the need to incorporate synthesized data from a wide range of studies in economic analyses of CHC screening and treatment, as well as the importance of incorporating the associated uncertainty surrounding these estimates.
This review included a significant amount of new data compared to a previously published meta-analysis (McLernon 2008). However, further research is still needed in certain subgroups of CHC patients.

Poster 49

Demographics and Clinical Outcomes for HCV-Positive Individuals in Southern Saskatchewan - The Regina Qu'Appelle HCV Cohort

Alexander Wong, Regina Qu'Appelle Health Region; Sarah Craddock, Regina Qu'Appelle Health Region; Sabyasachi Gupta, Regina Qu'Appelle Health Region; Dennaye Fuchs, Regina Qu'Appelle Health Region; Maria Folk, Regina Qu'Appelle Health Region; Cara Benz Tramer, Regina Qu'Appelle Health Region; Maurice Hennink, Regina Qu'Appelle Health Region; Tania Diener, Regina Qu'Appelle Health Region

Background:
Saskatchewan currently faces a unique hepatitis C (HCV) epidemic characterized by high rates of injection drug use and disproportionate representation of Indigenous persons. The Regina Qu'Appelle Health Region Infectious Diseases Clinic (RQHR IDC) serves as a tertiary referral site for HCV-positive individuals across southern Saskatchewan. To address the need for epidemiologic and clinical data to inform the epidemic, the RQHR IDC developed a comprehensive database for its HCV-positive individuals, the Regina Qu'Appelle HCV Cohort (RQHC). The development of the RQHC and current demographic and clinical data from the cohort are discussed.

Methods:
The cohort consists of all individuals with HCV viremia seen by the RQHR IDC from January 1/16 onwards. This includes individuals seen in the RQHR IDC and various outreach settings within urban Regina (community-based clinics and correctional facilities), but not individuals seen in rural and on-reserve settings. Using a customized electronic medical record, epidemiologic and clinical data is collected by clinic staff at each encounter and is standardized within the charting system to maximize data accuracy. Individual records with missing data were excluded from this analysis.

Results:
The RQHC consists of 766 patients. 316 of 766 persons (41.3%) were female, 255 of 766 persons (33.3%) were 35 years of age or younger. Indigenous peoples accounted for 64.2% (401/625) of the cohort. 210 of 766 individuals (27.4%) were co-infected with HIV. The predominant HCV genotypes represented were 1a (351/640, 54.8%) and 3 (197/640, 30.8%), comprising over 85% of the cohort with genotyping data. 320 of 644 individuals (49.7%) with Fibroscan data were F2 or greater (≥ 7.1 kPa), with 122 of these having F4 fibrosis (>12.5 kPa). 93 patients with genotype 1a HCV had baseline resistance testing, only 2 individuals were found to have clinically significant NS5A resistance-associated substitutions.

115 prescriptions for direct-acting antivirals (DAAs) were written between January 1/16 and March 31/17 in the RQHR IDC. Of these, 72 were for SOF/LDV, 18 were for PrOD +/- RBV, and 10 were for EBR/GZR. 82 prescriptions were written between April 1/17 and June 30/17; 57 were for SOF/VEL, 14 were for EBR/GZR, and 10 were for SOF/LDV. As of September 11, 129 persons had completed treatment and 50 were on treatment. Of 129 who had completed therapy, 77 achieved SVR12, 34 were pending SVR12, 5 relapsed or reinfected, 11 were lost to follow-up, and 2 deceased.

Conclusions: The RQHC informs the current HCV epidemic in southern Saskatchewan, with disproportionate representation of Indigenous peoples, women, and young persons 35 years of age and younger. Despite improved access to DAA therapy, relatively few persons are being treated. The numbers of individuals in southern Saskatchewan treated with DAAs must rapidly increase to realize WHO elimination targets by 2030.

Poster 50

SPATIAL ANALYSIS OF HCV INFECTION IN BRITISH COLUMBIA, CANADA

Zahid Butt, University of British Columbia; Naveed Janjua, BC-CDC; Sunny Mak, BC Centre for Disease Control; Dionne Gesink, University of Toronto; Mark Gilbert, BC Centre for Disease Control; Jason Wong, BC Centre for Disease Control; Amanda Yu, BC Centre for Disease Control; Stanley Wong, BC Centre for Disease Control; Maria Alvarez, BC Centre for Disease Control; Mei Chong, BC Centre for Disease Control; Jane Buxton, BC Centre for Disease Control; Mark Tyndall, BC Centre for Disease Control; Mel Krajden, University of British Columbia

Background:
'Core areas' of transmission for bacterial sexually transmitted infections have been described previously; however, research on characterizing core areas for chronic viral infections such as hepatitis C virus (HCV) is limited.

Purpose:
We aimed to identify distinct core areas of HCV infection in British Columbia, Canada during 1990-2013 using geographic mapping and spatial analysis methods.

Methods:
The British Columbia Hepatitis Testers Cohort was used to estimate HCV rates for all BC residents tested for HCV or HIV (~1.5 million) from 1990 to 2013. HCV core areas were identified both spatially and temporally for five time periods (1990-1993, 1994-1998, 1999-2003, 2004-2008 and 2009-2013) by conducting thematic mapping, kernel density estimation, hotspot analysis and cluster analysis (discrete Poisson) at the Census dissemination area level (smallest geographic area for which data were available) in ArcGIS and SatScan.

Results:
All spatial analytic methods showed consistency in identifying HCV core areas. 1) KDE showed core area expansion from the downtown of major cities in Metro Vancouver (MV), Vancouver Island, and Northern BC during 1990 to 1998, to smaller cities in MV and Interior BC from 2000 onward. 2) HSA showed statistically significant hot spots in MV (Vancouver downtown), Northern BC (Prince George) and Vancouver Island from 1990 to 2008 with expansion to other urban areas in MV (Surrey and Abbotsford) from 1990 to 2013. 3) Spatiotemporal cluster analysis (adjusted for injection drug use, HCV testing, age group, sex, material and social deprivation) revealed a persistent most likely cluster in MV (Vancouver downtown) from 1990 to 2008 with secondary clusters in urban areas in Northern and Interior BC. A secondary cluster was observed for Vancouver Island from 1990 to 2003. Recently (2009-13), the most likely cluster was observed in Northern BC (Prince George) with a secondary cluster in MV (Vancouver).

Conclusions:
Persistence of areas with high HCV rates in same geographic areas of Vancouver and Prince George over past two decades suggest that these are most likely core areas of HCV transmission. Other clusters were identified but were not consistent across all methods and time-frames suggesting they could be outbreak areas or areas with higher transmission activity than other geographic areas. Identification of core areas can assist in targeting interventions to these areas and can help evaluate the impact of programs and interventions over time.

Poster 51

A Descriptive Epidemiology of Hepatitis C Cases Referred for Specialized Care in Newfoundland and Labrador, 1996-2014

Jennifer Leonard, Memorial University of Newfoundland; Mary Malebranche, University of Calgary; Dawn King, Eastern Health

Background:
Since its discovery in 1989, chronic infection with the hepatitis C virus (HCV) has become an increasingly recognized public health concern worldwide. Despite this growing awareness, our understanding of the epidemiology and demographic distribution of HCV infection in Canada, specifically in Atlantic Canada, remains limited.

Purpose:
There is currently little published data on the demographic and clinical profile of HCV positive individuals in Newfoundland and Labrador (NL) outside provincial public health reports, which are unable to capture the full spectrum of relevant demographic and clinical data on individuals infected with HCV in the province. The purpose of this study is to address this knowledge gap.

Methods:
A retrospective cohort study of 714 HCV positive individuals referred for specialized HCV care in St. John's, NL, between 1996 and 2014, was conducted. Data was obtained through a standardized and comprehensive manual chart review and access to a database comprised of sociodemographic and clinical data on individuals referred for specialized HCV care in St. John's.

Results:
767 individuals were referred for specialized HCV care during the study period of which 714 were included in our analysis. This represents 57.5% of HCV positive cases identified by the province's public health department during the same timeframe. HCV infection was more common in men (68.2%) and in urban dwellers (74.8%). The majority of cases were HCV Genotype 1 (52.1%). Intravenous and intranasal drug use were the most common self-reported risk factors for HCV transmission. High loss to follow-up rates were noted in those referred from the province's correctional system.

Conclusion:
This study demonstrates that many well-documented epidemiologic characteristics of HCV positive inidividuals in Canada hold true for individuals referred for specialized HCV care in Newfoundland and Labrador. Most notably it shows that specific attention needs to be paid to HCV positive inidividuals referred for specialized care from the province's correctional system as they are at highest risk for loss to follow-up in specialized care. This study provides important insights into the demographic and clinical profile of individuals referred for HCV-related care in Newfoundland and Labrador and fills a gap in our current understanding of HCV positive individuals in this Atlantic province. These findings can help inform future directions for HCV-related health policy, resource allocation and clinical care initiatives in NL and across Canada.

Poster 52

WHO ARE WE LEAVING BEHIND? COMPARING RATES OF OPIATE AGONIST TREATMENT INITIATION ACCORDING TO PREFERRED OPIOID OF ABUSE AMONG PEOPLE WHO INJECT DRUGS IN MONTREAL

Andreea Adelina Artenie, Université de Montréal; Julie Bruneau, CRCHUM; Élise Roy , Université de Sherbrooke; Institut national de santé publique du Québec ; Emmanuel Fortier, Université de Montréal; Nanor Minoyan, Université de Montréal / CRCHUM; Didier Jutras-Aswad, Research Centre of the Centre Hospitalier de l'Université de Montréal; Department of Psychiatry, Université de Montréal

Background:
Opiate agonist therapy (OAT) is considered key in hepatitis C virus (HCV) prevention among people who inject drugs (PWID). Despite concerns surrounding the substantial diversion of prescription opioids (PO) to the illicit market, and the high risk of HCV infection associated with PO injection, little is known about the access to OAT among street-based drug users whose drug of choice is PO, and how it compares to those who prefer heroin.

Purpose:
The main objective of this study was to assess and compare rates of OAT initiation among PWID according to preferred opioid of abuse (PO vs heroin).

Method:
Data were drawn from HEPCO, a prospective cohort study of active PWID followed between 2004 and 2011 in Montreal. At six-month intervals, participants were interviewed to collect information on socio-demographics, recent (past month or past six months) drug use behaviours and OAT initiation. For this study, PWID were eligible if they indicated, at baseline, i) their preferred drug of abuse to be heroin or PO and ii) not being on OAT within the past six months, and were followed-up at least once. Participants were censored following first episode of OAT reported during follow-up. First, the baseline characteristics of participants were compared, according to drug of choice. Then, for each group, rates of OAT initiation were calculated using the person-time method, and cumulative incidences, based on Kaplan-Meier estimates, were compared using the log–rank test.

Results:
At baseline, 163 PWID (median age: 29.6, 76.1% of male gender) were eligible for this analysis, of whom 63 (38.7%) reported preferring PO and 100 (61.3%) indicated preferring heroin. While no differences were found for age and gender, relative to those preferring heroin, those whose drug of choice was PO were more likely to also report smoking cocaine (68.3% vs 47.0%) and using sedatives (60.3% vs 42.0%), injecting daily (50.8% vs 30.0%) and at a higher frequency [≥3 injections/day (60.3% vs 36.0%)], living in unstable housing conditions (65.1% vs 31.0%) and injecting mostly in public (54.0% vs 36.0%; all p-values < 0 .05). Overall, PWID contributed 210.53 person-years (p-y) of follow-up. PWID indicating PO as their drug of choice had a lower rate of OAT initiation relative to those indicating heroin [incidence rates: 34.1 per 100 p-y (95% confidence interval (CI): 24.3 – 45.0) vs 54.6 per 100 p-y (95% CI: 45.4 – 63.7); log-rank p-value: 0.03].

Conclusion:
Compared to those preferring heroin, participants whose drug of choice was PO were more likely to present characteristics potentially placing them at greater risk of HCV infection. Further, our findings suggest that this group were significantly less likely to initiate OAT. Additional research is needed to examine optimal strategies to engage PWID whose drug of choice is PO in addiction treatment.

Poster 53

Peers4Wellness: Creating Indigenous Ways of HCV Care and Support Utilizing the Peer Navigation Concept

Angela Thomson, Nicola Valley Institue of Technology; Terry Howard, Independent; Sadeem Fayed, SFU; Alexandra King, University of British Columbia

Background
In Canada, the rates of Hepatitis C virus (HCV) are at least five times higher among Indigenous Peoples in Canada (IPC), particularly Indigenous women. Yet, IPC are underrepresented in HCV health care programs, likely due to the lack of Indigenous ways of care and support. Utilizing the concept of conventional peer navigation (PN), we will provide an Indigenous approach to address the under engagement of IPC with HCV health care. In Indigenous culture, it is critical to build relationships and trust before developing any care model. PN provides a promising concept to be re-contextualized to meet the specific needs of Indigenous people with lived HCV and/or HIV experiences and will provide evidence for improving health care engagement.

Purpose
This study begins with building relationships and trust with Indigenous communities. In doing so, we will address some of the gaps in PN literature and practice, with a focus on Indigenous women (cis- and trans-gender) with lived HCV and/or HIV experience in Vancouver and the surrounding region. It involves a three-pronged sharing circle consultation with the following community stakeholders: 1) Indigenous women with lived HCV and/or HIV experience, 2) peer navigators, and 3) community organizations. Study findings will explore a gendered Indigenous perspective to inform the development of a peer-led support model to improve engagement in HCV and HIV health care.

Methods
Peers4Wellness is an Indigenous Peer-led Community Based Research project. It applies a "Two-eyed-Seeing" framework which emphasizes sharing circle data collection, and weaves Indigenous and Western methods together. Sharing circle methodology imbued with Indigenous philosophies and protocols will be used as the main data collection method for participants and peer navigators. Individual interviews will be used for consultation with community organizations. Study findings will be synthesized through community-led participatory data coding and analysis.

Results
We have been successfully engaging the community to build the relationships and trust necessary for sharing circle recruitment. In developing our sharing circle model, we carefully considered the special vulnerabilities and needs of our research participants. This ensured protection of the cultural and personal safety of women participants, and respected Indigenous practice. The study includes a total of five sharing circles, five interviews and a total of 40 research participants. We expect the majority of participants to have HCV lived experience. We expect to conclude our study in the Spring of 2018.

Conclusion
This study engages Indigenous communities to address some of the research and practice gaps in relation to HCV health care engagement and peer support among IPC. It introduces an innovative Indigenous model of peer support for IPC with lived HCV and/or HIV experience. Peers4Wellness embodies a reconciliation-based research approach which emphasizes both Indigenous and Western paradigms.

Poster 54

Real-World Effectiveness of Sofosbuvir-based Regimens for Treatment of Hepatitis C Genotypes 1-3: BC Hepatitis Testers Cohort (BC-HTC)

Maryam Darvishian, University of British Columbia; Mel Krajden, University of British Columbia; Alnoor Ramji, University of British Columbia; Eric Yoshida, University of British Columbia; Stanley Wong, BC Centre for Disease Control; Mei Chong, BC Centre for Disease Control; Darrel Cook, BC Centre for Disease Control; Zahid Butt, University of British Columbia; Maria Alvarez, BC Centre for Disease Control; Nuria Chapinal, BC Centre for Disease Control; Nazrul Islam, Harvard University; Hasina Samji, BC Centre for Disease Control; Mark Tyndall, BC Centre for Disease Control; Naveed Janjua, BC-CDC

Background
To assess the effectiveness of ledipsavir/sofosbuvir (LDV/SOF), ledipsavir/sofosbuvir/ribavirin (LDV/SOF/RBV), and sofosbuvir/peginterferon/ribavirin (SOF/PEG/RBV) for genotype 1 (GT1) and sofosbuvir/ribavirin (SOF/RBV) and SOF/PEG/RBV for genotype 2 (GT2) and 3 (GT3) in routine medical practice using a large population based Canadian cohort.

Methods
The British Columbia Hepatitis Testers Cohort (BC-HTC) includes individuals tested for HCV (~1.7 million) between 1990-2016 linked with data on medical visits, hospitalizations, cancers, prescription drugs and mortality. HCV patients who were prescribed LDV/SOF, LDV/SOF/RBV, and SOF/PEG/RBV for GT1 and SOF/RBV and SOF/PEG/RBV for GT2 and GT3 until December 31, 2016 were included in the study. Outcome was sustained virological response (SVR) assessed at 12 weeks post treatment based on the intention to treat approach. Logistic regression was used to identify factors that were associated with SVR.

Results
Among GT1 patients, 1834, 28 and 75 individuals initiated LDV/SOF, LDV/SOF/RBV, and SOF/PEG/RBV, respectively. 170 and 16 GT2 patients and 294 and 53 GT3 patients initiated SOF/RBV and SOF/PEG/RBV, respectively. The overall SVR rate among patients in GT1 treated with LDV/SOF, LDV/SOF/RBV, and SOF/PEG/RBV was 93.7%, 96.47%, and 85.4%, respectively. The overall SVR rate among SOF/RBV and SOF/PEG/RBV treated patients in GT2 was 93.5% and 81.2%, respectively. The overall SVR rate among SOF/RBV and SOF/PEG/RBV treated patients in GT3 was 80.9% and 90.6%, respectively.

In the multivariable model for GT1 and LDV/SOF regimen, male gender (SVR: 92.3% vs 96.5%; OR: 0.43; 95% CI 0.26-0.71), cirrhosis (SVR: 88.8% vs 94.6%; OR: 0.46; 95% CI 0.28-0.77), and treatment duration of less than 8 weeks (SVR: 62.9% vs. 94.5%; OR: 0.09; 95% CI 0.04-0.21); and for SOF/PEG+RBV regimen, treatment duration 24 weeks (SVR: 68.7% vs 89.8%; OR: 0.02; 95% CI 0.00-0.42) were significantly associated with lower SVR rate. In SOF+RBV treated patients with GT2, treatment duration of less than 12 weeks (SVR: 33.3% vs. 94.5% OR: 0.02; 95% CI 0.00-0.43) and previous HCV treatment (SVR: 85.1% vs. 96.7%; OR: 0.22; 95% CI 0.05-0.94) and with GT3, male gender (SVR: 75.7% vs. 88.9% OR: 0.33; 95% CI 0.16-0.69) and HCV-RNA of 243860- 989317 (IU/ml) (SVR: 67.1% vs. 86.4% OR: 0.29; 95% CI 0.13-0.65) were significantly associated with lower SVR.

Discussion
In this real-world cohort, high SVR rates with LDV/SOF ± RBV among GT1 infected patients and lower SVR with SOF/RBV and SOF/PEG/RBV among GT1, GT2 and GT3 are similar to the data reported from clinical trials and other real-world cohorts. Male gender, presence of cirrhosis, and treatment duration mainly less than 12 weeks were significant negative predictors of SVR. These data confirm the high effectiveness of LDV/SOF regimens among GT1 patients in a real-world setting, and highlight the sub-optimal SVR of SOF/RBV and SOF/PEG/RBV for GT1, GT2, and GT3.

Poster 55

The impact of hepatitis C diagnosis on substance-use behaviors in patients engaged in opioid agonist therapy

Hooman Farhang Zangneh, University of Toronto, Toronto Centre for Liver Disease; Jordan Feld, To; Hemant Shah, University of Toronto, Toronto Centre for Liver Disease; David Marsh, Northern Ontario School of Medicine; Joe Eibl, Northern Ontario School of Medicine; Graham Gauthier, Northern Ontario School of Medicine; David Pellegrini, Northern Ontario School of Medicine

Background:
Opioid misuse is a public health crisis in many populations. In Canada, the province of Ontario has more than 50,000 opioid-dependent persons who are engaged in opioid agonist therapy (OAT), using mainly methadone and suboxone. Hepatitis C Virus (HCV) infection, with an estimated prevalence of 0.3%-0.9% among all Canadians, is more common in this population. Many experts advocate for testing all OAT patients for chronic HCV infection. To date, the impact of HCV infection diagnosis on the substance use behaviors of OAT patients is unknown. and we aim to explore that here.

Purpose:
To explore the impact of hepatitis C diagnosis on substance use behavior while on opioid agonist therapy

Methods:
We conducted a retrospective cohort analysis using the electronic health data, urine toxicology and antibody-based HCV infection screening information from a network of 47 addiction treatment clinics in Ontario from 2007 to 2013. We used a logistic regression analysis determine the impact of HCV infection diagnosis on substance-use behaviors for patients engaged in OAT.

Results:
2406 individuals were identified amongst the 47 clinics who were screened for HCV infection. 527 (21.9%) individuals tested positive for anti-HCV Ab. Those who screened positive for HCV were 32.6% more likely to significantly alter their substance-use behaviors (aOR=1.326; CI95% = 1.08-1.63; p=0.008) and reduce their consumption of non-prescribed opioids according to urine toxicology after the anti-HCV Ab screening when compared to when their HCV-AB status was not clear. Patients who were diagnosed with HCV infection subsequently had a significantly lower proportion of positive urine drug screens, including non-prescribed opioids (aOR=1.346), benzodiazepines (aOR=1.545), and cocaine (aOR=1.551).

Conclusion:
We have demonstrated that HCV infection screening can have a positive impact on substance-use behavior among patients engaged in OAT in decreasing their substance use. Expansion and universal screening of OST clients for HCV infection should be encouraged.

Poster 56

Can healthcare-associated HCV outbreaks occur when intravenous medication vials are accessed with clean needles and syringes for use in multiple patients?

Selena Sagan, McGill University; Julie Magnus, McGill University; Sophie Breton, Queen's University; Rachel Phelan, Queen's University; Melanie Jaeger, Queen's University; Janet van Vlymen, Queen's University; Andrew Day, Kingston General Hospital Research Institute

Background:
Healthcare-associated hepatitis C virus (HCV) outbreaks continue to occur despite widespread implementation of infection control guidelines. In Ontario alone, there have been four independent HCV outbreaks documented in outpatient endoscopy clinics in the past 5 years, resulting in 14 new HCV infections. Thorough investigation of each outbreak concluded that contaminated medications, administered by the anesthesiologist, were the likely source of patient-to-patient transmission. Despite these findings, the anesthesiologists denied reusing needles and syringes to access multidose vials. While it is clearly unacceptable to reuse needles or syringes, it is a recognized practice to share multidose medication vials between patients provided new needles and syringes are used with aseptic technique.

Purpose:
We hypothesized that when caring for HCV-infected patients, anesthesiologists may inadvertently contaminate the vial diaphragm, and that subsequent access with sterile needles and syringes can transfer HCV into the medication where it remains stable in sufficient quantities to infect subsequent patients.

Methods:
We simulated contamination of multidose medication vials in healthcare settings using cell culture-derived HCV (HCVcc) to determine: 1) whether HCV can be transferred, via a sterile needle and syringe, into a medication vial if the rubber access diaphragm is contaminated; 2) whether HCV remains viable in commonly used medications in sufficient quantities over time to initiate an infection; and 3) whether cleaning with 70% isopropyl alcohol is sufficient to eliminate infectivity. In addition, we surveyed 546 anesthesiologists across Canada to assess how common reuse of multidose medication vials is in clinical practice and how contamination risks are mitigated.

Results:
Contamination of the rubber diaphragm of medication vials with 33 uL (mean volume of an accidental drop) of HCVcc (800,000 IU/mL) and subsequent access with sterile needles and syringes resulted in contamination of the vial contents in sufficient quantities of HCV to initiate an infection in cell culture. Second, HCV remains viable for ≥72h in several commonly used medications. Third, a single wipe of the vial diaphragm with 70% isopropyl alcohol was not sufficient to eliminate HCV infectivity. Importantly, 83.6% of anesthesiologists reported sometimes or routinely reusing medication vials for multiple patients and only 11.7% reported using the recommended cleaning procedure of scrubbing the vial diaphragm for 10 s and allowing it to dry.

Conclusions: HCV can be transferred, via sterile needles and syringes, into medication vials if the diaphragm is contaminated with medically relevant quantities of HCV and the virus remains stable in several commonly-used medications over time. Furthermore, a single wipe of the vial diaphragm with 70% isopropyl alcohol is not sufficient to eliminate HCV infectivity. Given these findings, as well as our survey responses, we recommend investment in education and knowledge translation across medical specialties, division (or elimination) of multidose vials, and investment in single-dose vials to minimize nosocomial HCV infections.

Poster 57

Real World Implications of Hepatitis C Infection and Treatment in Nova Scotia

Siena Davis, Mount Allison University; Lisa Barrett, Dalhousie University

Background.
Direct-acting antiviral (DAA) medications have been shown to be very effective at curing hepatitis C virus (HCV) in clinical trials. However, these studies typically include highly adherent populations. Many of these trials have also excluded individuals who have comorbidities affecting the efficacy of the DAA medications (eg. HIV co-infection), or who are a member of a vulnerable population (eg. intravenous drug users).

Purpose.
In order to determine the efficacy of DAA medications within Nova Scotia, the results of HCV treatment from different groups of individuals infected with HCV must be examined. This information may be used to determine sustained viral response (SVR) rates with DAA medications, as well as to view qualitative trends within the population. These findings may be used to inform policy on funding for these medications and update the model of care for HCV in Nova Scotia. The primary outcome of this project was to evaluate the rates of SVR in the population. The secondary outcomes were to investigate trends in demographics of this HCV population.

Method.
Information was collected from the medical charts of 258 individuals who were seen at the infectious diseases clinic of the Queen Elizabeth II Health Sciences Center (QEII HSC) in Nova Scotia from 2011 until 2017 for HCV care. A database was compiled and analyzed in order to view SVR rates among subpopulations and summarize demographics of the HCV population.

Results.
Overall, DAA treatments were more effective than previous interferon-based treatment regimens (SVR 87% vs. 78%), along with less relapsed or failed treatment outcomes. People who inject drugs (PWID) currently or in the past had 83% SVR compared to those who never used intravenous drugs (86%). Those co-infected with HIV had a lower SVR compared to those without (79% vs. 98%). Treatment-experienced individuals had a higher SVR compared to those that were treatment naïve (100% vs. 85%). HCV genotype 1(1a in particular) was most common, followed by genotype 3a. There was a wide range of liver fibrosis scores (F0 to F4). The most common age demographic was between 25 and 34 years, followed by ages 55-64, and the cohort was primarily male (69% vs. 31% female). Most individuals (71%) were previous PWID, with only 9% currently injecting drugs. HIV co-infection was present in 17% of the population.

Conclusions. The database of HCV patients seen in the infectious disease clinic at the QEII HSC demonstrates that the outcomes of DAA treatment were very successful for all groups of individuals including PWID, those co-infected with HIV and people who had previous HCV treatment. These trends may be used to inform new policy and update the model of care in Nova Scotia to work towards HCV eradication in the future.

Poster 58

Socio-demographic Characterization of Calgary's Cohort of the Surveillance of Persons Who Inject Drugs (PWID) for Hepatitis C Virus (HCV) Seroconversion in Inner City Clinics Study

Faustyna Zietara, University of Calgary; Gisela Macphail , CUPS & University of Calgary; Pamela Crotty, University of Calgary; Carla Coffin, Department of Medicine, University of Calgary; Michael Houghton, University of Alberta; D. Lorne Tyrrell, University of Alberta

Background:
Approximately 60% of incident HCV infections are due to intravenous drug use. The ability to engage PWID in prevention, testing and treatment for HCV remains challenging.

Purpose:
Understanding the sociodemographic characteristics of PWID could inform the need for additional resources, target screening initiatives and treatment programs.

Methods:
Our institution was part of a larger prospective cohort study to enroll HCV negative PWID in order to assess candidates for the HCV vaccine. All participants provided written informed consent at the time of study enrolment and completed an interviewer-administered questionnaire. Data were gathered to document drug use, sexual health, viral hepatitis/ HIV testing history, and community services utilization.

Results:
In total, data were collected from 239 PWID (median age 40, 82% M, 65% Caucasian, 19 % Aboriginal, 0.8% (2/239) HIV+). 28% (67/239) were anti-HCV positive (median age 41, 73% M, 72% Caucasian, 1.5% (1/67) co-infected with HIV). 55% (37/67) were referred for further follow-up and testing, but 45% were lost to follow-up. The drug most commonly injected was crystal methamphetamine (39%), anti-HCV+ participants reported using more opiates than HCV - people; morphine (23% vs. 11% p < 0 .05), the anti-HCV+ group reported using less crystal methamphetamine and cocaine (usually by non-injection routes). 29% of the anti-HCV+ group had been enrolled in a methadone program compared to 9% of the HCV – group (P< 0.005). There was no significant difference in history of previous incarceration (78% vs. 79%), and only 10% of both groups reported IDU during their incarceration. The majority of the migration to Calgary was interprovincial (usually Edmonton), followed by British Columbia and Ontario. Both groups also reported similar number of sexual partners in the last six months (usually 1 partner or 2-5 partners), however a high proportion did not use condoms (24% HCV- group vs. 40% of the antiHCV+ group P < 0 .05). Although, 66% of the group reported previous HCV testing, ~ 32 % of the antiHCV+ group reported testing over 4 years ago, compared to 14% of the HCV negative (P< 0.05). 79% of the total cohort and 73% of the antiHCV+ group reported previous HIV testing.

Conclusion:
In this cohort study of 239 PWID in Calgary, we note significant differences in injection drug use in HCV+ vs. anti-HCV persons, as well as a longer interval since last HCV testing. More HCV+ people had engaged with opiate substitution services, making these sites vital in HCV programs. Additional identification of sociodemographic risk factors in PWID and long term follow up is important to understand trends on high-risk behaviour, improve access to healthcare and community services and to ultimately reduce HCV risk, increase testing and HCV treatment.

Poster 59

What is Killing People with HCV infection? Analysis of population based cohort in Canada

Mel Krajden, Naveed Janjua, BC-CDC; Mel Krajden, University of British Columbia; Darrel Cook, BC Centre for Disease Control; Stanley Wong, BC Centre for Disease Control; Zahid Butt, University of British Columbia; Amanda Yu, BC Centre for Disease Control; Nuria Chapinal, BC Centre for Disease Control; Maryam Darvishian, University of British Columbia; Nazrul Islam, Harvard University; Maria Alvarez, BC Centre for Disease Control; Mark Tyndall, BC Centre for Disease Control

Background:
The causes of death among HCV positive and HCV negative individuals to understand the relative contributions of HCV acquisition risks, viral sequelae, and other mortality causes were compared.

Methods:
The BC Hepatitis Testers Cohort (BC-HTC) includes all individuals tested for HCV or reported to public health as a HCV case from 1990-2016 linked to their corresponding administrative data. ICD-10 codes were used to classify mortality as: 1) liver-related (including decompensated liver disease, liver cancer, HCV, non-alcoholic and alcoholic liver disease, other types of hepatitis); 2) acquisition risk-related (including drug and HIV-related,); and 3) all other mortality causes. We compared proportions of mortality causes among HCV positive and negative individuals overall and by birth cohort: born < 1 945, 1945-64 and ≥1965.

Results:
Of 1,372,391 individuals in the BC-HTC, 72,491 (5.3%) were HCV positive. Overall, 24.6% (17,834/72,491) of HCV positive compared to 9.0% (117,304/1,299,900) of HCV negative individuals died by June 2017. Median age at death was 56 vs. 75 yr., respectively. Deaths from acquisition risks- and liver- related causes, respectively were: negatives 2.6%/6.4%; spontaneous clearers 17.6%/ 15.3%; HCV RNA positive 17.5%/27.7%; those with SVR 11.5%/ 27.2%; and No SVR 9.9%/51.8%. Causes of death for birth cohorts < 1 945, 1945-64 and ≥1965 among HCV negatives and positives, respectively, were: 1) liver-related: 5.3%/25.8%; 10.2%/26.8% and 5.3%/ 7.6%; 2) acquisition risk-related: 0.3% / 2.7%, 4.6% /20.9% and 17.8% / 46.5%; and 3) all other mortality causes: 94.5% / 76.8%, 85.2% / 52.3% and 76.8% / 45.9%. People in the ≥1965 birth cohort who were HCV RNA positive or spontaneously cleared infection had higher acquisition related mortality while those in the 1945-64 birth cohort who were HCV RNA positive and those who failed treatment had the highest liver related mortality.

Conclusions:
Compared to HCV negative individuals, HCV positive individuals are more likely to die from drug related and liver related causes, and less likely to die from non-liver related causes. The contribution of drug related deaths is substantially higher in younger birth cohorts, while liver related deaths are more common in the 1945-64 birth cohort. These results demonstrate that curative HCV treatments, while likely to reduce deaths from viral sequelae, will not reduce acquisition risk mortality common in younger cohorts. These findings help quantify the need for comprehensive harm reduction programming to reduce overall mortality in persons with ongoing HCV acquisition risks.

Poster 60

Establishing a multi-centre prospective observational cohort study to document and analyse the hepatitis C cascade of care among people who inject drugs: the Virtual Cascade of Care Cohort (VCCC) study

Stine Hoj, Université de Montréal; Benedickt Fischer, University of Toronto; Michel Alary, Université Laval; Brian Conway, Vancouver Infectious Diseases Centre; Alexandra King, University of British Columbia; Chris Greenaway, McGill University; Didier Jutras-Aswad, Research Centre of the Centre Hospitalier de l'Université de Montréal; Department of Psychiatry, Université de Montréal; Élise Roy , Université de Sherbrooke; Institut national de santé publique du Québec ; Gerry Mugford, Memorial University; Jason Grebely, Kirby Institute, UNSW Sydney; Louise Balfour, The Ottawa Hospital; Marina Klein, McGill University; Mark Tyndall, BC Centre for Disease Control; Renee Masching, Canadian Aboriginal AIDS Network; Thomas Kerr, University of British Columbia; Wendy Wobeser, Queen's University; Julie Bruneau, CRCHUM

Background:
People who inject drugs (PWID) are the principal group at risk of hepatitis C virus (HCV) infection, with injection drug use estimated to contribute over 60% of total HCV disease burden in Canada. Advances in treatment suggest that HCV could be eliminated as a public health threat by 2030. However, the combination of high prevalence and low treatment uptake in PWID suggests that this will not be achievable without greatly increased engagement in health services. There is a lack of robust longitudinal data describing the entire HCV cascade of care in PWID, and a need for research to guide treatment scale-up in vulnerable populations.

Purpose:
The Virtual Cascade of Care Cohort (VCCC) is an innovative multi-centre observational prospective cohort study designed by the Canadian Network on Hepatitis C. Focusing on vulnerable populations of current and former PWID, it aims to: (i) document the entire HCV cascade of care, from community to post-treatment; (ii) identify modifiable determinants of HCV care/treatment within the theoretical framework of 'candidacy'; (iii) examine the long-term impact of HCV care/treatment on liver and non-liver comorbidities; and (iv) estimate the incidence and correlates of post-treatment reinfection.

Method:
VCCC combines in-person data collection at baseline with 'virtual' prospective follow-up through health administrative databases (data linkage). Participants will complete one study visit, comprising a ten-minute questionnaire; rapid HCV antibody testing; and collection of a dried blood spot panel for RNA detection and genotyping. During the visit, permission will be sought to access individual records from clinic, hospital, laboratory and pharmacy visits held in federal and provincial databases. Periodic linkages to this data will inform on multiple outcomes (HCV testing and diagnosis, physician visits, hospitalisations, treatment access, liver and non-liver related comorbidities, cause of death) for the next five years. Baseline data will inform on barriers and facilitators to care not available in health administrative databases (questionnaire) and enable preliminary detection of HCV infection outside a clinical setting (biological testing).

The target population includes people who have ever injected drugs; are vulnerable to unmet healthcare needs; and engage with some community services. HCV-negative (including previously treated) individuals are eligible to participate. Recruitment will take place in community-based harm reduction and addiction services with no linkage to HCV care, and may therefore exclude the most marginalised and/or least vulnerable individuals. Pilot sites will be located in Québec and Alberta with the intention of expanding throughout Canada.

Conclusion: VCCC provides a middle ground between cohort studies (which may struggle to retain vulnerable participants) and data linkage methodologies (which rely solely on secondary data), and has the potential to become a rich pan-Canadian data source to study HCV infection and care among a relatively hidden population, hard to capture through traditional clinical cohorts or population-based studies.

Poster 61

An Economic Evaluation of Emergency Department Population-Based Hepatitis C Screening Strategies in Canada

Andrew Mendlowitz, University of Toronto, David Naimark, Sunnybrook Hospital, William WL Wong, School of Pharmacy, University of Waterloo, Wanrudee Isaranuwatchai, Centre for Excellence in Economic Analysis Research (CLEAR), St. Michael's Hospital, Murray Krahn, Toronto Health Economics and Technology Assessment Collaborative (THETA), University of Toronto

Background: An estimated 220,000 Canadians live with chronic hepatitis C viral (HCV) infection, of which 44% are unaware of their diagnosis. Of those infected, it is estimated that 1 in 4 will develop cirrhosis and 1 in 8 will die from HCV-related causes. Newly approved medications have revolutionized the treatment of HCV infection, but finding and treating cases before complications develop is difficult due to HCV's asymptomatic nature. Emergency department (ED) patients have been associated with a higher prevalence of HCV infection when compared to the general population. Previous studies examining ED infectious disease screening have resulted in a higher prevalence of newly diagnosed infections and more cases of infection linked to timely care. Recently, the Canadian Task Force on Preventative Health Care recommended against population-based HCV screening strategies, citing a lack of evidence of their effectiveness. Although studies have analyzed wide-scale population screening, few have examined alternative screening strategies such as targeting high-risk populations including ED patients.

Purpose: This study aims to perform an economic evaluation of ED-based HCV screening strategies in Canada.

Method: A microsimulation state-transition model was developed. Two scenarios, (1) screening of the general ED population and (2) ED screening of those between 51 to 69 years of age (baby boomer cohort), were compared to no screening from the public healthcare payer perspective. Distinct measures of ED HCV prevalence, screening test uptake rate, and health utilities from published literature were used to model ED-specific screening strategies. Simulated direct-acting antiviral treatment regimens were based on treatment guidelines and effect estimates obtained from published sources. Quality-adjusted life-years (QALYs) and costs in 2016 Canadian dollars were predicted over a lifetime time horizon using a 1.5% discount rate. Sensitivity analyses were performed to characterize any uncertainties in parameter estimates and findings.

Result(s): Preliminary results demonstrated screening and subsequent treatment of ED patients would prevent 144 and 37 HCV-related deaths per 10,000 people screened for the general population and baby-boomer scenarios, respectively. ED general population screening was associated with an average cost increase of $1,948 and a QALY increase of 0.18 relative to no screening ($10,822/QALY). Baby boomer cohort screening was associated with an average cost increase of $559 and a QALY increase of 0.03 relative to no screening ($18,633/QALY). After accounting for uncertainty, both ED screening scenarios were likely to be cost-effective when compared to no screening at willingness-to-pay thresholds greater than $20,000 per QALY gained.

Conclusion: ED screening demonstrates the potential to be a cost-effective strategy that can play a role in broader population-based efforts to eradicate HCV. This analysis may provide the first step towards the development of pilot studies that can further determine mechanisms of implementation, the feasibility and the acceptance of ED-based HCV screening strategies.

Poster 62

Values, Preferences, and Acceptability of Hepatitis C Testing and Treatment in the Homeless and Vulnerably Housed: a Scoping Review.

Adam Palayew[1,2], Harneel Kaur[2,3], Olivia Magwood[2,4], Christina Greenaway[1,5,6], Alain D. Mayhew[2], Janet Hatcher-Roberts[7,8], Kevin Pottie[2,3,9]

1. *Department of Epidemiology, Biostatistics, and Occupational Health, McGill University, Montreal, Canada.*
2. *C.T. Lamont Primary Health Care Research Centre, Bruyère Research Institute, Ottawa ON*
3. *Faculty of Medicine, University of Ottawa, ON, Canada*
4. *Department of Population Medicine, University of Guelph, Guelph ON*
5. *Division of Infectious Diseases, Jewish General Hospital, McGill University, Montreal, Canada*
6. *Center for Clinical Epidemiology of the Lady Davis Institute for Medical Research, Jewish General Hospital*
7. *Senior Technical Advisor, Canadian Society for International Health*
8. *WHO Collaborating Centre for Knowledge Translation and Health Technology Assessment in Health Equity, Center for Global Health, University of Ottawa, ON, Canada*
9. *Centre for Global Health Institute of Population Health, University of Ottawa, ON, Canada*

Background: The WHO has called for the elimination of viral hepatitis as a public health concern by the year 2030. However, if this goal is to be met, marginalized and underserved populations, who account for a disproportionate burden of the disease, need to be tested and successfully linked to treatment and care. In Canada, at least 235,000 people experience homelessness in a year. This segment of the population often has poor access to health care, comorbidities, such as mental health issues, and engage in high-risk behaviours such as intravenous drug use. However, there is little evidence about the perceptions of the homeless and vulnerably housed towards testing and treatment for HCV, specifically the values, preferences, and acceptability of hepatitis C testing and treatment. Therefore, we conducted a scoping review to map and summarize relevant literature pertaining to this topic.

Method: We searched the following databases from January 1st, 2011 to July 8th, 2017; MEDLINE, EMBASE, PsychINFO, and CINAHL. The Google search engine was used to search for grey literature from organizations that were selected *a priori*: WHO, Health Canada, CDC, and PHAC. Two reviewers independently screened the titles and abstracts, followed by full text assessment of relevant citations for eligibility. Disagreements were resolved by consensus or by a third reviewer. Two reviewers extracted the data, disagreements were resolved through consensus.

Results: In total, we identified 968 eligible studies for screening by title and abstract, 28 full-text articles. In the end, four studies met the inclusion criteria. We found evidence that the homeless and vulnerably housed persons did not strongly value hepatitis C testing and treatment; rather they prioritized other issues such as housing, and community-based and primary health care treatment for acute diseases. Furthermore, homeless individuals were found to prefer treatment with limited side effects. HCV testing through a community-based screening program was reported to be highly acceptable (97%), and patient confidence to undergo and complete interferon-based treatment was 72.9% among the homeless and vulnerably housed. The main motivations for seeking treatment were taking care of one's health and following the advice of their physician. There was no direct evidence on values, preferences, or acceptability for newer direct-acting antiviral (DAA) treatment regimens.

Conclusions: Our scoping review identified a limited number of studies with only one study directly focusing on the homeless population, while the three other studies provided enough sub-group details to determine the response of homeless, and vulnerably housed individuals. The key findings of this scoping review are that more research is needed to more accurately assess the values, preferences, and acceptability, of hepatitis C testing and treatment especially in relation to DAA medications, and that homeless populations are more concerned with housing issues and community base treatment of primary health care issues.

Poster 63

Exploring the impacts of medicalization and the limits of traditional public health approaches to HCV prevention in the spaces where people use illicit drugs

Gillian Kolla, University of Toronto, Carol Strike, University of Toronto

Background: Making sterile injection materials easily available to people who inject drugs is key to the prevention of hepatitis C infection. The expansion of harm reduction programs, which distribute sterile injection materials while also providing education on hepatitis C, has been a key focus of public health intervention.

Purpose: This paper examines the impact of the "Satellite Sites", a program in which people who use drugs are employed by a community health centre to run satellite harm reduction programs within their own homes. This paper examines the interplay of medicalization and criminalization in these sites, and its impact on HCV vulnerability among people who inject drugs.

Method: Using data from an ethnographic study, including observations within the Satellite Sites and interviews with key members of the program, this paper explores the process, effects and limits of medicalizing the spaces where people gather to use illicit drugs, and turning them into a formal public health intervention.

Results: Turning the spaces where people gather to use drugs into sites of public health intervention has resulted in the medicalization of these sites. During their work, Satellite Site workers distribute drug use equipment and safer sex supplies, including needles and syringes, crack kits, and condoms; provide education on safer drug use; intervene in overdoses; and administer naloxone for overdose reversal. The process of medicalization has positively impacted the availability and accessibility of sterile injection equipment for people who inject drugs. The interactions between police and the Satellite Sites is also improved by medicalization. However, there are limits to the effects of medicalization under the current regime of criminalization of drug possession and distribution. Since these limits are due to the structural forces, including criminal law and the nature of illicit drug markets, it may not be possible to counteract them using traditional Public Health intervention methods.

Conclusion: Public Health authorities need to consider that effective HCV prevention is impeded by the effects of structural forces such as drug laws and the operation of illicit drugs markets when designing interventions. To achieve effective HCV prevention, a change in focus may be necessary, including examining the potential benefits that may stem from the decriminalization and regulation of currently illicit drug markets on the health of people who use illicit drugs and are vulnerable to HCV infection.

Participants list – Liste des participants

First Name	Last Name	Organization	Email Address
Mohamed	Abdel Hakeem	University of Pennsylvania	m.s.abdel.hakeem@gmail.com
Christopher	Ablenas	University of Ottawa	cablenas@uottawa.ca
Liza	Abraham	St. Michael's Hospital	lizaabraham72@gmail.com
Juan G	Abraldes	University of Alberta	juan.g.abraldes@ualberta.ca
Anupam	Adhikari	Centre de recherche du Centre hospitalier de l'Université de Montréal	bosein.anupam@gmail.com
Fatema	Alalkim Alzaabi	Vancouver General Hospital	Falalkim@gmail.com
Khalid	Alharbi	McMaster University	Khalid.alharbi02@gmail.com
Arshia	Alimohammadi	Vancouver Infectious Diseases Centre	arshia.alimohammadi@vidc.ca
Jason	Altenberg	South Riverdale Community Health Centre	sfish@catie.ca
Kehinde	Ametepee	Simon Fraser University	kametepe@sfu.ca
Karen	Anand		karenanand@rogers.com
Aslam	Anis	University of British Columbia	aslam.anis@ubc.ca
Mina	Antonios	McKesson Canada	mina.antonios@mckesson.ca
Shelly	Archibald	Sioux Lookout First Nations Health Authority	Shelly.Archibald@slfnha.com
Camille	Arkell	Canadian Aids Treatment Information Exchange	carkell@catie.ca
Andreea Adelina	Artenie	Centre de recherche du Centre hospitalier de l'Université de Montréal	adelina.artenie@gmail.com
Jacqueline	Atkinson	North End Community Health Centre	jatkinson@nechc.com
Felix	Audet	Point de Reperes	sfish@catie.ca
Ceilia	Bai	Gilead Canada	ceilia.bai@gilead.com
Michael	Bailey	Canadian Aids Treatment Information Exchange	mbailey@catie.ca
Ricardo	Baptista-Leite	Catolica University of Portugal	ricardo.baptistaleite@gmail.com
Patrick	Barber	Gilead Sciences Canada Inc.	patrick.barber@gilead.com
Lara	Barker	Canadian Aids Treatment Information Exchange	lbarker@catie.ca
Lisa	Barrett	Dalhousie University	lisa.barrett@nshealth.ca
Julie	Beaulac	The Ottawa Hospital	jbeaulac@toh.ca
Shelley	Beckstead	Street Health Centre	shelleyb@streethealth.kchc.ca
Estelle	Bene	Merck Canada Inc.	estelle.bene@merck.com
Amine	Benmassaoud	Royal Free London NHS Foundation Trust	amine.benmassaoud@mail.mcgill.ca
Annie	Bernier	McGill University	annie.bernier@mail.mcgill.ca
Diane	Bigras	Gilead Sciences Canada Inc.	diane.bigras@gilead.com
Marc	Bilodeau	Centre hospitalier de l'Université de Montréal	marc.bilodeau@umontreal.ca
Mawuena	Binka	BC Centre for Disease Control	mawuena.binka@bccdc.ca
Samantha	Bland	Dalhousie University	samantha.bland@dal.ca
Sharon	Bojarski	William Osler Health System	Sharon.Bojarski@williamoslerhs.ca
Apoorva	Bollu	University of British Columbia	ap.bollu@gmail.com

Meredith	Borman	University of Calgary	mborman@ucalgary.ca
Brent	Bostrom	AbbVie Canada	brent.bostrom@abbvie.com
Danny	Braaten	Positive Living Fraser Valley	sfish@catie.ca
Heather	Breen	Merck Canada Inc.	heather.breen@merck.com
Jen	Brenner	Liver Care Canada	jen.brenner@livercarecanada.com
Kennet	Brysting	Gilead Canada	kennet.brysting@gilead.com
Terri	Buller-Taylor	BC Centre for Disease Control	terri.buller-taylor@bccdc.ca
Zahid	Butt	University of British Columbia	zahid.butt@ubc.ca
Carmen	Cabral	PerCuro Clinical Research	carmen@percuro.ca
Leanne	Cadden	Salmon Arm Liver Clinic	leanne.cadden@interiorhealth.ca
Kate	Campbell	Gilead Sciences Canada Inc.	kate.campbell@gilead.com
Camelia	Capraru	VIRCAN/ Toronto Centre for Liver Disease	camelia.capraru@uhnresearch.ca
Jasmin	Chahal	McGill University	jasmin.chahal@mail.mcgill.ca
Justin	Chan	New York City Health & Hospitals, Correctional Health Services	justin.chan@mail.harvard.edu
Nuria	Chapinal	BC Centre for Disease Control	nuria.chapinal@phsa.ca
Michael	Cheng	University of Toronto	mly.cheng@mail.utoronto.ca
Norma	Choucha	Centre de recherche du Centre hospitalier de l'Université de Montréal	norma.choucha@canhepc.ca
Geoff	Christie	Gilead Sciences Canada Inc.	geoffrey.christie@gilead.com
Conan	Chua	University of Toronto	conan.chua@mail.utoronto.ca
Karen	Chuk	GMD Pharma Solutions	kchuk@gmdpharma.ca
Sila	Cocciolillo	McGill University	sila.coccio@gmail.com
Carla	Coffin	University of Calgary	cscoffin@ucalgary.ca
Che	Colpitts	University College London	c.colpitts@ucl.ac.uk
Brian	Conway	Vancouver Infectious Diseases Centre	brian.conway@vidc.ca
Adele	Cook	AIDS Saskatoon	sfish@catie.ca
Curtis	Cooper	University of Ottawa	ccooper@toh.ca
Sophie	Cousineau	McGill University	sophie.cousineau@mail.mcgill.ca
Sarah	Craddock	Regina General Hospital	sarah.craddock@saskhealthauthority.ca
Shelley	Crawford	Saskatchewan Health Authority	scrawford@paphr.sk.ca
Angela	Crawley	Ottawa Hospital Research Institute	acrawley@ohri.ca
Pam	Crotty	University of Calgary	pcrotty@ucalgary.ca
Brandi	Cull	Reseau ACCESS Network	brandic@reseauaccessnetwork.com
Evan	Cunningham	University of New South Wales	ecunningham@kirby.unsw.edu.au
Morven	Cunningham	Toronto Centre for Liver Disease	morven.cunningham@uhn.ca
Ecaterina	Damian	Canadian Society for International Health	edamian@csih.org
Eric	Dang	Streetworls	sfish@catie.ca
Dustin	Dapp	Simon Fraser University	ddapp@sfu.ca
Krystyna	Dart	Specialty Pharma Solutions	kdart@specialtypharmasolutions.ca
Maryam	Darvishian	University of British Columbia	maryam.darvishian@bccdc.ca

Ray	Davidson	ASK Wellness Society	sfish@catie.ca
Siena	Davis	Mount Allison University	ssdavis@mta.ca
Christina	De Castro	McGill University	christina.decastro@muhc.mcgill.ca
Isabelle	Defoy	AbbVie Corporation	isabelle.defoy@abbvie.com
Isabel	Deslongchamps	Merck Canada Inc.	isabel.deslongchamps@merck.com
Gretty	Deutsch	Merck Canada Inc.	Gretty.deutsch@merck.com
Anna	DeWolff	Salmon Arm Liver Clinic	adewolff@telus.net
Melisa	Dickie	Canadian Aids Treatment Information Exchange	mdickie@catie.ca
Victor	Dong	University of Alberta	vdong@ualberta.ca
Jean Dieunel	Dor	Université Lumière	dorolivier92@gmail.com
Matthew	Driedger	University of Ottawa, Faculty of Medicine	mdrie032@uottawa.ca
Laura	Duma	Liver Care Canada	laura.duma@live.com
Carol	Dupasquier	Canadian Association of Hepatology Nurses	dupasquier@shaw.ca
Laurie	Edmiston	Canadian Aids Treatment Information Exchange	ledmiston@catie.ca
Rachael	Edwards	CUPS Health Education Housing	rachaele@cupscalgary.com
Stephanie	Eiloart	Rx Infinity	stephanieeiloart@gmail.com
Magdy	Elkhashab	Toronto Liver Centre	melkashabmd@yahoo.ca
Aysegul	Erman	University of Toronto	aysegul.erman@mail.utoronto.ca
Gary	Fagan	Canadian Liver Foundation	gfagan@liver.ca
Hooman	Farhang Zangneh	University of Toronto	hooman.f.zangneh@mail.utoronto.ca
Sadeem	Fayed	Simon Fraser University	sfayed@sfu.ca
Jordan	Feld	University Health Network	jordan.feld@uhn.ca
Suzanne	Fish	Canadian Aids Treatment Information Exchange	sfish@catie.ca
Jennifer	Flemming	Queen's University	flemmij@hdh.kari.net
Amanda	Fletcher	CTAC	amanda@ctac.ca
Jo-Ann	Ford	Vancouver General Hospital	joann.ford@vch.ca
Pam	Ford	Regina Internal Medicine	slarpd@gmail.com
Lorraine	Fradette	Centre de recherche du Centre hospitalier de l'Université de Montréal	lorraine.fradette@canhepc.ca
Dennaye	Fuchs	Regina General Hospital	dennaye.fuchs@saskhealthauthority.ca
Antonio	Galante	Liver Transplant Program	antonio.galante@uhn.ca
Margaret	Gale-Rowe	Public Health Agency of Canada	margaret.gale-rowe@canada.ca
Lesley	Gallagher	Saskatchewan Infectious Disease Care Network	lesley.gallagher@vch.ca
Veeral	Gandhi	Pharmacy.ca	veeral@pharmacy.ca
Lisa	Gauthier	Gilead Canada	lisa.gauthier@gilead.com
Adam	Gehring	Toronto Centre for Liver Disease	adam.gehring@uhnresearch.ca
Peter	Ghali	McGill University	peter.ghali@muhc.mcgill.ca
Amanda	Giacomazzo	Canadian Aids Treatment Information Exchange	agiacomazzo@catie.ca
Lee	Goneau	Public Health Ontario	lee.goneau@oahpp.ca

Sonja	Gould	Liver Care Canada	sonjagould@cogeco.ca
Shauna	Granger	Dr. Wiesinger's Office	shauna.granger@hotmail.com
Jason	Grebely	The Kirby Institute, New South Wales University	jgrebely@kirby.unsw.edu.au
Nagma	Grewal	Queen's University	12ng23@queensu.ca
Del	Grimstad	AIDS Vancouver Island	sfish@catie.ca
Jen	Grochocinski	Canadian Aids Treatment Information Exchange	jgrochocinksi@catie.ca
Mary	Guyton	Sherbourne Health Center	mguyton@sherbourne.on.ca
Karin	Hagen	Merck Canada Inc.	karin.hagen@merck.com
Jodi	Halsey-Brandt	Merck Canada Inc.	jodi.halsey-brandt@merck.com
Sundeep	Hansra	University of Toronto	hansra_soni@hotmail.com
Janet	Hatcher Roberts	University of Ottawa - Bruyère Research Institute	Jhatcherroberts@gmail.com
Sandra	Hawker	South Health Campus	sandrahawker9@gmail.com
Sarah	Haylock-Jacobs	University of Calgary	Shaylock@ucalgary.ca
John H.	Hii	Traveller's Medical Service & Geographic Medicine	caledon53@gmail.com
Elita	Ho	Gilead Canada	Elita.Ho@gilead.com
Stine	Hoj	Université de Montréal	stine.hoj@umontreal.ca
Julie	Holeksa	Vancouver Infectious Diseases Centre	julie.holeksa@vidc.ca
Anita	Howe	BC Centre for Excellence in HIV/AIDS	ahowe@cfenet.ubc.ca
Emmanuelle	Huchet	CMU du Quartier Latin	ehuchet@me.com
Shohan	Illsley	Manitoba Harm Reduction Network	sfish@catie.ca
Brendan	Jacka	Centre de recherche du Centre hospitalier de l'Université de Montréal	brendan.jacka@umontreal.ca
Naveed	Janjua	BC Centre for Disease Control	Naveed.Janjua@bccdc.ca
Harry	Janssen	University Health Network	harry.janssen@uhn.ca
Erika	Jaramillo	Hospital General de México	jaramillo2502@gmail.com
Lindsay	Jennings	PASAN	sfish@catie.ca
Janelle	Johnson	University of Alberta	jjohnson@ualberta.ca
Christie	Johnston	Canadian Aids Treatment Information Exchange	cjohnston@catie.ca
Hsiao-Ming	Jung	Albany Medical Clinic, Liver Clinic	hjung@albanyclinic.ca
Didier	Jutras-Aswad	Centre hospitalier de l'Université de Montréal	didier.jutras-aswad@umontreal.ca
Shelina	Karmali	CTAC	shelina@ctac.ca
Kelly	Karn	Specialty Rx	kkarn@parkwoodns.com
Melissa	Kelley	Memorial University	Melkelley08@gmail.com
Susan	Kelso	AbbVie Canada	susan.kelso@abbvie.com
Janine	Kemming	University Hospital Freiburg	janine.kemming@uniklinik-freiburg.de
Alexandra	King	University of Saskatchewan	alexandra.king@usask.ca
Zak	Knowles	Canadian Aids Treatment Information Exchange	zknowles@catie.ca
Hin Hin	Ko	University of British Columbia	hinnih@gmail.com
Beverley	Kok	University of Alberta Hospital	beverley.kok@gmail.com

Gillian	Kolla	University of Toronto	gillian.kolla@utoronto.ca
Sreelakshmi	Kotha	Toronto General Hospital	Sreelakshmi_kotha@yahoo.com
Rob	Kozak	University of Toronto	rob.kozak@gmail.com
Murray	Krahn	Toronto General Hospital	murray.krahn@theta.utoronto.ca
Victor	Kramer	Merck Canada Inc.	victor.kramer@merck.com
Lisette	Krassenburg	University Health Network	lisette.krassenburg@uhn.ca
Nadine	Kronfli	McGill University	nadine.kronfli@medportal.ca
Rasika	Kunden	University of Saskatchewan	rasika.kunden@usask.ca
Hadi	Kuriry	Toronto General Hospital	h.kuriry@live.com
Rivka	Kushner	Canadian Aids Treatment Information Exchange	rkushner@catie.ca
Dimitriana	Kuzyk-Bernier	Mount Carmel Cliinic	demikb@shaw.ca
Jeff	Kwong	Institute for Clinical Evaluative Sciences	jeff.kwong@utoronto.ca
Myriam	Lachapelle	John Howard Society New Brunswick	sfish@catie.ca
Clemence	Laforce	Coverdale Clinic	clemencelaforce@msn.com
Douglas	Laird	University of Victoria	bioxyzen@yahoo.ca
Alain	Lamarre	INRS	alain.lamarre@iaf.inrs.ca
Charlotte	Laniece	McGill University	charlotte.laniece@mail.mcgill.ca
Stéphanie	Laporte	Programme national de mentorat sur le VIH et les hépatites	coordination_vih@pnmvh.org
Georg	Lauer	Massachusetts General Hospital/Harvard Medical School	glauer@mgh.harvard.edu
Noemie	Laverdure	Sainte-Justine Hospital	youpi548@gmail.com
Frederick	Lavigne	AbbVie Canada	frederick.lavigne@abbvie.com
Regan	Lavoie	Street Health Centre	reganl@streethealth.kchc.ca
John	Law	University of Alberta	llaw@ualberta.ca
Loretta	Layton	AbbVie Canada	loretta.layton@abbvie.com
Jeffrey	Lazarus	ISGlobal, Hospital Clínic, University of Barcelona	Jeffrey.Lazarus@isglobal.org
Robyn	LeBlanc	John Howard Society New Brunswick	sfish@catie.ca
Roger	LeBlanc	Clinique OPUS	rogerpleblanc@me.com
Lori	Lee	Canadian Mental Health Association	lorilee327@gmail.com
Marise	Lemieux	Gilead Sciences Canada Inc.	marise.lemieux@gilead.com
Jennifer	Leonard	Memorial University	leonards@nl.rogers.com
Isabelle	Létourneau	Canadian Institutes of Health Research - Institute of Infection and Immunity	isabelle.letourneau@crchudequebec.ulaval.ca
Bernadette	Lettner	South Riverdale CHC	blettner@srchc.com
Marcelle	Levy	AbbVie Corporation	marcelle.levy@abbvie.com
Seng	Liem	University Health Network	k.s.liem@erasmusmc.nl
Liang-Tzung	Lin	Taipei Medical University	ltlin@tmu.edu.tw
Jimin (Nancy)	Liu	Halton Healthcare Services	nliu@haltonhealthcare.com
Ching-Hsuan	Liu	Dalhousie University	julia.chliu@gmail.com
Hongqun	Liu	Canadian Network Undertaking against Hepatitis C	hliu@ucalgary.ca

Lewis	Liu	Princess Margaret Cancer Tower	lewy.liu@mail.utoronto.ca
Allaina	Lucier	Sanguen	sfish@catie.ca
Carrielynn	Lund	Canadian Aboriginal AIDS Network	carriel@caan.ca
Daryl	Luster	Pacific Hepatitis C Network ,AHC, CanHepC	dluster@telus.net
Ann	Ma	University of Toronto	ma.ann.thu@gmail.com
Alex	MacDonnell	HepNS	director@hepns.ca
Nimâ	Machouf	Clinique de Médecine Urbaine du Quartier Latin	nmachouf@cmql.ca
Shona	Mackenzie	Parkdale Community Health Centre	Shonamac@sympatico.ca
Sonya	MacParland	University of Toronto	sonya.macparland@uhnresearch.ca
Gisela	Macphail	CUPS Health Education Housing	gisela.macphail@ahs.ca
Jessica	Mak	University of Toronto	jessica.mak@uhn.ca
Nick	Mapara	Vela Diagnostics	nickm8870@gmail.com
Alyssa	Margeson	The Moncton Hospital	alyssa.margeson@horizonnb.ca
Alison	Marshall	The Kirby Institute, New South Wales University	amarshall@kirby.unsw.edu.au
Valérie	Martel-Laferrière	Centre hospitalier de l'Université de Montréal	vmlaferriere@gmail.com
Steven	Martin	Alberta Children's Hospital	stevenr.martin@ahs.ca
Renee	Masching	Canadian Aboriginal AIDS Network	reneem@caan.ca
Andrew	Mason	University of Alberta	andrew.mason@ualberta.ca
Sabrina	Mazouz	Centre de recherche du Centre hospitalier de l'Université de Montréal	mazouz.sabrina@gmail.com
Matt	McCoy	Gilead Canada	matthew.mccoy@gilead.com
Mark	McGovern	Merck Canada Inc.	mark.mcgovern@merck.com
Gina	McGowan	Government of British Columbia	gina.mcgowan@gov.bc.ca
Liza	McGuinness	Hepatitis Education Canada/BCCDC	liza.mcguinness@bccdc.ca
David	McLay	Canadian Aids Treatment Information Exchange	dmclay@catie.ca
Shawna	McLean	Correctional Service Canada	Shawna.McLean@csc-scc.gc.ca
Orlando	McLeish	Positive Living Fraser Valley	sfish@catie.ca
Andrew	Mendlowitz	University of Toronto	andrew.mendlowitz@mail.utoronto.ca
Jason	Mercredi	AIDS Saskatoon	sfish@catie.ca
Nanor	Minoyan	Centre hospitalier de l'Université de Montréal	nanorminoyan@gmail.com
Robert	Mitchell	University of British Columbia	rmitch86@gmail.com
Wes	Miyai	Merck Canada Inc.	wes.miyai@merck.com
Gerald	Mugford	Memorial University	gmugford@mun.ca
Dylana	Mumm	Gilead Sciences Canada Inc.	dylana.mumm@gilead.com
Armstrong	Murira	Institut Armand Frappier	armstrong.murira@iaf.inrs.ca
Blaise	Myette	Advanced Care Specialty Pharmacy	bmyette@gmdpharma.ca
Lindsay	Myles	Liver Care Canada	lindsay.myles@livercarecanada.com
Kate	Newcombe	CUPS Health Education Housing	KateN@cupscalgary.com
Lucy	Newman-Hogan	University of Guelph	lucynewmanhogan@gmail.com

Frederic	Nguyen	University of Ottawa	fnguy006@uottawa.ca
Susanne	Nicolay	Wellness Wheel	sfish@catie.ca
Claudia	Nigro	BC Hepatitis Program	claudia.nigro@vch.ca
Howard	Njoo	Public Health Agency of Canada	howard.njoo@canada.ca
Kelly	O'neill-Beard	Liver Care Canada	Kelly28291@hotmail.com
Erin	O'Halloran	Gilead Canada	erin.ohalloran@gilead.com
Sharon	Oldford	Dalhousie University	sharon.oldford@dal.ca
Annika	Ollner	Toronto Community Hep C Program - Sherbourne Health Centre	aollner@sherbourne.on.ca
Adam	Palayew	McGill University	apalayew@gmail.com
Michelle	Paquin	Coverdale Clinic	mpaquin@coverdaleclinic.com
Robyn	Parsons	Vancouver Infectious Diseases Centre	robyn.parsons@vidc.ca
Nishi	Patel	University of Calgary	nishi.patel@ucalgary.ca
Diane	Perreault	Clinique de gastroentérologie de Lanaudière	diane.perreault@gmail.com
Laila	Peterson	PerCuro Clinical Research	laila@percuro.ca
Shane	Phillips	Positive Living Fraser Valley	sfish@catie.ca
Pam	Pickering	ASK Wellness Society	sfish@catie.ca
Margaret	Poitras	All Nations Hope	sfish@catie.ca
Kathryn	Poldre	VIRCAN / Toronto Centre for Liver Disease	kathyapoldre@gmail.com
Ann	Port	Ottawa Hospital	aport@toh.ca
Melanie	Provost	Merck Canada Inc.	Melanie.provost@merck.com
Michel	Quintas	Gilead Sciences Canada Inc.	michel.quintas@gilead.com
Jennifer	Ralph	Canadian Institute of Health Research	jennifer.ralph@cihr-irsc.gc.ca
Alnoor	Ramji	University of British Columbia	ramji_a@hotmail.com
Homie	Razavi	Center for Disease Analysis Foundation	hrazavi@cdafound.org
Rebekah	Rittberg	Internal Medicine Resident	rittberr@myumanitoba.ca
Patreka	Roach	VIRCAN / Toronto Centre for Liver Disease	patreka.roach@vircan.ca
Eve	Roberts	Hospital for Sick Children	eve.roberts@dal.ca
Yoima	Rodriguez	Clinique OPUS	yoima.rodriguez@cliniqueopus.com
Jonathan	Roger	McGill University	jonathan.roger@muhc.mcgill.ca
Tim	Rogers	Canadian Aids Treatment Information Exchange	trogers@catie.ca
Natalia	Rosário	Centre de recherche du Centre hospitalier de l'Université de Montréal	nataliarosario@id.uff.br
Carmine	Rossi	McGill University	carmine.rossi@mail.mcgill.ca
Elise	Roy	University of Sherbrooke	elise.roy@usherbrooke.ca
Chris	Rueda-Clausen	University of Alberta	ruedacla@ualberta.ca
Yasmin	Saeed	University of Toronto	yasmin.saeed@mail.utoronto.ca
Sahar	Saeed	McGill University	sahar.saeed@mail.mcgill.ca
Selena	Sagan	McGill University	selena.sagan@mcgill.ca
Noem	Sain	McKesson Canada	noem.sain@mckesson.ca
Danae	Sale	Canadian Association of Hepatology Nurses	admin@cahn.ca

Nabeel	Samad	University of Manitoba	nbsamad@gmail.com
Beate	Sander	University Health Network	beate.sander@uhnresearch.ca
Dena	Schanzer	Public Health Agency of Canada	dena.schanzer@canada.ca
Wendy	Schaufert	Alberta Health Services	schau4t@gmail.com
Maria	Schmit	GI Research Institute	maria.a.schmit@gmail.com
Richard	Schreiber	University of British Columbia	rschreiber@cw.bc.ca
Giada	Sebastiani	McGill University	giada.sebastiani@mcgill.ca
Sejal	Shah	Specialty Pharma Solutions	sshah@specialtypharmasolutions.ca
Hemant	Shah	University of Toronto	hemant.shah@uhn.ca
Alexandra	Shingina	University of Washington	alexandra.shingina@mail.utoronto.ca
Naglaa	Shoukry	University of Montréal Hospital Research Centre	naglaa.shoukry@umontreal.ca
Avtar	Singh	Punjabi Community Health Services	sfish@catie.ca
Lucy	Smith	Memorial University	lucy.smith@mun.ca
Melissa	Smith	Saskatchewan Infectious Disease Care Network	mlg014@mail.usask.ca
Hugo	Soudeyns	Centre Hospitalier Universitaire Sainte-Justine	hugo.soudeyns@recherche-ste-justine.qc.ca
Alexander	Southward	McGill University	alexander.southward@mail.mcgill.ca
Shelby	St. Amour	Island Health Authority	shelby.stamour@viha.ca
Maria	Stavrakis	Jewish General Hospital	mstavrakis@jgh.mcgill.ca
Matthew	Stewart	Dalhousie University	mt272675@dal.ca
Marie-Josee	St-Pierre	AbbVie Canada	marie-josee.st-pierre@abbvie.com
Myriam	St-Pierre-Lussier	Université de Sherbrooke	myriam.st-pierre-lussier@usherbrooke.ca
Ken	Sun	University of Alberta	ksun3@ualberta.ca
Tracy	Swan		tracyswannyc@gmail.com
Fozia	Tanveer	Canadian Aids Treatment Information Exchange	ftanveer@catie.ca
Shannon	Taylor	CAHN/ACS Pharmacy	radioshan@gmail.com
Taylor	Teal	AIDS Vancouver Island	sfish@catie.ca
Angela	Thomosn	Nicola Valley Institute of Technology	angelapaul712@gmail.com
Michael	Trauner	Medical University of Vienna	michael.trauner@meduniwien.ac.at
Janie	Trepanier	Merck Canada Inc.	janie.trepanier@merck.com
Mario	Trudel	Gilead Sciences Canada Inc.	mario.trudel@gilead.com
Keith	Tsoi	McMaster University	ktsoi@mcmaster.ca
Shanell	Twan	Streetworks	sfish@catie.ca
Mark	Tyndall	BC Centre for Disease Control	mark.tyndall@bccdc.ca
D. Lorne	Tyrrell	University of Alberta	lorne.tyrrell@ualberta.ca
Taryn	Tyrrell	LAIR Centre	ttyrrell@laircentre.com
Marla	Ullman	Rx Infinity	kwang@rxinfinity.ca
Rob	Urbanic	Gilead Canada	robert.urbanic@gilead.com
Kathryn	Van de Ven	HepCare	kathryn.v@hepcare.ca

Aaron	Vanderhoff	VIRCAN / Toronto Centre for Liver Disease	aaron@vircan.ca
Anu	Vig	Merck Canada Inc.	anu.vig@merck.com
Lynn	Vignola	Ottawa Liver Centre	Lynnvignola@sympatico.ca
Jean-Philippe	Wallach	Nanaimo Regional General Hospital	jp.wallach@gmail.com
Lori Lee	Walston	LAIR Centre	lorileewalston@gmail.com
Bessie	Wang	Gilead Sciences Canada Inc.	bessie.wang@gilead.com
Heiner	Wedemeyer	Essen University Hospital	heiner.wedemeyer@gmail.com
Chantelle	Weir	AIDS Committee of Newfoundland and Labrador	sfish@catie.ca
Marianne	Wiebe	Mount Carmel Clinic	mwiebe@mountcarmel.ca
Wendy	Wobeser	Queen's University	wlw@queensu.ca
Cathy	Woldanski	The Group Health Centre	woldanski_c@ghc.on.ca
Sheryl	Wolfstadt	Coverdale Clinic	sherylmwolf@gmail.com
William WL	Wong	University of Waterloo	wwlwong@uwaterloo.ca
Josephine	Wong	Toronto General Hospital	josephine.wong@theta.utoronto.ca
Alexander	Wong	University of Saskatchewan	awong37@gmail.com
Jessica	Woolfson	The Hospital for Sick Children	jessica.woolfson@sickkids.ca
Kipp	Wotherspoon	Gilead Sciences Canada Inc.	Kipp.Wotherspoon@gilead.com
Gerard	Yetman	AIDS Committee of Newfoundland and Labrador	sfish@catie.ca
Colina	Yim	Toronto General Hospital	colina.yim@uhn.ca
Yukun	Zhao	Canadian Aids Treatment Information Exchange	yzhao@catie.ca
Blake	Ziegler	GMD Pharma Solutions	bziegler@gmdpharma.ca
Faustyna	Zietara	University of Calgary	fzietara@ucalgary.ca
Donna	Zukowski	Canadian Association of Hepatology Nurses	dzukow@shaw.ca

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Thank you! We couldn't have done it without you
Merci! Nous n'aurions pas pu le faire sans vous