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

8th Canadian Symposium on Hepatitis C Virus

8ème Symposium canadien sur le virus de l'hépatite C

May 24, 2019 – 24 Mai 2019

Hotel Bonaventure, Montréal. QC

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 8th 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, health, 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 Montreal! 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 8e 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 Montréal!

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.

Selena Sagan, PhD
McGill University

Giada Sebastiani, MD
McGill University

Biographies of Co-Chairs

Selena Sagan, McGill University, Montréal, Canada – Chair

Biography

Dr. Selena M. Sagan, Ph.D. is an Assistant Professor, Department of Microbiology & Immunology, and Associate Member of the Department of Biochemistry, McGill University. Dr. Sagan received her Ph.D. from the University of Ottawa. She completed her postdoctoral fellowship training in Department of Microbiology & Immunology at Stanford University. Dr. Sagan is a Canada Research Chair in *RNA Biology and Viral Infections* and her laboratory studies positive-strand RNA viruses of the *Flaviviridae* family (including Hepatitis C virus, Dengue virus and Zika virus). The main focus of her research program is RNA-RNA and protein-RNA interactions at the host-virus interface.
www.saganlab.com

Giada Sebastiani, McGill University, Montréal, Canada – Co-Chair

Biography

Giada Sebastiani is Associate Professor of Medicine at McGill University and Clinician Scientist at the Research Institute of McGill University Health Centre in Montreal, Canada. She provides clinical services in the Division of Gastroenterology and Hepatology. She received a medical degree and specialized in internal medicine at the University of Padua, Italy. She had training in clinical and basic research at Harvard Medical School (US), University College of London (UK), University of Bordeaux (France) and Lady Davis Institute for Medical Research (Montreal, Canada). Her work focuses on fatty liver disease, liver fibrosis and non-invasive diagnostic tools in liver disease. She is author of 68 articles in peer-reviewed journals (including Hepatology, Journal of Hepatology, Clinical Infectious Diseases, AIDS; h-index=27, total number of citations=3,000), 15 book chapters, 120 conference publications at national and international congresses. She has been invited speaker in 60 international congresses and universities, including European, Asian Pacific, Mexican, Italian and Canadian Associations for the Study of the Liver. She was awarded the prestigious Clinical Research Salary Award from Fonds Recherche Sante Quebec. Other honors include: honorary membership of the Romanian Association for the Study of the Liver; Emerging Stars in Hepatology Award (Asian Pacific Association for the Study of the Liver, 2010); Top 10 cited papers 2006-2008 Award by Journal of Hepatology - European Association for the Study of the Liver.

Program – Programme

Improving diagnosis: how to reach the undiagnosed population

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: Rod Russell, Memorial University & Vanessa Meier-Stephenson, University of Calgary

08h15 - 08h35 Remaining Challenges in HCV Research
Ralf Bartenschlager, University of Heidelberg, Heidelberg, Germany

08h35 - 08h55 Single-cell RNA Sequencing to Describe the Cellular Microenvironment of the Liver
Sonya MacParland, University of Toronto, Toronto, Canada

08h55 - 09h15 Questions/Panel Discussion

Oral Presentations

09h15 - 09h27 Targeting HCV-induced Epigenetic Reprogramming for HCC Chemoprevention Post Cure
Nourdine Hamdane, University of Strasbourg, Strasbourg, France

09h27 - 09h39 Identification of the Domain to Which miR122 and Other small RNAs Annealing Promotes the HCV Lifecycle
Rasika Kunden, University of Saskatchewan, Saskatchewan, Canada

09h39 - 09h51 Analysis of Programmed Cell Death Induced by HCV Infection
Lingyan Wang, Memorial University, St. John's, Canada

09h51 - 10h11 Coffee Break – Pause café

Social, Cultural, Environmental, and Population Health Research
Co-Chairs: Marina Klein, McGill University & Abdool Yasseen, University of Toronto

10h11 - 10h31 Diagnostic Testing for Hepatitis C Infection: Where Are We Now and What Does the Future Hold?
Stuart C. Ray, Johns Hopkins University School of Medicine, Baltimore, USA

10h31 - 10h51 Hepatitis C and HIV Testing from Dried Blood Spots: Simplifying Testing to Broaden Community-Based Screening
John Kim, Public Health Agency of Canada, Winnipeg, Canada

10h51 - 11h11 Questions/Panel Discussion

Oral Presentations

11h11 - 11h23 Estimation of an Individual-Level Deprivation Index for HIV/HCV co-infected Persons
Adam Palayew, McGill University, Montréal, Canada

11h23 - 11h35 Opioid Agonist Treatment and Risk of Hepatitis C Virus Infection Among People who Inject Drugs: The Overlooked Role of Dosage Adequacy
Andreea Adelina Artenie, Université de Montréal, Montréal, Canada

11h35 - 13h00 Lunch and poster session – Diner et présentation des affiches **: St-Laurent 1-3**
CanhepC evaluation will take place between 12h00-13h00 to allow trainees to have lunch

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

Clinical Research
Co-Chairs: Lisa Barrett, Dalhousie University & Sahar Saeed, McGill University

13h00 - 13h20 Risk of HCC following Hepatitis C Treatment
Hashem B. El-Serag, Baylor College of Medicine, Houston, USA

13h20 - 13h40 Liver Fibrosis Staging in Hepatitis C
Keyur Patel, University Health Network, Toronto, Canada

13h40 - 14h00 Questions/Panel Discussion

Oral Presentations

14h00 - 14h12 Never Too Old to be DAA Treated for Hepatitis C
Curtis cooper, University of Ottawa, Ottawa, Canada

14h12 - 14h24 Feasibility of Rapid Hepatitis C Point-of-Care RNA Testing and Linkage to Care at an Integrated Supervised Consumption Site in Toronto, Canada
Bernadette Lettner, South Riverdale Community Health Centre, Toronto, Canada

14h24 - 14h36 Engaging Vulnerable, Treatment Naïve Persons Living with Hepatitis C in Same-Day Treatment
Shawn Greenan , Health PEI, Halifax, Canada

14h36 - 14h56 Coffee Break – Pause café

Health Services Research
Co-Chairs: Naveed Janjua University of British Columbia & Aysegul Erman, University of Toronto

14h56 - 15h16 Feasibility and Cost of Hepatitis C Elimination
Jagpreet Chhatwal, Harvard Medical School, Boston, USA

15h16 - 15h36 Testing and Linkage with Care Strategies for HCV Among Immigrants and Newcomers
Christina Greenaway, McGill University, Montreal, Canada

15h36 - 15h56 Questions/Panel Discussion

Oral Presentations

15h56 - 16h08 The Hepatitis C Virus (HCV) Cascade of Care in a Canadian Provincial Prison: Implications for HCV Micro-elimination
Nadine Kronfli, McGill University, Montréal, Canada

16h08 – 16h20 State-specific Direct Medical Costs of Hepatitis C in Ontario: A Population-Level Study
Alexander Haines, THETA, Toronto, Canada

16h20 - 16h32 Assessment of Hepatitis C Screening Strategies in Different Community Settings in a Canadian Metropolitan Area
Camelia Capraru, Toronto Centre for Liver Disease/VIRCAN, UHN, Toronto, Canada

16h32 - 17h15 **Panel discussion:** Engaging People with Lived Experience to Improve Hepatitis C Diagnosis and Linkage-to-Care in Programming and Research
Dopamine, Montreal, Quebec, Access Place, Prince Albert, Saskatchewan, Toronto Community Hepatitis C Program, Ontario
Moderator: Christopher Hoy, CATIE, Knowledge Specialist, Community Hepatitis C Programming

17h15 – 17h25 CanHepC trainee Awards Ceremony

17h25 – 17h30 CanHepC Symposium Closing Remarks
Selena Sagan and Giada Sebastiani, McGill University, Montreal, Canada

17h30 – 17h40 Canadian Liver Meeting Opening Remarks
Marc Bilodeau, Université de Montreal, Montreal, Canada

17h40 – 18h30 **Launch and panel discussion:** Blueprint to inform hepatitis C elimination efforts in Canada - **LIVE**
Presenter/moderator: Jordan Feld (University of Toronto). Panel: Melisa Dickie (CATIE), Lindsay Jennings (Prisoners HIV/AIDS Support Action Network), Julie Bruneau (Université de Montréal), Mel Krajden (University of British Columbia), and Marina Klein (McGill University)

18h30 **Canadian Liver Meeting Opening Reception**

Committees – Comités

Organizing Committee - Comité organisateur

Selena Sagan, McGill University, Chair
Giada Sebastiani, McGill University, Co-Chair

Curtis Cooper, University of Ottawa
Melisa Dickie, CATIE
Jordan Feld, University Health Network
Lesley Gallagher, CAHN
Jason Grebely, UNSW Sydney
Naveed Janjua, University of British Columbia
Alexandra King, University of Saskatchewan
Naglaa Shoukry, Université de Montréal
Joyce Wilson, University of Saskatchewan

Adelina Artenie, Université Montréal and Brendan Jacka, Université de Montréal, trainee representatives

Norma Choucha, CRCHUM, Symposium Coordinator

Session Chairs - Modérateurs de sessions

Biomedical Research
Rod Russell, Memorial University
Vanessa Meier-Stephenson, University of Calgary

Social, Cultural, Environmental, and Population Health Research
Marina Klein, McGill University
Abdool Yasseen, University of Toronto

Clinical Research
Lisa Barrett, Dalhousie University
Sahar Saeed, McGill University

Health Services Research
Naveed Janjua University of British Columbia
Aysegul Erman, University of Toronto

Abstract Reviewers - Réviseurs des résumés

Biomedical Research

Mohamed Abdel Hakeem, University of Pennsylvania
Che Colpitts, University College London
Angela Crawley, University of Ottawa
John Law, University of Alberta
Sonya MacParland, University of Toronto
Thomas Michalak, Memorial University
John Pezacki, University of Ottawa
Rodney Russell, Memorial University
Joyce Wilson, University of Saskatchewan

Social, Cultural, Environmental, and Population Health Research

Julie Bruneau, Université de Montréal
Renée Mashing, CAAN
Brendan Jacka, Université de Montréal
Carrielynn Lund, CAAN
Gerry Mugford, Memorial University
Sahar Saeed, McGill University

Clinical Research

Marc Bilodeau, Université de Montréal
Brian Conway, Vancouver Infectious Diseases Centre
Curtis Cooper, University of Ottawa
Marina Klein, McGill University
Sam Lee, University of Calgary
Valerie Martel-Laferriere, Université de Montréal
Vanesssa Meier-Stephenson, University of Calgary
Marie Louise Vachon, Université de Montréal

Health Service Research

Adelina Artenie, Université de Montréal
Jason Grebely, UNSW Sydney
Naveed Janjua, University of British Columbia
Murray Krahn, University of Toronto
Jeff Kwong, University of Toronto
Alison Marshall, UNSW Sydney
Carmine Rossi, University of British Columbia
Beate Sanders, University of Toronto

Speaker Biographies and Abstracts – Biographies des conférenciers et résumés

Biomedical Research

Ralf Bartenschlager, University of Heidelberg, Heidelberg, Germany

Biography

Ralf Bartenschlager, Department of Infectious Diseases, Molecular Virology, Heidelberg University Hospital, Im Neuenheimer Feld 345, 69120 Heidelberg; Division "Virus-associated carcinogenesis", German Cancer Research Center, Im Neuenheimer Feld 242, 69120 Heidelberg, Germany

Ralf Bartenschlager is molecular biologist by training and interested in the complexities of the interactions between viruses and their host cells. His work centers on hepatitis viruses, notably hepatitis C and B virus (HCV and HBV, respectively) and comparative analyses with flaviviruses (Dengue and Zikavirus). One research direction in the Bartenschlager lab deals with the strategies used by HCV and HBV to establish persistence with a focus on the innate antiviral defense. Another direction centers on the cell biology of the replication cycle of these viruses, how they exploit host cell factors and pathways for efficient replication and how this relates to virus – host evolution. Finally, knowledge gained from these studies is used to develop novel antiviral strategies, focusing on host cell dependency factors that hold promise for the development of broad-spectrum antiviral drugs.

Abstract

Counteraction of innate antiviral defense by persistent hepatitis viruses

Infections with the Hepatitis B and C virus (HBV, HCV) are a major risk factor for chronic liver disease, with both viruses having a high propensity to establish persistence. While HCV is a positive-strand RNA virus replicating in the cytoplasm in membranous replication organelles, HBV is a pararetrovirus, replicating its pregenomic RNA via reverse transcription within the nucleocapsid. To establish persistence, both viruses have developed efficient strategies to overcome innate antiviral immunity. In the case of HCV we found that it blocks the interferon activation pathway via MAVS by proteolytic cleavage of this signaling molecule. However, it still induces a strong interferon response in vitro and in vivo and is highly sensitive to the antiviral program induced by this cytokine. Moreover, HCV does not actively suppress the TLR3 signaling pathway but keeps the TLR3-induced response low via release of exosomes containing viral replication intermediates. In contrast, HBV is a prototypic "stealth" virus passively bypassing the interferon system at all levels of sensors and antiviral effectors. This might be the result of the long-term coevolution of HBV with its host over geologic eras.

Sonya MacParland, University of Toronto, Toronto, Canada

Biography

Dr. MacParland is an early career researcher and Scientist in the Toronto General Hospital's Transplant Program and an Assistant Professor in the University of Toronto's Departments of LMP and Immunology. Dr. MacParland's research program is focused on translating fundamental knowledge about the immune biology of the liver into clinical applications. Dr. MacParland and her research team are using advanced genomics including single cell RNA sequencing to describe the microenvironment of the healthy human liver (***Nature Communications; 2018****)* as a platform to examine how liver immune dysregulation drives liver diseases, including chronic viral infection and inflammatory liver fibrosis. They will also examine how the liver immune environment can be therapeutically manipulated using nanoparticles to slow or reverse ongoing damage.

Abstract

Single-Cell RNA Sequencing to Describe the Cellular Microenvironment of the Liver

The liver is vital for human metabolism and immune function. A reference map of the healthy human liver landscape at single cell resolution is critical to understanding the pathogenesis and treatment of liver disease. This landscape has been difficult to describe, mainly because fresh human liver tissue access is scarce and the tissue is difficult to fractionate without damaging fragile resident cell populations. One approach to creating an unbiased map of the human liver cellular landscape is to combine careful dissociation of relatively large segments of fresh, healthy human liver with single cell RNA sequencing (scRNA-seq). This talk will present an unbiased examination of the cellular landscape of the normal human liver *via* scRNA-seq. We identify 20 hepatic cell populations from the transcriptional profiling of 8444 cells obtained from liver grafts of five healthy neurologically deceased donors (NDD). By examining the most differentially expressed (DE) genes of each cluster, and using known landmark genes or characterizing markers known from cell-specific gene expression, flow cytometry, or immunohistochemical examinations of human liver tissue, we find distinct populations of hepatocytes, endothelial cells, cholangiocytes, hepatic stellate cells, KCs, B cells, conventional and non-conventional T cells and NK cells. These evaluations uncover aspects of the immunobiology of the liver, including the presence of two distinct populations of liver resident macrophages with inflammatory and non-inflammatory/immunoregulatory functions. The development of scRNA-seq transcriptional reference maps of the human liver microenvironment provides a framework for understanding the cellular basis of human liver function and disease and a benchmark for the development new cell-based and immunomodulatory therapies to treat and prevent liver disease.

Social, Cultural, Environmental, and Population Health Research

Stuart C. Ray, Johns Hopkins Univ Sch of Med, Baltimore, USA

Biography

Stuart Ray, MD FACP FIDSA serves as Professor of Medicine, Oncology, and Health Sciences Informatics at Johns Hopkins University School of Medicine, Vice Chair of Medicine for Data Integrity and Analytics, and Director of the Laboratory for Integrated NanoDiagnostics. He is a faculty member of the graduate programs in Immunology and Pharmacology, and is a member of the ASCI.

After receiving his M.D. from Vanderbilt he went to Johns Hopkins Hospital for residency and chief residency on the Osler Service. During his ID fellowship there, he studied HIV sequence variation and immunology, co-mentored by Drs. Robert Bollinger and Robert Siliciano. During his fellowship he began work on a software program called SimPlot, distributed free of charge, that has been used in about 2000 publications. In 1997 Dr. Ray joined the JHU SOM faculty and, mentored by Dr. David Thomas, has focused on the sequence variation of HCV as it reveals fundamental mechanisms of viral control and evasion.

Abstract

Diagnostic Testing for Hepatitis C Infection: Where Are We Now and What Does the Future Hold?

HCV diagnosis is a rate limiting step in elimination campaigns worldwide. Unlike many other viral infections, HCV infection marked by high-level viremia, greatly simplifying diagnosis. For reasons of cost, screening begins with testing for antibodies, in spite incomplete sensitivity and low specificity for infection - approximately 30% of people with positive HCV EIA are not infected with HCV, and this proportion will rise as elimination campaigns progress. There is a need for Affordable, Sensitive, Specific, User-friendly, Rapid and robust, Equipment-free and Deliverable to end-users (ASSURED) diagnostics for HCV. Steps toward this goal have been made but more innovation is needed, from research to regulation.

John Kim, Public Health Agency of Canada, Winnipeg, Canada

Biography

Dr. John Kim is the Chief of the National Laboratory for HIV Reference Services (NLHRS) at the National Microbiology Laboratory's JCWilt Infectious Disease Center in Winnipeg, MB. Along with the NLHRS he has extensive experience in testing including reference services for HIV/HTLV, monitoring proficiency in Canadian public health and hospital labs and support for all PHAC's Track surveillance surveys of key populations.

Recently they have engaged with several First Nations communities to increase testing opportunities for blood borne infections using dried blood spots. This novel intervention uses a model of engagement and ownership to ensure community uptake and includes Chief/council approval and training of local healthcare workers in the collection of DBS. This model has helped address empowerment, stigma, racism and reduce health inequities associated with inadequate access to testing.

Clinical Research

Hashem B. El-Serag, Baylor College of Medicine, Houston, USA

Biography

Dr. El-Serag obtained his medical degree from Al-Arab Medical University in Libya, completed his internship and residency in internal medicine (1995) at Greenwich Hospital, Yale University, Connecticut, and completed a fellowship in clinical gastroenterology (1997) at the University of New Mexico, Albuquerque, New Mexico, where he also earned a master's degree in public health (1998). In 1999, Dr. El-Serag joined the Michael E. DeBakey VA Medical Center and Baylor College of Medicine (BCM) in Houston, where he later became Chief of the Section of Gastroenterology and Hepatology (2007-2016). In 2017, he was selected to serve as Chairman of the Department of Medicine at BCM.

Dr. El-Serag's research focuses on the clinical epidemiology and outcomes of several digestive disorders, including GERD, Barrett's esophagus, esophageal adenocarcinoma, hepatocellular carcinoma and hepatitis C. He has obtained more 50 funded research grants including those from NIH, VA and Cancer Prevention Research Institute of Texas (CPRIT). He has more than 450 published papers to his credit including those published in *New England Journal of Medicine, JAMA, Annals of Internal Medicine and Gastroenterology*. He served multiple national leadership roles including Editor-in-Chief for *Clinical Gastroenterology and Hepatology* (2012-2017) and President Elect for the American Gastroenterological Association (2019). Dr. El-Serag's achievements have been recognized in multiple national and international awards as well as selection into the American Society for Clinical Investigators (ASCI) and American Association of Physicians (AAP).

Abstract

Risk of HCC following Hepatitis C Treatment

Patients with active HCV-induced cirrhosis are at particularly high risk for the development of HCC, with an annual incidence of HCC ranging from 3% to 10%. Sustained virologic response (SVR) with DAA has emerged as the most dominant modifier of HCC in patients with HCV. Other than cirrhosis, the residual role of most traditional risk factors among those with active untreated or uncured HCV is unclear; these factors include older age, male sex, Hispanic ethnicity, and possibly diabetes, obesity, smoking, HCV genotype, and HIV or HBV coinfection. Growing data consistently illustrate a considerable (50%–80%) and steady HCC risk reduction over time of de novo HCC among those achieving DAA-related SVR. DAAs offer a chance of cure for patients with advanced cirrhosis, older patients, and those with alcohol use—all characteristics independently associated with risk of HCC in HCV. Despite these historical differences, in a systematic review of 26 studies on de novo HCC occurrence (IFN, n = 17; DAA, n = 9), there was no evidence for differential HCC occurrence or recurrence risk after SVR from DAA and IFN-based therapy. However, despite the relative reduction in risk of HCC, the absolute risk of HCC persists relatively high (>1% per year) at least for the first several years in patients with DAA-induced SVR. These estimates exceeded the cutoffs beyond which HCC surveillance may become cost effective. In contrast, the risk of HCC was low in almost all patients without cirrhosis, with the exception of patients with a high baseline Fibrosis-4, suggesting presence of advanced fibrosis. Based on these data, HCC surveillance is likely to continue to be needed for all patients with cirrhosis or advanced fibrosis at the time of SVR. The extent of reduction of HCV-related HCC is also dependent on screening and detection of HCV-infected cohorts and the dissemination of DAA treatments. .

Keyur Patel, University Health Network, Toronto, Canada

Biography

Dr. Patel received his Bachelor of Medicine degree from the University of Southampton, United Kingdom and completed his clinical fellowships in Internal Medicine and Gastroenterology/Hepatology in Western Australia. He completed a 3-year post-doctoral research fellowship in Clinical and Translational Research in viral hepatitis at Scripps Clinic and Research Foundation, San Diego, CA and Duke Clinical Research Institute, Durham NC. He joined the Division of Gastroenterology at Duke University in 2004, and remained on faculty until relocating to UHN Toronto in October 2015. His research interests include early phase clinical therapeutic trials for viral hepatitis and fibrosis, and the development of biomarkers of fibrosis.

Abstract

Liver Fibrosis Staging in Hepatitis C

Liver biopsy is still regarded as the best method for staging hepatic fibrosis in chronic liver disease, but the semi-quantitative scoring systems used for staging do not quantify linearity of fibrosis deposition or reflect actual matrix content. In the DAA era, histologic risk assessment in chronic hepatitis C has mostly been replaced by non-invasive tests for determination of fibrosis stage, prior to treatment and after achieving SVR. These non-invasive tests were initially developed in relation to a cross-sectional and binary assessment of semi-quantitative histological scores to help guide IFN-based treatment decisions in CHC. Current non-invasive tools to estimate fibrosis utilize both biochemical and physical characteristics. Serum biomarker algorithms include a combination of either "direct markers", that are mostly complex proteins involved in extracellular matrix remodeling, or "indirect markers", that are relatively simple biochemical tests which estimate disease severity. Several imaging elastography modalities are now available as point-of-care tests for determination of liver stiffness measure (LSM) as a surrogate measure of fibrosis severity. The diagnostic accuracy of these non-invasive tests is essentially similar for advanced fibrosis stages, although there may be clinical utility to using a combined serum marker and imaging approach to improve diagnostic accuracy. These tests may have additional prognostic utility, and are frequently used in clinical practice to assess for changes in fibrosis stage after DAA treatment. However, currently available non-invasive diagnostic tools cannot reliably differentiate adjacent fibrosis stages, and have not been validated for assessment of post-SVR fibrosis regression, or following patients at risk of disease progression.

Health Services Research

Jagpreet Chhatwal, Harvard Medical School, Boston, USA

Biography

Jagpreet Chhatwal, PhD is an assistant professor at Harvard Medical School and a senior scientist at Massachusetts General Hospital. His research is centered in decision science, data analytics, and health economics. Dr. Chhatwal's work on hepatitis C has informed several highly-debated questions surrounding the cost-effectiveness of hepatitis C treatments and elimination of hepatitis C. In partnership with the World Health Organization, he also developed an online modeling tool, the *Hep C Calculator*, that allows policymakers from 28 countries to evaluate the cost-effectiveness of hepatitis C treatment in those countries. His work on hepatitis C has been featured in leading media such as The Wall Street Journal, Forbes, and National Public Radio.

Abstract

Feasibility and Cost of Hepatitis C Elimination

The World Health Assembly recently pledged to eliminate hepatitis C virus (HCV) as a public health threat by 2030. To achieve HCV elimination, the World Health Organization (WHO) launched a global strategy with an ambitious goal of diagnosing 90% of HCV-infected people and treating 80% of all eligible people. Despite the availability of highly-effective, new direct-acting antivirals (DAAs), treatment uptake remains low in most countries. In addition, the cost of providing population-level HCV testing and treatment to reach HCV elimination goal could be exorbitant. This talk will present the feasibility and cost of HCV elimination in several countries, if HCV elimination can become cost-saving, challenges to achieve elimination, and potential solutions to make elimination feasible by taking innovative approaches such as new diagnostics and financing mechanisms.

Christina Greenaway, McGill University, Montreal, Canada

Biography

Christina Greenaway is an infectious disease physician, clinician researcher and internationally recognized expert in migrant health. Her research focuses on identifying and addressing infectious disease health disparities among migrants. To achieve this, she had conducted observational studies, retrospective cohort studies with large linked administrative datasets, systematic reviews, economic analyses and has developed screening and clinical guidelines for migrants in Canada and Europe. She has found that HCV-infected immigrants were more likely to have end stage liver disease and hepatocellular cancer (HCC) at diagnosis and were less likely to be drug users, compared to the Quebec born population and, were only diagnosed a mean of 10 years after arrival. These data highlight the need to screen those born in HCV endemic countries and link those found to be positive to care and treatment. To further micro-elimination efforts among the foreign-born population she is leading a CIHR funded multi-province study using linked administrative databases to map the HCV care cascade in key risk groups, including migrants. She is also partnering with a leading HCV community organization in Montreal in a culturally and linguistically adapted HCV community outreach program in the Pakistani population to enhance HCV screening and treatment.

Abstract

Testing and Linkage with Care Strategies for HCV Among the Immigrant Population

The foreign-born population represents 35% of people living with chronic Hepatitis C Virus (HCV) in Canada. Immigrants face unique barriers to accessing HCV care. Despite having a 2-fold higher prevalence of HCV than the Canadian-born population, there is no routine HCV screening program for immigrants, contributing to late diagnosis and severe liver outcomes. Furthermore, many recent immigrants face cultural and linguistic barriers to accessing healthcare, and may benefit from decentralized services, such as community-based screening. Microelimination strategies, which tailor HCV elimination interventions in specific geographic regions and populations, may hold the key to overcoming health-system barriers that confront the foreign-born population. In this presentation, the barriers and enablers for HCV screening, linkage to care, and treatment completion for the migrant population will be reviewed. An example of an outreach program "Aagahi" (Urdu for "Awareness") among the Montreal Pakistani community developed in partnership with the Centre Associatif Polyvalent d'Aide Hépatite C (CAPAHC) will be presented. This program will provide culturally and linguistically adapted HCV educational outreach in several community venues, with point of care testing and support for linkage to care and treatment for those found to be HCV positive. The lessons learned from the Aagahi program will inform microelimination strategies geared at reaching the migrants living with chronic HCV in Canada and other countries with large migrant populations.

Panel discussion

Christopher Hoy, CATIE, Knowledge Specialist, Community Hepatitis C Programming

Biography

Christopher Hoy is a Knowledge Specialist in Hepatitis C Community Health Programming at CATIE. In this role, he has national and province-specific roles in sharing community programming practices and building capacity for frontline service providers. Christopher has previously worked in a variety of public health communications and policy roles in Ontario and has a Master of Public Health from the University of Guelph.

Blueprint to inform a Hepatitis C Elimination Strategy in Canada

Jordan Feld, University of Toronto, Toronto, Canada

Biography

Dr. Feld 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.

Oral Abstracts – résumés oraux

Biomedical Research

Oral presentation at 09h15 - ID: 48

Targeting HCV-induced epigenetic reprogramming for HCC chemoprevention post cure

Nourdine Hamdane, Institute for Viral and Liver Diseases, Frank Jühling, Institute for Viral and Liver Diseases, Emilie Crouchet, Institute for Viral and Liver Diseases, Christine Thumann, Institute for Viral and Liver Diseases, Houssein El Saghire, Institute for Viral and Liver Diseases, Shen Li, Division of Surgical Oncology, Massachusetts General Hospital Cancer Center, Harvard Medical School, Naoto Fujiwara, Liver Tumor Translational Research Program, Simmons Comprehensive Cancer Center, University of Texas Southwestern Medical Center, Atsushi Ono, Liver Tumor Translational Research Program, Simmons Comprehensive Cancer Center, University of Texas Southwestern Medical Center, Nabeel Bardeesy, Massachusetts General Hospital Cancer Center, Harvard Medical School, Christian Schmidl, Regensburg Centre for Interventional Immunology (RCI) and University Medical Center of Regensburg, Christoph Bock, CeMM Research Center for Molecular Medicine of the Austrian Academy of Sciences, Kazuaki Chayama, Department of Gastroenterology and Metabolism, Applied Life Sciences, Institute of Biomedical & Health Sciences, Hiroshima University, Yujin Hoshida, Liver Tumor Translational Research Program, Simmons Comprehensive Cancer Center, University of Texas Southwestern Medical Center, Bryan C. Fuchs, Division of Surgical Oncology, Massachusetts General Hospital Cancer Center, Harvard Medical School, Mirjam B. Zeisel, Inserm U1052, CNRS UMR 5286, Cancer Research Center of Lyon (CRCL), Université de Lyon (UCBL), François H.T. Duong, Institute for Viral and Liver Diseases, Thomas F. Baumert, Institute for Viral and Liver Diseases

Background: Chronic hepatitis C virus (HCV) infection is a major cause of hepatocellular carcinoma (HCC). Although curative treatment reduces the overall HCC incidence, the management of patients with advanced fibrosis where the HCC risk persists following cure is challenging. Epigenome alterations have been shown to cause transcriptional reprogramming associated with cancer.

Purpose: Given the persistent risk of hepatocarcinogenesis in patients with advanced fibrosis following viral cure we investigated whether HCV-induced epigenetic and transcriptomic changes persist and drive liver disease and HCC post sustained virologic response (SVR). Moreover, we explored whether virus-induced epigenetic modifications could be used as therapeutic target for chemoprevention of HCC in cell-based and animal models.

Methods: We focused on the analysis of persistent epigenome changes in HCV-infected and direct acting antiviral (DAA)-cured patients to identify HCC epi-driver genes and screened for epidrugs targeting transcriptional changes promoting liver disease and carcinogenesis.

Results: RNA-Seq and ChIP-Seq mapping of H3K27ac-mediated transcriptional changes in liver tissues from non-infected, HCV-infected or DAA-cured patients enabled us to identify persistent epigenetic changes on putative epi-driver genes associated with cancer-related pathways. Using a state-of-the-art HCV cell culture model, we uncovered several epi-drugs reversing the transcriptional reprogramming associated with liver disease progression and HCC development in patients. The functional impact of the compounds on gene expression and disease biology was validated by CRISPR/Cas9-mediated knockout of chromatin modifiers or readers targeted by epi-drugs and a DEN/choline-deficient high-fat-diet mouse model modeling liver disease and hepatocarcinogenesis of advanced fibrosis.

Conclusion: The identification of epi-driver genes relevant for liver carcinogenesis will contribute to identify biomarkers to predict the risk of liver disease progression and HCC development in patients. Furthermore, epi-drugs provide a novel perspective to treat liver disease progression and prevent HCC post HCV cure.

Oral presentation at 09h27 - ID: 61

Identification of the domain to which miR122 and other small RNAs annealing promotes the HCV lifecycle

Rasika Kunden, University of Saskatchewan, Philipp Schult, University of Heidelberg CIID , Tyler Mrozowich, Dept of Chemistry and Biochemistry, University of Lethbridge, Trushar Patel, Dept of Chemistry and Biochemistry, University of Lethbridge , Volker Lohmann, University of Heidelberg CIID , Joyce Wilson, University of Saskatchewan

The genome of Hepatitis C Virus (HCV) is 9.6 kb positive sense RNA which contains a polyprotein coding region, a 5'UTR and a 3'UTR. Its efficient replication requires host microRNA (small RNA), miR-122, annealing to two sites on its 5' UTR. However, the mechanism of replication promotion remains incompletely understood.

We recently found that annealing of perfect match siRNAs to HCV 5'UTR can also promote HCV replication as efficiently as miR-122, when siRNA-mediated target cleavage was abolished, using Ago2 knockout cells (Ago2KO). This finding provided us with a method to test other small RNAs to map the locations on the HCV genome to which small-RNA annealing can promote HCV replication.

To identify regions where small-RNA annealing can promote HCV replication several 19bp siRNAs targeting different sites on the HCV genome were tested. Replication promotion was assessed in Ago2 knockout cells and the activity of miR-122 was blocked using miR-122 antagonist. We found that siRNAs annealing between nucleotides 13 and 44 in HCV 5'UTR, promoted replication, and siRNAs annealing within IRES, NS5B and 3'UTR regions, including other predicted miR122 binding sites, did not. Efficient replication promotion required a minimum of 15 annealing nucleotides and a 19bp siRNA. Targeting nucleotides 19-37 by a single siRNA promoted replication most efficiently and was more effective than binding of miR-122 to both annealing sites. Replication promotion efficiency decreased as the siRNA target site moved away from this region and was abolished if the siRNA target included nucleotide 45.

To gain more insight into the mechanisms by which small RNAs induce the viral life cycle, we monitored the interaction of miR-122 with the HCV genome by Fluorescence in-situ hybridization (FISH). Preliminary data suggests that HCV colocalizes with miR-122 at early time points after transfection, supporting the concept of an involvement in early stages of the virus infection cycle. Colocalization was also evident at later stages suggesting possible roles in ongoing virus replication.

Thus, we have defined the RNA domain that is pivotal for enhancement of virus amplification by small RNA annealing. We were also able to observe HCV and miR122 colocalization at various time points suggesting potential roles throughout all stages of the viral replication cycle. Future studies will characterize how HCV translation, replication, genome stability and RNA structures are modulated by small-RNA annealing to better understand the mechanism by which miR-122 promotes HCV replication.

Oral presentation at 09h39 - ID: 149

Analysis of Programmed Cell Death Induced by HCV Infection

Lingyan Wang, Memorial University, Hannah Wallace, Memorial University , Jingyi He, Memorial University of Newfoundland , Maria Licursi, Memorial University of Newfoundland, Vipin Shankar Chelakkot, Memorial University of Newfoundland, Michael Grant, Memorial University, John Pezacki, University of Ottawa, Kensuke Hirasawa, Memorial University of Newfoundland, Rod Russell, Memorial University of Newfoundland

Background: Virus infection results in host cell death via various modes of programmed cell death. Pyroptosis is a caspase-1-dependent form of cell death that is considered an inflammatory form of cell death. Therefore, pyroptosis may play roles in the development of liver pathogenesis and hepatocellular carcinoma in HCV-infected individuals.

Purpose: The objective of this study was to identify cellular mechanisms by which HCV infection induces programmed cell death.

Methods: Infection and transfection experiments were performed in Huh-7.5, Huh-7.5 nucleotide-binding oligomerization domain-like receptor containing pyrin domain 3 (NLRP3) CRISPR-knockout, Huh-7.5 caspase-3 CRISPR-knockout and Huh-7.5 caspase-1 CRISPR-knockout cells. The expression of pro-caspase-1, cleaved (c)-caspase-1, pro-caspase-3, c-caspase-3, HCV core protein and GAPDH were determined by Western blotting. HCV replication was determined by virus titration assay.

Results: When Huh-7.5 cells were infected with HCV *in vitro* at MOI=1, we observed activation of caspase-1 (pyroptosis) at 2 days after infection and activation of caspase-3 (apoptosis) at 3 days after infection. HCV infection did not induce pyroptosis in NLRP3 knockout Huh-7.5 cells at day 2. We observed lower levels of virus titer in Huh-7.5 caspase-3 knockout and Huh-7.5 NLRP3 knockout cells compared to control Huh-7.5 cells. The ratio of extracellular to intracellular titer was reduced in Huh-7.5 NLRP3 knockout and Huh-7.5 Caspase-3 knockout cell lines compared to control Huh-7.5 cells.

Conclusion: Pyroptosis is induced earlier than apoptosis during HCV infection. Moreover, NLRP3 is involved in pyroptosis induced by HCV infection. Finally, program cell death promotes HCV replication most likely through enhancement of virus spread. The findings from this study have the potential to identify mechanisms underlying chronic liver inflammation and viral spread in HCV patients.

Social, Cultural, Environmental, and Population Health Research

Oral presentation at 11h11 - ID: 106

Estimation of an individual-level deprivation index for HIV/HCV co-infected persons

Adam Palayew, McGill University , Alexandra M. Schmidt, McGill University Department of Epidemiology, Biostatistics, and Occupational Health , Sahar Saeed, McGill University , Curtis Cooper, U Ottawa , Valerie Martel-Laferriere, Centre de Recherche du Centre hospitalier de l'Université de Montréal , Marina Klein, McGill University Health Centre

Background: HIV/HCV coinfected individuals are often marginalized, and of lower socio-economic status, which plays an important role in health outcomes. These factors are difficult to measure and are often constructed using aggregated data, which fails to capture individual heterogeneity. Furthermore, traditional indices that try and capture this information are often designed for the general population and are not generalizable to more marginalized populations. We developed an individual-level index that encapsulates social, material, and lifestyle variables for participants in the Canadian Coinfection Cohort (CCC), a publically funded prospective cohort of 1842 HIV/Hepatitis C co-infected individuals actively recruiting from 18 centres across Canada.

Purpose: To use the rich and individual-level data of the CCC to better quantify the spectrum of deprivation in HIV/HCV co-infected individuals. To do this by creating a single individual score for every participant by aggregating information from multiple variables.

Methods: We fit a Bayesian factor analysis model based on 8 dichotomous variables: income > $1500 per month, education > high school, employment, identifying as homosexual, unstable housing, injection drug use in last 6 months (IDU6m), past incarceration, and self-reported depression measured at baseline CCC visit for all participants. Variables included in the model were selected based on an exploratory data analysis, which consisted of significance testing with chi-squared tests set an alpha of 0.05 and multiple joint correspondence analyses to examine the grouping of the responses to the variables visually. For the variables included in the model, we estimated a severity parameters, which considers how likely an item was to be reported, and discriminatory parameters, denoting the ability of a variable to distinguish between levels of the index. Additionally, we estimated an individual parameter for every subject, which is the index.

Results: We analyzed 1642 complete cases (of 1842 enrolled participants) for the 8 variables. In the full model, we found incarceration, education, income, and employment had the highest absolute values of the discriminatory parameter, suggesting that these variables were more likely to distinguish between different levels of the index. Furthermore, we found that past history of incarceration, depression, and IDU6m were the variables with the highest severity parameter meaning that those 3 items were the most likely to be reported. The person with the highest score had: education ≤ high school, a history of incarceration, IDU6m, was heterosexual, unemployed, with income < $1500, reported depression, and was unstably housed. In contrast, those with the lowest score had the entirely opposite profile.

Conclusion: We estimated a novel individual-level index incorporating social, material, and lifestyle components which may be useful in studying access to treatment and other health outcomes in HIV/HCV co-infected Canadians.

Oral presentation at 11h23 - ID: 157

Opioid agonist treatment and risk of hepatitis C virus infection among people who inject drugs: The overlooked role of dosage adequacy

Andreea Adelina Artenie, Université de Montréal **,** Nanor Minoyan, Université de Montréal / CRCHUM , Brendan Jacka, Centre de Recherche du CHUM, Stine Hoj, Centre de Recherche du CHUM, 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, Lise Gauvin, Université de Montréal, Geng Zang, CRCHUM, Julie Bruneau, Université de Montréal

Background: According to clinical-practice guidelines for the management of opioid use disorders, for most patients, optimal opioid agonist treatment (OAT) dosage is ≥60mg/day for methadone and ≥16mg/day for buprenorphine. Increasing evidence also highlights the importance of patients' perceptions in driving favorable OAT outcomes. While OAT is considered key in preventing hepatitis C virus (HCV) transmission among people who inject drugs (PWID), the role of OAT dosage adequacy in HCV prevention is unclear. In the context of an ongoing global movement to eliminate HCV as a public health threat by 2030, and in light of evidence that OAT scale-up will be central to achieving this goal, this study seeks to improve our understanding of how to optimise OAT provision to prevent HCV transmission.

Purpose: We investigated the joint association of clinically-indicated and patient-perceived adequate OAT dosage levels with HCV infection risk among OAT-eligible PWID.

Methods: Data were drawn from HEPCO, an open, prospective cohort study of initially HCV RNA- (Ab+/-) PWID in Montreal (2004-2017). At 6- or 3-month intervals, participants were tested for HCV Ab/RNA to determine new HCV infection (primary or reinfection), and completed behavioral questionnaires, self-reporting: current OAT enrolment (yes/no), prescribed dose (high defined as: ≥60mg/day if methadone; ≥16mg/day if buprenorphine) and perceived dosage adequacy (adequate/inadequate). The exposure was defined as a five-level variable: no OAT, OAT high dose/perceived adequate, OAT high dose/perceived inadequate, OAT low dose/perceived adequate and OAT low dose/perceived inadequate. Time-varying Cox regression analyses were fit, adjusting for gender, injection duration, previous HCV infection and recent cocaine injection, unstable housing and incarceration.

Results: Of 513 participants (median age: 35; 78% male), 168 acquired HCV over 1423 person-years (p-y) of follow-up [HCV incidence: 12/100 p-y (95% confidence interval (CI): 10-13)]. For the 1589/3421 study visits where OAT was reported, dosage adequacy was recorded as: 37% high dose/perceived adequate, 12% high dose/perceived inadequate, 36% low dose/perceived adequate and 15% low dose/ perceived inadequate. Compared to those not on OAT, PWID prescribed a high OAT dose had a lower HCV risk *if dosage was perceived adequate*[(adjusted hazard ratio (aHR): 0.40 (95% CI: 0.21-0.78)], yet results were inconclusive *if perceived inadequate* [(aHR: 0.59 (95%CI: 0.24-1.44)]. Additionally, compared to those not on OAT, PWID prescribed a low OAT dose had a similar HCV risk *if dosage was perceived adequate*[aHR: 1.17 (95%CI: 0.71–1.92)], and a higher risk *if perceived inadequate* [aHR: 1.98 (95%CI: 1.13–3.45)].

Conclusion: HCV infection risk varies substantially according to a combined indicator of OAT dosage adequacy informed by clinical guidelines and patient perceptions. Findings suggest that simply scaling-up OAT uptake may not be enough to decrease HCV transmission among PWID, and that the adequacy of OAT dosage should be considered in our HCV prevention efforts.

Clinical Research

Oral presentation at 14h00 - ID: 15

Never too old to be DAA treated for Hepatitis C

Stephen Shafran, University of Alberta, Sergio Borgia, William Osler Health System, Karen Doucette, University of Alberta, Chrissi Galanakis, Ottawa Hospital Research Institute, Curtis Cooper, University of Ottawa

Background and aims: Elderly patients were seldom treated for HCV in the IFN era due to side effects of treatment. IFN-free DAA therapy has minimal side effects making treatment feasible for many more patients, including the elderly. We report demographic and outcome data on all patients over 75 years of age who were treated for HCV with DAA therapy in 3 Canadian clinics.

Purpose: To determine the safety and efficacy of DAA therapy elderly patients.

Methods: All HCV-infected patients greater than 75 years treated with DAAs without IFN were included. Information on demographics, treatment and outcomes were collected at 3 Canadian sites (Ottawa, Edmonton and Brampton). Fibrosis score was determined by transient elastography.

Results: 78 patients were included in the analysis. Patients were female (63%) with a mean age of 79 (SD 3.5, range 75-88 years; 36% were ≥ 80 years) and Caucasian (56%). Seventy (90%) were treatment naïve, 35% were genotype 1b-infected , 18% with genotype 1a, 22% with genotype 2, 6.4% with genotype 3 and 9% with genotype 4. The mean METAVIR fibrosis score was 2.8 (SD 1.2) with 78% having fibrosis scores ≥F2. 41% had cirrhosis. The main HCV treatments consisted of SOF/VEL (33%), SOF/LDV (32%) and EBR/GZR (17%). 13 of 78 (17%) received ribavirin (RBV)-containing regimens with daily doses of 400 mg (n=1), 600 mg (n=1), 800 mg (n=3), 1000 mg (n=8). 92% (57/62) with outcome results achieved SVR. No virologic failures occurred. SVR was 98% (n=48/49) with non-RBV regimens and 69% (9/13) for RBV-recipients. Two deaths (ESLD, HCC), 1 discontinuation of all HCV medications at week 2, and 1 LTFU occurred in RBV recipients. Mean on-treatment nadir hemoglobin in RBV recipients was 95 g/L (SD 22.1, range 57-128). RBV dose was reduced in 3/13 cases and was later discontinued in 2 of these 3 patients. Three received on-treatment PRBC transfusions.

Conclusions: Safety and efficacy of RBV-free DAA therapy is similar to that of younger adults. RBV-specific complications are frequent and without evidence of improved SVR in the elderly.

Oral presentation at 14h12 - ID: 41

Feasibility of rapid hepatitis C point-of-care RNA testing and linkage to care at an integrated supervised consumption site in Toronto, Canada

Kate Mason, South Riverdale Community Health Centre, Bernadette Lettner, South Riverdale Community Health Centre, Erin Mandel, University Health Network, Frank Crichlow, South Riverdale Community Health Centre, Jason Altenberg, South Riverdale Community Health Centre, Jeff Powis, Toronto Community Hep C Program, Jordan Feld, Toronto Centre for Liver Disease

BACKGROUND: In Canada, most new cases of Hepatitis C (HCV) occur among people who inject drugs, yet relatively few engage in HCV care or initiate antiviral treatment. The recent expansion of supervised injection/consumption services (SCS) across Canada offer a new and unique opportunity to engage people who use drugs in HCV care.

PURPOSE: To evaluate the feasibility of rapid, point-of-care HCV RNA testing and subsequent linkage to HCV care among service users of a small-scale SCS co-located within a primary care community health centre in Toronto.

METHODS: The SCS can accommodate up to 5 injections/consumptions at a time with an average of 10 unique person visits daily. Posters in the consumption area, staff referrals, and word of mouth advertised study participation to registered SCS service users who inject drugs and were not currently engaged in HCV antiviral treatment. An onsite HCV treatment nurse completed baseline surveys with participants to capture socio-demographics and history of HCV care. Testing was also conducted by the HCV treatment nurse 2.5 days per week using a HCV Viral PCR Finger-Stick assay, allowing for RNA results within 1 hour. Other SCS staff (Nurses, Health Promoters, Harm Reduction Workers) provided additional post-testing counseling when required. Participants that tested positive for HCV RNA were connected with the onsite HCV treatment and support program. RESULTS: 79 service users consented to participate in the first five months. Two were removed for ineligibility. Of 77 participants, 65% were male with an average age of 42 years. Two thirds (66%) had unstable/no housing and 68% reported daily injection drug use. More than half (57%) reported a history of HCV testing. Of these, only two reported they had received RNA testing and nearly half (49%) didn't know what type of HCV testing they had received. Of those tested in the SCS,13 results were invalid. Five participants agreed to repeat testing. Of the 66 valid tests, 32% (N=21) were positive. Of those testing positive, 10 have started further HCV assessments at the health centre, 3 are attending a weekly HCV education and support group, one has completed treatment and one participant died due to accident.

CONCLUSIONS: Interest in POC testing was high, as was engagement in HCV care among those found to be HCV RNA positive. Testing uptake remains limited primarily by the low number of new and unique service users at the SCS. Ongoing access to the HCV treatment nurse within the SCS and SCS staff with lived experience of HCV likely facilitated linkage to care. POC RNA testing can successfully position SCS as an alternative single point of HCV care access, allowing for more integrated care and increased HCV treatment uptake among people who inject drugs.

Oral presentation at 14h24 - ID: 169

Engaging vulnerable, treatment naïve persons living with hepatitis C in same-day treatment

Shawn Greenan, Health PEI, George Carruthers, Dalhousie University, Lisa Barrett, Dalhousie University

Background To eliminate viral hepatitis C (HCV) for vulnerable populations need to exist. The greatest barrier to HCV elimination is engaging people to initiate and complete HCV treatment after positive diagnosis. Rapid, same-day treatment for Human immunodeficiency virus (HIV) has demonstrated both better HIV and non-HIV related health care engagement.

Purpose: To determine if the rapid, same-day access to HCV treatment improves engagement for vulnerable, treatment naïve persons living with HCV in both in HCV and non-HCV health care.

Methods: Persons living with HCV are identified and referred to Canada's Prince Edward Island Phase 2 Provincial, Coordinated HCV Elimination Program through the Department of Public Health, community providers, or 'bring a friend' strategies. The Elimination Program facilitate baseline blood work, conduct pre-visit, drug-drug interaction checks, and schedule an initial appointment within 1-2 weeks of bloodwork. Treatment naïve individuals without contraindications are offered glecaprevir/pibrentasvir treatment at the first visit. Self-reported medication adherence, side effects, sustained virological response (SVR12), and attendance at scheduled opioid substitution therapy (OST) clinic visits are recorded.

Results: Patients assessed between February and October 2018 were included. 102 patients were referred and 73 (71.5%) were seen for an initial appointment. 71/73 (97.2%) treatment naïve individuals started treatment, 67/71 (94.3%) on the first visit. Of those who attended the first visit and did not start immediately, 5 had medication interactions requiring adjustment, and 1 person was pregnant. There were 3 discontinuations for non-HCV related medical reasons, and 1 person was lost to follow-up before SVR. To date, all 52 people past the treatment completion date finished treatment, and 23/32 have documented SVR12 (9 people did not have SVR12 bloodwork but completed full treatment course). Importantly, individuals with difficulty attending OST appointments before HCV treatment had improved attendance at appointments after HCV treatment start. Attendance at non-HCV health care appointments was variably improved. No safety issues were noted.

Conclusions: Rapid treatment start is safe, and has a very high rate of successful HCV and non-HCV care engagement. Same day, first visit HCV health treatment start should be explord as an HCV elimination tool.

Health Services Research

Oral presentation at 15h56 - ID: 8

The hepatitis C virus (HCV) cascade of care in a Canadian provincial prison: Implications for HCV micro-elimination

Nadine Kronfli, McGill University , Camille Dussault, McGill University Health Centre , Bertrand Lebouché, McGill University , Marina Klein, McGill University Health Centre , Joseph Cox, McGill University

Background: Hepatitis C virus (HCV) micro-elimination efforts must target sub-populations such as people in prison; however, most Canadian provincial prisons lack systematic HCV screening and care programs. The HCV cascade of care has never been assessed among people in Canadian correctional facilities.

Purpose: We characterized the HCV care cascade among people in Quebec's largest all-male provincial prison, l'Établissement de détention de Montréal (Bordeaux).

Methods: We conducted a retrospective analysis of all HCV-related laboratory tests requested for Bordeaux inmates between July 1, 2017 and June 30, 2018. We defined seven HCV cascade of care steps: 1) Total sentenced inmates; 2) HCV screened (via HCV-antibody); 3) HCV-antibody positive; 4) HCV RNA tested; 5) HCV RNA positive; 6) Linked to care (defined as having been evaluated by an HCV care provider); and 7) Initiated treatment. Proportions of inmates at each step were measured using denominator-numerator linkage. We also calculated the proportion screened for HCV (step 2) among inmates sentenced for at least one month, during which time screening should be feasible.

Results: Of the estimated 7743 sentenced inmates between July 2017 and June 2018, 345 (4.5%) were screened for HCV; 39 (11.3%) were HCV-antibody positive; 36 (92.3%) received HCV RNA testing; 17 (57.2%) were HCV RNA positive; 11 (64.7%) were linked to care; and 2 (18.2%) were initiated on treatment. Restricting the analysis to inmates sentenced for at least one month (n=3097) increased the proportion of inmates screened for HCV to 11.1%.

Conclusions: Our findings confirm that a very small proportion (4.5%) of men at a Canadian provincial prison were screened using on-demand HCV testing. Screening was the major rate-limiting step while progression along the HCV cascade of care thereafter, in the absence of formal HCV care pathways, was better than expected. Treatment initiation rates were also low in the absence of linkage to care programs. In order to eliminate HCV in this sub-population, adopting universal opt-out HCV testing should be considered a necessary first step.

Oral presentation at 16h08 - ID: 75

State-specific direct medical costs of Hepatitis C in Ontario: A population-level study

Alexander Haines, Toronto Health Economics and Technology Assessment Collaborative, Zhan Yao, Institute for Clinical Evaluative Sciences, Hla-Hla Thein, University of Toronto, William WL Wong, School of Pharmacy, University of Waterloo, Murray Krahn, Toronto Health Economics and Technology Assessment Collaborative (THETA), University of Toronto

Background: With an effective cure in place and ambitious targets put forward by the World Health Organization to eliminate HCV by 2030, a large body of research has turned to identifying the most effective and cost-effective way to screen and identify undiagnosed cases of HCV. An important component of answering this question is the cost savings associated with curing a case of HCV before the individual develops end stage liver disease. Current Canadian cost estimates are over 10 years old and do not describe the cost of HCV in the granular detail required for economic modelling; such as differentiating between decompensated cirrhosis (DC) and hepatocellular carcinoma (HCC).

Purpose: To estimate the cost to the provincial payer associated with nine different HCV-related health states: no cirrhosis, compensated cirrhosis, DC, HCC, HCC & DC, liver transplantation, liver related death, other death, and cured HCV.

Method: We conducted a population-based retrospective cohort study using administrative health data from databases held at the Institute for Clinical and Evaluative Studies (IC/ES). Patients diagnosed with chronic HCV infections from 2003-2014 were identified using Public Health Ontario laboratory data. Time from HCV diagnosis until the end of follow-up was allocated to nine mutually exclusive health states. States were defined using a validated set of diagnosis, procedure and death codes. Direct medical costs per 30 day period were then calculated for each state based on the resource use utilized whilst spending time in said state.

Results: Our preliminary results identified 48,239 patients meeting our inclusion criteria. The following is the average 30-day cost calculated for each health state:

Health state	N (%) that spent (> 1 day) in each health state	Cost per 30 days spent in each health state (2018 CAD $)
No cirrhosis	43,568 (90.3%)	$798
Cured HCV (RNA negative results after chronic diagnosis established)	6,422 (13.3%)	$660
Compensated cirrhosis	4,970 (10.3%)	$1,487
Decompensated cirrhosis	3,151 (6.5%)	$3,659
Hepatocellular carcinoma	550 (1.1%)	$4,238
HCC and DC	485 (1.0%)	$8,753
Liver transplantation	372 (0.8%)	$4,539
Liver related death (average over	3,201 (6.6%)	$11,202

last 6 months of life)		
Non-liver related death (average over last 6 months of life)	5,278 (10.9%)	$8,801

Conclusions: Our estimates are significantly higher than previous Canadian HCV estimates, but congruent with other published Ontario and international costs. The true economic benefit of curing HCV may be underestimated if current cost estimates are used. Our estimates also provide additional detail by breaking down the exact advanced stage liver disease diagnosis and separating out the patients who are cured. These robust estimates will be important for estimation of the economic benefits of population-level HCV control.

Oral presentation at 16h20 - ID: **112**

Assessment of Hepatitis C Screening Strategies in Different Community Settings in a Canadian Metropolitan Area

Camelia Capraru, Toronto Centre for Liver Disease/VIRCAN, UHN**,** Bettina Hansen, Institute of Health Policy, Management and Evaluation, Aaron Vanderhoff, University of Toronto, Steven Marc Friedman, Emergency Medicine, University Health Network, Kathy Bates, Emergency Department, Toronto Western Hospital, Tony Mazzulli, Mount Sinai Hospital , Danielle Porplycia, Department of Emergency Medicine, University Health Network, Bentley McCormack, Toronto Centre for Liver Disease, UHN, Joshua Juan, Toronto Centre for Liver Disease, UHN, Hsiao-Ming Jung, Albany Medical Clinic , Hemant Shah, University of Toronto, Toronto Centre for Liver Disease, Jordan Feld, Toronto Centre for Liver Disease, Harry Janssen, Toronto Centre for Liver Disease

Background and Aims:

It is estimated that over 45% of individuals with chronic hepatitis C virus (HCV) infection in Canada remain undiagnosed. Understanding current rates of HCV diagnosis and linkage to care in different community settings is critical information for developing future screening strategies.

To evaluate HCV screening strategies in three different community settings: emergency department (ED), medical walk-in clinic (MC) and community outreach (CO).

Methods:

We implemented birth cohort (1945-1975) HCV testing in the ED and MC, and universal testing during CO. Blood samples in the ED were collected by finger prick on Dried Blood Spot (DBS) collection cards and tested for anti-HCV with reflex to HCV RNA. In the MC and CO, we used anti-HCV point-of-care testing followed by HCV RNA on DBS card. Patients with positive HCV RNA were linked to care.

Results:

5,144 individuals were tested during 1.5 years; 142 (2.8%) were HCV reactive (Table). Seropositivity varied among all three groups: 1.8% (95%CI 1.2%-2.4%) in the ED, 0.4% (95%CI 0.1%-0.7%) in the MC and 5.3% (95%CI 4.3%-6.3%) in the CO. Of Ab positives, 117 (82.4%) underwent HCV RNA testing. 61 (82.4%) out of 74 HCV RNA positives were linked to care. Compared to the general population the HCV prevalence was significantly higher in the CO (5.3% vs. 0.7%; $p < 0.0001$), and in the ED (1.8% vs. 0.7%; $p < 0.0001$). The MC group exhibited similar seropositivity as the general population (0.4% vs. 0.7%; $p = 0.12$).

Conclusions:

The HCV prevalence in the CO and ED was significantly higher than the general Canadian population. Using DBS for HCV testing ensured high HCV RNA test uptake. Screening efforts in populations with higher prevalence, such as the ED and outreach programs, were higher yield and still resulted in good linkage to care.

	HCV Ab tests				
Characteristics	**Total** N = 5114	**ED** N = 1639 (32.0%)	**MC** N = 1452 (28.4%)	**CO** N = 2023 (39.6%)	p-value
Age *(median, range)*	56 (15-97)	58 (35-74)	51 (15-97)	54 (16-97)	< 0.0001
Male *n (%)*	2354 (46.0)	850 (51.9)	591 (40.7)	913 (45.2)	< 0.0001
HCV Ab Positives *n (%)*	142 (2.8)	29 (1.8)	6 (0.4)	107 (5.3)	< 0.0001
HCV RNA Tests *n/HCV Ab positives (%)*	117/142 (82.4)	26/29 (89.7)	5/6 (83.3)	86/107 (80.4)	0.531
HCV RNA Positives *n/HCV RNA tests (%)*	74/117 (63.2)	18/26 (69.2)	4/5 (80.0)	52/86 (60.5)	0.443
Linkage to Care *n/HCV RNA positives (%)*	61/74 (82.4)	14/18 (77.8)	3/4 (75.0)	44/52 (84.6)	0.474

Posters – Affiches

Biomedical Research

ID: 184

Transcriptional reprogramming of exhausted T cells upon cure of chronic disease is not paralleled by epigenetic recovery

Mohamed S. Abdel-Hakeem, University of Pennsylvania (Primary Presenter, Pierre Tonnerre, Harvard University , Jean-Christophe Beltra, University of Pennsylvania , Sasikanth Manne, 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, 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. **Here, we aim to determine the mechanisms of recovery from exhaustion following non-immunological cure of chronic disease**. For this, we seized the unique opportunity of chronic HCV cure by DAAs to examine whether Tex in cured patients differentiate to recovered T cells (Trecov) with better functional and durable memory profile. In parallel, we examined differentiation of Tex "cured" from chronic infection by adoptive transfer from LCMV-clone13 infected mice into antigen-free mice. The LCMV well-defined tractable mouse model enabled us to dissect cellular and molecular mechanisms underlying recovery, as well as the subset dynamics and recall capacity of Trecov upon re-exposure to the antigen compared to Tex and memory T cells (Tmem). Our results revealed recovery of some phenotypic markers of Tmem and partial recovery from dysfunction, but some "scars" of Tex persisted. For example, expression of the memory marker IL-7 receptor (CD127) increased and the Tex marker PD-1 decreased on Trecov, suggesting differentiation toward memory, but expression of IL-7R was still lower and PD-1 expression higher when compared to bona fide Tmem. Recovery was associated with preferential survival of the Tex subset with progenitor properties, identified by intermediate expression of PD-1 and being TCF1+ TIM3–, however cellular conversion also occurred. Transcriptional profiling using single-cell RNAseq indicated that Trecov gene-expression profile resembles Tmem in many respects, but remains similar to Tex cells in other features, confirming our phenotyping results. We tested how these changes impacted a key memory feature, recall response upon antigen re-encounter, and our mouse challenge experiments revealed that although Trecov recall capacity was better than Tex, it was still inferior to Tmem on a per cell basis. To investigate whether the transcriptional and functional scars have epigenetic roots, we performed ATACseq to measure chromatin accessibility in Trecov. Our analysis suggests that Trecov have not recovered epigenetically to the same extent as their transcriptional recovery. Together, these results suggest that following elimination of persistent antigenic stimulation previously-exhausted T cells recover some Tmem properties, while other aspects remain "scarred" from their exhaustion history. These studies are enhancing our understanding of mechanisms of Tex recovery, and could identify novel immunotherapeutic strategies.

Funded by NIH. MSA is a CRI, FRQS, CanHepC Fellow.

ID: 148

Neutrophils are the major producers of the pro-fibrogenic cytokine IL-17A in non-alcoholic fatty liver (NAFLD)

Mohamed Abdelnabi, CrCHUM, University of Montreal (Primary Presenter), Manuel Flores, CRCHUM, Thomas Fabre, CRCHUM, Soucy Geneviève , Université de Montréal , Naglaa Shoukry, CRCHUM,

Background: Due to the rise in obesity among adults, NAFLD-related liver fibrosis has become a major health challenge with a complex pathogenesis and limited therapies. Liver fibrosis occurs via the production of collagen by activated hepatic stellate cells (HSC) in response to persistent tissue damage and inflammation. This response can be modulated by pro-inflammatory cytokines such as IL-17A that is produced by intrahepatic immune cells (IICs) and hence can influence liver fibrosis progression (Frideman S.L. et al. 2015). We have demonstrated that IL-17A promotes fibrosis by sensitizing HSCs to the suboptimal doses of TGF-β via increasing cell surface expression of TGF-β-RII (Fabre T. et al. 2014). Furthermore, IL-17A producing cells, primarily neutrophils, were enriched in livers with advanced fibrosis (F3-F4) irrespective of the aetiology. This finding was validated *in vivo* in CCl_4 model of chronic liver injury (Fabre T. et al. 2018). In this study, we wanted to extend our findings to a more physiological model such as NAFLD.

Purpose: We hypothesize that IL-17A producing cells enhance NAFLD-related fibrosis. Our main goal is to define the cellular sources of IL-17A implicated in this process.

Methods: We have established a mouse model of NAFLD using male and female C57BL/6N mice (age 6-8 weeks) fed high fat diet (HFD, 40% Kcal fat+ 40% Kcal carbohydrate (including fructose) +2%cholesterol)) vs chow diet (CD, 18%Kcal fat+ 24%Kcal protein) for 15 or 30 weeks (Wk). IL-17A+ cells were characterized in liver tissues by using immunofluorescence (IF). Visiopharm software was used for IF image analysis and quantification. H&E, Oil Red O and Picro Sirius red (PSR) staining were used to evaluate liver inflammation, steatosis and fibrosis, respectively. Moreover, we evaluated NAFLD-associated metabolic abnormalities using weekly body weight measurement, glucose tolerance test and fat mass analysis.

Results: Mice on HFD developed liver injury, steatosis and inflammation at 15 and 30Wk as compared to corresponding CD mice. Moreover, mice-fed HFD for 30Wk tended to have intense liver inflammation compared to 15Wk, as evidenced by H&E staining. We observed an increase in NAFLD-related fibrosis at 30 Wk HFD mice as compared to 15 Wk (mean of PSR +ve area=4.3 vs 2.7, P=0.0491). This finding was associated with an increase of IL-17A+ cells at 30Wk HFD as compared to 15 WK (mean density [cells/mm^2)] of IL-17A+ cells= 9 vs 0.8, P<0.0001). Neutrophils (Ly6G+) were the major IL-17A producers and the density of IL-17A producing neutrophils correlated with fibrotic area (PSR +ve area) at 30 Wk (r=0.7524, P<0.0001).

Conclusion: Our data suggest an active role for IL-17A+ neutrophils in NAFLD-related fibrosis.

ID: 172

Immune Restoration of Hepatitis C Virus-specific T cells following Direct Acting Antiviral Therapy in Acute Hepatitis C Virus- infected Patients

Julia Casey, University of Toronto , Sonya McParland, University of Toronto ,Vera Cherepanov, Toronto Centre for Liver Disease Jordan Feld, University of Toronto

Background: Chronic Hepatitis C Virus (HCV) infection is defined by an exhausted immune phenotype. Exhaustion develops in a step-wise and progressive manner, varies in severity, and results in ineffective HCV-specific antiviral T cell responses. Previous data from our lab show that cure of chronic infection with direct-acting antivirals (DAA) leads to partial reversal of T cell exhaustion in some patients. We hypothesize that *treatment of early/acute infection* with DAA will further improve immune restoration, leading to responses similar to those seen with spontaneous HCV clearance, which may increase protection against reinfection.

Aim: Characterize the HCV-specific immune response before, during and after *treatment of acute/early infection* with both interferon (IFN) and DAA regimens and compare to responses with treatment of chronic infection.

Methods: We will assess the impact of DAA and IFN-based therapies on HCV-specific T cell responses in peripheral blood during treatment of early/acute HCV infection using enzyme-linked immunospot (ELISPOT) and flow cytometry. We will evaluate strength and breadth of T cell responses to overlapping HCV peptides using ELISPOT to quantify IFNγ cytokine secretion by HCV-specific T cells throughout treatment. We will identify HCV-specific T cells using HLA-A2 or B27-restricted HCV pentamers and assess frequency and phenotype including expression of exhaustion (PD-1, TIM-3) and memory marker (CD127) expression. Responses will be compared at baseline to those during and after therapy and between treatment type (IFN vs DAA). Evolution of responses over the course of therapy and follow-up will be compared to individuals treated during chronic HCV infection and responses in individuals who spontaneously cleared HCV infection without treatment. Clinical data including age, sex, BMI, HCV RNA level and IL28B/IFNL4 genotype will be available for correlation analysis.

Results: Stored samples from clinical trials of acute/early and chronic HCV with IFN and DAA-based therapy have been identified. To date, ELISPOT data from spontaneous clearers (n=4) and healthy controls (n=10) are available. Broad HCV-specific responses were seen in 3 of 4 spontaneous clearers and were strongest in NS3 and NS5A but were also detected in NS5B, Core, E1 and E2. Data from treated patients will be available at the time of the meeting with planned comparisons as shown below.

Conclusions: Conclusions will be made when more data is available.

Samples to be analyzed:

Group		N=
Spontaneous Resolution	Acute	10
DAA Treated	Acute	15
	Chronic	15
IFN Treated	Acute	15
	Chronic	15

Acute and chronic responses (both IFN-based and DAA therapies) will be compared to individuals who spontaneous cleared HCV infection without treatment.

ID: 66

miR-122 as well as hAgo interactions with the HCV genome alter the secondary structure of the viral 5' terminus and promote functional IRES formation

Jasmin Chahal, McGill University, Luca Gebert, The Scripps Research Institute, Hin Hark Gan , New York University, Edna Camacho , McGill University, Kristin C. Gunsalus , New York University and New York University Abu Dhabié, Ian MacRae, The Scripps Research Institute, Selena Sagan, McGill Universityé ,

Background: Hepatitis C virus (HCV) is a positive-sense RNA virus that interacts with a liver specific microRNA, miR-122. miR-122 binds to two sites on the 5' untranslated region (UTR) of the viral genome and *promotes* HCV RNA accumulation. Previous studies suggest two major mechanisms for miR-122: 1) protection of the viral 5' triphosphate moiety from pyrophosphatase activity and subsequent RNA decay; and 2) an RNA chaperone-like change in structure to promote viral translation. Through biophysical analyses we provide additional evidence to support the RNA chaperone-like mechanism and provide insight into the role of human Argonaute (hAgo) proteins in this process.

Purpose: To investigate how hAgo2:miR-122 binding alters the structure of the HCV 5' UTR.

Methods: We performed biophysical analyses, including isothermal titration calorimetry (ITC), electrophoretic mobility shift assay (EMSA), Selective 2' Hydroxyl Acylation analyzed by Primer Extension (SHAPE) as well as computational modeling to investigate the structure of the wild-type and G28A mutant HCV 5' UTR in the presence and absence of hAgo2:miR-122.

Results: Our data suggests that hAgo2:miR-122 binding to the wild-type HCV 5' UTR suppresses an alternative structure (termed $SLII^{alt}$) and promotes formation of the functional internal ribosomal entry site (IRES, SLII-IV). In contrast, the G28A mutation, which was initially isolated from patients who underwent antisense miR-122 inhibitor therapy and was subsequently shown to have reduced reliance on miR-122, was shown to favour formation of the IRES even in the absence of miR-122. Furthermore, despite the close proximity between the miR-122 sites, two hAgo2:miR-122 complexes are able to bind to the HCV 5' terminus simultaneously and SHAPE analyses revealed further alterations to the structure of the 5' UTR to accommodate these complexes. Computational modeling of the hAgo2:miR-122 complexes with the IRES-40S suggests that hAgo2 is likely to form additional interactions with the HCV IRES (specifically at SLIIa) which is supported by SHAPE analyses, and these interactions may further stabilize the viral IRES and promote HCV translation.

Conclusions: Our data provides a new model for hAgo2:miR-122 interactions with the HCV genome. Specifically, we predict that the HCV 5'UTR initially takes on an alternative conformation in the absence of miR-122 ($SLII^{alt}$). Binding of hAgo2:miR-122 to Site 2 acts in an RNA chaperone-like manner to convert the 5' terminus to SLII, allowing formation of the viral IRES (SLII-IV). The SLII conformation then allows recruitment of hAgo2:miR-122 to Site 1, which protects the 5' triphosphate moiety from pyrophosphatase activity and viral RNA decay. To accommodate hAgo2:miR-122 at Site 1, the auxiliary interactions with the Site 2-bound hAgo2:miR-122 are destabilized, but this complex is further stabilized by interactions with the HCV IRES. This model is supported by our biophysical data and provides novel insight into the mechanisms of miR-122-mediated viral RNA accumulation.

ID: 80

Interrogating the role of the poly(rC)-binding protein 2 (PCBP2) in the HCV life cycle

Sophie Cousineau, McGill University **,** Selena Sagan, McGill University

Background:

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. In particular, the poly(rC)-binding protein 2 (PCBP2) is known to mediate the stability and expression of a number of cellular transcripts, and is 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 the 5' and 3' untranslated regions, which are known to play important roles in viral translation and replication. However, the exact mechanism(s) by which PCBP2 affects HCV replication still remain to be elucidated.

Purpose:

We aimed to identify the specific step(s) of the viral life cycle that are affected by PCBP2.

Methods:

We used the HCV cell culture system (specifically the JFH-1_T viral strain and Huh-7.5 cell line) to assess how viral protein expression, viral RNA accumulation, and the production of infectious viral particles is affected by siRNA-mediated knockdown of PCBP2. To examine PCBP2's effects on specific steps of the viral life cycle, we carried out assays for viral translation, genome stability, RNA replication, and packaging. Viral translation and genome stability was assessed using a RNA replication-deficient luciferase reporter virus (the J6/JFH-Renilla-GNN viral construct). RNA replication was assessed using a packaging-deficient luciferase reporter virus (a J6/JFH-ΔE1-p7-Renilla viral construct).

Results:

Knockdown of PCBP2 leads to ~2-fold reductions in HCV protein expression, RNA accumulation, and infectious particle production. Using a RNA replication-deficient luciferase reporter virus, we found that PCBP2 knockdown did not alter viral translation nor the rate of decay of its genome. When we conducted these assays with a replication competent but packaging-deficient viral construct, we found that although PCBP2 knockdown leads to a decrease in luciferase activity, viral RNA accumulation was not reduced to the same extent. We are thus investigating whether PCBP2 modulates the switch between translation and viral RNA replication. Current work aims to clarify this interaction, and further assess if PCBP2 plays concurrent roles in viral packaging, egress, or viral entry.

Conclusions:

PCBP2 knockdown disrupts HCV RNA accumulation in Huh-7.5 cells. While the exact mechanism of PCBP2-mediated regulation is unclear, we have found that it does not promote viral translation or genome stability. We anticipate that further clarifying this PCBP2-HCV interaction will provide a model for the PCBP2-mediated regulation of viral RNA accumulation.

ID: 64

Visualization of HCV Proteins using Fluorescent Unnatural Amino Acids

Leah Jane Fitzgerald Curnew, Memorial University of Newfoundland **(Primary Presenter)**, Kate McNicholas, Memorial University of Newfoundland, Bridgette Green, Memorial University of Newfoundland, Jackie Barry, Memorial University of Newfoundland , Hannah Wallace, Memorial University, Lingyan Wang, Memorial university, John Pezacki, University of Ottawa, Rod Russell, Memorial University of Newfoundland

Background: The study of a viral protein depends on the ability to visualize that protein, which typically relies on the availability of an antibody that specifically recognizes that protein. Unfortunately, it is sometimes difficult to generate a "good" antibody for a protein of interest. To circumvent this issue, recombinant versions of proteins can be engineered containing various tags, such as HA or His, for which numerous antibodies are commercially available, and of course proteins of interest can also be fused to naturally fluorescent proteins such as GFP. However, although such methods are powerful and have facilitated the discovery of relevant findings for many proteins, the structural impact of such tags can affect the function and topology of a protein, resulting in the appearance of artefactual results.

Purpose: The study of the Hepatitis C Virus (HCV) protein p7 is limited due to the lack of useful commercially available antibodies. The ability to visualize individual viral proteins by microscopy allows for better understanding of the structure and function of p7, and HCV infections in the context of pathogenesis. In this study, we employed the fluorescent unnatural amino acid (UAA) called Anap (3-[(6-acetyl-2-naphthalenyl)amino]-L-alanine) to label HCV proteins. The ultimate goal would be to fluorescently label HCV p7, but to validate our system we have initiated these studies first in the context of the well-characterized HCV Core protein.

Method: Huh-7.5 cells were co-transfected with HCV Core plasmids containing amber stop codons at various positions throughout the coding sequence, along with a second plasmid coding for the tRNA and orthogonal synthetase that facilitates the incorporation of Anap. Three days post-transfection, cells were fixed and stained for Core protein, followed by fluorescent microscopic analysis to visualize Core protein. In this system Core protein can then be observed through conventional indirect immunofluorescence, as well as direct fluorescence from the incorporated Anap.

Result(s): To date, we have optimized transfection protocols to allow efficient expression of the tRNA and synthetase required for Anap incorporation and are able to visualize our mutant Core proteins containing Anap at numerous amino acid positions. Currently, we have succeeded to substitute Anap into 11 different positions within Core, including substitutions for tryptophan, tyrosine and phenylalanine residues.

Conclusion(s): Viral proteins can be directly visualized using unnatural amino acid technology, and this ability will allow us to perform functional studies on HCV p7 that have not been possible to date. Once we identify optimal positions within Core and p7 for Anap incorporation, we will be able generate fluorescently-labelled infectious viruses that will have use in basic virological and immunological studies.

ID: 73

Neutrophils and mast cells are major producers of IL-17A in hepatocellular carcinoma

Manuel Flores, CRCHUM, Thomas Fabre, CRCHUM, Mohamed Abdelnabi, CrCHUM, University of Montreal, Soucy Geneviève , Université de Montréal, Marc BILODEAU, CHUM , Simon Turcotte, CRCHUM , Naglaa Shoukry, CRCHUM

Background:

Hepatocellular Carcinoma (HCC) is the third cause of cancer-related death worldwide. IL17A is upregulated in HCC and correlates with poor survival. Several studies link IL-17A to fibrosis progression and poor prognosis of HCC. However, the identity of the cellular sources of IL-17A and their target cells in the tumor tissue remain elusive. Furthermore, the activity of Th17 cells, the classical producers of IL-17A, can be regulated by regulatory T cells (Tregs).

Hypothesis and Objective:

We hypothesize that IL-17A from different cellular sources drives transition from fibrosis to HCC and HCC progression. Our primary objective is to define the cellular sources of IL-17A and their location within the tumor tissue and their interaction with Tregs that may modulate their activity in HCC as well as other target cells.

Methods:

We developed a strategy combining multiplex immunofluorescence (IF), histochemistry (HC) and advanced image analysis to map IL-17A+ cells and Tregs *in situ* in formalin fixed paraffin embedded (FFPE) HCC tumor tissue samples (tumor, peritumor and adjacent non tumoral tissue) obtained from our institutional Biobank (n=14). We optimized a strategy for the analysis of digitalized images that combines the image analysis tools of Tissuealign™, Visiomorph™, and HISTOmap™ (Visiopharm). This strategy allowed us to quantify and spatially resolve specific cell populations in tissue compartments.

Results

Tissue heat maps demonstrate opposite compartmentalization of IL-17A+ cells and Tregs, where IL-17A+ cells are enriched in the peritumoral compartment and Tregs intratumorally. Tregs density was significantly higher intratumorally compared to non-tumoral adjacent tissue ($p=0.0093$), and the IL-17A/Treg ratio was significantly reduced inside the tumor ($p=0.0098$). We identified tumor associated neutrophils (TANs) and mast cells as the main source of IL-17A, accounting for up to 90 % of the total IL-17A+ cells. IL-17A+ TANs were located all over the tissue while mast cells were restricted to peritumoral and intratumoral fibrotic lesions.

Conclusions:

Our data demonstrated opposite compartmentalization of IL-17A+ cell and Tregs in the tumor microenvironment, and identified neutrophils and mast cells as major sources of IL-17A in HCC with distinct localization. The role of these cells, particularly neutrophils, needs to be more deeply evaluated in the pathogenesis of HCC.

ID: 108-

Association of IL-10 and MTP gene polymorphisms with severity of HCV-induced liver fibrosis in an Egyptian cohort

Amr A. Hemeda, Future University In Egypt, Amal A. Mohamed, National Hepatology and Tropical Medicine Research Institute, Ramy K. Aziz, Cairo University , Mohamed S. Abdel-Hakeem, Cairo University, Marwa Ali-Tammam, Future University in Egypt

Complications of hepatitis C virus (HCV) chronic infection cause ~400,000 deaths worldwide annually. One complication, liver fibrosis, is influenced by host genetic factors. Genes influencing fibrosis include immune and metabolic genes, such as interleukin 10 (IL-10) and microsomal triglyceride-transfer protein (MTP) encoding genes. Thus, association of these genes with HCV-induced fibrosis represents an attractive biomarker. This study aims to test whether polymorphism in IL-10 and MTP genes is associated with differential fibrosis induced by HCV genotype 4 (HCV-gt4) in a cohort of Egyptian chronic patients. A hundred blood samples were collected from fibrotic chronic HCV-gt4 patients, and genomic DNA was tested for polymorphisms by PCR-RFLP. We used logistic regression to analyze the association between allele frequencies and liver fibrosis. Our results show that for IL-10 gene the frequencies of nucleotides A and C at position 627 were 26% and 74%, respectively. For the MTP gene, the frequencies of nucleotides T and A at position 400 were 37% and 62%, respectively. Regression analysis indicated a significant association of IL-10 A allele with less advanced stages of fibrosis compared to C (p = 0.018). Combined haplotype analysis for both genes showed significant association of less advanced fibrosis with having allele A in both IL-10 and MTP compared to other haplotype combinations (p = 0.006). These findings suggest that alleles A/627 and A/400 for genes IL-10 and MTP, respectively, are associated with less advanced HCV-gt4-induced fibrosis. Identifying reliable biomarkers correlated with HCV-gt4-induced fibrosis severity would significantly impact the personalized plans for prophylaxis and treatment of patients at risk.

ID: 20

Role of NS5A phosphorylation in HCV RNA translation modulation

Mangyung Kandangwa, University of Saskatchewan, Qiang Liu, VIDO-InterVac, University of Saskatchewan

Hepatitis C virus (HCV) non-structural protein 5A (NS5A) is a pleiotropic protein and is indispensable for viral propagation and assembly. Regarding HCV RNA translation, we have previously demonstrated that HCV-1b NS5A downregulates viral RNA translation by binding to the poly U/UC region in the 3'UTR.

NS5A is a phospho-protein with two phosphorylation states: hypo- and hyper- phosphorylation. Phosphoproteomics and genetic mutation studies have pinpointed a cluster of serine residues (S222, S225, S229, S232, S235, and S238) in the low complexity sequence I region responsible for N5SA hyper-phosphorylation. Phosphorylation status of NS5A has been considered to have a significant impact on its functions. With the intention of identifying a possible role of NS5A phosphorylation in HCV translation, we performed extensive mutation analysis of these serine residues.

Using genomic HCV-1b translation reporter RNA and phosphorylation–ablated alanine (S-A) NS3-NS5A mutants, we found that S229A and S238A mutants lost their ability to downregulate HCV RNA translation, whereas phosphorylation-mimetic aspartic acid (S-D) mutation on the same sites rescued translation downregulation by NS5A. This suggests that phosphorylation at S229 and S238 is essential for NS5A to downregulate the translation. In contrast, the S232D and S235D NS3-NS5A mutants no longer downregulate the translation, while this function was rescued with alanine mutation, suggesting de-/ un-phosphorylation of these sites is important for NS5A to downregulate the translation. Interestingly, the alanine or aspartate mutation at S222 and S225 was found to have no effect on translation downregulation by NS5A, suggesting that phosphorylation at these sites may not regulate NS5A's role in translation. Lastly, we generated alanine or aspartic acid mutations at the six serine residues (S6A, or S6D) NS3-NS5A mutants to mimic hypo- or hyper-phosphorylated NS5A, respectively. We found that both S6A and S6D mutants did not downregulate HCV RNA translation. These results suggest that a certain ratio of hypo- and hyper-phosphorylated NS5A species is crucial for NS5A to modulate HCV RNA translation. This function of NS5A may be regulated through cascading events resulting in phosphorylation at S229 and S238 and/or de-/un-phosphorylation at S232 and S235. This phosphorylation and/or de-phosphorylation cascade may be mediated through various kinases and phosphatases. We are currently investigating the role of casein kinase 1α (CK1α). Our study will provide additional insights into the functions of NS5A phosphorylation.

ID: 186

A global prophylactic HCV vaccine is effective against antibody escape mutants

John Law, University of Alberta **,** Owen Smith, University of Alberta , Francine Cheung, University of Alberta , Juthika Kundu, University of Alberta , Michael Logan, University of Alberta , Elzbieta Dudek, University of Alberta , Darren Hockman, University of Alberta , Amir Landi, University of Alberta , Chao Chen, University of Alberta.ca , Catalina Prince, University of Alberta , Kevin Crawford, University of Alberta , Mark Wininger, University of Alberta , Lia Firth, University of Alberta , Drew Nahirney, University of Alberta , Janelle Johnson, University of Alberta , D. Lorne Tyrrell, University of Alberta , Michael Houghton, University of Alberta

Both humoral and cellular responses play important roles in protection against HCV infection. We are developing a combination vaccine containing a second generation gpE1/gpE2 envelope glycoprotein heterodimer (derived from a Fc fusion precursor) to elicit broadly cross-neutralizing antibodies along with conserved HCV T cell antigens to broaden cross-protective cellular immunity. In support of the protective role of neutralizing antibody, many cross-neutralizing monoclonal antibodies (Mab) capable of preventing or ameliorating infection have been identified. However, viral escape mutants have also been reported to these Mabs. For example, mutation of serine 417 in gpE2 has rendered the Mab AP33 ineffective. However, we show that our vaccine antisera retain the ability to neutralize infection against HCV encoding the N417S escape mutation because the vaccine elicits cross-neutralizing antibodies targeting many different epitopes. We have also examined escape mutations to other cross-neutralizing antibodies such AR3a, AR5a and HC33.1 and HC84.26. While these recombinant viruses able to reduce efficiency of neutralization by these monoclonal antibodies, our vaccine induced antisera maintain similar neutralization activity against theses mutant as well as wild type virus. This data showed a proof of principle where our vaccine can induce protective antibody capable to block virus escape. Such data provides encouragement that our vaccine candidate (currently under GMP manufacturing for initiation of clinical trials) will provide both optimal and global protection for the millions of people at risk of HCV infection.

ID: 199

Biodistribution of Gold Nanoparticles in a Hepatitis-induced Tumor Model

Lewis Liu, Max Ma, Ben Ouyang, Justin Manuel, Danielle Ings, Annie Chen, Xu-Chun Chen, Sagar Marwah, Rahul Gupta, Blair Gage, Sai Chung, Damra Camat, Michael Cheng, Manmeet Sekhon, Kyryl Zagorovsky, Oyedele Adeyi, Juan Echeverri, Dagmar Kollmann, Warren C.W. Chan, Thomas I. Michalak, Ian D. McGilvray, Sonya A. MacParland

Background: Hepatocellular carcinoma (HCC) is the third leading cause of cancer related death worldwide and the major cause of death in patients suffering from chronic hepatitis B or hepatitis C (HBV/HCV) infection (Idilman et al. 1998; Lupberger and Hildt 2007). Current treatment options for HCC include surgical interventions, radiotherapy, and chemotherapeutic agents. Importantly, no current treatments are capable of selectively targeting cells that promote HCC tumor progression, and HCC recurrence is common. We aim to design a nanoparticle (NP) based therapy that targets immunoregulatory TAMs within the tumor microenvironment of HCC in a manner that promotes anti-tumor immunity. We are using the *in vivo* pre-clinical woodchuck hepatitis model of Woodchuck Hepatitis Virus (WHV) induced HCC to test our therapy. Woodchucks are naturally infected with WHV and is the only animal model that spontaneously develops HCC on an intact immunological background. In addition, given that WHV and HBV induced HCC share many similar characteristics, the woodchuck model is capable of effectively recapitulating hepatitis infection in humans, and therefore, represents one of the most robust animal systems to test new HCC therapies.

Purpose: In order to validate the effectiveness of therapeutic nanoparticles in this animal system, an assessment of nanoparticle biodistribution must be conducted first.

Methods: We injected 7 woodchucks (3 healthy, 4 WHV+ tumor bearing) intravenously with 60nm gold nanoparticles to identify the biodistribution, cellular uptake, and subcellular localization of these particles. We performed inductive coupled mass spectrometry (ICP-MS) on woodchuck organs and tumors to assess the biodistribution of these particles. In addition, we performed flow cytometry, confocal and electron microscopy to investigate the cellular and subcellular distribution of these particles.

Results: We find that the liver is the primary organ that facilitates uptake of these particles and the subcellular localization of these particles are primarily distributed in CD14+ cells.

Conclusions and Significance: The discrepancy between pre-clinical animal models and clinical performance and translation is largely attributed to the lack of tumor models that can recapitulate human cancers. The pre-clinical woodchuck model is the only animal system that incorporates spontaneous tumor development as a result of chronic hepatitis infection. By identifying the biodistribution of injected nanoparticles in this animal system, we hope that this will establish the basis to test future nanoparticle-based therapies for the treatment of HCC.

ID: 168

Investigating microRNA-122-mediated protection of the Hepatitis C Virus genome

Ismatul Rahman, McGill University , Jasmin Chahal, McGill University , Annie Bernier, McGill University , Selena Sagan, McGill University

Background: Hepatitis C virus (HCV) recruits two molecules of the liver-specific microRNA-122 (miR-122) to the 5' end of its genome. While microRNAs usually repress gene expression, the interaction of miR-122 with the HCV genome promotes viral RNA accumulation in cultured cells. Our lab has previously shown that two cellular pyrophosphatases, DOM3Z and DUSP11, limit HCV RNA accumulation and that miR-122 is able to protect the HCV genome from pyrophosphatase activity and subsequent exonuclease-mediated decay. However, this was demonstrated through depletion studies and the requirements for miR-122-mediated protection of the HCV genome remain unclear.

Purpose: To demonstrate a direct association of miR-122-mediated protection of the 5' end of HCV genome from pyrophosphatases DOM3Z and DUSP11 and to determine the substrate requirements for DOM3Z and DUSP11 activities.

Methods: We sub-cloned wild-type (WT) DOM3Z and DUSP11 into a bacterial expression vector and created catalytic mutants (CM) for both pyrophosphatases using site directed mutagenesis. The WT and CM pyrophosphatases were expressed in bacteria and purified by HisTrap purification, size exclusion chromatography and fast protein liquid chromatography (FPLC). We developed an *in vitro* pyrophosphatase assay using ^{32}Pγ-phosphate-labeled *in vitro* transcribed HCV RNA (nucleotides 1-117).

Results: Sanger sequencing confirmed successful bacterial expression constructs for both WT and CM DOM3Z and DUSP11. SDS-PAGE and Western blot analyses have confirmed expression and purification of these pyrophosphatases. The *in vitro* pyrophosphatase assay was optimized using commercial Calf Intestinal Alkaline Phosphatase (CIP) and we are currently optimizing the assay to assess DOM3Z and DUSP11 activity and substrate requirements. We plan to use this assay to explore miR-122-mediated protection of the 5' terminus of the HCV genome as well as to explore several miR-122 inhibitor resistance-associated mutations that are predicted to confer protection from pyrophophatase activity, even in the absence of miR-122.

Conclusion: In conclusion, we were able to express and purify both the WT and CMs of the DOM3Z and DUSP11 pyrophosphatases. We are currently working to optimize our *in vitro* pyrophosphatase assay and we hope that this will demonstrate a direct protection mechanism for miR-122 against pyrophosphatase activity. Moreover, we expect that resistance associated mutations identified in patients who underwent miR-122 inhibitor-based therapy are associated with reduced susceptibility to pyorphosphatase activity. This will further elucidate the role of miR-122 in the HCV life cycle and may help to explain novel resistance associated mutations to miR-122 inhibitors in the clinic.

ID: 69

Investigating the role of PCBP1 in the HCV life cycle

Marylin Rheault[1], Sophie E. Cousineau[2], and Selena M. Sagan[1, 2]
[1]Department of Biochemistry, McGill University
[2]Department of Microbiology & Immunology, McGill University

Background:

Hepatitis C virus (HCV) recruits a number of cellular factors to its genome to perform various functions throughout its life cycle. Poly(rC)-binding protein 1 (PCBP1) is a highly abundant RNA binding protein that is implicated in modulation of translation, mRNA stability, and has been demonstrated to play a role in several positive-strand RNA virus infections. PCBP1 has previously been shown to associate with the HCV genome and its depletion limits viral RNA accumulation in cell culture. Interestingly, although we observed an overall decrease in viral RNA accumulation upon depletion of PCBP1, we observed an overall increase in viral particle production.

Purpose:

We hypothesize that PCBP1 may play a role in promoting viral egress or packaging. Moreover, since PCBP1 has three hnRNP K-homology (KH) domains that are implicated in RNA binding, we hypothesize that one or more of them are involved in its interaction with the viral RNA. We hope to elucidate the role of PCBP1 in the HCV life cycle as well as the importance of PCBP1's KH domains in performing this function.

Method:

To investigate this, we created C-terminal FLAG-tagged recombinant wild-type PCBP1 and KH domain mutant plasmids. We tested these in transient expression assays and created stable cell lines that will be used to explore the role of the KH domains in the HCV life cycle. We plan to perform siRNA-mediated knockdown of endogenous PCBP1 during infection with HCV. We will assess the effects on HCV infection by using established assays for viral protein expression (Western blot), viral RNA accumulation (Northern blot and qRT-PCR), and viral particle production (focus-forming unit assay).

Results:

We have confirmed that the C-terminal FLAG-tagged recombinant wild-type and mutant PCBP1 constructs are expressed in Huh-7.5 cells. Moreover, the stable cell lines generated which express the FLAG-tagged protein in a continuous manner are still permissive to HCV infection, resulting in an improved model in which to study the role of PCBP1 in the HCV life cycle.

Conclusion:

PCBP1 knockdown results in a decrease in HCV RNA accumulation, but an increase in viral particle production. However, the precise role of PCBP1 in the HCV life cycle remains to be clearly elucidated. We have developed a system to study PCBP1 and assess the role of each of the individual KH domains by generating mutant constructs and cell lines that stably express our recombinant proteins. We hope that analysis of these mutants in the context of viral infection will help precisely define the role of PCBP1 in the HCV life cycle.

ID: 143

Deciphering the role of DDX3X-HCV RNA in HCV pathogenesis

Vanessa Meier-Stephenson, Universities of Calgary and Lethbridge, Corey Nelson, Dept of Chemistry and Biochemistry, University of Lethbridge, Tyler Mrozowich, Dept of Chemistry and Biochemistry, University of Lethbridge, Joyce Wilson, University of Saskatchewan, Carla Coffin, Department of Medicine, University of Calgary, Trushar Patel, Dept of Chemistry and Biochemistry, University of Lethbridge

Background: Approximately 71 million people worldwide are chronic HCV carriers, including >240,000 Canadians, all of whom are at elevated risk of developing hepatocellular carcinoma[1]. Despite advances made in direct-acting-antiviral therapies, many questions remain unanswered regarding the interaction of this virus with the host's cellular proteins and their link with liver pathology and oncogenesis.

Upon cellular invasion, host proteins, including the helicase, DDX3, are exploited for viral propagation. In fact, DDX3 has been shown to be essential for HCV viral replication, where knockdown studies of DDX3 resulted in a 95% reduction in HCV RNA[2]. DDX3 has also been implicated in HCV-associated hepatic steatosis through influences on lipid metabolism pathways[3]. Interestingly, both these processes are mediated by DDX3 interaction with the 3'-UTR of HCV[3,4]. There are also numerous links with DDX3 and oncogenesis highlighting this host protein as an important target[5-9].

Purpose: Through the rigorous study of the key DDX3-HCV 3'-UTR RNA interaction, the precise structural features necessary for this interaction with be determined, that will enable downstream inhibitor development and pathogenesis studies.

Methods: We designed triple-host (expressible in E. coli, HEK293 or sf9 cells) cDNA constructs of DDX3 that can express full-length protein and individual domains. Protein products were purified through affinity and size-exclusion chromatography. The HCV 3'-UTR was cloned and produced using in vitro transcription. Electrophoretic mobility shift assays and microscale thermophoresis were employed to study interactions between DDX3 and the 3'-UTR of HCV RNA to identify which domains are responsible for mediating the interaction. As well, small-angle X-ray scattering (SAXS) will be performed on the individual fragments and the interacting partners to inform solution structure models.

Results: We have designed ten cDNA constructs for expression and purification of DDX3 protein. We have optimized in vitro transcription protocols for purification of HCV RNA fragments. We are collecting data on low-resolution structures of HCV RNA and of DDX3X-HCV RNA. We will also evaluate binding affinities between RNA and protein using biochemical assays.

Conclusions: The determination of the precise structural features of the DDX3-HCV-3'-UTR interaction will enhance understanding of HCV-associated liver pathogenesis and potentially enable the development of inhibitors to selectively disrupt these pathologic processes.

[1]Canadian Task Force. Hepatitis C Virus. 2017; https://canadiantaskforce.ca/hepatitis-c-clinician-summary/. Accessed Feb, 2019. [2]Ariumi Y, et al. J Virol. 2007;81(24):13922-13926. [3]Pene V, et al. J Virol. 2015;89(10):5462-5477. [4]Saito T, et al. Nature. 2008;454(7203):523-527. [5]Schweitzer CJ, et al. J Virol. 2017. [6]Zhao L, et al. Am J Cancer Res. 2016;6(2):387-402. [7]Ariumi Y. Front Genetics. 2014;5:423. [8]Bol GM, et al. Mol Cancer. 2015;14:188. [9]Chang PC, et al. Oncogene. 2006;25(14):1991-2003.

ID: 150

Inflammasome Activation and its Role in HCV-Induced Pyroptosis

Hannah Wallace, Memorial University, Lingyan Wang, Memorial University, Vipin Shankar Chelakkot, Memorial University of Newfoundland, Michael Grant, Memorial University, John Pezacki, University of Ottawa, Kensuke Hirasawa, Memorial University of Newfoundland, Rod Russell, Memorial University of Newfoundland

BACKGROUND:

Pyroptosis, a form of inflammatory programmed cell death, is induced after activation of an inflammasome, which ultimately results in pore formation and cell lysis. One factor in the pathology associated with Hepatitis C virus (HCV) infection is caspase-3-mediated apoptosis (non-inflammatory) which is thought to contribute to liver cirrhosis/fibrosis in chronically-infected patients. Recently it was shown that both apoptosis and pyroptosis occur in cultured human hepatocyte-like cells infected with HCV as well as in uninfected bystander cells. In the context of other viral infections, pyroptosis has been shown to be beneficial to the virus in some contexts or act as an innate antiviral response potentially benefitting the host in others. We aim to clarify this discrepancy in the context of HCV infection, but what is clear already is that liver cells are dying.

PURPOSE:

The current research aims to detect universal inflammasome components (cleaved caspase-1, ASC) in HCV-infected cells and to study the effect of pyroptosis on HCV infection.

METHODS:

Optimization of a protocol using anti-ASC antibodies and/or FAM-FLICA probes has been used effectively to visualize ASC or caspase-1, respectively, in HCV-infected cells *in vitro*. Cell lines that have universal inflammasome components knocked out as well as inhibitors of these components will be used to determine the effect that inhibition of pyroptosis has on the virus.

RESULTS:

Higher levels of ASC as well as caspase-1 were consistently observed in HCV-infected cells compared to uninfected cells, indicating more inflammasome activation occurs in infected cells. Inhibition of inflammasome activation using knockout cell lines or inhibitors showed virus titer was decreased when inflammasome-induced pyroptosis was inhibited.

CONCLUSION:

In conclusion, these data confirm the presence of pyroptosis in HCV-infected cells and specifically demonstrate the involvement of the inflammasome. These results suggest that pyroptosis is a mechanism used by HCV to cause pathology associated with infection.

Social, Cultural, Environmental and Population Health Research

ID: 36

Hepatitis C cascade of care and factors associated with treatment uptake among people who inject drugs in British Columbia in 2017

Sofia Bartlett, BC Centre for Disease Control, Amanda Yu, BC Centre for Disease Control, Margo Pearce, BCCDC, Hasina Samji, BC Centre for Disease Control, Mawuena Binka, BC CDC, Maria Alvarez, BC Centre for Disease Control, Geoff Mckee, British Columbia Centre for Disease Control, Zahid Butt, University of British Columbia, Stanley Wong, BC Centre for Disease Control, Maryam Darvishian, University of British Columbia, Carmine Rossi, British Columbia Centre for Disease Control, Mark Gilbert, BC Centre for Disease Control, Jason Wong, BC Centre for Disease Control, Mark Tyndall, BC Centre for Disease Control, Mel Krajden, University of British Columbia, Naveed Zafar, BCCDC

Background: Removal of restrictions on public reimbursement for direct acting antivirals (DAAs) is expected to increase treatment rates among people living with hepatitis C virus (HCV), particularly among People Who Inject Drugs (PWID). We constructed 2017 HCV care cascades for PWID and non-PWID living with HCV infection in British Columbia (BC), and investigated factors associated with HCV treatment uptake.

Purpose: Assessing gaps in HCV care cascades among PWID and non-PWID is essential to monitoring progress towards HCV elimination goals and ensuring equitable treatment access.

Method: The BC Hepatitis Testers Cohort (BC-HTC) was used for this analysis. BC-HTC includes all individuals tested for HCV in BC since 1990, linked to data on prescription drugs, medical visits, hospitalizations and mortality data. We defined six care cascade stages: 1) anti-HCV diagnosed; 2) RNA tested; 3) RNA positive; 4) genotyped; 5) initiated treatment; and 6) achieved post-treatment sustained virologic response (SVR). People diagnosed with HCV infection were stratified by history of injecting drug use based on a previously validated algorithm (recent PWID, $\leq$3 years; past PWID, >3 years ago; or never PWID). Factors associated with treatment uptake were assessed using multiple logistic regression.

Results: In 2017, 52,987 individuals were diagnosed anti-HCV positive in BC. Among those, 22% were recent PWID, 17% past PWID and 61% never PWID. RNA or genotype testing was highest among recent PWID, and lowest among never PWID. HCV treatment initiation was 38% (2698/7081) among recent PWID, compared to 46% (2016/4350) among past PWID, and 60% (10162/16812) among never PWID. Among HCV RNA positive PWID, a major mental illness diagnosis (recent PWID; adjusted odds ratio [AOR] 1.10; 95% Confidence Interval [CI] 1.01-1.20, past PWID; AOR 1.24; 95%CI 1.12-1.39), HIV coinfection (past PWID; AOR 1.64; 95%CI 1.42-1.89) and cirrhosis (past PWID; AOR 1.58; 95%CI 1.30-1.99) were associated with treatment uptake. Factors negatively associated with treatment uptake included being in most materially (recent PWID; AOR 0.78; 95%CI 0.67-0.92) or socially deprived quintiles (recent PWID; AOR 0.72; 95%CI 0.60-0.86, past PWID; AOR 0.67; 95%CI 0.54-0.82), and unknown residential location (recent PWID; AOR 0.22; 95%CI 0.12-0.40, past PWID; AOR 0.40; 95%CI 0.24-0.66).

Conclusion(s): For PWIDs, progression through the HCV care cascade has improved since DAAs became more widely available but remains lower than among non-PWIDs. Associations between major mental illness diagnosis, HIV infection, and treatment uptake among PWID may be due to more frequent engagement with social or health services among people with these diagnoses. The negative association between treatment uptake and material and social deprivation among PWID suggests additional support may be required to facilitate HCV treatment uptake among highly marginalized people. Further investigation in to the negative association between unknown residential location and treatment uptake among PWID is warranted, as this may relate to homelessness.

ID: 177

Who are the real transformational leaders? From peer educators to peer navigators

Magali Boudon, DOPAMINE

Dopamine is a Montréal-based community organization located in the Hochelaga-Maisonneuve neighbourhood, with the mission to help, support, and work alongside people who use drugs.

It has been ten years since Dopamine initiated the Dopalliés project, with the goal of mobilizing participants to adopt and promote more secure behaviours through educative workshops aiming to prevent the transmission of HIV/AIDS, Hepatitis C and other STIBBs. Each year approximately fifty participants of the Dopalliés project become progressively equipped with prevention knowledge and act as peer educators in their own community.

This change in our educative approach has had a direct impact in the community: participants finally wanted to start treatment. However, they remained confronted by structural barriers: a health care system that is not adapted to their life situation.

Consequently, Dopamine developed a new service in partnership with CAPAHC (Centre Associatif Polyvalent d'Aide Hépatite C) and the Lotus project was born. The project provides personalized accompaniment services in partnership with the Quartier Latin clinic. A team of dedicated health professionals work to adapt and modify services so that a minimum of ten participants each year can access and adhere to treatment and avoid reinfection.

Despite the willingness of health professionals to adapt to this specific population, participants still faced cultural barriers: when an institution must accommodate diverse adult needs, it has the reflex to infantilize and to offer privileges that can then be revoked. Ultimately, the institution loses confidence in the patient because they are unable to adapt to its formal functions.

Subsequently, the organization has continued its reflections in order to further adapt health care services to better suit the needs of people who use drugs. In order to complement the services offered by the Lotus project in collaboration with its partners, Dopamine created a medical clinic at the drop-in centre called Dopamed.

This new clinic aims to engage service users of Dopamine who are already implicated in various projects offered by the organization. In this new structure, two peers are responsible for the reception of patients and the functioning of the clinic. They are the first visionaries and decision makers of the structure and culture of the Dopamed clinic. Decisions are made collectively between team members including peers, doctors, nurses, and the intervention team.

People who have had positive experiences with Dopamine's services and projects are able to use their experiential knowledge to become peer navigators. They are able to turn their fear of being stigmatized into a desire to take care of themselves! They are the true transformational leaders of social and medical change.

ID: 79

Acceptability, Availability and Preference of Different Methods of Communication Among Vulnerable Patients at Risk for Hepatitis C

Samuel Delisle-Reda, Centre de Recherche du Centre hospitalier de l'Université de Montréal, Julie Bruneau, CRCHUM, Valerie Martel-Laferriere, Centre de Recherche du Centre hospitalier de l'Université de Montréal

Background: Despite increased availability of HCV treatment, the rate of treatment among people who use drugs (PWID) is still very low. Frequent attrition due to the difficulty reaching PWID through conventional methods of communications after HCV Ab screening and before confirmatory testing is a potential modifiable factor to improve the cascade of care in this vulnerable population.

Purpose: The aim of this study was to determine which methods of communication are acceptable and available to PWID when communicating with their healthcare professionals. We also evaluated if participants had access to their preferred methods.

Method: This cross-sectional study was conducted in HEPCO, a research cohort based in Montreal, between June and August 2018. Participants included French-speaking PWID and who were at-risk or currently infected with HCV. Answers were self-recorded on RedCap 8.5.0 with the assistance of an investigator, when required. Methods of communication of interest included: phone, standard mail, friends/family/professional (secondary contact), pharmacist, emails, text messages and social media. To be considered available to a user, a given method had to fulfill pre-set criteria (e.g.: phone: owing a functional device and phone number). Availability of preferred methods of communication was evaluated. To determine acceptability, participants were asked if they were comfortable using the different methods of communication with their medical team. Regarding preferences, participants had to classify the different methods of communication from the most preferred to the least preferred. Proportions of acceptability, availability and preferences of each of the method were examined.

Results: Amongst the 96 participants, median age was 45 years old (IQR: 37-52), 85.4% were male and 25.0% were homeless. The majority (78.1%) of participants were actively injecting drugs and 60.4% have been infected with HCV. Overall, 95.7% of participants had access to at least one method of communication. Secondary contacts, standard mail and phone were the most available and acceptable methods of communication (table). Most participants favoured phone calls, followed by mail and contact through their pharmacist. There were discrepancies between availability and preferences: 66.7%, 62.2% and 50% of those who preferred mail, phone or pharmacist were effective users, respectively.

Conclusion: The results show that mail and phone remained the most available, most acceptable and preferred methods of communication with patients at-risk for HCV or HCV-infected. However, some participants perceived being more effective users than they actually were. This study highlights the importance of adapting practices and communication tools when engaging PWID in care, with the involvement of alternative modes of communications and reach-out, including peers and community based organizations.

	Acceptability	Availability	Preferred method of communication n=94*	Availability of preferred method of communication
Phone	89.6%	50%	43 (45.7%)	28/43 (62.2%)

Standard mail	80.2%	60.4%	15 (16.0%)	10/15 (66.7%)
Secondary contact	82.3%	80.2%	11 (11.7%)	7/11 (63.6%)
Pharmacist	79.2%	29.2%	12 (12.8%)	6/12 (50%)
Email	65.6%	31.3%	5 (5.3%)	3/5 (60%)
Text message	60.4%	32.3%	5 (5.3%)	5/5 (100%)
Social media	26%	27.1%	0%	-

*Two participants excluded. Three participants preferred phone applications (3.2%).

ID: 182

Delivery of HCV Care to Remote and Indigenous Alberta Communities via Telehealth

Kate Dunn, Alberta Health Services, Cari Egan, Alberta Health Services, Kienan Williams, Alberta Health Services, Samuel Lee, University of Calgary, Susan Tallow Christenson, Blood Tribe Department of Health

Background: Hepatitis C Virus (HCV) infections represent a major public health burden in Canada, affecting approximately 350,000 individuals. Although HCV is curable with highly effective direct-acting antivirals (DAA), conventional models of medical care (referral to specialists) have been access barriers to the curative therapy for remote and Indigenous communities. HCV prevalence is 2-4 times higher with Indigenous communities in Alberta where treatment rates are also the lowest. Factors contributing to these health inequities include: stigma, public and primary care provider knowledge gaps, and policies that restrict DAA prescribing to select groups of specialists who practice in urban areas. This centralized care model forces individuals from remote and/or hard-to-reach Indigenous communities to travel to urban centres for HCV care amplifying the inequity. We therefore adapted the New Mexico ECHO (Extension for Community Health Outcomes) model of telehealth by videoconferencing in a hub-and-spoke model to deliver HCV care.

Purpose: Improve access to HCV care by telehealth (ECHO HCV Outreach Project) with collaboration from the Alberta Sexually Transmitted and Blood-Borne Infections Operational Strategy and Action Plan (STBBI OSAP) in Indigenous communities.

Methods: Collaboration between ECHO HCV Outreach project, STBBI OSAP, Indigenous community leadership, Indigenous Elders and local healthcare teams facilitated improved HCV screening, de-stigmatization, treatment access, and supported community healthcare providers to effectively access specialized liver care for Indigenous HCV patients. These patients were all treated in their local communities without travelling to a specialist. Various approaches were used to improve HCV public awareness, de-stigmatization, testing, and treatment compliance, including: initial visits to Indigenous communities by ECHO and STBBI OSAP personnel to implement the program; enlisting key community leaders and Elders; public lectures and media campaigns; incentive programs to improve therapy adherence; peer navigators; and preceptorship training for non-specialist physicians and nurses working in Indigenous communities.

Result(s): The Alberta ECHO HCV program started in October 2015 as biweekly videoconferences with 5 remote 'spoke' sites and the Calgary 'hub'. Despite several attempts to enlist Indigenous communities, none participated until ECHO started collaborating with STBBI OSAP in December 2017. Eight communities have joined the program since then, using the expertise, connections and implementation abilities of STBBI OSAP in Indigenous communities. To date, 26 Indigenous HCV patients have been treated locally through the ECHO videoconferences, with 100% SVR (11/11 patients). Four Healthcare Providers from Indigenous communities have completed preceptorships and are participating regularly in the telehealth sessions with the goal of ultimately becoming independent HCV treaters. Several more Indigenous communities plan to join the program in 2019.

Conclusion(s): A culturally-sensitive multidisciplinary telehealth program developed in collaboration with STBBI OSAP and its substantial network has dramatically improved access to HCV care in remote and Indigenous Alberta communities.

ID: 1

The health impact of policies delaying direct-acting antiviral treatment for chronic hepatitis C: a decision-analytic approach

Aysegul Erman, University of Toronto, William WL Wong, School of Pharmacy, University of Waterloo Jordan Feld, University of Toronto, 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 (DAAs) are highly effective, but expensive treatments for chronic hepatitis C (CHC). To manage costs, drug plans worldwide have rationed access to DAAs in various ways, making timely access to treatment a challenge for patients.

Purpose: To quantify the health impact of delaying DAA therapy.

Method: A decision-analytic model was developed to quantify the health impact of delaying DAAs for CHC subgroups stratified by age, fibrosis level, viral genotype and injection drug use over their lifetime. The health impact of delaying therapy was quantified in terms of quality-adjusted life expectancy (quality-adjusted life years, or QALYs) and life expectancy (years).

Result(s): Deferring DAAs for patients with no or mild fibrosis (F0/F1) for periods of time between 1-5 years is unlikely to result in any loss in life expectancy and leads only to marginal losses of 0.02-0.06 QALYs per year of delay. However, delaying treatment for 30-50-year-olds with advanced fibrosis or cirrhosis (≥F3) for as little as a year results in a considerable health loss (0.25-1.04 QALYs and 0.19-1.53 years). Reimbursement criteria that limit DAA access for those with substance use are associated with large health losses. People who actively inject drugs with advanced fibrosis or cirrhosis (≥F3) may lose 0.18-1.05 QALYS and 0.13-1.16 years from delaying treatment, despite the risk of reinfection and competing mortality. Results are robust to parameter uncertainty and key assumptions.

Conclusion(s): The current study presents estimates of the health impact of policies that delay therapy for various CHC subgroups considering the effects of age, disease severity, genotype and injection drug use. Our results I suggest that patients with at least moderate fibrosis (F2) and especially those with advanced fibrosis (≥F3) should have access to prompt therapy, regardless of high-risk behaviors such as drug use.

ID: 55

Peers4Wellness: Indigenous Model for Supportive HCV and HIV Care

Candice Norris, Indigenous Wellness Research Group, Sharon Jinkerson- Brass, Indigenous Wellness Research Group, Emily Scotton, Indigenous Wellness Research Group, Sadeem Fayed, Simon Fraser University, Indigenous Wellness Research Group, Malcolm King, University of Saskatchewan, Alexandra King, University of Saskatchewan

Background: The rate of hepatitis C (HCV) among First Nations, Inuit and Métis, the Indigenous peoples of Canada, is 5X higher than non-Indigenous people in Canada. This gap is magnified for Indigenous females, who are over-represented among those living with HCV in Canada. This trend is counter mirrored in HCV care, where Indigenous people and Indigenous females, in particular, are under-represented. Peer navigation (PN) has been emerging as a promising innovative approach to enhance engagement in health care; PN might be of particular value from an Indigenous perspective due to its wellness resonant elements. However, the current landscape of PN research and practice is lacking an Indigenous focus, as well as a HCV and co-infection focus. This study is aimed at addressing this gap

Purpose: Peers4Wellness (P4W) is an Indigenous peer-led community-based participatory research study. It involved an assessment of needs for supportive HCV and HIV care among Indigenous women (cis- and trans-gendered) in Vancouver and Fraser Valley, British Columbia. Specifically, the study explored the feasibility of applying PN as a springboard for developing an Indigenous model for supportive HCV and HIV care. This involved consultations with three groups of community stakeholders: Indigenous women with lived HCV and/or HIV experiences, peer navigators and community organizations.

Method: This study (n=47) applied qualitative Indigenous research methodology. It used *Two-eyed Seeing* as a research framework to weave together Indigenous and Western paradigms. Data collection included Sharing Circles and conversational interviews. Data analysis applied a dualistic (Indigenous and Western) thematic content analysis approach. Data collection and analysis involved a participatory process that is co-led by the community and academia

Results: The findings underline the need for Indigenous-specific and wellness-centered HCV/HIV supportive care for Indigenous women in Vancouver and Fraser Valley. The study underscores some gaps in support services across the HCV/HIV care cascades. It outlines key pillars for Indigenous models of supportive HCV/HIV care, including: 1) mobilize community capacity for healing and self-management, 2) address the intersecting socio-cultural inequities uniquely experienced by Indigenous women with HCV/HIV, and 3) respond to Indigenous wholistic conceptualization of HCV/HIV burden and care. The results also indicate that peer support, from an Indigenous perspective, is needed as an approach to strengthen community resilience against HCV/HIV by promoting collective identity and cultural connection. Finally, the study leads to a new hypothesis regarding the application of Indigenous research as a HCV/HIV intervention. Many of the research participants have indicated that their involvement in a P4W sharing circle have supported their HCV/HIV healing journeys.

Conclusion: P4W will introduce an innovative Indigenous model for supportive HCV/HIV care to improve the wellness and HCV/HIC health care outcomes among Indigenous women in Vancouver and Fraser Valley. We expect that this model will scalable and transferable.

ID: 90

Implication of the 'cheque effect' in HCV transmission: Determinants of short-term changes in drug consumption behaviour following receipt of a significant cheque among people who inject drugs in Montréal, Canada

Stine Hoj, Centre de Recherche du CHUM, Phélix Bussière, Université de Montréal, Brendan Jacka, Centre de Recherche du CHUM, Julie Bruneau, Université de Montréal

Background

Injection drug use (IDU) accounts for the majority of hepatitis C (HCV) burden in Canada. Prevention strategies have not ended HCV transmission among people who inject drugs (PWID), possibly reflecting situational influences on injecting risk behaviour. Disbursement of social assistance payments has been associated with intensified drug use and related harm, but little is known about the implication of 'cheque effects' in HCV risk.

Purpose

This study examines short-term changes in drug injection behaviour surrounding receipt of a significant cheque, and relationships to known determinants of HCV risk.

Method

Data were collected from an open prospective cohort of people who inject drugs (PWID) in Montréal, Canada (HEPCO, 2011-2017). Participants (aged ≥18 and injected drugs within six months preceding recruitment) completed three-monthly questionnaires capturing sociodemographic and recent drug use characteristics, including two days before/after receipt of a significant cheque in that month. Analysis was restricted to visits where participants reported any consumption of illicit drugs and receipt of a cheque.

Descriptive statistics compared proportions of participants reporting any IDU and any receptive syringe sharing (McNemar's test) and the median number of injections (Sign test) in the two days before/after cheque receipt. Individual-level change in injection frequency before/after cheque receipt was analysed using a hurdle model to assess the relative (1) odds and (2) rate of any increase in injection frequency, with respect to the unstable housing, cocaine use, frequent injection (past month), incarceration (past three months), and enrolment in opiate agonist therapy (current). Analyses adjusted for age, gender, ethnicity, education, age at first injection, monthly income, and income source. Cluster-robust standard errors were obtained via a sandwich estimator.

Results

In total, 705 participants [at baseline 82% male; 92% white; median age 40 (IQR: 31-48); 91% receiving welfare or other government benefits] provided 4787 eligible assessments.

The overall prevalence of IDU (65% vs. 38%), prevalence of receptive syringe sharing (2.3% vs. 1.0%), and median number of injections (3 vs. 0) were each significantly greater in the two days following cheque receipt, compared to the two days before.

At the individual level, 44.4% of observations showed a change in the number of injections, of which 97% increased injection frequency. Past-month frequent injection, cocaine use, and unstable housing increased both (1) the odds and (2) the rate of increase in the number of injections. Enrolment in OAT boosted the odds of an increased number of injections, but reduced the rate of increase among those who did inject more. Finally, recent incarceration reduced the odds of an increase in the number of injections.

Conclusion

Drug injection behaviour differs in the days following receipt of a significant cheque. Past-month cocaine use, frequent injection, and unstable housing exacerbated these 'cheque effects', potentially acting as a temporal link in the causal pathway to HCV infection.

ID: 2

Recent sexual behaviour is not associated with HCV recurrent infection among men who inject drugs in Canada.

Brendan Jacka, Centre de Recherche du CHUM, Marina Klein, McGill University Health Centre, Nanor Minoyan, Université de Montréal / CRCHUM, Sahar Saeed, McGill University, Carmine Rossi, British Columbia Centre for Disease Control, Geng Zang, CRCHUM, Andreea Adelina Artenie, Université de Montréal, Didier Jutras-Aswad, Research Centre of the Centre Hospitalier de l'Université de Montréal; Department of Psychiatry, Université de Montréal, Curtis Cooper, University of Ottawa, Julie Bruneau, Université de Montréal

Background

Although hepatitis C virus (HCV) infection is both preventable and curable, acquisition remains high among key affected populations, particularly people who inject drugs (PWID) and men who have sex with men (MSM). Substantial recurrent HCV infection has been reported in both these populations, and increased uptake of highly effective direct acting antivirals increases the pool of individuals susceptible to recurrent infections. Considering the complex interplay between sexual behaviour and drug consumption, a better understanding of HCV recurrent viremia in sexual minorities is necessary and timely.

Purpose

The aim of this study was to examine the rate of and factors associated with HCV recurrent viremia among PWID in Canada, stratified by recent sexual activity.

Methods

Participants in the HEPCO (Montreal; 2011-2017) and Canadian Coinfection Cohort (CCC, pan-Canadian; 2004-2018) studies were eligible if HCV antibody positive and HCV RNA negative with $\geq$1 follow-up visit. Eligibility for HEPCO was injection drug use in past six months at cohort enrolment, while CCC was open to any participant with HIV/HCV coinfection (in this analysis, restricted to participants reporting recent injection drug use at enrolment or follow-up). Comprehensive behavioral and socio-demographic questionnaires and HCV RNA testing was undertaken at enrolment and 3/6-month intervals, depending on cohort. Sexual activity (time-varying, past 3/6-months) was categorised as: 1) no sexual partner, 2) opposite sex partner only, or 3) $\geq$1 same sex partner. We defined HCV recurrence as a positive HCV RNA test among individuals having previously cleared the virus, consistent with current clinical definitions. Time-to-event methods were used to calculate recurrence rates and factors associated (clustered by site and adjusting for age, recent incarceration, cocaine injection, heroin injection, prescription opioid injection, and psychedelic consumption).

Result

At baseline, 436 males were eligible [median age: 48 years (IQR: 42-53); 57% HIV-positive], and reported cocaine injecting (45%), heroin injecting (19%), prescription opioid injecting (20%), and amphetamine injecting (9%). In total, 90 HCV recurrent infections occurred in 1101 person-years [8.18 events per 100 person-years (PY)] with no difference in incidence by sexual behaviour group: no sex (8.31 per 100py), opposite sex only (8.35 per 100py), and $\geq$1 same sex partner (6.57 per 100py). Similarly, in Cox regression analysis there was no association between risk of HCV recurrent viremia and recent sexual behaviour: no sexual partner (Hazard ratio: 1.30, 95% CI: 0.69, 2.46) and opposite sex partner only (HR: 1.23, 95% CI: 0.68, 2.40) compared to $\geq$1 same sex partner.

Conclusion

On these cohorts of PWID, reporting recent same sex partners was not associated with greater risk of HCV recurrent viremia. Further studies of event-level sexual and injecting risk behaviours are necessary to further elucidate the role of sexual behaviour in HCV transmission.

ID: 95

Can the misalignments between the priorities of public health authorities and people who use drugs provide insights to help improve programs addressing hepatitis C risk?

Gillian Kolla, University of Toronto

Background: The "Satellite Sites", are a low-barrier harm reduction program where people who use drugs are employed by a community health centre to run satellite harm reduction programs within their own homes. This program aims to reduce health harms, including the transmission of hepatitis C through the provision of sterile injection equipment and education. While the priorities of people who use drugs, and those of public health authorities are often in alignment, moments of compromise, or misalignment of priorities can occur. This paper examines whether an examination of the misalignments between the priorities of public health authorities and those of people who use drugs can provide insights to help improve harm reduction programs addressing hepatitis C risk.

Methods: Data from an ethnographic study, including 6 months of participant observation in Satellite Sites, and 20 qualitative interviews with Satellite Site Operators (SSO), clients and program managers were collected; thematic analysis was used to examine key themes.

Results: The key priority of Satellite Site clients is to obtain a steady supply of good quality drugs. In contrast, the key priority of public health is the reduction of health-related harms as HIV and hepatitis C transmission. When priorities align (for example, clients seek out syringes to preserve vein health and naloxone for overdose), public health interventions are successful. Misalignment of priorities is often due to neglect on the part of public health to consider the primacy of drug supply issues to people who use drugs (including maintaining access to a good, affordable drug supply; ensuring money to buy drugs, and ensuring access to drugs to ward off withdrawal). A focus on the individual-level behaviours that increase risk of disease transmission by public health programs can be seen by people who use drugs as a refusal to address their key priorities.

Conclusions: Examination of the misalignments between the priorities of public health programs and people who use drugs reveals that an examination of the structural factors (including structural violence and functioning of drug markets due to criminalization) that contribute to health risks is necessary. Attention to structural factors exposes how criminalization of illicit drug use contributes to the inability of people to put in place public health best practice guidelines, and may be contributing to risk of hepatitis C transmission. Public health authorities must consider a change in focus, including an examination of how safer supply programs and decriminalization of drug use may reduce hepatitis C transmission and improve the health of people who use drugs.

ID: 35

Trends in hepatitis C virus (HCV) seroprevalence and associated risk factors among men who have sex with men (MSM) in Montreal from 2005 to 2018, results from three cross-sectional surveys

Charlotte Laniece Delaunay, McGill University, Joseph Cox, McGill University, Marina Klein, McGill University Health Centre, Gilles Lambert, Institut National de Santé Publique du Québec, Mathieu Maheu-Giroux, McGill University

Background

HCV epidemics among HIV-positive MSM have been reported in Europe, North America, and Australia since the late 1990s. Evidence suggests that sexual transmission of HCV occurs among HIV-positive MSM without a history of injection drug use (IDU). Recent cases of sexual transmission of HCV from HIV-positive to HIV-negative MSM have also raised concerns about potential spill-over effects of the HIV-HCV syndemic to HIV-negative MSM. Building on the existing literature on risk factors for HCV infection among MSM, this study aims to examine changes in HCV seroprevalence from 2005 to 2018 in Montreal MSM and to identify biological, social, and behavioural factors associated with HCV seroprevalence.

Methods

We used data from three cross-sectional studies conducted in 2005 (Argus 1, n=1,808), 2008-2009 (Argus 2, n=1,260) and 2018 (Engage, n=1,086) among Montreal MSM. The Argus surveys used convenience (2005) and time-location (2008-2009) sampling methods. To allow for robust computation and comparison of prevalence estimates, the Argus surveys were standardized on age, income, sexual orientation, and first language learned to the Engage respondent-driven sample. We then pooled the three surveys and conducted modified-Poisson regression analyses to identify factors associated with HCV seroprevalence. Finally, we compared prevalence estimates of previously identified correlates in 2005, 2008-2009, and 2018. Anti-HCV seropositivity was defined as an antibody reactive test at the time of study.

Results

Our results show a relatively stable HCV seroprevalence among MSM from 6.3% (95% confidence interval (CI): 5.1–7.6%) in 2005, 7.2% in 2008-2009 (95% CI: 5.0–9.4%), and 7.6% (95% CI: 4.5–10.8%) in 2018. In a multivariable modified-Poisson regression, history of IDU (adjusted prevalence ratio (APR): 10.1, 95% CI: 6.8–14.9), age (APR for age 30-44: 3.5, 95% CI: 1.8-6.7; for age 45 and over: 4.8, 95% CI: 2.4, 9.3; reference group: age under 30), sexual orientation other than gay or homosexual (APR: 2.9, 95% CI: 2.0–4.2), and HIV-positive status (APR: 2.1, 95% CI: 1.4–3.0), were associated with an increased risk of anti-HCV seropositivity. Inversely, annual income equal or superior to 30,000 dollars (APR: 0.4, 95% CI: 0.3–0.7) was associated with a decreased risk of anti-HCV seropositivity. No association was found between anti-HCV seropositivity and first language other than French or English, self-reported risky sexual behaviour (condomless anal sex with a known discordant or unknown serostatus partner in the last six months), having had sex with more than 10 or 20 men in the last six months, current or past syphilis infection, or year of data collection.

Conclusions

These preliminary findings suggest a stable HCV seroprevalence among Montreal MSM from 2005 to 2018, and a strong association between anti-HCV seropositivity and IDU. We will further explore potential risk factors of anti-HCV seropositivity in this population (e.g. other aspects of risky sexual practices such as "chemsex", history of other sexually-transmitted infections).

ID: 59

Hepatitis C incidence rate among people who inject drug (PWID) in British Columbia from 2000 to 2015

Yiqiao Li, BC Center for Disease Control , Stanley Wong, BC Centre for Disease Control, Zahid Butt, University of British Columbia, Carmine Rossi, British Columbia Centre for Disease Control, Jason Wong, BC Centre for Disease Control, Amanda Yu, BC Centre for Disease Control, Mawuena Binka, BCCDC, Maria Alvarez, BC Centre for Disease Control, Mel Krajden, University of British Columbia, Naveed Zafar, BCCDC

Background: Global Health Sector Strategy on Viral Hepatitis aims to reduce new hepatitis C virus (HCV) infections by 80% by 2030. However, countries lack systems to monitor incidence of HCV. We estimated the HCV incidence over time among people who inject drugs (PWID) at population level to provide proof of concept for incidence monitoring.

Purpose: To estimate the HCV incidence over time and identify risk factors among PWID in British Columbia, Canada.

Methods: This study utilized data from the BC Hepatitis Testers Cohort (BC-HTC). Incidence was defined as a positive anti-HCV, RNA, or genotype test following a negative anti-HCV test among PWID, assessed based on a previously validated algorithm using administrative data. Annual incidence rates for HCV primary infection from 2000 to 2015 were estimated using a log-binomial regression model and were stratified by birth cohorts (1974) to observe change in risk over time. Adjusted incidence rates (aIR) were calculated controlling for risk factors.

Results: Of the 42,568 participants identified, 4,066 HCV seroconversions occurred over 318,613 person-years (PY) of follow-up. The overall incidence rate was 1.28/100PY. Between 2000 and 2011, the annual aIR decreased steadily from 4.01 to 1.00/100PY. The aIR then rose to 1.49/100PY in 2015. Factors associated with elevated risk of infection include: younger birth cohort (1965-1974: RR:1.9, 95%CI: 1.02,3.6), history of illicit opioid use (RR:2.5, 95%CI: 2.3,2.7), stimulant misuse (RR:1.77, 95%CI: 1.7,1.9), HIV coinfection (RR:3.6, 95%CI: 3.1,4.1), HBV coinfection (RR:1.9, 95%CI: 1.6,2.2), material deprivation (RR:1.5, 95%CI: 1.4,1.7) and social deprivation (RR:1.6, 95%CI: 1.4,1.8).

Conclusion: A slight increase in HCV incidence rate since 2011 was mainly driven by the younger birth cohort and introduction of enhanced testing in 2010. People with HIV or HBV coinfection, opioid and stimulant misuse, social and material deprivation are at higher risk of HCV infection. HCV treatment and prevention programs need to address comorbidities and include harm reduction strategies like opioid substitution therapy and access to social services to achieve HCV elimination goals.

ID: 114

A LONGITUDINAL EVALUATION OF TREATMENT OF HCV INFECTION AMONG PEOPLE WHO USE DRUGS (PWUD)

Tianna Magel, Vancouver Infectious Diseases Centre, Julie Holeksa, Vancouver Infectious Diseases Centre, Astou THIAM, Vancouver Infectious Diseases Centre, Letitia Chu, Vancouver Infectious Diseases Centre, Rossitta Yung, Vancouver Infectious Diseases Centre, David Truong, Vancouver Infectious Diseases Centre, Brian Conway, Vancouver Infectious Diseases Centre

Background: People who use drugs (PWUD) constitute the majority of prevalent and incident HCV infections in the developed world. Although they have had access to treatment since the era of interferon (IFN)-based regimens, such access has increased significantly since the availability of more active, safer and simpler all oral combination therapy. There are few data about the long-term outcomes of PWUD treated in the IFN era and the impact of increased availability of HCV therapy on treatment uptake among PWUD.

Purpose: To document the outcomes of PWUD treated in the IFN era and the impact of increased availability of all-oral HCV therapy.

Method: We undertook a retrospective analysis of all HCV treatment starts among PWUD at our centre from 2001 to the present. We extracted demographic and disease stage information, as well as treatment response rates. We evaluated long-term outcomes, including overall mortality, liver-related morbidity and HCV re-infection rates. We analyzed IFN and non-IFN based treatments to compare the characteristics of patients accessing treatment as well as treatment responses. Another analysis was conducted among patients who were re-treated after initial therapeutic failure.

Result(s): Overall, 307 active/recent PWUD patients have been treated for HCV infection, 42 on IFN (6/36 platelets < 150/>150) 265 (51 cirrhotic/ 214 non-cirrhotic) on all-oral therapy. In patients on IFN, the success rate was 34/42 (81%) as measured by sustained virologic response at 24 weeks post-HCV treatment (SVR24). Of the 22 individuals having received prior IFN-based HCV treatment, SVR24 rate was 16/22 (73%). Among patients on all-oral therapy, the overall success rate (SVR12) was 252/265 (95%). Of the 70 individuals having received prior HCV treatment, SVR12 rate was 58/70 (83%). There are 4 cases of confirmed reinfection in this group (0.77 per 100 person- years), 5 confirmed cases of hepatocellular carcinoma (HCC) among cirrhotics (3.3 per 100 person-years) and 10 individuals are since deceased, 4 due to an opioid overdose. The key differences between the two populations is the greater success rates of SVR for HCV in the all-oral cohort.

Conclusion(s): Although some PWUD accessed IFN-based HCV treatment in specialized centres such as ours and responded to it, the availability of all-oral therapy has led to increased access in patients with less advanced disease. High SVR12 rates to all-oral treatments are observed, consistent with those observed in clinical trials. Patients who initially failed IFN-based therapy have also benefited from these programs. There is a low rate of HCV reinfection in our setting. Our program has successfully pivoted to non-IFN based treatment and increased treatment access for HCV-infected PWUD. This will be an important part of the community-based response to achieve the WHO goals to eliminate HCV infection as a public health concern by 2030.

ID: 100

Combined coverage of harm reduction interventions and rates of primary and recurrent hepatitis C virus infection in a community-based cohort of people who inject drugs

Nanor Minoyan, Université de Montréal / CRCHUM, Andreea Adelina Artenie, Université de Montréal, 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, Geng Zang, CRCHUM, Marie-Ève Turcotte, Research Centre of the Centre Hospitalier de l'Université de Montréal, Julie Bruneau, Université de Montréal

Background: Needle-syringe programs (NSP) and opioid agonist therapy (OAT) form the basis of harm reduction among PWID. Recent modelling studies suggest a continued role for these interventions within the context of hepatitis C virus (HCV) elimination efforts. Empirical evidence regarding their combined prevention benefit is, however, lacking. Further, no studies have estimated whether NSP and OAT are similarly associated with infection risk among HCV-naïve and previously-infected PWID.

Objectives: To estimate the rate of HCV infection and its association with NSP/OAT coverage among PWID in Montreal i) overall and ii) among HCV-naïve and previously-infected PWID.

Design: Data were drawn from an ongoing prospective longitudinal cohort study of PWID (HEPCO). Participants were followed every 6 months from January to November 2010, and every 3 months thereafter. At each visit, interviewer-administered questionnaires elicit sociodemographic and behavioural data, and blood samples are collected for subsequent HCV-RNA and antibody testing. Participants eligible for this analysis reported past-6-month injection at recruitment, past 3/6-month opioid use/OAT enrolment, and tested HCV-Ab-negative (at risk of primary HCV) or Ab+/RNA-negative (at risk of HCV recurrence).

Measures: OAT coverage was defined by self-reported current dose, categorized according to recent clinical guidelines: high (≥60mg/day methadone, ≥16mg buprenorphine); low (<60mg/day methadone, <16mg buprenorphine); none. Complete NSP coverage was defined as exclusively reporting safe needle-syringe sources in the past 3/6 months. Combined coverage was defined as: full=high-dose OAT/100% safe sources of NSP; minimal=low-dose OAT/<100% safe sources of NSP; partial=other OAT/NSP combinations. For all coverage variables, participants reporting no recent injection were categorized apart. HCV infection was defined as the date between the last negative and first positive antibody or RNA test, as appropriate.

Analyses: Multivariable Cox regression models estimated associations between NSP/OAT coverage and time-to-HCV-infection, overall and stratified by subgroups at risk of primary and recurrent HCV. Analyses were adjusted for age at baseline (<30, ≥30), gender (m/f), and cocaine injection frequency (continuous). Exposure variables and cocaine injection frequency were coded as time-updated. Participants were censored at the date of infection, loss to follow up, or May 2017, whichever occurred first.

Results: 56 primary and 50 recurrent HCV events were observed over 526 and 657 respective person-years of follow-up: IR_P=10.6/100py; IR_R=7.6/100py. Full coverage of harm reduction was associated with a 70% and 62% reduced risk of HCV acquisition, compared to partial and minimal coverage, respectively. High-dose OAT was associated with a 66% and 77% reduction in HCV infection risk, compared to low-dose-OAT and no OAT, respectively. NSP coverage alone was not significantly associated with HCV incidence. Estimates were similar among HCV-naïve and previously-infected PWID.

Conclusions: Full coverage of harm reduction interventions, particularly high-dose OAT, should be promulgated alongside treatment-as-prevention approaches to reduce ongoing HCV transmission among both HCV-naïve and previously-infected PWID.

ID: 179

Operationalizing the risk environment: spatial distribution of people who inject drugs and hotspots of social injecting activity in Montreal, Canada

Nanor Minoyan, Université de Montréal / CRCHUM, Andreea Adelina Artenie, Université de Montréal, Stine Hoj, Centre de Recherche du CHUM, Brendan Jacka, Centre de Recherche du CHUM, Didier Jutras-Aswad, Research Centre of the Centre Hospitalier de l'Université de Montréal; Department of Psychiatry, Université de Montréal, Marie-Pierre Sylvestre, Université de Montréal / CRCHUM, Julie Bruneau, Université de Montréal

Background: Active people who inject drugs (PWID) are considered a priority population in global efforts to reduce ongoing hepatitis C virus (HCV) transmission. It is acknowledged that drug harms are concentrated within specific social and geographic spaces ("risk environments"). Identifying these spaces may improve targeting of treatment and prevention activities.

Aims: i) To map and describe the geographic spaces occupied by PWID in Montreal between 2004 and 2017; ii) Identify areas demonstrating heightened clustering ("hotspots") of social injecting activity; iii) Assess potential period effects reflecting an evolving drug epidemic.

Methods: Data were drawn from the HEPatitis COhort (HEPCO), an ongoing longitudinal cohort study established in 2004 to examine individual and contextual determinants of HCV infection. Participants eligible for recruitment reside in the Greater Montreal Area, are aged ≥18 years, and self-report drug injection in the previous 6 months. At regular scheduled visits (six-monthly from 2004 to 2010, three-monthly thereafter), trained interviewers collect sociodemographic and behavioural data, and HCV antibody (2004–) and RNA (2010–) testing is performed. Geographic spaces: Participants report the 6-digit postal code of the place they have slept most often in the past month ("dwelling location") and of the location of their most recent injection episode with (an)other person(s) present ("injecting location"), if applicable.

Analyses: Spatial analyses were performed using a combination of software with spatial analytic functionality (ArcGIS/R/GeoDa). Period effects were assessed by analyzing two sub-periods separately (2004-2010, 2011-2017). Postal codes were geocoded using open-source Google software, and spatial analyses were performed to describe the overall distribution of participant dwelling and injecting locations. Hotspot identification is ongoing; the Getis-Ord Gi* statistic will be used to identify areas demonstrating statistically significant clustering of social injecting locations (under a null hypothesis of random distribution of locations across the Montreal island).

Results: A total of 1540 participants have been recruited since 2004, reporting a total of 9489 dwelling postal codes (2296 unique) and 3892 injecting postal codes (1416 unique). Across both time periods, injecting locations were more concentrated in the downtown Montreal area, as compared to dwelling locations. The mean centre of dwelling and injecting locations has remained stable over time, however, the deviation of participants from that centre is greater in the latter period, suggesting geographical expansion over time. Preliminary results of hotspot analyses suggest a core area focused in the downtown/old town centre that has expanded over time, with an additional pocket emerging in the southwest portion of the island.

Implications: The approach proposed in this study may be used to identify areas that favour HCV transmission and related harms among PWID, and where scale up of both existing and novel interventions is urgently needed.

ID: 45

A Two-eyed Seeing Approach to Wholistic Healing and Wellness for People with Drug Use Experience

Candice Norris, Indigenous Wellness Research Group, Willie Ermine, First Nations University of Canada, Norma Rabbitskin, Sturgeon Lake Health Centre, Matthew Fischer, Indigenous Wellness Research Group, April Roberts-Poitras, Sturgeon Lake First Nation, Emily Scotton, Indigenous Wellness Research Group, Kehinde Ametepee, Simon Fraser University, Sandi Mitchell, Indigenous Wellness Research Group, Terry Howard, Independent, Malcolm King, University of Saskatchewan, Jack Haight, Canadian Aboriginal AIDS Network, Donald Turner, Canadian Aboriginal AIDS Network, Stewart Gonzales, Indigenous Wellness Research Group, Alexandra King, University of Saskatchewan

Purpose: This peer-developed and -led pilot research explores the use of wellness and cultural activities as health and substance use interventions for First Nations and Métis people who use drugs. Community members with lived experience, Elders, researchers and knowledge users, came together in this pilot interventional research using land- and culture-based healing.

Background: Substance use is typically seen by Western society through an individualistic framework, where current health status results from poor decision-making and lifestyle choices and deemed reparable through individual willpower. However, an Indigenous health determinants framework, which emphasizes structural and sociocultural impacts on health, especially colonization, better explains Indigenous over-representation in substance use and related conditions (e.g., hepatitis B/C, HIV). Indigenous peoples have historically used land-based retreats for wholistic wellness. More recently, these are being explored for their effectiveness in restoring connections and promoting healing in the context of substance use. The Medicine Wheel Spirit Shadow Dance (MWSSD) was developed by people living with HIV, many of whom had a history of substance use, as a wholistic, strengths-based approach to promote self-exploration and healing based on medicine wheel teachings.

Methodology: A land- and culture-based retreat which included the MWSSD, with post-retreat activities, was designed as a healing intervention with contextualization by Knowledge Holders for their specific communities. This was piloted in two sites – a First Nation community in Saskatchewan and an urban Indigenous community in British Columbia. A Two-eyed Seeing multi-pronged evaluation included qualitative analysis of intra- and post-retreat sharing circles, self-reflexivity, and an innovative First Nation self assessment tool.

Findings: Preliminary findings identified elements of land- and culture-based healing that are effective at restoring and promoting wellness for Indigenous people who use drugs. The MWSSD provides a shame-free space for sharing of and both individual and collective learning from deeply personal narratives.

ID: 99

Characterization and identification of gaps within the HCV cascade of care among ethnic groups: a population-based cohort study

Margo Pearce, BCCDC, Hasina Samji, BC Centre for Disease Control, Sofia Bartlett, BC Centre for Disease Control, Maryam Darvishian, University of British Columbia, Zahid Butt, University of British Columbia, Carmine Rossi, British Columbia Centre for Disease Control, Maria Alvarez, BC Centre for Disease Control, Mawuena Binka, BCCDC, Amanda Yu, BC Centre for Disease Control, Stanley Wong, BC Centre for Disease Control, Mel Krajden, University of British Columbia, Jason Wong, BC Centre for Disease Control, Mark Gilbert, BC Centre for Disease Control, Geoff Mckee, British Columbia Centre for Disease Control, Mark Tyndall, BC Centre for Disease Control, Eric Yoshida, University of British Columbia, Naveed Zafar, BCCDC

Background: Some minority ethnic groups in Canada are disproportionately affected by HCV infection cmpared to the majority, and may benefit most from recent advances in treatment efficacy and tolerability. Population-level monitoring of people living with hepatitis C (HCV) across the cascade of care is an important method to identify gaps and develop interventions tailored to the needs of different ethnic groups.

Purpose: To describe the burden of HCV and identify gaps within the HCV cascade of care across ethnic groups in British Columbia (BC).

Methods: We analyzed the BC Hepatitis Testers Cohort which included 1.7 million people who tested for HCV, HIV, reported cases of hepatitis B, and active tuberculosis in BC from 1990-2017. Test results were linked to medical visits, hospitalizations, cancers, prescription drugs, and mortality data. Name recognition software was validated using surveillance data where self-reported ethnicity was routinely collected; this process identified five ethnic groups: South Asian (SA), East Asian (EA), European/White (EW), Other (African/Caribbean/Black, West Asian, and Latin American), and Unknown. Six HCV care cascade stages were identified: 1) antibody diagnosed 2) RNA tested; 3) RNA positive; 4) genotyped; 5) initiated treatment; and 6) achieved sustained virologic response (SVR). 2017 HCV care cascade results were stratified by ethnic group.

Results: An estimated 52,987 people were HCV antibody-positive in BC in 2017. Of those, the ethnicity breakdown was: 90.1% EW, 4.2% EA, 4.1% SA, 1% Other, and 0.6% Unknown. Among HCV antibody-positive EW people, 82.5% had RNA testing, and of those RNA positive, 88% (25,434) were genotyped. Of those genotyped, 52% (13,124) initiated treatment, with 90% achieving SVR. Among HCV antibody-positive EA people, 83% (1,839) had RNA testing, and of those RNA positive, 89% (1,121) were genotyped. Of those genotyped, 67% (755) initiated treatment, with 93% reaching SVR. Among HCV antibody-positive SA people, 90% (1,933) had RNA testing, and of those RNA positive, 70% (1,344) were genotyped. Of those genotyped, 62% (777) initiated treatment, with 89% achieving SVR. Among HCV antibody-positive people within the Other ethnicity category, 81% (444) had RNA testing, and of those RNA positive, 92% (283) were genotyped. Of those genotyped, 47% (134) initiated treatment, with 92% achieving SVR. Of participants with Unknown ethnicity, 81% (254) received RNA testing, and of those RNA positive, 85% (159) were genotyped. Of those genotyped, 54% (86) initiated treatment, with 88% achieving SVR.

Conclusions: Gaps in the HCV cascade of care are affecting each ethnic group, most notably for treatment initiation. Lower genotyping within the SA population is of concern. Other/Unknown ethnicity groups had markedly lower rates of RNA testing, genotyping, and treatment initiation. Public health programmers and policy makers must consider involving community members living with HCV in design and delivery of culturally-safe HCV care.

ID: 101

The Cedar Project: Childhood sexual abuse is a risk factor for hepatitis C infection among young Indigenous people who use drugs in Canada

Margo Pearce, BCCDC, Kate Jongbloed, UBC, Wenecwtsin Christian, Splatsin Secwepemc Nation, Eric Yoshida, University of British Columbia, Martin Schechter, UBC, Patricia Spittal, UBC

Background: Hepatitis C (HCV) infection disproportionately impacts Indigenous people in Canada. Indigenous communities are concerned that historical and lifetime traumas stemming from colonization may be contributing to the HCV epidemic.

Purpose: Few studies have explored the longitudinal effects of childhood sexual abuse or physical abuse on HCV risk. Under the direction of our Indigenous governance, the Cedar Project Partnership, we sought to better understand the association of sexual and physical abuse within a cohort of young Indigenous people who have used drugs.

Methods: The Cedar Project is an ongoing cohort study involving young Indigenous people who have used illicit drugs in Vancouver and Prince George, British Columbia, Canada. This study included participants who completed the Childhood Trauma Questionnaire (CTQ) and returned for a follow-up study visit between 2007 and 2016. The CTQ determined experience and severity of sexual and physical abuse, which was dichotomized (none vs. any). Multivariate generalized estimating equations (GEE) explored relationships between sexual abuse and physical abuse and multiple longitudinal adverse health outcomes, adjusting for potential confounders. Adjusted odds ratios (AOR) and 95% confidence intervals (CI) were calculated.

Results: Overall, 420 participants (55% women, 29.5% living with HCV, mean age 24 years) completed the CTQ and had at least one follow-up. In total, 60.2% of participants reported experiencing childhood sexual abuse and 79.2% reported experiencing childhood physical abuse. Sexual abuse was associated with having a parent who attended a government residential school (p=0.002). In multivariate analyses, sexual abuse was associated with 88% higher odds of sex work involvement (95% CI: 1.12-3.16); 93% higher odds of sexual assault (95% CI: 1.07-3.48); 2.5-fold greater odds of high frequency cocaine injection (95% CI: 1.2-4.86); 91% higher odds of binge injection (95% CI: 1.19-3.06); and 67% greater odds of HCV infection (95%CI: 1.05-2.66) in the previous six months. In multivariate analyses, physical abuse was associated with 88% higher odds of inconsistent condom use (95% CI: 1.3-2.7) and 84% higher odds of binge injection drug use (95% CI: 1.15-2.95) in the previous six months. Physical abuse was marginally associated with having an STI in the previous six months (AOR: 1.52; 95% CI: 0.94-2.48; p=0.09).

Conclusion: Childhood sexual and physical abuse experiences continue to negatively impact the wellbeing of young Indigenous people. Direct acting antiviral therapy may lead to HCV eradication if delivered effectively to populations who will benefit the most from cure. HCV infection may be a marker of previous sexual abuse among Indigenous patients. As a result, clinicians must provide trauma-informed and culturally safe liver care and HCV treatment options for Indigenous patients.

ID: 165

Comparing perceptions of illness among patients with chronic liver disease

Izza Sattar, University of Toronto, Joel Karkada, Toronto General Hospital, Nechama Lipton, University of Toronto, Harry Janssen, Toronto Centre for Liver Disease, Bettina Hansen, Institute of Health Policy, Management and Evaluation, Jordan Feld, Toronto Centre for Liver Disease

Background: When diagnosed with a chronic disease, patients' understanding of their illness and its severity may influence the steps they take towards its management. In chronic liver disease, perception of disease severity may be particularly challenging due to its lack of attributable symptoms.

Purpose: The purpose of this study was to examine the relationship between disease perception and disease severity (as measured by degree of liver fibrosis) among patients with various chronic liver diseases.

Method: We administered the Brief Illness Perception Questionnaire (Brief IPQ) to patients at the Toronto Centre for Liver Disease who had been diagnosed with or were receiving treatment for non-alcoholic fatty liver disease (NAFLD), hepatitis B infection (HBV) or hepatitis C infection (HCV), including patients who had achieved sustained virological response (HCV-SVR). Patients were categorized by fibrosis stage as early (F0-2) versus late (F3-4). Greater IPQ scores indicate perception of more severe illness. Individuals with HIV, liver cancer, decompensated cirrhosis or severe comorbidities were excluded.

Results: A total of 465 participants completed the Brief IPQ. Scores were higher in those with advanced compared to mild fibrosis in only NAFLD and SVR patients ($p < 0.0005$ for both). Among low fibrosis patients, the mean score for SVR patients was significantly lower when compared to mean scores for all other groups (30.64 for HBV, 33.91 for HCV, and 30.37 for NAFLD; $p < 0.0005$ for all three comparisons). As well, among high fibrosis patients, the mean score for NAFLD patients was significantly higher than mean scores for all other groups (33.18 and $p = 0.001$ for HBV, 35.04 and $p = 0.017$ for HCV, and 32.07 and $p < 0.0005$ for SVR). Lastly, for the question assessing how much patients perceived treatment to help their illness, both the high and low fibrosis NAFLD groups had significantly greater mean scores compared to all other high ($p = 0.002$ for HBV, $p < 0.0005$ for HCV and SVR) and low fibrosis groups ($p = 0.057$ for HBV and $p < 0.0005$ for HCV and SVR) respectively.

Conclusions: Patients with chronic liver disease seen generally have accurate perception of their disease severity and the efficacy of treatment. The Brief IPQ proved to be a useful and reliable test for assessing disease perception, which may have value for assessing individuals' understanding of and engagement in their disease management.

ID: 185

Systematic review of the efficacy of DAAs in the treatment of HCV genotype 6

Julie Tan, McMaster University, Khurram J Khan, McMaster University, Keith Tsoi, St. Joseph's Healthcare Hamilton

BACKGROUND: Multiple direct-acting antiviral agents (DAA) are now available for the treatment of hepatitis C virus (HCV) with the goal of cure. Of the estimated 185 million HCV infections worldwide, genotype 6 accounts for approximately 2.5%, and is mainly prevalent in South east and East Asian populations. Few of the clinical study data available for DAA efficacy have focused on this genotype. However, in Canada, where genotype 6 patients represent predominantly an immigrant population, information regarding the efficacy of DAAs on this genotype may guide treatment in this often marginalized patient cohort. We have therefore conducted a systematic review of the efficacy of DAAs in the treatment of HCV genotype 6.

METHODS: We searched Pubmed, Embase, and the Cochrane Library for keywords "hepatitis c", "genotype 6", and "direct-acting antiviral genotype 6" producing 432 hits. We included studies on adults infected with HCV genotype 6, with or without cirrhosis or prior treatment, using DAA treatment and sustained virologic response at 12 weeks (SVR12) as the outcome. We excluded conference proceedings, studies including viral co-infection, and studies where number of genotype 6 patients could not be discerned.

RESULTS: A total of 23 studies were analyzed for a total of 717 patients. Studies consisted of 3 randomized controlled trials, 17 Phase 2 and 3 open label clinical trials, 4 retrospective studies, as well as 1 comparative open label study. Sofosbuvir/Velpatasvir with or without Voxilaprevir produced 100% SVR12 in 153 patients with and without cirrhosis or prior treatment. SVR12 was achieved in all 8, 12, and 24 week regimens with this regimen. Glecaprevir/Pibrentasvir yielded a 98% SVR12 for 107 of 109 patients. Sofosbuvir/Ledipasvir achieved 91% SVR12 in 270 of 296 patients. Sofosbuvir/Daclatasvir achieved SVR12 at a rate of 97% in 37 of 38 patients. Sofosbuvir/Simeprevir found SVR12 in 100% of 3 patients. Elbasvir/Grazoprevir achieved SVR12 in only 69%, 45 of 65 patients. Sofosbuivir/Ribavirin produced SVR12 in 100% of 53 patients. These DAAs were generally well tolerated, however, event rate was small for major adverse events. Where data regarding polymorphisms in NS3, NS5A, and NS5B were available, these did not show consistent effect regarding treatment efficacy. However, emerging in vitro data suggest that particular substitutions may be associated with highly resistant subtypes of genotype 6.

CONCLUSIONS: There is an overall consistent and high rate of SVR12 for most DAAs against genotype 6, particularly amongst the pangenotypic combinations Sofosbuvir/Velpatasvir and Glecaprevir/Pibrentasvir, where cirrhosis status and prior treatment history had minimal impact. Our data support the use of pangenotypic regimens in the less-studied genotype 6 population.

ID: 46

Stamsh Slhanay Lhawat: Warrior Women Healing

Bernice Thompson, Indigenous Wellness Research Group, Candice Norris, Indigenous Wellness Research Group, Sharon Jinkerson- Brass, Indigenous Wellness Research Group, Emily Scotton, Indigenous Wellness Research Group, Terry Howard, Indigenous Wellness Research Group, Kehinde Ametepee, SIMON FRASER UNIVERSITY, Malcolm King, University of Saskatchewan, Alexandra King, University of Saskatchewan

The importance of culture and ceremony in infectious disease treatment with Indigenous women."

Purpose: This study captures the experiences and wisdom of a group of Indigenous women from Vancouver's Downtown Eastside (DTES) in the development of a culture- and land-based, Indigenous-led, wellness program for urban Indigenous women which includes strategies for wellness and prevention of diseases such as HCV, and other infectious and chronic diseases.

Background: Indigenous women are traditionally the matriarchs and healers in their communities. However, colonization, patriarchy, oppression, trauma and persistent structural inequities have denied many their connection to wellness. While urban Indigenous women have been invisible in health service planning and program development, they remain over-represented among victims of violence and diseases. Indigenous health and primary healthcare researchers have recommended equity-oriented, culturally safe, trauma- and violence-informed care as a wise practice for Indigenous people experiencing health inequities. Few interventions are aimed at improving the health and wellness of Indigenous women and their families through wholistic perspectives based on Indigenous knowledges, spirituality and ceremony.

Methodology: Four sets of Elder-led sequential sharing circles, supplementary conversational interviews and a land-based retreat - all grounded in culture- and land-based activities - were held with 23 Indigenous women who reside in the DTES. Data collection and analyses were guided by Indigenous research methodologies. In addition, research team members and participants were included in the planning of the Nəc̓amat Indigenous Women's Village of Wellness 2018 hosted by Vancouver Coastal Health.

Findings: Based on ongoing analyses, the findings specify the necessity of culture and ceremony, families and meaningful relationships, and the creation of safe spaces for Indigenous women to thrive in their journey to wellness. The underlying impacts of the intersection of colonialism, systemic racism and gender significantly affect their lived realities. Most importantly, these findings reveal the importance of resilience and willingness to lead and direct HCV- specific and other health programming and services for urban Indigenous women.

ID: 51

Uptake of testing, linkage to care, and treatment for hepatitis C infection among people who inject drugs in Australia: The ETHOS Engage Study

Heather Valerio, The Kirby Institute, UNSW Sydney, Maryam Alavi, The Kirby Institute, UNSW Sydney, David Silk, The Kirby Institute, UNSW Sydney, Carla Treloar, Centre for Social Research in Health, UNSW Sydney, Andrew Milat, NSW Health, Adrian Dunlop, Newcastle Pharmacotherapy Service, Jo Holden, NSW Health, Charles Henderson, NUAA, Janaki Amin, Faculty of Medicine and Health Sciences, Phillip Read, Kirketon Road Centre, Louisa Degenhardt, National Drug and Alcohol Research Centre, UNSW Sydney, Gregory J Dore, The Kirby Institute, Jason Grebely, Kirby Institute, UNSW Sydney

Background: People who inject drugs (PWID) are at high risk of hepatitis C virus (HCV) infection but have poor access to HCV treatment in most settings. Unrestricted direct-acting antiviral (DAA) therapy has been available in Australia since March 2016. Further data is needed on uptake of HCV DAA therapy among PWID and the impact of treatment on HCV prevalence.

Purpose: Our objective was to evaluate burden of HCV and the extent of, and factors associated with, engagement with the HCV cascade of care among PWID in an era of unrestricted DAA therapy access.

Method: ETHOS Engage is an observational cohort study collecting demographic, behavioural and clinical data among PWID attending drug treatment clinics and needle and syringe programs in Australia. All PWID underwent point-of-care (POC) HCV RNA testing via Xpert® HCV Viral Load Finger-Stick assay. Multivariate logistic regression models were used to identify demographic and behavioural factors associated with treatment uptake.

Results: Between May and November 2018, 507 PWID were enrolled. Overall, 70% had injected drugs in the last month, and 70% were currently receiving opioid substitution therapy (OST). Of all enrolled, 73% (n=370) were ever HCV-infected (Ab positive), and 58% (n=296) were ever chronic HCV-infected (RNA positive or prior treatment). Among those Ab positive (n=370), 76% had previously been tested for HCV RNA. Among those with evidence of current or past chronic HCV (n=296), 86% had ever been linked to care and 68% had ever received treatment for HCV. Uptake of HCV therapy was high across sub-populations, including those with current and no OST (71%, 59%) recent injecting (last month) (70%), and heroin (68%), other opioid (57%) and amphetamine (70%) injecting in the last month. In adjusted analysis, no factors were associated with treatment uptake. Among those with a POC HCV RNA result at enrolment, 26% had current HCV infection (HCV RNA+ve), 33% had treatment-induced clearance, 17% spontaneous clearance, and 23% were uninfected (HCV Ab-ve). The proportion with current HCV infection was similar across demographic and behavioural sub-populations.

Conclusion: The DAA era in Australia has produced high treatment uptake and lowered HCV viraemia among PWID attending drug treatment and needle syringe programs. To reach elimination targets, subgroups of PWID may require additional support to encourage further screening and engagement with HCV care.

Clinical Research

ID: 181

Barriers to the uptake, adherence, and efficacy of hepatitis C treatment with direct-acting antivirals: a review of reviews

Ayoub Abulkhir, McGill University , Kim Engler, MUHC , Nadine Kronfli, McGill University , Joseph Cox, McGill University , Giada Sebastiani, McGill University , Isabelle Vedel , McGill University , Bertrand Lebouché, McGill University

Background

The new direct acting-antiviral (DAA) therapies are highly efficacious, well-tolerated, and of short duration. Despite these advances in therapy, there remains several barriers to treatment initiation, adherence, completion, and/or success, including deficiencies in screening, diagnosis, and access to care as well as the high cost of DAA. There is a need to better characterize barriers and to assess their impact on the use of DAAs, as well as related adherence and success in curing hepatitis C virus (HCV).

Methods

We thus conducted a review of reviews and searched PubMed and Embase for relevant articles. Three concepts were targeted: 1) HCV, 2) HCV treatment, and 3) barriers to HCV treatment. Eligibility criteria included English-language; reviews of any type, published between 2014-2018, that concerned western countries; presented results on second generation DAA and HCV treatment initiation, adherence, completion, and/or success. The review title, abstract or results also needed to mention "barriers" to HCV treatment or its synonyms. Records were imported to Endnote (version X8) and duplicates were removed. Two researchers screened the titles and abstracts to identify records for full text examination which they subsequently assessed for inclusion. We conducted a thematic synthesis of barriers to the use of DAA.

Results

A total of 374 records were screened for inclusion. From these, 36 were retained for full text review. Six reviews met the eligibility criteria. The synthesis revealed three types of barriers:

1. Patient-related barriers: clinical factors are the major barrier to HCV treatment in the era of DAA. Medical co-morbidity is a the most common barriers to DAA. Other barriers include, personal preferences not to start DAA, fear of the diagnosis and treatment side effects, and concerns about drug-drug interactions. Lack of knowledge about the HCV treatment cascade, the outcomes and the complications of not being treated. Commuting difficulties to the HCV clinic.
2. Socio-behavioural barriers: barriers cited most frequently were factors such as use of illicit drugs, alcohol abuse, low education, unemployment, financial burdens, unstable housing, and chaotic lifestyle, and problems with public transportation.
3. Healthcare system-related barriers: the most frequently mentioned barriers were poor management of side effects by healthcare professionals, inadequate physician and health care provider knowledge, high treatment cost, insurance plans that do not cover DAAs, and government restriction of treatment with DAAs.

Conclusion

This review of review offers an extensive portrait of barriers to uptake, adherence and completion of DAA treatment of HCV in western countries.

These results might be useful for clinicians in adapting treatment plans so as to mitigate potential barriers ultimately promoting person-centered approach. A better understanding of the barriers that are most important could be understood by using survey-based Delphi methods.

ID: 178

Tracing Progression through the Cascade of Care among Patients with Hepatitis C Infection in a specialised Clinic

Ruoke Chen, Université de Montréal, Emmanuelle Huchet, Clinique de Médecine Urbaine du Quartier Latin, Marc Poliquin, Clinique de Médecine Urbaine du Quartier Latin, Jean-Guy Baril, Clinique de Médecine Urbaine du Quartier Latin, Pierre Coté, Clinique de Médecine Urbaine du Quartier Latin, Alexandra Hamel, Clinique de Médecine Urbaine du Quartier Latin, Serge Dufresne, Clinique de Médecine Urbaine du Quartier Latin, Antoine Cloutier-Blais, Clinique de Médecine Urbaine du Quartier Latin, Danièle Longpré, Clinique de Médecine Urbaine du Quartier Latin, Benoit Trottier, Clinique Médicale du Quartier Latin, Nima Machouf, Clinique de Médecine Urbaine du Quartier Latin

Background: The hepatitis C virus (HCV) is a major public health problem. Since 2009, hepatitis C has been declared an epidemic in Montreal. However, with the current simplified direct-acting antivirals (DAAs) therapy regimens, HCV elimination becomes a feasible target.

Purpose: We describe the current state of HCV infected patients attending health services in Urban Medical Clinic Quartier Latin (CMUQL), which is one of the most important centers in Montreal. It specializes mainly in the screening, treatment and clinical follow-up of HIV and HCV. CMUQL is a low threshold clinic and offers drug substitution / maintenance program as well. In order to evaluate the effectiveness of HCV care of the clinic, we build this CMUQL HCV care cascade.

Method: Lab data, medical follow-up, liver stiffness and treatment information are all registered in the electronic medical chart (EMC). All patients with positive HCV antibody were identified and included in this analysis. HCV positive patients with more than two medical visits were considered to be linked in care. We went through each HCV positive patient's file to trace if the person had HCV RNA testing, underwent fibrosis assessment (by either biopsy, ultrasound or fibroscan), began and completed treatment, and achieved sustained virologic response (SVR). For patients with HCV re-infection or multiple treatments, we considered only the last situation which probably overestimates the SVR because there were more multiple treatments (n=88 patients) than cases of re-infection (n=29 patients).

Results: A total of 1291 antiHCV+ patients were identified. Of these HCV positive patients, 1254 (97%) were linked to care, 1066 (83%) had an RNA test, 761 (59%) underwent liver fibrosis assessment and 78 (6%) cleared the virus spontaneously. In our cohort of patients, 876 had received treatment (68% of antiHCV+ patients or 72% of those who needed treatment). While 70 are still on treatment, 703 (89%) reached the end of treatment. Finally among treated patients, 62 are waiting for the 3 months post-treatment evaluation (3m-postTx) and 699 achieved SVR which represent 94% of 3m-postTx patients. With a conservative evaluation and imputing the previous success-rate to the patients who are still on treatment, we estimate that 65% of our antiHCV+ patients are now free of HCV.

Conclusions: Analyses showed that in an HIV/HCV specialized clinic with substitution program and holistic care, maintaining patients into care could be successful. The largest gap in the HCV care cascade was seen in fibrosis assessment (resolve now with possibility of indoor fibroscan) and initiating treatment. Greater emphasis on linking patients to clinical evaluation and treatment is necessary in order to achieve the elimination of hepatitis C as a public health threat.

ID: 169

Engaging vulnerable, treatment naïve persons living with hepatitis C in same-day treatment

Shawn Greenan, Health PEI, George Carruthers, Dalhousie University, Lisa Barrett, Dalhousie University

Background To eliminate viral hepatitis C (HCV) for vulnerable populations need to exist. The greatest barrier to HCV elimination is engaging people to initiate and complete HCV treatment after positive diagnosis. Rapid, same-day treatment for Human immunodeficiency virus (HIV) has demonstrated both better HIV and non-HIV related health care engagement.

Purpose: To determine if the rapid, same-day access to HCV treatment improves engagement for vulnerable, treatment naïve persons living with HCV in both in HCV and non-HCV health care.

Methods: Persons living with HCV are identified and referred to Canada's Prince Edward Island Phase 2 Provincial, Coordinated HCV Elimination Program through the Department of Public Health, community providers, or 'bring a friend' strategies. The Elimination Program facilitate baseline blood work, conduct pre-visit, drug-drug interaction checks, and schedule an initial appointment within 1-2 weeks of bloodwork. Treatment naïve individuals without contraindications are offered glecaprevir/pibrentasvir treatment at the first visit. Self-reported medication adherence, side effects, sustained virological response (SVR12), and attendance at scheduled opioid substitution therapy (OST) clinic visits are recorded.

Results: Patients assessed between February and October 2018 were included. 102 patients were referred and 73 (71.5%) were seen for an initial appointment. 71/73 (97.2%) treatment naïve individuals started treatment, 67/71 (94.3%) on the first visit. Of those who attended the first visit and did not start immediately, 5 had medication interactions requiring adjustment, and 1 person was pregnant. There were 3 discontinuations for non-HCV related medical reasons, and 1 person was lost to follow-up before SVR. To date, all 52 people past the treatment completion date finished treatment, and 23/32 have documented SVR12 (9 people did not have SVR12 bloodwork but completed full treatment course). Importantly, individuals with difficulty attending OST appointments before HCV treatment had improved attendance at appointments after HCV treatment start. Attendance at non-HCV health care appointments was variably improved. No safety issues were noted.

Conclusions: Rapid treatment start is safe, and has a very high rate of successful HCV and non-HCV care engagement. Same day, first visit HCV health treatment start should be explored as an HCV elimination tool.

ID: 25

Ophthalmic Complications of Non Alcoholic Fatty Liver disease: A cross sectional Observational clinical study

Dr. Patrick Basu, Cornell University Medical Center ,NY **,** Nimy John, St. Vincent Hospital , Aloysius Madhok, JJP VAMC Icahn School of Medicine at Mount Sinai

Objective:

This study reveals a unique ocular complication of NAFLD - Premature Cataract formation in a Non-Diabetic cohort of NAFLD.

Method:

Four Hundred (n=400) NAFLD patients were initially recruited from age group 50 to 60 with BMI >30%. The mean HbA1c was less than 7.1. The mean weekly Alcohol consumption was less than 30 grams. Patients underwent Serum NAFLD score analysis, abdomen sonogram, ECHO, Carotid Doppler for atheroma Volume, Fibroscan for Base Line fibrosis and Ophthalmic Evaluations. All patients were placed on strict regulated Weight loss and exercise for 6 months. All patients had measurement of Leptin, Adiponectin, Retinol Binding Protein 4, Triglyceride, HOMA score, TNF Alfa levels prior to the study. Patients also underwent sleep studies to look for sleep apnea.

Patient Characteristics	
Male	213
Female	187
Age group	50 to 60
Age (Median)	57
BMI (Mean)	25.7
Race	
Asian	128/400 (32%)
Caucasian	35/400 (8.75%)
African American	23/400 (5.75%)
Hispanic	78/400 (19.5)
Pacific Islander	136/400 (34%)
Baseline Serum Triglyceride (Median)	**273**
HbA1c	**6.5–7.1 (Median–6.7)**
HOMA Score (Median)	**2.9**
Leptin (Median)	**7.3**

TNF Alfa (Median)	**2.9**
Liver/Spleen Ratio	**1.33**
Hypertension	
Male	133
Female	82
Acanthosis Nigricans	
Male	156
Female	96
Carotid Atheroma (Mean)	**> 56%**
Male	22%
Female	14%
MRE fat (Mean)	**> 69%**
Male	123
Female	98
Genetic Assay	
PLPAL P 3 Homozygotes	51%
NCAN Homozygotes	26%
APOC3 Homozygotes	54%

Table 1

Results:

Characteristics of patients with Premature cataract

No of Patients with premature cataract formation	278/400 (69.5%)
BMI (Mean)	Greater than 32%
HOMA score (Median)	3.6 (High)
Leptin (Median)	7.3 (High)
TNF Alpha (Median)	2.8 (high)
Adiponectin levels (Median)	0.7 (Low)
Sleep Apnea Score	Moderate (3 times per sleep in 8 hours)

Serum Triglyceride (Median) 273 mg/dl (Elevated)

Conclusion:

Our study showed that NAFLD is associated with early development of Cataract formation in NAFLD, especially in the subgroup of high Inflammatory markers (High levels of TNF Alfa and Leptin, Sleep apnea, High Triglyceride levels, Elevated HOMA score and Moderate Atheroma load with normal Glucose Homeostasis). Patients with NAFLD will benefit with regular ophthalmologic evaluations to screen for premature cataract development.

ID: 26

Sofosbuvir, Velpratasvir, Veloxpravir Efficacy in 12 week treatment in triple infected (Chronic Hepatitis C, Chronic Hepatitis B and HIV} Geno 3 naive population: An open level prospective clinical trial - SOLVVE – C

Dr. Patrick Basu, Cornell University Medical Center ,NY**,** Nimy John, St. Vincent Hospital, Aloysius Madhok, JJP VAMC Icahn School of Medicine at Mount Sinai

Objectives:

This study evaluates the efficacy and safety of Sofosbuvir, Velpratasvir, and Veloxpravir in the treatment of triple infection with HBV, HIV, and HCV (Genotype 3).

Methods;

Twenty-two (n = 22) HCV treatment-naive patients with Triple Infection (HIV HBV HCV Genotype 3) were recruited for the study.

Patients with HIV were on Atripla for over three years with HIV with Undetectable Viral load and HBV Viral load Undetectable. HCV infected patients had a Median Viral load of 3 million IU and Genotype 3 prior to treatment.

Demographics:

Patient Characteristics					
Race	**No of Patients**		**Mode of transmission**		
	Males	**Females**	**IVDU**	**MSM**	**Blood transfusion**
African-American	1	0	1	0	0
Caucasian	1	0	0	1	0
Haitian	2	0	0	0	2
Asian	0	18	1	0	17
India	0	4	1	0	3
Pakistan	0	12	0	0	12
Bangladesh	0	2	0	0	2
Total	4	18	2	1	19
Mean Age	56 (44 – 68)				
Mean BMI	27 (21 – 29.6)				
Mean Fibrosis	F3				
Patient HBV characteristics					

Race	**No of Patients**		**Genotype**					
	Males	**Females**	**A**	**B**	**C**	**D**	**G**	**H**
Asian	0	18	0	1	5	12	0	0
India	0	4	0	1	0	3	0	0
Pakistan	0	12	0	0	3	9	0	0
Bangladesh	0	2	0	0	2	0	0	0
Caucasian	1	0	1	0	0	0	1	0
African-American	1	0	1	0	0	0	1	0
Haitian	2	0	0	0	0	0	2	2

HBV Characteristics

HBeAg Negative	19
HBeAg Positive	3
HBsAg Positive	22
HBcAb Positive	22

Results:

Results

Duration of treatment	HCV Viral load	
	Viral load - Undetectable	Viral load detectable
a. Fourth week	18/21	3/21 detectable, 200 copies mean
b. Eighth week	18/21	3/21 detectable
c. Twelfth week	18/21	
d. Twenty fourth week	18/21	

Resistance-associated substitution	**Pre-therapy**	**Post-therapy**
RAS 31	1	3
RAS 36	0	1
RAS 93	1	1

Conclusion:

The study demonstrates the efficacy of DAAs in 12-week treatment with an SVR of 87% in a very challenging triple infected cohort, with significant efficacy, tolerability, and safety. A larger trial is needed to validate the results.

ID: 152

Risks of hepatitis C virus reactivation in a real life population of oncology patients treated in an academic center

Catherine-Audrey Boutin, Université de Montréal, Jean-Philippe Adam, CHUM , Dominic Martel, Centre de recherche du Centre hospitalier de l'Université de Montréal , Stephane Doucet, Centre de recherche du Centre hospitalier de l'Université de Montréal , Valerie Martel-Laferriere, Centre de Recherche du Centre hospitalier de l'Université de Montréal

Background Chemotherapy has been associated with a theoretical risk of hepatitis C virus (HCV) reactivation. A recent prospective study illustrated a 23% incidence of HCV reactivation and a 43% incidence of hepatitis flare in chronic HCV carriers receiving chemotherapy. However, little is known about the amplitude of viral replication, the incidence of subsequent hepatic exacerbation during and after chemotherapy and the impact on chemotherapy treatment.

Purpose We aimed to describe the occurrence of hepatitis flare and HCV reactivation (HCVr) at the Centre hospitalier de l'Université de Montréal (CHUM), a tertiary academic center.

Method In this case-series, we included patients with chronic HCV receiving chemotherapy at our institution over a period of 5 years. Inclusion criterias consisted of patients aged 18 years and older with detectable HCV RNA who received intravenous chemotherapy for the treatment of hematological or solid cancers between August 2013 and June 2017. We excluded patients with undetectable HCV RNA, hepatocellular carcinoma, liver metastases or other etiologies of hepatic disease including chronic HBV and NAFLD. The primary objective was to identify hepatic flares defined as elevation of alanine aminotransferase (ALT) 3 times above the upper limit of normal. Secondary objectives were to assess HCVr (HCV-RNA ≥1 log10 IU/mL when compared to baseline value), hepatic decompensation, mortality and the impact on the chemotherapy treatment plan. Descriptive statistics were used.

Results A total of 11 patients with chronic HCV were identified among the 5761 oncology patients who received intravenous chemotherapy at the CHUM. Only 36% of all patients followed from 2015 to 2017 were tested for HCV with a prevalence of chronic HCV of less than 1%. Seven patients were treated for solid cancers while 4 patients received chemotherapy for hematological malignancies. All patients were HCV treatment naïve and three showed previous exposure to HBV, none with chronic infection. Four patients displayed a FIB-4 between 1.45 and 3.25 while seven patients had a FIB-4 score less than 1.45. Five patients experienced a hepatic flare with median maximal ALT value of 139 U/L (IQR 133-237). Only 2 patients met criteria for HCVr with a median RNA increase of 1.16 log IU/mL (IQR 1.11-1.20). One patient presented with both HCVr and a hepatic flare. Only one patient required chemotherapy discontinuation following the hepatic flare. No hepatic decompensation or mortality following hepatic flare were observed.

Conclusion We identified a very small number of HCV cases among our oncology population receiving intravenous chemotherapy. Possible explanations include under-diagnosis and strict selection criteria for chemotherapy, including ECOG, social factors and exclusion of advanced liver disease. We observed HCVr and hepatic flares, but only one clinical consequence on the cancer treatment. HCV screening is encouraged among patients undergoing chemotherapy to allow close follow-up of hepatic function and seamless care for future HCV treatment.

ID: 89

Profile of Patients with Chronic HCV Infection initiating DAA Treatment in Canada based on Risk for HCV Transmission: The Real-World C-RESPECT Study

Brian Conway, Vancouver Infectious Diseases Centre **,** Daniel Smyth, The Moncton Hospital , Rejean Thomas, Clinique medicale l'Actuel , Alexander Wong, Regina Qu'Appelle Health Region , Giada Sebastiani, McGill University , Curtis Cooper, University of Ottawa , Hemant Shah, University of Toronto, Toronto Centre for Liver Disease , Estelle Bene, Merck Canada Inc, Ritesh Kumar, Merck & Co. Inc. ,Ted Watson, Merck Canada Inc.

Background: Populations at high risk for Hepatitis C virus (HCV) infection include people who inject drugs (PWID) and men who have sex with men (MSM); identified as "core transmitters" (CT) for the maintenance of the epidemic in the developed world. Understanding the clinical and social characteristics of these groups is important to guide clinical care.

Purpose: The aim of this analysis was to describe and compare the disease parameters, sociodemographic characteristics, and behaviors of Core Transmitters (CT), both PWID and MSM, and non-CT HCV-infected patients treated with direct-acting antiviral (DAA) in clinical care across Canada.

Methods: C-RESPECT is an ongoing, prospective, observational study of HCV-infected patients treated with DAAs. In this interim analysis, patients enrolled between 03/2017 and 09/2018 were included.

Results: A total of 236 participants (CT: 131; non-CT: 105) were considered. Baseline demographics and characteristics among CT and non-CT patients are shown in Table 1. Overall, significant differences were observed between groups in age, socioeconomic status, food/housing security, incarceration, genotype, current smoking, BMI, and fatigue score. The most common comorbidities were chronic pain (CT: 24.4%; non-CT: 18.1%), non-alcoholic fatty liver disease (CT: 4.6%; non-CT: 15.2%), and diabetes (CT: 4.6%; non-CT: 10.5%).

Conclusion: The results of this analysis have shown that significant differences exist at the time of DAA initiation in the profile of CT and non-CT patients being treated for HCV infection. Future analyses will compare response to therapy between these two groups with an emphasis on factors associated with non-response. Long-term follow-up of CT patients will also be undertaken to evaluate the incidence and correlates of re-infection post-SVR12.

Table 1: Patient Demographics and Characteristics at Baseline by Group

Parameter	CT n=131	Non-CT n=105	P-Value
Age: years, mean (SD)	45.0 (11.5)	56.3 (10.1)	**<0.001 (S)**
Male gender, n (%)	87 (66.4%)	77 (73.3%)	0.251 (P)
Caucasian, n (%)	107 (81.7%)	88 (83.8%)	0.107 (F)
Currently insecure about food/housing, n (%)	48 (36.6%)	24 (22.9%)	**0.020 (P)**
Ever incarcerated, n (%)	77 (58.8%)	35 (33.3%)	**<0.001 (P)**

Smoker, n (%)	109 (83.2%)	48 (45.7%)	**<0.001 (P)**
Illicit drug use, n (%)	104 (79.4%)	30 (28.6%)	**<0.001 (P)**
BMI, kg/m^2, mean (SD)	26.3 (6.5)	25.7 (6.1)	**0.008 (W)**
Previous HCV infection, n (%)	17 (13.0%)	19 (18.1%)	0.263 (P)
Patient genotype, n (%)			
1a	58 (44.3%)	46 (43.8%)	**0.040 (F)**
1b	7 (5.3%)	14 (13.3%)	
3	50 (38.2%)	23 (21.9%)	
4	1 (0.8%)	2 (1.9%)	
Mixed	2 (1.5%)	2 (1.9%)	
Hepatic fibrosis assessment performed, n (%)	102 (77.9%)	78 (74.3%)	0.607 (P)
Fatigue severity score, mean (SD)	41.8 (14.6)	34.6 (15.6)	**0.001 (W)**

ID: 16

Direct Acting Antiviral Exposure and Sustained Virologic Response Do Not Influence Liver Steatosis in Most Patients

Chrissi Galanakis, Ottawa Hospital Research Institute, Erin Kelly, The Ottawa Hospital , Cynthia Tsien, University of Ottawa, Thomas Shaw-Stiffel, The Ottawa Hospital, Gary Garber, The Ottawa Hospital Raymond Corrin, The Ottawa Hospital, Curtis Cooper, University of Ottawa

Background and Aims: HCV infection perturbs lipid homeostasis and steatosis. Influence of DAA exposure and SVR on liver steatosis is uncertain. Controlled Attenuation Parameter (CAP) is an accepted non-invasive method for evaluating steatosis.

Purpose: To determine changes in liver steatosis following HCV treatment with DAA therapy.

Methods: HCV patients treated with DAA at The Ottawa Hospital Viral Hepatitis Program, Ottawa, Canada with available baseline (BL) and post-treatment (PT) CAP data obtained by transient elastography (TE) were included in this evaluation. PT CAP score defined as the most recent value obtained at least six months post DAA treatment. BL characteristics and co-morbid conditions were obtained from chart review. Excess alcohol (ETOH) use was assessed in the year prior to starting treatment. Advanced fibrosis and cirrhosis were defined as TE scores >9.0 and >12.5 kPa, respectively. Changes in CAP score from BL to PT were determined by Wilcoxon Signed rank tests and mean differences between patient groups were assessed by Wilcoxon rank-sum test with significance levels at $p < 0.05$.

Results: 64 patients were included. Patients were male (70%), had a mean age of 57 years (SD 8.4) with a mean weight of 80 kg (SD 16.8). 51 (80%) were genotype 1-infected, 8 (13%) had diabetes (DM), 15 (23%) used excess ETOH and 4 (6%) were HIV co-infected. BL CAP was 249 dB/m (SD 56) and fibrosis score was 21.3 kPa (SD 17.8). 50 (78%) had advanced fibrosis and 36 (56%) were cirrhotic. PT CAP scores were 263 dB/m (SD 62) (measured 424 days (SD 170) post treatment completion). Overall, no change in CAP score was observed from BL to PT ($p=0.11$). 23/64 (36%) had a decrease (>5%) in CAP score, 33 (52%) had an increase (>5%) and 8 (12%) had no change. Those with S3 steatosis (CAP > 286) had a decrease in CAP (mean difference -18.5 dB/m) while patients without S3 steatosis had greater CAP scores PT (mean difference 22.9 dB/m, $p=0.04$). CAP score increased PT in DM (mean difference 56 dB/m, $p=0.02$) and in HIV (mean difference 93 dB/m, $p=0.01$) patient groups. No change in PT CAP was observed for sex ($p=0.33$), excess ETOH ($p=0.24$), genotype 3 infection ($p=0.99$), advanced fibrosis ($p=0.26$), cirrhosis ($p=0.54$) and SVR ($p=0.07$).

Conclusions: DAA and HCV cure are not associated with short term change in liver steatosis in most patient populations. Steatosis was noted to increase post treatment in those with DM, in those without severe baseline steatosis and in HIV seropositive treatment recipients. These observations require further validation and explanation.

ID: 50

Hepatitis C virus reinfection following antiviral treatment among people who inject drugs: a systematic review and meta-analysis

Behzad Hajarizadeh, The Kirby Institute, Evan Cunningham, UNSW Sydney, Heather Valerio, The Kirby Institute, UNSW Sydney , Marianne Martinello, The Kirby Institute, UNSW Sydney, Matthew Law, The Kirby Institute, UNSW Sydney, Naveed Zafar, BCCDC , Håvard Midgard, Oslo University Hospital, Olav Dalgard, Akershus University Hospital, John Dillon, University of Dundee, Matthew Hickman, University of Bristol, Julie Bruneau, Université de Montréal, Gregory J Dore, The Kirby Institute, Jason Grebely, Kirby Institute, UNSW Sydney

Background: Among individuals with ongoing injecting drug use (IDU), hepatitis C virus (HCV) reinfection following successful therapy can compromise treatment outcome. However, there are little data on HCV reinfection following successful therapy among people who inject drugs, particularly in the era of direct-acting antiviral therapy.

Purpose: This systematic review assessed HCV reinfection rate after treatment among people with recent IDU and those receiving opioid substitution therapy (OST).

Methods: Bibliographic databases and conference abstracts were searched for studies assessing HCV reinfection rate after treatment among people with recent IDU or those receiving OST. Meta-analysis was used to cumulate reinfection rates and meta-regression to explore factors associated with heterogeneity across studies.

Results: Twenty-two eligible studies were included [total person-years follow-up (PYFU)=5112], including sub-population data of people with recent IDU (19 studies, PYFU=4116) and people receiving OST (11 studies, PYFU=1905). Recent IDU definition varied across studies (IDU during HCV treatment or post-treatment follow-up most commonly used). HCV reinfection rate was 5.4 per 100 PYFU (95%CI: 3.2, 8.9) among people with recent IDU, and 2.7 per 100 PYFU (95%CI: 1.4, 5.4) among those receiving OST. Reinfection rate was comparable between post-interferon-containing therapy (4.6 per 100 PYFU; 95%CI: 2.4, 8.8), and post-DAA therapy (3.4 per 100 PYFU; 95%CI: 2.3, 5.1). In stratified analysis, reinfection rate was 1.3 per 100 PYFU (95%CI: 0.5, 3.2) among people receiving OST with no recent IDU, 3.6 per 100 PYFU (95%CI: 1.5, 9.1) among those with recent IDU who also received OST, and 4.6 per 100 PYFU (95%CI: 2.1, 10.3) among those with recent IDU, not receiving OST. In adjusted meta-regression analysis, longer follow-up was significantly associated with lower reinfection rate [adjusted Rate Ratio (aRR) for each year increase in mean/median follow-up: 0.79 (95%CI: 0.67, 0.92; P=0.005), while using end of treatment as the start point of time-at-risk of reinfection, compared to 12 weeks post-treatment (SVR12) or later, was significantly associated with higher reinfection rate (aRR: 2.54 (1.28, 5.04; P=0.011). Diagnosis of reinfection following end of treatment was based on virus sequencing data, or genotype-switch.

Conclusion: Post-treatment HCV reinfection rate was the highest among people with recent IDU, not receiving OST. Higher rate in studies assessing reinfection from the end of treatment and lower rate in studies with longer follow-up suggested higher risk of reinfection early post-treatment. Harm reduction services are required to reduce the reinfection risk while regular post-treatment HCV assessment is required to detect and treat reinfection early.

ID: 11

Nonalcoholic fatty liver disease increases the risk of incident cardiometabolic complications and all-cause mortality in HIV-infected persons

Thomas Krahn, Mcgill University Health Centre , Nadine Kronfli, McGill University , Julian Falutz, Mcgill University Health Centre , Giovanni Guaraldi, University of Modena and Reggio Emilia , Marina Klein, McGill University Health Centre , Ruth Sapir-Pichhadze, Mcgill University Health Centre , Philip Wong, McGill University , Marc Deschenes, McGill University , Peter Ghali, McGill University , Giada Sebastiani, McGill University

Background: Non-alcoholic fatty liver disease (NAFLD) has been linked with extra-hepatic diseases, including all-cause mortality and the development of cardiometabolic comorbidities such as type II diabetes mellitus (T2DM), dyslipidemia, hypertension and chronic kidney disease. Cardiometabolic comorbidities and liver diseases are both major contributors to morbidity and mortality in people living with HIV (PLHIV). Aging PLHIV are also at particular risk of NAFLD. We hypothesized that the presence of NAFLD and associated liver fibrosis will increase the incidence of cardiometabolic comorbidities and all-causes death in PLHIV.

Methods: The LIVEr disease in HIV (LIVEHIV) Cohort Study is a routine screening program for NAFLD and liver fibrosis in PLHIV running at the McGill University Health Centre. Since 2013, participants undergo yearly transient elastography (TE) examination with associated controlled attenuation parameter (CAP), in addition to routine clinical measurements, biochemical parameters, imaging studies, and subspecialty referrals. NAFLD was defined as a CAP value ≥248 dB/m and the exclusion of alcohol abuse. Significant liver fibrosis was defined as a TE value ≥7.1 kPa. Incidence rates were computed as event per 1000 person-years (PY). Kaplan-Meier survival analysis, the log rank test, and adjusted Cox proportional hazard models were computed.

Results: Until August 2018, 777 PLHIV (mean age 49, 77% males, 34% coinfected with hepatitis C virus, mean CD4 619) were included. Prevalence of NAFLD and significant liver fibrosis at baseline was 30% and 27%, respectively. During a median follow-up period of 44 months, the incidence rate of hypertension, chronic kidney disease, dyslipidemia and T2DM was 3.1, 2.1, 3.7 and 1.6 per 1000 PY, respectively. NAFLD predicted development of hypertension ($p=0.005$), dyslipidemia ($p<0.001$), and T2DM ($p<0.001$). There were 35 deaths, yielding a mortality rate of 1.0 per 1000 PY. Both significant liver fibrosis and NAFLD predicted all-cause mortality (see Table 1). On multivariable analysis, NAFLD was an independent predictor of incident T2DM (adjusted hazard ratio [aHR]=2.1, 95% CI 1.0-4.7) after adjustments. Significant liver fibrosis was also an independent predictor of all-cause mortality (aHR=6.5, 95% CI 1.3-35.0).

Conclusion: PLHIV with NAFLD are at risk of incident cardiometabolic comorbidities and increased all-causes mortality. Screening strategies for NAFLD and liver fibrosis may help identify patients benefitting from early referral strategies and more aggressive management of cardiometabolic risk. Improved monitoring of liver health in PLHIV could lead to better targeting of lifestyle modification and management of comorbidities for greater longevity.

Table 1. Incidence rates of all-cause mortality by NAFLD and significant liver fibrosis status and relative log-rank test result.

Condition	**Incidence rate of mortality**	**p-value**
NAFLD present	1.2 per 1000 PY	0.001
NAFLD absent	0	

Significant liver fibrosis present	1.1 per 1000 PY	0.010
Significant liver fibrosis absent	0.1 per 1000 PY	

ID: 156

Toronto HCC risk index (THRI) and albumin predict low risk of hepatocellular carcinoma (HCC) after sustained virological response (SVR) in HCV infection

Jason Lau, Toronto Centre for Liver Disease, Lisette Krassenburg, Toronto Centre for Liver Disease, Wayel Zanjir, Toronto Centre for Liver Disease, Firass Georgie, Toronto Centre for Liver Disease, Orlando Cerocchi, University of Toronto, Emily Stotland, Toronto Centre for Liver Disease, Heidy Morales, Toronto Centre for Liver Disease, Harry Janssen, Toronto Centre for Liver Disease, Bettina Hansen, Institute of Health Policy, Management and Evaluation, Jordan Feld, Toronto Centre for Liver Disease

Background:

Current guidelines recommend hepatocellular carcinoma (HCC) surveillance for all F3/F4 after sustained virological response (SVR), however not all patients with advanced fibrosis are at equally high risk of HCC. HCC surveillance is unlikely to be cost effective if the incidence is below 1.3%/year.

Purpose: This study aimed to identify factors associated with a low enough risk of HCC post-treatment to forego HCC surveillance.

Method:

Data were collected from the Toronto Centre for Liver Disease from 06/2006 to 10/2018 for all patients with advanced fibrosis (AST-to-platelet ratio index≥1, FIB-4≥1.45, liver stiffness≥9.5 kPa or biopsy≥F3) who achieved HCC. Toronto HCC risk index (THRI) combines age, sex, etiology, and platelet count to categorize patients with F4 as low (THRI<120), intermediate (THRI=120-240), or high HCC risk (THRI>240). Baseline patient data were collected at start of treatment and patients were followed from end of treatment until HCC occurrence, transplant, or death. Cox regression was used to identify factors associated with a low risk of HCC post-treatment.

Results:

Of 1,093 F3/F4 patients who achieved HCC, 397 (36.3%) received interferon-based and 696 (63.7%) received direct-acting antiviral therapy. Median age was 57.7 (IQR 52.1-63.1) years, 420 (38.4%) were female and 703 (64.3%) had cirrhosis. Patients were followed for median 1.4 (0.6-2.9) years: 4.1 (1.4-7.7) years for interferon patients and 1.0 (0.4-1.7) years for direct-acting antiviral patients. Forty-one (3.8%) patients developed HCC. By multivariable analysis, higher albumin and lower THRI were associated with decreased HCC risk. Baseline albumin >40 g/L (HR=0.228 (0.101-0.516), P<0.001) and THRI <120 (HR=0.317 (0.098-1.029), P=0.056) predicted a lower risk of HCC. Prognosis was improved in patients with albumin >40 g/L or THRI <120, and best in patients with albumin >40 g/L and THRI <120. Of 541 (49.5%) patients with albumin >40 g/L, 7 (1.3%) developed HCC (incidence = 0.52% per person-year) and none of the 137 patients with albumin >40 g/L and THRI <120 developed HCC.

Conclusion:

Among hepatitis C patients with F3/F4 and HCC, patients with baseline THRI<120 and albumin >40 g/L have a very low risk of HCC. If confirmed with longer follow-up, HCC surveillance could be avoided in these individuals.

ID: 41

Feasibility of rapid hepatitis C point-of-care RNA testing and linkage to care at an integrated supervised consumption site in Toronto, Canada

Kate Mason, South Riverdale Community Health Centre, Bernadette Lettner, South Riverdale Community Health Centre, Erin Mandel, University Health Network, Frank Crichlow, South Riverdale Community Health Centre, Jason Altenberg, South Riverdale Community Health Centre, Jeff Powis, Toronto Community Hep C Program, Jordan Feld, Toronto Centre for Liver Disease

BACKGROUND: In Canada, most new cases of Hepatitis C (HCV) occur among people who inject drugs, yet relatively few engage in HCV care or initiate antiviral treatment. The recent expansion of supervised injection/consumption services (SCS) across Canada offer a new and unique opportunity to engage people who use drugs in HCV care.

PURPOSE: To evaluate the feasibility of rapid, point-of-care HCV RNA testing and subsequent linkage to HCV care among service users of a small-scale SCS co-located within a primary care community health centre in Toronto.

METHODS: The SCS can accommodate up to 5 injections/consumptions at a time with an average of 10 unique person visits daily. Posters in the consumption area, staff referrals, and word of mouth advertised study participation to registered SCS service users who inject drugs and were not currently engaged in HCV antiviral treatment. An onsite HCV treatment nurse completed baseline surveys with participants to capture socio-demographics and history of HCV care. Testing was also conducted by the HCV treatment nurse 2.5 days per week using a HCV Viral PCR Finger-Stick assay, allowing for RNA results within 1 hour. Other SCS staff (Nurses, Health Promoters, Harm Reduction Workers) provided additional post-testing counseling when required. Participants that tested positive for HCV RNA were connected with the onsite HCV treatment and support program. RESULTS: 79 service users consented to participate in the first five months. Two were removed for ineligibility. Of 77 participants, 65% were male with an average age of 42 years. Two thirds (66%) had unstable/no housing and 68% reported daily injection drug use. More than half (57%) reported a history of HCV testing. Of these, only two reported they had received RNA testing and nearly half (49%) didn't know what type of HCV testing they had received. Of those tested in the SCS,13 results were invalid. Five participants agreed to repeat testing. Of the 66 valid tests, 32% (N=21) were positive. Of those testing positive, 10 have started further HCV assessments at the health centre, 3 are attending a weekly HCV education and support group, one has completed treatment and one participant died due to accident.

CONCLUSIONS: Interest in POC testing was high, as was engagement in HCV care among those found to be HCV RNA positive. Testing uptake remains limited primarily by the low number of new and unique service users at the SCS. Ongoing access to the HCV treatment nurse within the SCS and SCS staff with lived experience of HCV likely facilitated linkage to care. POC RNA testing can successfully position SCS as an alternative single point of HCV care access, allowing for more integrated care and increased HCV treatment uptake among people who inject drugs.

ID: 161

Transcriptomic analyses of the immune response during HCV re-infections

Sabrina Mazouz, CRCHUM, Nathalie Bedard, (CRCHUM), Omar Khedr, CRCHUM, Julie Bruneau, Université de Montréal, Naglaa Shoukry, CRCHUM

Background: Development of efficient vaccines against chronic viral infections like HCV is hampered by our limited understanding of the cellular and molecular pathways that form a potent protective memory immune response that is effective in "real-life" settings. Transcriptome analysis of primary and memory responses in murine models of viral infection demonstrated that different gene clusters distinguish effector and memory T cells, with memory T cells becoming imprinted with transcriptional programs that reduce exhaustion and facilitate rapid proliferation and long-term survival[1]. Our results during acute primary HCV infection demonstrate activation of pathways associated with innate immune activation, interferon signaling, and reduced B cell signatures[2]. Transcriptomic signatures of memory responses during a real-life human viral re-exposure remain unexplored.

Purpose: The goal of this proposal is to compare the transcriptomic and functional signatures of immune response to primary HCV infection versus reinfection and their contribution to long term protective immunity.

Methods: As a preliminary analysis, we selected 6 patients, from our Montreal cohort of people who inject drugs, who became re-infected after spontaneously clearing an initial HCV infection. Among them, four successfully resolved the subsequent re-exposure, while two became chronically infected. For this analysis, PBMC samples collected at baseline (Pre-infection), early acute (~ 4 weeks), late acute (~ 12 weeks) and follow-up phase (~ 48 weeks) of each infection episode of reinfection were used to perform bulk RNA-seq.

Results: Similar to primary infection, principal component analysis (PCA) of the top variable 500 genes showed complete separation of early acute time-points from the baseline and follow-up time points, unveiling a clear separation between virus-positive versus virus-negative samples, in resolvers. Such distinct PCA signatures were not observed in chronics. Modules differentially regulated during each episode were determined using blood transcriptome modules (BTM) with an FDR <0.74. BTM analyses in resolvers revealed global down-regulation of different immune modules, at the early acute time-point, apart from two modules that are up-regulated in all patients: the immunoregulation-monocytes, T and B cells, and the myeloid, dendritic cell activation via NFkB modules. In contrast, there was no common pattern of differentially expressed BTMs with most of the modules being up-regulated overtime in chronics.

Conclusions and future directions: As compared to primary acute infection, resolution of the second infection is associated with a shorter duration and magnitude of viremia. Thus, acute HCV re-infection might be missed or elicits a non-detectable transcriptional response in total PBMCs of resolvers. The response may be limited to a small subset of immune cells. To answer this issue, we will increase the number of patients with shorter time differences between the baseline and the acute time-points and focus on T cell targeted or single cell RNA-seq.

References:

1. Doering TA et al, *Immunity 2012*

2. Rosenberg BR et al, *PLoS Pathogens 2018*

ID: 52

High incidence of drug-drug interactions with hepatitis C direct-acting antivirals in patients that have been hospitalized during their treatment

Laurence Messier, Centre hospitalier de l'Université de Montréal, Virginie Verreault, Centre hospitalier de l'Université de Montréal , Philippe Arbour, Centre hospitalier de l'Université de Montréal **,** Chloé Trudeau, Centre hospitalier de l'Université de Montréal, Suzanne Marcotte, Centre hospitalier de l'Université de Montréal, Nancy Sheehan, McGill University Health Centre; Faculté de pharmacie, Université de Montréal, Valerie Martel-Laferriere, Centre de Recherche du Centre hospitalier de l'Université de Montréal, Michèle Bally, Centre de recherche du Centre hospitalier de l'Université de Montréal, Ludovick Larocque-Laplante, Centre hospitalier de l'Université de Montréal, Dominic Martel, Centre de recherche du Centre hospitalier de l'Université de Montréal

Background: Direct-acting antivirals (DAAs) remain a challenge regarding drug-drug interactions (DDIs). Incidence of DDIs with DAAs in ambulatory cohorts is well established, but has not been assessed in inpatient populations.

Purpose: The study aims to assess the cumulative incidence of DDIs between DAAs and co-medications of patients hospitalized in the course of their hepatitis C virus (HCV) treatment. Secondary objectives are to assess the severity of DDIs and their predictive factors, and to measure virological success and describe hospital pharmacists' interventions.

Method: MONTREAL-C is a retrospective single-centre study. Patients hospitalized from December 2013 to December 2017, and treated with interferon-free DAA regimens were included and assessed for cumulative incidence of DDIs. Occurrence and severity of DDIs were evaluated using online drug interaction checker tools and, in the absence of available data, by a committee of three pharmacists with clinical expertise in HCV treatment. Predictive factors for DDIs were identified with univariate and multivariate logistic regressions analyses using Stata (IC version 14.2). Treatment success was evaluated with the achievement of a sustained virologic response at week 12 (SVR). All other statistical analyses were performed with SPSS (IBM SPSS Statistics, Version 25).

Results: A total of 113 inpatients, accounting for 164 hospitalizations, were included. The median number of co-medications per hospitalization was 15 (interquartile range, IQR 10-20). Overall, 68.1% (95% CI 59.4%-76.9%) of patients and 64.6% (95% CI 54.7%-73.4%) of hospitalizations presented at least one potential DDI with a DAA regimen. Among the 235 DDIs identified, 3.8% were classified as contraindicated. Most frequently involved co-medications in DDIs in this study were gastric acid modifiers. Female gender (odds ratio (OR) 2.91 95% CI 1.21-7.00; $p = 0.017$) and polypharmacy of more than 10 co-medications (OR 5.64 95% CI 2.48-12.85; $p < 0.001$) were identified as predictive factors for DDI in the multivariate logistic regression analysis. Despite numerous DDIs and many patients treated with sofosbuvir/ribavirin (38%), 87.5% of patients achieved SVR. Out of the 56 interventions performed by hospital pharmacists, 53.6% were related to management of DDIs.

Conclusions: This is the first study to report data on patients that have been hospitalized during their HCV treatment. Inpatients are at high risk for DDIs where polypharmacy is frequent. SVR rates remained high in patients being hospitalized during their HCV treatment. Caution is warranted to identify and manage DDIs in inpatients on DAAs and hospital pharmacists can play a key role.

ID: 141

Correlation Between Baseline FIB4 and APRI Scores With Transient Elastography Prior To Hepatitis C Therapy In British Columbia

Robert Mitchell, University of British Columbia **,** Seyed Amir Mohajerani, GI Research Institute, Pacific Gastroenterology Associates , Steven Pi, University of British Columbia , Hin Hin Ko, University of British Columbia , Alnoor Ramji, University of British Columbia

Background: Measurement of hepatic fibrosis is an essential step in the initial assessment of patients with chronic hepatitis C virus (HCV). In recent years, non-invasive measurement of fibrosis in HCV has involved the use of transient elastography (TE). This modality of fibrosis measurement is not widely available outside of tertiary hepatology clinics. HCV treatment has become simpler, more widespread, and in some regions is being initiated by general practitioners. For this to continue to occur, widely available methods of non-invasive hepatic fibrosis measurement must be explored. Fibrosis-4 (FIB4) and AST to platelet ratio index (APRI) are simple, easily available methods of non-invasive fibrosis measurement. The 'real-world' utility of these tests in Canada is lacking.

Purpose: To assess the performance of APRI and FIB4 in predicting fibrosis for patients with HCV, using transient elastography as a 'gold-standard' comparison.

Methods: Retrospective chart review was conducted from patient data collected at two hepatology clinics in British Columbia between January 2006 and January 2019. Baseline demographics, TE (FibroScan) scores, and laboratory parameters for calculation of FIB4 and APRI were collected. Only patients with complete evaluation prior to HCV therapy were included.

Results: 1530 patients were reviewed, and 1226 had baseline transient elastography measures were enrolled in the study. The mean age of patients was 61.4 ±8.9 years. When utilizing TE as the 'gold standard' for fibrosis (F) level, the mean baseline FIB4 and APRI compared to TE stage F1 were 1.6±0.99 and 0.66±0.5, for F2 were 2.03±1.21 and 0.95±0.86, for F3 were 3.01±2.31 and 1.67±1.79, and for F4 were 5.33±3.6 and 2.7±2.8, respectively. Based on Spearman correlation analysis, FIB4 correlation to fibrosis ($r=0.57$, $p<0.001$) was higher than APRI correlation to fibrosis ($r=0.45$, $p<0.001$). In those persons with FIB4<1.45 and APRI<0.7, TE F1 fibrosis was 77% and 71%, respectively. In persons with FIB4>3.25 and APRI>2, the proportion of correct fibrosis stage F4 was 69% and 66%, respectively. In persons with FIB4 <1.45 and APRI<0.7 the proportion of stage F3,4 fibrosis by TE was 6% and 17% respectively.

Conclusion: Persons with low FIB4 scores (and to a lesser extent, low APRI scores) can accurately exclude the absence of extensive fibrosis, as measured by TE. Conversely, FIB4 and APRI are not accurate in assessing for the presence of advanced fibrosis. FIB4 may be useful as a fast, easily accessible, bedside 'rule-out' tool for advanced fibrosis in the real-world HCV treatment setting.

ID: 103

Increased Risk of Renal insufficiency In Chronic Hepatitis B Patients on Treatment With Tenofovir disporoxylate fumarate (TDF) Compared To Lamivudine

Nick Pang, University of British Columbia**,** Seyed Amir Mohajerani, GI Research Institute, Pacific Gastroenterology Associates, Yousef Alshamli, University of British Columbia, Hin Hin Ko, University of British Columbia, Alnoor Ramji, University of British Columbia

Background: The long-term use of Tenofovir disporoxylate fumarate (TDF) is associated with proximal tubular dysfunction in HIV and less often in Chronic Hepatitis B (CHB) patients. There is minimal 'real-world' Canadian data on the incidence and risk factors for developing renal insufficiency.

Purpose: The primary aim was to compare the proportion of CHB patients developing renal insufficiency between patients being treated with TDF and those being treated with Lamivudine (LAM) which is standard of care in British Columbia. The secondary aim was to evaluate risk factors for the development of renal insufficiency in these CHB patients.

Methods: In a retrospective study in an academic tertiary clinic between 2014 and 2019, 345 patients were enrolled in the study. All patients had to be on a minimum of 1-year of either TDF or LAM. Renal function using GFR (mL/min) levels were measured prior to treatment initiation and every 3-6 months. GFR<60 mL/min was defined as renal insufficiency. Data collected included patient demographics, and risk factors for renal insufficiency including advanced age (>65), diabetes mellitus, and hypertension.

Results: A total number of 345 patients were included in the study, with 174 patients treated with Tenofovir (TDF) and 171 with Lamivudine (LAM). The mean (±SD) age was 55.4±12.2 in TDF group and 59.17±12.1 in LAM. Out of the 171 LAM patients, 74 were female and 97 were male, and in TDF group, 41 were female and 133 were male. The mean GFR at baseline was 89.7 mL/min ±15.8 in TDF group, and 91.7 mL/min ±13.05 in the LAM group (p=0.36). Cirrhosis (Fibroscan >12.5) was present in 35 out of 174 (20%) of patients on TDF, and 4 out of 171 (2%) on LAM. No patient in LAM group developed renal insufficiency. In the TDF group 16 (9.1%) of 174 patients had a decrease in GFR level to <60 mL/min. The baseline GFR in these 16 patients was 69.3 mL/min ±8.7 and nadir mean GFR was 48.6 mL/min ±7.3 (P=0.01). Out of these 16 patients, 4 patients were switched to Entecavir; and GFR subsequently increased in these patients to 58 mL/min ±8.9 which was significantly higher than their lowest GFR point (48.6±7.3) (p=0.01). The duration of TDF therapy before a decrease of GFR<60 mL/min was 4.25 ±1.9 years. Two risk factors were present in 10 (62%) of the 16 TDF patients with GFR <60 mL/min, whereas only 5 (3%) of 158 persons who did not develop renal insufficiency.

Conclusion: In a 'real-world' setting CHB patients treated with TDF were more likely to have GFR <60 mL/min compared to those on LAM therapy. The impact of TDF on renal function appears to be more profound when there is a presence of 2 risk factors for renal disease.

ID: 144

Health utilities in chronic hepatitis C patients with advanced liver disease

Yasmin Saeed, Leslie Dan Faculty of Pharmacy, University of Toronto**,** Arcturus Phoon, Toronto Health Economics and Technology Assessment (THETA) Collaborative, University Health Network, Josephine Wong, Toronto Health Economics and Technology Assessment (THETA) Collaborative, University Health Network, Jordan Feld, Toronto Centre for Liver Disease, David Wong, Toronto Centre for Liver Disease, Hemant Shah, University of Toronto, Toronto Centre for Liver Disease, Julie Bruneau, Université de Montréal, Zeny Feng, University of Guelph, Nicholas Mitsakakis, TORONTO GENERAL HOSPITAL, Jeff Powis, South Riverdale Community Health Centre, Welson Ryan, Toronto Health Economics and Technology Assessment (THETA) Collaborative, University Health Network, Valeria Rac, Toronto Health Economics and Technology Assessment (THETA) Collaborative, University Health Network, Karen Bremner, Toronto Health Economics and Technology Assessment (THETA) Collaborative, University Health Network, 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) can progress to cirrhosis, decompensated cirrhosis (DC), and/or hepatocellular carcinoma (HCC) if untreated. Health utility is a preference-based approach to measuring health-related quality of life on a 0-1 (dead-full health) scale. There are limited utility data from CHC patients with advanced liver disease.

Purpose: To measure the impact of liver disease severity on health utilities in patients with CHC.

Methods: We recruited CHC patients from the liver, pre-liver transplant, and gastrointestinal oncology clinics at the University Health Network, Toronto, Ontario. Trained interviewers administered the Health Utilities Index (HUI) Mark 2/3, EuroQol-5D (EQ-5D), time trade-off (TTO), and visual analogue scale (VAS) utility instruments, and collected sociodemographic and clinical information. Regression analysis was used to examine the impact of liver disease severity on utilities with adjustments for sociodemographic and clinical factors.

Results: Utilities were collected from 175 patients. Most were male (61%) with an average age of 58 years. Most patients were born in Canada (59%), most were unemployed (62%), and many had a history of mental health disorders (35%).

The mean ± standard error HUI2 utilities were: no cirrhosis 0.811 ± 0.174 (n=74); compensated cirrhosis 0.755 ± 0.203 (n=33); DC 0.723 ± 0.236 (n=31); HCC 0.764 ± 0.226 (n=25); HCC+DC 0.680 ± 0.221 (n=12). Stratifying by Child-Pugh class (cirrhotic patients only), HUI2 utilities were: Class A 0.761 ± 0.209 (n=59); Class B 0.710 ± 0.231 (n=33); Class C 0.676 ± 0.260 (n=8).

The regression analysis showed that compensated cirrhosis (coefficient: -0.06), DC (-0.06), and HCC+DC (-0.07) were associated with similar reductions in utility compared to no cirrhosis; while HCC (-0.09) was associated with a greater reduction. Immigrants (+0.06) and those with successfully treated CHC (+0.08) had higher utilities; while unemployment (-0.11) and a history of mental health disorders (-0.08) were associated with substantially lower utilities. Only the covariates for unemployment and mental health reached statistical significance ($p<0.05$).

Results from the other utility instruments showed similar trends. The TTO instrument was associated with the highest utilities and the HUI3 was associated with the lowest utilities.

Conclusions: Our results suggest that CHC patients with advanced liver disease experience substantial impairment in health utility, although impairment was less than expected for DC and/or HCC. These findings are similar to previous research, and may be related to selection effects. Stratifying disease severity by Child Pugh class showed a clearer association with health utility than liver disease stage.

Factors associated with marginalization such as unemployment and mental illness clearly affected global health status (reduced utility scores) in these patients.

This research can improve our understanding of the burden of advanced CHC and the benefits of treatment and elimination efforts.

ID: 5

Elevated HCV reinfection rates after cure or spontaneous clearance among HIV-infected and uninfected men who have sex with men

Carmine Rossi, British Columbia Centre for Disease Control, Zahid Butt, University of British Columbia, Maryam Darvishian, University of British Columbia, Stanley Wong, BC Centre for Disease Control, Amanda Yu, BC Centre for Disease Control, Mawuena Binka, BCCDC, Maria Alvarez, BC Centre for Disease Control, Mel Krajden, University of British Columbia, Naveed Zafar,

Background and Aims: Increasing rates of hepatitis C virus (HCV) infection associated with ongoing risk activity have been reported after successful cure or viral clearance, particularly among HIV-infected men who have sex with men (MSM). There has been considerably less information on HCV reinfection risk factors in this population. We assessed factors associated with reinfection after treatment-induced or spontaneous clearance (SC) in both HIV-infected and uninfected MSM in British Columbia, Canada.

Method: We identified HIV-infected and uninfected MSM who achieved sustained virologic response (SVR) to HCV treatment or had SC with ≥1 subsequent HCV RNA measurement in the British Columbia Hepatitis Testers Cohort. Crude reinfection rates per 100 person-years (PYs) were calculated. Cox regression was used to model adjusted hazard ratios (HRs) and 95% confidence intervals (CI) for reinfection, overall, and by HIV status.

Results: We identified 1,349 HCV-infected MSM with SVR (n=856) and SC (n=493), of which 349 (26%) were HIV-positive. HIV-infected MSM were more likely to have achieved viral clearance through SVR (76% vs. 59%), had histories of injection drug use (IDU; 41% vs. 21%), alcohol use (22% vs. 14%) and mental health disorders (47% vs. 28%), compared to HIV uninfected. A total of 98 reinfections were identified, yielding an overall reinfection rate of 1.9 per 100 PY (1.0 for SVR patients and 2.7 per 100 PY for SC). HIV-infected MSM had higher rates of reinfection (3.1 vs. 1.6 per 100 PY) than HIV uninfected individuals. In multivariable analysis, age < 35 years (HR 3.1, 95% CI: 1.2, 8.1), cure through SVR (HR 0.2, 95% CI: 0.1, 0.4), HIV infection (HR 2.0, 95% CI: 1.3, 3.1), problematic alcohol use (HR 2.0, 95% CI: 1.2, 3.3), IDU (HR 2.7, 95% CI: 1.6, 4.3) and mental health (MH) counseling (HR 0.2, 95% CI: 0.1, 0.4) were independently associated with reinfection, overall. Among HIV-infected, age < 35 years (HR 2.7, 95% CI: 1.0, 7.5) and MH counseling (HR 0.4, 95% CI: 0.1, 0.9) remained associated with reinfection, but IDU (HR 1.9, 95% CI: 0.8, 4.2) was less strongly associated. Among HIV uninfected, alcohol use (HR 3.0, 95% CI: 1.7, 5.7) and IDU (HR 2.7, 95% CI: 1.5, 4.9) remained the largest independent predictors of reinfection.

Conclusion: Rates of HCV reinfection remain elevated among HIV-infected and uninfected MSM. Ongoing substance use is driving reinfection among HIV-negative MSM, while sexual transmission may be more important among HIV-positive MSM.

ID: 183

Homelessness impact on active drug use among hepatitis C infected population

Astou THIAM, Vancouver Infectious Diseases Centre **,** Rossitta Yung, Vancouver Infectious Diseases Centre , Tianna Magel, Vancouver Infectious Diseases Centre , Julie Holeksa, Vancouver Infectious Diseases Centre , Letitia Chu, Vancouver Infectious Diseases Centre , David Truong, Vancouver Infectious Diseases Centre , Brian Conway, Vancouver Infectious Diseases Centre

Background: The elimination of hepatitis C virus (HCV) infection as a public health concern is in within reach. However, certain populations may have reduced access to curative all-oral HCV therapy, despite systematic outreach initiatives

Purpose: Our aim is to evaluate the impact of unstable housing and its correlates on the use of drugs among inner city vulnerable populations receiving direct acting agents HCV treatment.

Method: We conducted a retrospective analysis of all patients receiving all-oral HCV therapy at our centre between 03/14-12/17. The effect of the homelessness variable (and its correlates) on successful HCV therapy was measured by statistical analyses using Chi square and logistic regression models with SPSS IBM V24

Results: We included 215 participants, 74% (160/215) males, 39% active/recent (83/215), 49% remote drug users (106/215), median age of 56 years old, 15% HIV co-infected patients (32/215) ; SVR was achieved in 91.2 % (196 / 215) cases. With respect to the primary variable of interest, 28% (60/215) had unstable housing and 13% (28/215) were homeless). Homelessness was significantly associated with active drug use (68%, 19/28) compared to the non-homeless population (34%, 64/187); (chi square test: 11.6; p=0.001). All homeless participants were active or remote drug users. Homeless participants were much less likely to achieve HCV cure (71.4%; 20/28 versus 94.1%; 176/187; $p < 0.001$). The predictors of active drug use were homelessness, aged between 49-40 and coinfection [OR: 4.32; CI: 95% (1.77-10.54); $p = 0.001$], [OR: 4.05; CI: 95% (1.84-8.90); $p = 0.001$] and [OR: 2.54; CI: 95% (1.13-5.72); $p = 0.024$] respectively.

Conclusions: In our cohort, homelessness was the driving factor of failure of HCV therapy and strongly associated with active drug use. Engagement of this population in HCV care must include measures to address housing needs and addiction care to maximize the public health benefit of this intervention.

ID: 88

Two decades of HCV epidemic in Manitoba: outcomes of chronic HCV infection

Julia Uhanova, University of Manitoba, Casandra Dolovich, University of Manitoba, Robert Tate, University of Manitoba, Gerald Minuk, University of Manitoba

Background: Due to a worldwide epidemic, chronic hepatitis C virus (HCV) infection have become important social and health care issues resulting in an increased demand for hospital-based and outpatient health care. Utilizing two decades of public and administrative health data, we documented 20-year longitudinal trends in the epidemiology and clinical outcomes of HCV infection in a large population-based cohort with a provincial population of approximately 1.3 million. Following the first diagnosed case of HCV infection in 1991, approximately 450 newly reported cases have been identified in Manitoba yearly. In recent years the numbers have been declining, so that 7,827 residents have been diagnosed with hepatitis C over 20 years.

Methodology: This longitudinal study utilized the Manitoba Public Health, administrative and clinical databases (Figure 1). The Hepatitis C research database links hospital discharge abstracts, physician services claims records, community pharmacy prescription data, population registry and viral hepatitis surveillance and clinical data for all persons diagnosed with hepatitis C in Manitoba and age-, sex-, region-matched population controls in the ratio of 1:5. We aimed to document trends in the following important variables: incidence and prevalence of newly reported chronic HCV infection, liver disease-related morbidity, rates of hepatic decompensation, including rates of liver transplant and hepatocellular carcinoma, and mortality.

Results: Total all-cause mortality among chronic hepatitis C cases was much higher than among controls (18.6% vs 5.3%, $p<0.0001$). Individuals with chronic HCV infection had 5.95 times the risk of dying as compared to the controls (AOR 5.95, 95% CI 5.44-6.51, $p <0.0001$). Out of 7,828 cases with chronic HCV infection, 9% developed decompensated cirrhosis compared to 1% of controls. Thus, 5.7% of HCV cases and 0.55% of controls developed esophageal varices, 3.65% vs. 0.42% had ascites. Among HCV-infected persons, 136 cases of HCC occurred compared to 38 cases among controls. 44 cases and 40 controls underwent liver transplant. The proportion of decompensated cirrhosis was similar between males (9.4%) and females (8.5%), $P>0.2$. Almost half of the HCV-infected cases with decompensated disease had multiple events (e.g. ascites and varices) compared to only 18% of controls ($P<0.0001$). Time to first decompensated event from the first diagnosis of HCV infection was 4.7 years, at the mean age of 48 yrs. Of note, 70% of chronic HCV cases and 40% of controls with decompensated cirrhosis had died during the study period (1992-2012).

Conclusions: This research database allowed for a precise and multidimensional focus on various clinico-demographic features and longitudinal variations of the outcomes of chronic HCV infection. There is a significant increase in all-cause mortality related to chronic HCV infection, both for men and women. Decompensated liver disease occurred with a similar frequency in men and women.

Health Services Research

ID: 134

NPs as site champions in HCV case-finding and treatment in primary care

Mia Biondi, Toronto General Hospital, University Health Network**,** Hemant Shah, University of Toronto, Toronto Centre for Liver Disease, Jordan Feld, Toronto Centre for Liver Disease, Cheryl Dale, SpecialtyRx Solutions

Background: The CASL HCV Clinical Practice Guidelines recommend HCV birth cohort screening; however there has yet to be uptake studies in primary care in Ontario (PC). Primary care providers (PCPs) are also often the first point of contact for at-risk populations. In particular, Nurse Practitioners (NPs) have been shown to be more likely than their physician colleagues to work with youth; those who are homeless; spend more time in street outreach; and accommodate walk-ins. A recent US study demonstrated that although visits to PCPs following a positive HCV RNA are increasing and greatly exceed specialty; PC treatment initiation remains low. Yet, data from the ASCEND trial demonstrated that once treatment is initiated, SVR rates in PC are significantly higher than specialty; with appointment adherence highest among NP-treaters. In many provinces, NPs currently prescribe DAA therapy, though novel methods to engage NPs has not occurred. Thus, the aim of this study was to assess the feasibility of a systematic approach for PC NPs to become HCV site champions.

Methods: We engaged NPs within two models of PC in London, Ontario. The first, included 30 NPs from Canada's largest family health team (FHT), with 19 sites, and 150,000 patients. In FHT models, an NP sees clients rostered to several GPs. In the second organization, a Nurse Practitioner-Led Clinic (NPLC), with two sites, 4 NPs act as MRPs. Although much smaller, many NPLCs serve populations at-risk for HCV acquisition. NPs received a one-day NP/hepatologist-led training, and ongoing continuing education. NPs were encouraged to screen as per the guidelines; and organically develop approaches to engage team members. As screening rates were already high in the NPLC, the objective was to chart review and create a HCV-free NPLC. NPs were given intake and treatment algorithms, and the number and types of inquiries from NPs were recorded. Questions requiring specialist consult were answered by a hepatologist.

Results: 11 NPs participated in the single day training. After 2.5 months of screening, FHT NPs have screened 192 individuals. Interestingly, one NP mailed requisitions for birth cohort screening for a single roster (902 patients), with 101 results received in one week. To date, no new positives have been identified within the FHT, but 4/7 NPs have initiated care with 6 known positive patients; 3 now on DAAs. Within the NPLC, one NP caseload has been reviewed; yielding 98 screens. Of this cohort 2/98 new RNA positives were identified, and 2/98 were known positives not engaged in care. All four have achieved SVR. The six months screening, treatment initiation, and SVR rates will be available at CanHepC.

Conclusions: Our study demonstrates that formalized initiatives to engage and educate NPs in screening and treatment of HCV has the potential to uncover innovative strategies, and create NP leaders in the treatment and elimination of HCV in Ontario.

ID: 140

Canadian Mental Health Association and Addictions Clinics: A Lean NP-Model of Hepatitis C Care

Cheryl Dale, SpecialtyRx Solutions , Ken Lee, Canadian Mental Health Association/ Addiction Services of Thames Valley , Rania Rabie, South Lake Regional Health Centre , Mia Biondi, Toronto General Hospital, University Health Network

BACKGROUND: The World Health Organization is promoting elimination of Hepatitis C (HCV). New therapies carry few side effects and less complex treatment regimens, making HCV treatment easier to manage and more tolerable for patients. This provides an opportunity to treat patients who were previously denied or ineligible due to comorbidities or barriers. A new model of care utilizing Nurse Practitioner (NP) HCV led clinics was established in Southwestern Ontario (SWO) within mental health and addictions clinics to meet the needs of patient populations who were unable to attend traditional clinics. Our aim was to evaluate if utilizing the "meeting the patient where they are at" model would increase engagement in treatment of HCV. We also decided that while wrap-around services within addictions centers may be helpful, this "lean" model of HCV treatment allowed the client to choose whether they desired these services. METHODS: In 2017, a single NP led HCV clinic was established within a Canadian Mental Health Association primary care clinic and a Rapid Access Addictions Medicine Clinic. Patients were assessed by an experienced hepatology NP and included onsite fibroscan when required. Treatment candidates engaged with a treatment nurse and pharmacy team. By 2018, other local practitioners started referring to the NP clinic, and 3 more sites were initiated. In early 2019, 2 additional NP led clinics were added due to demand for the service. RESULTS: In two years of utilizing this model, at three sites, NPs received 55 HCV referrals, despite these clinics being in the same region as multiple established treatment centres. Of these, 44/55 were HCV RNA positive, with 64% GT1a, 5% GT1b, 5% GT1 (unspecified), 18% GT2, and 7% GT3. Two patients were referred to local hepatology, due to suspected HCC and portopulmonary syndrome. Of the remaining 42, 35 have initiated treatment, with 55% not at SVR end-point. Among the 45% who completed treatment, 100% were undetectable at SVR12. An unexpected outcome is that, 5% of referrals are now coming from a mix of primary care providers, mental health and addictions nurses, counsellors, and peers of treated patients. The fourth treatment site was added in mid 2018 and referral, treatment initiation, and SVR data will be available at the CLM. CONCLUSIONS: This NP model of HCV care, led to barrier free, streamlined, efficacious care for HCV patients within settings where the patients were comfortable. Retention of patients with co-morbidities of addiction, and severe mental health issues was achieved, despite many patients having previously not returned to traditional clinics for care. New referral patterns and collaborations are resulting in increased treatment for difficult to reach patients. This quick to access HCV care, with an individualized approach to meeting patient needs offers another option for HCV care.

ID: 42

The potential impact of a provincial prison-based universal testing and treatment strategy on HCV transmission among people who inject drugs in Montréal, Canada: the mathematical modelling perspective

Arnaud Godin[1], Joseph Cox[1,2], Michel Alary[3,4,5], Nadine Kronfli[2], Mathieu Maheu-Giroux[1]

1-Department of Epidemiology, Biostatistics, and Occupational Health, McGill University, Montréal, Canada. 2-Division of Infectious Diseases/Chronic Viral Illness Service, Department of Medicine, Glen site, McGill University Health Centre, Montréal, Canada. 3- Centre de recherche du CHU de Québec, Axe Santé des populations et pratiques optimales en santé, Hôpital Saint-Sacrement, Québec, Canada. 4- Département de médecine sociale et préventive, Université Laval, Québec, Canada. 5- Institut national de santé publique du Québec, Québec, Canada.

Background: In Canada, the hepatitis C (HCV) burden is concentrated among current or former people who inject drugs (PWID). This key population faces high incarceration rates, and is most often in contact with the provincial prison system (sentence duration <2 years). PWID and people in prison have been identified as key populations for HCV acquisition and transmission. Programs are currently underway in Canada to treat all people with chronic HCV in federal prisons (sentence durations of ≥2 years). As a result of short direct-acting antivirals (DAAs) ranging from 8 to 12 weeks, people in provincial prisons could also be prioritized for treatment. However, universal HCV screening has not been implemented in these settings yet, which prevents the identification of those requiring treatment. Although a modeling study from Scotland (United Kingdom) suggested that scaling-up DAAs among incarcerated people could provide important prevention benefits, the evidence base for such interventions remains scarce in Canadian settings.

Purpose: The purpose of this study is to assess the potential population-level impact of a prison-based "test-and-treat" intervention on HCV transmission among PWID in Montréal.

Methods: We developed a dynamic compartmental model of HCV transmission in PWID in Montréal. The model is stratified by sex (male, female), incarceration status (never, currently, recently or previously released), and injecting status (active, past, and on Opioid Agonist Therapy). It was fitted in a Bayesian framework to detailed local epidemiological data from both prison-based bio-behavioral surveys (2003, 2014), and annual bio-behavioral surveys among PWID (2003-2014). Once calibrated, we explored the impact of a prison-based "test-and-treat" intervention. In this scenario, all PWID entering prison are tested and those chronically infected are treated. We estimated the 5- and 10-year impacts of this intervention on incidence proportions, as compared to a status quo counterfactual scenario where no person in prison is tested or treated for HCV.

Results: Our model is able to reproduce the HCV epidemic among PWID in Montréal, both inside and outside of prison settings. Scaling-up HCV testing and treatment in provincial prisons would lead to a 7.7% relative decrease in incidence among all active Montréal PWID (95% CrI: 4.6-12.2%) in 2023, five years after intervention implementation, reaching a 9.5% relative decrease in 2028 (95% CrI: 5.6-15.5%). The intervention would also yield the average treatment of 1.4% (95%CI: 0.9, 2.0%) of the total PWID population per year over the period.

Conclusion: Our preliminary results suggest that offering a universal HCV "test-and-treat" model in provincial prisons could change the course of the HCV epidemic in Montréal. These results are proportionally large, as only a small fraction of the population is treated. Finally, more in depth intervention scenarios will be modeled, as informed by a real-world prison-based HCV care cascade intervention study currently underway in Montréal.

ID: 167

Task shifting is a successful tool to sustain HCV care engagement

Barbara Goodall, Nova Scotia Health Authority**,** Yvonne Lynch-Hill, Nova Scotia Health Authority , Morgan MacNeil, Nova Scotia Health Authority , Lisa Barrett, Dalhousie University

Background: Hepatitis C virus (HCV) elimination requires coordinated scale up of both HCV diagnostics and therapeutics. In publicly funded health care systems, finding maximum efficiencies is paramount. In particular, revision of medically complex HCV care models is needed. One strategy is task shifting non-nursing roles to other skilled individuals, such as clerical staff.

Purpose: Determine the effect of skilled clerical staff on overall HCV wait times and treatment initiations.

Methods: A provincial HCV elimination strategy was developed, and intrinsic to the low cost business plan was maximized scope of practice. A medical clerk with advanced skills in database management and telephone based patient engagement was added to the HCV clinical team to complement an experienced nurse and physician. The required amount of time to engage each patient, as well as the wait times before and after engagement were measured.

Results: We collected data from 3 time periods: pre-clerk (Jan - Dec 2017), clerk (Dec 2017- Aug 2018), and post-clerk (Oct 2018). Treatment initiations were an average of 2.25, 15.3, and 3 patients per month respectively during each of the periods. Median wait time, in days, for the pre-clerk and clerk period was 140 (IQR 84-235) and 35 (IQR 21-63.75), respectively. First appointment attendance was 54.5%, 82.2%, and 14.3% ($p<0.05$, clerk vs post clerk period) respectively for the pre-clerk, clerk, and post-clerk time periods.

Conclusions: Task shifting initial HCV patient engagement from a nurse to skilled clerical personnel is a successful tool to gain rapid scale-up of patient treatment initiation. Models that encourage task shifting need to be supported longitudinally to maintain benefit in HCV elimination.

ID: 125

Estimating the prevalence of chronic Hepatitis C infection in British Columbia and Ontario using mathematical modelling and health administrative data

Abdullah Hamadeh, University of Waterloo , Alexander Haines, Toronto Health Economics and Technology Assessment Collaborative , Zeny Feng, University of Guelph , Hla-Hla Thein, University of Toronto , Naveed Zafar, BCCDC , Murray Krahn, Toronto Health Economics and Technology Assessment Collaborative (THETA), University of Toronto, William WL Wong, School of Pharmacy, University of Waterloo

Background

Though the landscape of care for patients with chronic hepatitis C (CHC) has changed rapidly, many infected individuals have not yet been identified. Population as well as targeted screening will play key roles in achieving the World Health Organization's (WHO) 2030 elimination targets. Key factors in planning national screening are the prevalence of CHC infection and the proportion of the CHC population that remains undiagnosed. There are few reliable sources for these rates.

Purpose

The objective of this study is to estimate the CHC prevalence and undiagnosed rates in British Columbia (BC) and Ontario by utilizing a model-based approach that is informed by provincial population-level health administrative data.

Methods

A two-step approach was used: Step 1) Two population-based retrospective analyses of administrative health data for a cohort of Ontarians (1999-2014) and a cohort of British Columbians (2000-2011) with CHC were conducted to generate population-level statistics of CHC-related health events. The annual numbers of CHC diagnoses, CHC-induced hepatocellular carcinoma (HCC) and decompensated cirrhosis (DC) were collected along with the annual numbers of newly-initiated CHC treatments. Step 2) We applied a back-calculation approach, using 1) a validated natural history model; and 2) a Bayesian Markov chain Monte Carlo (MCMC) algorithm to obtain historical prevalence and incidence estimates that are in line with the observed data collected in Step 1.

Results

Our population-level retrospective study found that, in BC and Ontario, the number of newly diagnosed CHC cases is declining yearly, while the complications of the disease are increasing. The population-weighted CHC prevalence rate was found to be 1.21% (1.03-1.42%) in BC in 2011 and 0.90% (0.82-1.00%) in Ontario in 2014. The population-weighted CHC undiagnosed rate was 25.6% (20.4-31.5%) in BC in 2011 and 37.7% (34.2-42.9%) in Ontario in 2014. Among baby-boomers, we estimate the CHC prevalence rate to be 2.57% (2.13-3.11%) in BC in 2011 and 1.88% (1.65-2.15%) in Ontario in 2014.

Conclusions

Compared to previously published nationwide figures, this study estimates higher CHC prevalence rates in BC and Ontario. Furthermore, while the overall undiagnosed rate in Ontario is comparable to reported national estimates, the corresponding rate in BC is estimated to be significantly lower.

Our study offers robust estimates based on the integration of a validated natural history model with provincial-level health administrative data on multiple HCV-related events. By using health administrative

data on specifically CHC health events, we have eliminated several sources of uncertainty that impact previously reported CHC prevalence and undiagnosed rate estimates. Our study thus provides vital evidence and information to help BC and Ontario make aggressive, timely and cost-effective moves to achieve WHO elimination targets.

ID: 117

Prevention of HIV transmission and optimization of HIV therapy among HCV-infected people who inject drugs (PWID) by engagement in long-term medical care

Julie Holeksa, Vancouver Infectious Diseases Centre, Tianna Magel, Vancouver Infectious Diseases Centre, Astou THIAM, Vancouver Infectious Diseases Centre, Letitia Chu, Vancouver Infectious Diseases Centre, Rossitta Yung, Vancouver Infectious Diseases Centre, David Truong, Vancouver Infectious Diseases Centre, Brian Conway, Vancouver Infectious Diseases Centre

Background and Aims: Among HCV-infected PWID, 10-20% are co-infected with HIV. Identification of HCV mono-infected PWID may provide us with an opportunity to prevent HIV acquisition as blood-to-blood transmission of HCV generally occurs more rapidly than for HIV.

Purpose: We wanted to assess the impact of long-term engagement in multidisciplinary care of HCV-infected active PWID on the rate of subsequent HIV seroconversion and response rates to antiretroviral therapy among HCV/HIV co-infected individuals.

Methods: We conducted a retrospective review of HCV-positive patients who initiated HCV treatment. All patients are enrolled in care addressing medical, social, psychological, and addictions-related needs. Outcomes of interest: rate of HIV seroconversion (HCV mono-infected) or response to antiretroviral therapy (HIV/HCV coinfected).

Results: 411 individuals were considered, of whom 78 were co-infected with HIV, 40 (51%) were active PWID. Demographics of HIV co-infection: mean age 55, 8% female, 10% homeless, 36% on opioid substitution therapy (OST). The majority (77/78, 99%) were on antiretroviral therapy, with 74/77 (96%) having full virologic suppression. The only correlate of absent/ineffective antiretroviral therapy was male sex (3/3). Among 333 mono-infected patients, 152 (46%) were active PWID. Demographics: mean age 56, 30% female, 12% homeless, 34% on OST. In 617 person-years of follow-up, there were no cases of HIV seroconversion.

Conclusion: Within HCV-infected PWID, long-term engagement in care (continuing after HCV treatment) is associated with excellent HIV treatment responses (exceeding WHO 90-90-90) in co-infected individuals and reduction in HIV acquisition despite ongoing high-risk behaviors in mono-infected individuals, confirming an additional benefit of providing HCV care to PWID.

ID: 118

PRELIMINARY RESULTS FROM A NOVEL MODEL OF HCV CARE IN OPIATE SUBSTITUTION THERAPY (OST) CLINICS: FIND 50

Julie Holeksa, Vancouver Infectious Diseases Centre, Tianna Magel, Vancouver Infectious Diseases Centre, Astou THIAM, Vancouver Infectious Diseases Centre, Letitia Chu, Vancouver Infectious Diseases Centre, Rossitta Yung, Vancouver Infectious Diseases Centre, David Truong, Vancouver Infectious Diseases Centre, Brian Conway, Vancouver Infectious Diseases Centre

Background: To support WHO elimination goals, various models have been proposed for the identification and engagement in care of individuals living with HCV infection. In Canada, the majority of incident cases occur among people who use drugs (PWUD). Models must be targeted to the needs of this unique group. We report on the preliminary success of an outreach model designed to engage this population in care.

Purpose: To assess the preliminary success of an outreach program designed to engage PWUD in HCV care.

Methods: We performed an interim analysis of all HCV+ patients encountered and engaged through our "Find 50" program. In this protocol, clinicians providing opioid substitution therapy (OST) pre-identify HCV-positive patients and coordinate their OST prescription renewal with a date when our HCV team is present on site at the OST clinic to perform clinical evaluations and specifically plan for HCV treatment. The process of laboratory and abdominal ultrasound testing, securing governmental approval for HCV medications, medication delivery, and evaluation of treatment efficacy is done by our centre remotely, in conjunction with OST clinic staff.

Results: At 3 half-day events (held 07-11/18), we have encountered 36 individuals infected with HCV, 8 newly diagnosed by point-of care antibody testing. Key demographics are: mean age 43 years, 25% female, 80% Caucasian, 11% Indigenous, 36% currently homeless or unstably housed, 94% reporting active substance use. 34/36 were found to be viremic, with two now in long-term follow-up to monitor for recurrent viremia. All 34 have been offered HCV treatment. Of these, 14 have since discontinued OST and additional measures are in place to secure follow-up. Of the remaining 20 individuals, 13 have started HCV treatment and 4 are scheduled to do so. On-treatment HCV RNA was done in 7 cases and was undetectable in all cases. End of treatment HCV RNA was done in 6/8 cases, with undetectable measures in 100% cases.

Conclusion: Many non-specialist clinics do not have the time or established infrastructure to provide HCV treatment without support, despite having a substantial HCV-infected population within their census. The "Find 50" model we propose provides an on-site service for patient assessment and remote coordination of HCV treatment to supplement routine OST-based care. This model is very efficient (36 patients evaluated and enrolled over 3 half-day clinics), insightful (8 patients newly diagnosed), effective (plan of care established for 17/20 viremic patients remaining engaged in care), and feasible (good adherence to treatment and high treatment efficacy). Surprisingly, among patients thought to be stably engaged in care, 14 (39%) discontinued OST in the period following initial contact with our program, supporting the need for additional measures to ensure they have access to curative HCV treatment. This approach could be an essential part of the

ID: 119

Hepatitis C virus (HCV)-infected People Who Use Drugs (PWUD) with cirrhosis: Need for urgent treatment of HCV infection to prevent liver-related complications

Julie Holeksa, Vancouver Infectious Diseases Centre, Tianna Magel, Vancouver Infectious Diseases Centre, Astou THIAM, Vancouver Infectious Diseases Centre, Letitia Chu, Vancouver Infectious Diseases Centre, Rossitta Yung, Vancouver Infectious Diseases Centre, David Truong, Vancouver Infectious Diseases Centre, Brian Conway, Vancouver Infectious Diseases Centre

Background: People who use drugs (PWUD) make up the largest proportion of incident and prevalent Hepatitis C virus (HCV) infections in Canada. These individuals have often become infected with HCV remotely, and remain undiagnosed or untreated, with a risk of end-stage liver disease and/or hepatocellular carcinoma (HCC) in up to 25% of those with chronic infection. Treatment of HCV can reduce incidence of HCC by as much as 71%, even in individuals who already have cirrhosis. Thus, engaging HCV-positive PWUD in curative HCV care and maintaining long-term engagement of those with cirrhosis (for HCC screening) is an important part of long-term treatment, along with addiction care.

Purpose: To assess the importance of engaging HCV+ PWUD with cirrhosis in long-term multidisciplinary care.

Methods: We conducted a retrospective chart review of all HCV-positive PWUD who have received direct-acting antiviral therapy at our centre, focusing specifically on those who were diagnosed with cirrhosis prior to treatment by transient elastography (FibroScan, or FS, >12.5 kPa) prior to treatment initiation. All individuals engaged at our centre have access to an integrated, multidisciplinary model of care to address their medical, social, psychological, and addictions-related needs.

Results: Since 2014, 348 eligible individuals have been initiated treatment at our centre, of whom 62 (18%) had cirrhosis at baseline. Demographic characteristics of those with cirrhosis include: mean age 59 years, 22% female, 22% HIV co-infected, 74% on opioid substitution therapy, 6% homeless or unstably housed, 25% with a diagnosed psychiatric issue, 23% engaged through community outreach programming. Of those on treatment, 55/60 (92%) have achieved sustained virologic response (SVR12, or cure of HCV infection), with 1 virologic relapse, and 4 individuals being lost to follow up. 2 individuals have completed treatment but are awaiting SVR bloodwork. Mean pre-treatment FS was 22.9 kPa ± 11. Mean post-treatment FS for those with available scores (n = 39) was 16.2 kPa ± 13, with 22 (56%) of those having a score in the non-cirrhotic range. All individuals remain under long-term care to assess for HCC, as well as for re-infection for those with ongoing risk behaviours.

Conclusion: These data demonstrate additional support for the continued expansion and prioritization of PWUD for HCV treatment. A significant proportion of these individuals already have advanced liver disease and require urgent treatment. These individuals have high cure rates, associated with reversal of fibrosis. This is associated with an improvement in quality of life, and may also enhance the benefit of their addiction care.

ID: 120

LOSS TO FOLLOW UP (LTFU): A KEY BARRIER TO POPULATION-BASED CONTROL OF HCV INFECTION

Julie Holeksa, Vancouver Infectious Diseases Centre, Tianna Magel, Vancouver Infectious Diseases Centre, Astou THIAM, Vancouver Infectious Diseases Centre, Letitia Chu, Vancouver Infectious Diseases Centre, Rossitta Yung, Vancouver Infectious Diseases Centre, David Truong, Vancouver Infectious Diseases Centre, Brian Conway, Vancouver Infectious Diseases Centre

Background: With the elimination of HCV as a public health concern being a feasible goal, we must ensure that measures of program efficacy are optimized. Following initiation of HCV treatment, some cohorts report loss to follow-up (LTFU) rates of 20% or more, reducing our ability to confirm cure or institute measures to reduce HCV re-infection risk and/or monitor for the development of hepatocellular carcinoma. We have evaluated the impact of a multidisciplinary intervention program on LTFU among inner city vulnerable populations receiving HCV treatment at our centre.

Purpose: To assess the impact of multidisciplinary care in mitigating LTFU in vulnerable populations receiving HCV treatment.

Methods: We have included all individuals initiating all-oral HCV therapy between 03/14-10/18. After initial engagement in care at our centre, patients are enrolled in a multidisciplinary program addressing all medical, social, psychological, and addictions-related needs in an integrated manner. Within this context, individualized patient support programs are designed to maintain follow-up and active outreach strategies are immediately instituted if a follow-up visit is missed. The purpose of this analysis was to document the rate and correlates of LTFU following initiation of HCV therapy.

Results: A total of 391 individuals have been initiated on treatment. Baseline demographic characteristics include: mean age 54, 26% female, 60% active/recent drug use, 30% alcohol use, 14% homelessness, 37% on OST, mean baseline FibroScan 11.6 kPa, 21% with cirrhosis at baseline. The overall success rate of HCV treatment (SVR12) rate is 91% by ITT analysis (298/328), 98% by mITT analysis, excluding non-virologic failures (298/304). The on-treatment LTFU rate was 3.6% (14). Characteristics of patients who were LTFU are: mean age 46, 43% female, 64% confirmed active ongoing injection drug use, 36% homeless, 43% with a diagnosed psychiatric issue, 50% on OST, mean baseline FibroScan 12.8 kPa, with 28% with cirrhosis at baseline. 4 cases of reinfection have been identified at our centre, all amongst patients who were LTFU during their treatment course and later re-engaged. Of those maintained in long-term care post SVR12, there have been no cases of recurrent viremia, despite ongoing injection drug use in 49% of individuals.

Conclusion: Low rates of LTFU can be achieved among inner city vulnerable populations engaged in HCV care within multidisciplinary programs with appropriate structures in place. Such approaches will be necessary to the control of HCV infection, as LTFU patients displayed more social vulnerability, including higher rates of homelessness and ongoing drug use, and appear to be at higher risk of HCV re-infection, as well as more often being cirrhotic at baseline.

ID: 115

HCV treatment outcomes among current and remote injection drug users (IDUs): real life data

Tianna Magel, Vancouver Infectious Diseases Centre, Julie Holeksa, Vancouver Infectious Diseases Centre , Astou THIAM, Vancouver Infectious Diseases Centre, Letitia Chu, Vancouver Infectious Diseases Centre, Rossitta Yung, Vancouver Infectious Diseases Centre, David Truong, Vancouver Infectious Diseases Centre, Brian Conway, Vancouver Infectious Diseases Centre

Background and Aims: A number of clinical trials (CO-STAR, D3FEAT, SIMPLIFY) have suggested that HCV treatment outcomes among active injection drug users (IDUs) is identical to that observed in other populations. It has been suggested that these data may not pertain to IDUs who would not be enrolled in such trials. Despite the recent publication of a meta-analysis on this subject, there is a need for more comparative data among current and remote IDUs treated for HCV under similar circumstances.

Purpose: To compare the outcome of HCV treatment and SVR12 in current and remote injection drug users.

Methods: A retrospective cohort analysis was performed on all HCV infected patients who were treated with Direct Acting Antivirals (DAAs) at our centre with a history of current or remote IDU between 04/14- 10/18. All participants had access to a multidisciplinary model of care addressing their medical, social, psychological, and addiction-related needs. The primary end point of this analysis was the achievement of SVR12 and its correlates, with a view to demonstrating whether active IDU was a correlate of treatment outcome when care was delivered to current and remote IDUs within the same setting.

Results: In this analysis, we compared 141 active and 88 remote IDUs who were evaluated at the SVR12 time point. Baseline demographic and disease characteristics for active and remote IDU, respectively: mean age 51.7 / 55.8 years, 78% / 70% male, 53% / 25% opiate substitution therapy, 36% / 25% alcohol use, 22% / 7% homelessness, 17% / 16% cirrhotic, 14% / 10% HIV co-infected. All oral HCV treatment for active and remote IDUs, respectively: 27% / 18% SOF/VEL, 17% / 23% SOF/LED, 13% / 15% ELB/GRAZ and 23% / 23% PrOD. Of the active IDUs that reached the SVR timepoint, 138/141 (98%) achieved SVR12 vs. 88/88 (100%) amongst remote IDUs by mITT analysis. Two active IDUs relapsed and one individual discontinued treatment due to medical complications unrelated to therapy. Four cases of reinfection have been identified, all amongst active IDUs at a rate of 1.6 per 100 person-years. Reinfection occurred at a mean of 50 weeks post SVR12 date.

Conclusion: Within a multidisciplinary care model, high SVR12 rates were achieved in both active and remote IDUs. Therapeutic failure and re-infection events occurred infrequently, but only among active IDUs. This supports the need to develop interventions to maintain these individuals in care during and after treatment to mitigate these risks and ensure that proper harm reduction interventions can be applied.

ID: 153

Transitioning from Interferon-based to direct antiviral treatment options: a potential shift in barriers and facilitators of treatment initiation among people who use drugs?

Iuliia Makarenko, McGill University, Andreea Adelina Artenie, Université de Montréal, Stine Hoj, Centre de Recherche du CHUM, Nanor Minoyan, Université de Montréal / CRCHUM, Brendan Jacka, Centre de Recherche du CHUM, Geng Zang, CRCHUM, Gillian Barlett-Esquilant, McGill University, Valerie Martel-Laferriere, Centre de Recherche du Centre hospitalier de l'Université de Montréal, Didier Jutras-Aswad, Research Centre of the Centre Hospitalier de l'Université de Montréal; Department of Psychiatry, Université de Montréal, Julie Bruneau, CRCHUM

Background: People who inject drugs (PWID) are the primary group at risk for hepatitis C virus (HCV) but faced multiple barriers to accessing interferon-based (IFN) treatment, including concerns about side effects among both patients and providers. Highly effective and tolerable IFN-free direct-acting antiviral (DAA) agents were first introduced in Canada in 2014, but data on treatment initiation remain scarce among PWID.

Purpose: This study examined temporal trends in HCV treatment initiation among PWID and associated factors during the periods pre- and post-availability of IFN-free DAA treatment.

Methods: A sample of 308 HCV RNA-positive PWID contributing 915.6 person-years of follow-up was drawn from an ongoing prospective community-based cohort study of PWID in Montreal, Canada. At three-month/one-year intervals between 2011 and 2017, participants completed an interviewer-administered questionnaire on socio-demographic characteristics, drug use behaviours and health service utilisation, including HCV treatment. Time-updated Cox regression models were used to examine associations between time to HCV treatment initiation and hypothesised barriers and facilitators. Final multivariate models were stratified by the period of DAA availability: 1) 2011-2013 – first DAAs available in combination with IFN-based regimens; 2) 2014-2017 – DAA IFN-free era.

Results: Participants were predominantly male (85.1%) with a median age of 42 years (IQR: 33, 50). Of 308 participants, 80 (26%) initiated HCV treatment during the follow-up period. Treatment incidence increased gradually between 2011 to 2017, from 1.6 (95% CI: 0.9–2.6) in 2011 to 12.7 (10.6–15.1) in 2017 (p-trend=0.0012). In multivariate analyses, seeing a primary care physician (DAA+IFN era: aHR=3.63, 95%CI [1.21–10.9]; DAA IFN-free era: 2.52 [1.10–5.77]) and frequent injection (0.23 [0.05–0.99] and 0.49 [0.24–0.99]) were associated with treatment initiation both pre- and post-introduction of IFN-free regimens. Cocaine injection was negatively associated with HCV treatment initiation during the DAA+IFN era (0.40 [0.18–0.90]) but this relationship attenuated slightly in the IFN-free era (0.64 [0.37–1.09]). Participants aged over 40 (2.27 [1.24–4.13]), those receiving opioid agonist therapy (OAT) (2.17 [1.19–3.94]), and those with previous HCV treatment experience (3.00 [1.75–5.15]) were more likely to initiate treatment during the latter period.

Conclusion: Among PWID recruited in a community setting in Canada, HCV treatment initiation has been increasing, however remains low and seeing a primary care physician remains a key facilitator. In the IFN-free DAA era, treatment was typically initiated by those already engaged with health services, either through enrolment in OAT or previous HCV treatment. These findings underscore that access to primary healthcare and OAT is essential but not enough to scale up treatment in this population.

ID: 22

Barriers and facilitators for engaging in HCV management and DAA therapy among general practitioners and drug and alcohol specialists – the practitioner experience

Alison Marshall, the Kirby Institute, University of New South Wales Sydney and the Centre for Social Research in Health, University of New South Wales Sydney**,** Jason Grebely, Kirby Institute, UNSW Sydney, Gregory J Dore, The Kirby Institute, Carla Treloar, Centre for Social Research in Health, UNSW Sydney

Background: Since the advent of interferon-free direct-acting antiviral (DAA) HCV therapies, many countries have reduced prescriber restrictions permitting HCV management in various settings outside of tertiary hospital-based clinics. However, there is limited knowledge of the practitioner experience in managing HCV DAA treatment, particularly those new to HCV-related care. Increased evidence is critical to inform healthcare delivery and policy and optimise the scale-up of DAA regimens globally.

Purpose: The aim of this qualitative study was to investigate barriers and facilitators for HCV management among: (1) general practitioners (GPs) who are opioid agonist therapy (OAT) prescribers; and, (2) drug and alcohol specialists in Australia.

Methods: In-depth, semi-structured interviews via telephone took place between September 2018 and February 2019. Practitioners with none/limited experience in HCV DAA prescribing (<20 patients total) and greater experience (>20 patients) were targeted for recruitment and questioned on barriers and facilitators (e.g. education/training, mentorship, HCV testing) to 'taking on' care in their clinic(s). Data were coded and analysed thematically.

Results: Among the 26 practitioners interviewed, the majority were surprised by the efficacy of DAA therapies and felt professionally rewarded by high cure rates. Notably, some practitioners expressed trepidation with liver disease staging and continued frustrations with implementation barriers, e.g. administrative burdens and lack of personnel, equipment, and infrastructure for HCV-related care. Practitioners with good mentorship and established pathways to referral services experienced comparatively fewer obstacles than practitioners with seemingly less support. Poor venous access and limited phlebotomy services were frequently elucidated as a barrier to HCV testing and subsequently, treatment initiation for people who inject drugs. Most practitioners were unsure as to how to best galvanise more GPs/OAT prescribers into HCV care and increase treatment uptake among PWID.

Conclusion: To achieve HCV WHO targets by 2030, practitioners require additional implementation support. Since HCV testing remains a substantial barrier to linkage to care, practitioners should be kept well-informed of developments in diagnostic technology and be provided with treatment 'work-up' support (e.g. nurse-led care). Findings highlight the importance of (initial) mentorship, especially for practitioners new to HCV care, with further evidence needed for practitioners based in rural and remote regions.

ID: 175

Partnering with the First Nations Community in Hepatitis C Research: Building Capacity with Healthcare Administrative Data and the Co-creation of Knowledge

Andrew Mendlowitz, University of Toronto**,** Jennifer Walker, Laurentian University, 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:

Hepatitis C viral (HCV) infection has been identified as having the highest burden among infectious diseases in Ontario. First Nations people in Ontario are represented in this epidemic, but no research has fully addressed the burden of HCV in this population. Recent data-linkage initiatives have provided the opportunity for researchers and First Nations organizations to partner for population-level studies using healthcare administrative data. In 2019, this partnership has translated to a collaboration with First Nations organizations to measure the health and economic burden of HCV in Ontario.

Purpose:

To describe how a relationship is being built between researchers at universities, ICES, and First Nations organizations to design a research project on HCV infection in First Nations populations in Ontario.

Method:

Relationship-building and creating a strong partnership between researchers and First Nations communities in the context of HCV research has involved the following steps: (1) building researcher understanding for First Nations ways of knowing and data sovereignty; (2) collaboration between academic researchers and First Nations organizations throughout the entire research process; (3) seeking the appropriate permissions and ensuring the study is respectful of First Nations data governance principles; and (4) ensuring that integrated knowledge translation and community-based research practices are used to involve and share information with First Nations partners throughout the project.

Results:

From the abovementioned steps, the research team in partnership with First Nations organizations have made the following progress: Researchers have received land-based cultural training and training in First Nations OCAP® (Ownership, Control, Access and Possession) principles which foster the understanding of First Nations ways of knowing and the ethical conduct of First Nations research. An ongoing partnership between academic researchers and the Ontario First Nations HIV/AIDS Education Circle (OFNHAEC) was established to explore how research findings can support community programming, and through the formalization of a research agreement, established the commitment and involvement of all parties throughout the research process. Seeking permission from the First Nations Data Governance Committee for access to First Nations healthcare administrative data at ICES has ensured that study findings will be beneficial to First Nations communities while mitigating the perpetuation of the stigma potentially associated with HCV research. In parallel to administrative data analyses, ongoing meetings with OFNHAEC and their co-involvement at each research step warrants that study results are interpreted in ways appropriate to the First Nations context.

Conclusion(s):

Through partnering with First Nations organizations and respecting First Nations data sovereignty principles, this research will contribute to emerging standards on how to meaningfully involve First Nations in research using healthcare administrative data. Building strong relationships with First Nations organizations ensures a collaborative approach to research that will empower First Nation communities to inform health services and influence policy and/or community action around HCV infection.

ID: 123

A population-based matched cohort study evaluating the healthcare costs of hepatitis B virus (HBV) in Ontario, Canada

Natasha Nanwa, ICES, Jeff Kwong, ICES, Jordan Feld, Toronto Centre for Liver Disease, Fangyun Wu, ICES, Beate Sander, THETA

Background: The economic burden of HBV in Canada is poorly understood.

Purpose: To evaluate mean attributable costs related to HBV from the Ontario Ministry of Health and Long-Term care perspective.

Methods: Using a matched-cohort incidence-based cost-of-illness approach, we identified infected subjects (individuals with HBV) from January 1, 2004 to December 31, 2014 using Public Health Ontario Laboratory data. This data was linked to ICES administrative data which represents publicly funded health services for nearly the entire Ontario population. Infected subjects were defined as having positive HBV surface antigen, DNA, or e-antigen. We included the latter as HBV testing in Ontario is not centralized. The index date corresponded to the date of the first positive specimen. We organized our cohort into three groups: no HBV-related complication; HBV-related complication prior to index date; and 3) HBV-related complication post index date. We used published literature and clinical expertise to define a HBV-related complication (e.g., jaundice, liver cancer). We adopted the phase-of-care approach to calculate costs (2017 Canadian dollars). Six phases were defined: 1) pre-diagnosis; 2) initial care; 3) continuing care; 4) HBV-related complication; 5) continuing care for HBV-related complication; and 6) final care. We hard matched at the initial and final phases. Our hard match variables included sex, age group, index year, rurality, neighbourhood income quintile, resource utilization bands (co-morbidities measure), and immigrant status (post 1985). We calculated the mean difference between matched pairs to determine the mean attributable phase-specific costs. Calculated costs were then combined with crude survival data to determine 1-, 5-, and 10-year costs. We stratified costs by age group, sex, immigrant status, and acute/chronic infection.

Results: We identified 41,469 infected subjects. Their mean age was 44 (standard deviation= 15, median=43) years old, with majority male (55%), immigrant (58%), moderate user of the healthcare system (45%), urban resident (96%), and among lowest income quintile (27%). Eight percent had a HBV-related complication prior to the index date and 12% had a HBV-related complication post index date. Our match rates were 89-93% for initial care and 100% for final care across groups. Mean attributable phase-specific costs ranged between -$27-$19 for pre-diagnosis, $167-$1,062 for initial care, $53-$407 for continuing care, $1,033 for HBV-related complication, $304 for continuing care for HBV-related complication, and $2,552-$4,281 for final care. Across groups, mean cumulative 1-, 5-, and 10-year costs ranged between $253-$3,066, $3,067-$20,349, and $6,128-$38,968, respectively. Infected subjects with HBV-related complication prior to index date, had the highest 10-year costs. Generally, costs were higher among males, long-term Ontario residents, 19 years and younger, and those with chronic infection.

Conclusions: We found HBV has long-term impact on healthcare costs. Our study quantifies the burden of HBV and aids decision making on strategies which may mitigate this costly infectious disease.

ID: 23

Eliminating a Structural Barrier: Impact of Removing Fibrosis Stage Restrictions on Hepatitis C Treatment Uptake among people co-infected with HIV

Sahar Saeed, McGill University, Erin Strumpf, McGill University, Erica Moodie, McGill University, Joseph Cox, McGill University, Sharon Walmsley, University Health Network, Curtis Cooper, University of Ottawa, Brian Conway, Vancouver Infectious Diseases Centre, Mark Hull, BC Center of Excellence, Lisa Barrett, Dalhousie University, Valerie Martel-Laferriere, Centre de Recherche du Centre hospitalier de l'Université de Montréal, Mark Tyndall, BC Centre for Disease Control, John Gill, Southern Alberta Clinic, Marina Klein, McGill University Health Centre

Background: Direct-acting antivirals (DAAs) have revolutionized Hepatitis C (HCV) treatments. Unfortunately, due to high costs, healthcare insurers have imposed restrictions limiting access to DAAs worldwide. In Canada, initially HCV treatments were only covered for people with significant liver fibrosis, but this criterion was removed differentially by provinces over time. In Quebec, restrictions were removed progressively between July 2014-July 2015 and then permanently as of March 2016. While in most other province's restrictions were lifted as of March 2017. Using this *natural experiment*, we evaluated the impact of removing fibrosis stage restrictions on HCV treatment initiation rates overall and specifically among people who inject drugs (PWID).

Methods: We used data from the Canadian HIV-HCV Co-Infection Cohort (CCC) which prospectively follows 1917 participants from 18 centers. Eligible CCC participants for this study were HCV RNA + residing in either BC, ON and QC. Using a difference-in-differences approach, we determined the impact of removing fibrosis stage restrictions on HCV treatment initiation, while accounting for time-invariant differences between provinces and secular trends. Negative binomial regression with generalized estimating equations were used to account for repeated outcomes. Time-fixed and varying predictors of treatment initiation including socio-demographic and clinical factors were evaluated. We further evaluated if the policy change reached the intended population by performing a difference-in-differences-in-differences analysis. Here a triple interaction term (between the time-varying policy change, province and an indicator for not having significant fibrosis) was the estimator of interest. Finally, we assessed a lagged exposure variable one year after provinces removed fibrosis stage restrictions to determine whether the effect of eliminating fibrosis stage restrictions persisted.

Results: Between 2011-2017, there were a total of 574 HCV treatment initiations. HCV treatment rates increased by 1.9 times (95% CI, 1.4, 2.5) after removing fibrosis stage restrictions accounting for temporal trends and time-invariant differences between provinces. Among PWID the impact appeared even stronger aIRR, 3.7 (95% CI, 1.9, 7.2). Adjustment for fixed and time-varying covariates did not change the effect of the policy change. Furthermore, there was evidence to support participants without significant liver fibrosis more likely to initiate treatment after restrictions were removed: aIRR, 1.7 (95% CI, 0.7, 3.9). Furthermore, treatment initiation rates were not sustainable as a decline in treatment initiation was observed one year following the policy change, IRR 0.8 (95% CI 0.6, 1.0).

Conclusion: This is the first study that quantifies the causal impact of eliminating a significant system-level barrier. While we found HCV treatment initiations increased following unrestricted access, this impact was only temporary. This confirms country-level observations of treatment initiations plateauing after an initial "warehousing effect". To meet the WHO targets of eliminating HCV by 2030, it will be essential for countries to minimize structural barriers and also adopt targeted interventions to maintain treatment initiation rates.

ID: 21

Vulnerable people with hepatitis C virus (HCV) benefit from the health services offered by Coopérative de solidarité SABSA Centre de recherche, Institut universitaire de pneumologie et de cardiologie

Isabelle Têtu, Clinique de solidarité SABSA **,** Jean-Pierre Grégoire, Faculté de pharmacie, Université Laval , Jocelyne Moisan, Faculté de pharmacie, Université Laval

Background: SABSA is a non-profit healthcare cooperative that offers medical and psychosocial integrated care and follow-up services to vulnerable people with HCV in Quebec City. SABSA is a nurse-led clinic that has consolidated a network of outreach services for people vulnerable to sexually transmitted and blood-borne infections in order to facilitate their access to anti-HCV treatment. By providing nursing, nutritional, psychosocial, pharmacological and logistical support in a strategic location, close to vulnerable clienteles, SABSA offers a "turnkey" service to gastroenterologists and infectious disease specialists who treat people with HCV.

Purpose: To describe the characteristics of the SABSA patients initiating a hepatitis C treatment and calculate the proportion of them who had a sustained virological response (SVR) 12 weeks after the end of their treatment.

Method: We included in a non-experimental cohort study all individuals who initiated a hepatitis C treatment at SABSA between January 1, 2012 and December 31, 2017. Data on individuals themselves, their illness, their concomitant diseases and their behaviors were collected on the day of treatment initiation. HCV RNA in the blood was measured 12 weeks after the end of treatment. The proportion of individuals with SVR was estimated at that time.

Results: Of the 171 individuals included in the study (women: 29.8%, median age: 52), 61 (35.7%) had attended only primary school, 97 (56.7%) were unemployed, 95 (55.6%) had a monthly income of <$1,000 and 102 (59.6%) had a criminal record. In regards to their health, 157 (91.8%) had ≥1 health problem in addition to their hepatitis C: 22 (12.9%) had a physical health problem, 42 (24.6%) had a mental health problem, and 93 (54.4%) had both a mental and a physical health problem; 93 (54.4%) were infected with a genotype 1a virus, 43 (25.2%) with a genotype 3 virus, 15 (8.8%) with a genotype 1b virus and 13 (7.6%) with a genotype 2 virus. A total of 137 (80.1%) individuals had contracted hepatitis C as a result of injection drug use. During their treatment, 158 individuals had ≥1 visit at SABSA (median: 5 visits). In regards of the follow-up scheduled 12 weeks after the end of their treatment, 35 (20.5%) individuals did not show up (3 had died, 2 were incarcerated, 2 were hospitalized, 4 had another reason and 24 an unknown reason). Of the 136 individuals who had a follow-up, 3 (2.2%) did not have a HCV RNA test. Of the remaining 133 individuals, 127 (95.5%) had SVR.

Conclusion: Despite the high vulnerability of patients treated at SABSA, the vast majority of those initiating a hepatitis C treatment were cured.

ID: 67

Making OraQuick Quicker: A hepatitis C point-of-care assay reduced to five minutes for viremic individuals

Aaron Vanderhoff, University of Toronto, David Smookler, University Health Network, Mia Biondi, Toronto General Hospital, University Health Network , Camelia Capraru, Toronto Centre for Liver Disease/VIRCAN, UHN, Bettina Hansen, Institute of Health Policy, Management and Evaluation, Hemant Shah, University of Toronto, Toronto Centre for Liver Disease, Harry Janssen, Toronto Centre for Liver Disease, Jordan Feld, University of Toronto

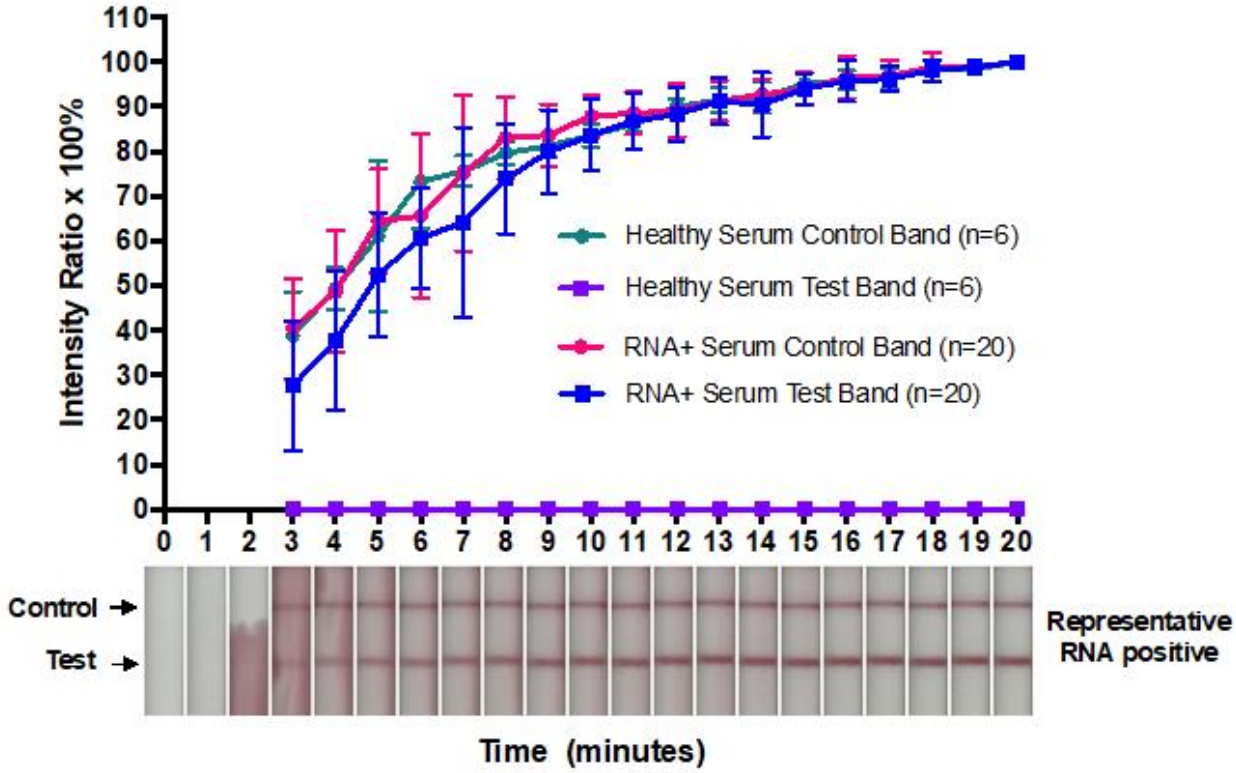
Background: Point-of-care testing for hepatitis C (HCV) increases access to screening for hard-to-reach populations and in settings with high test volumes or limited laboratory facilities. OraQuick HCV Rapid Antibody Test (OQ) is an FDA-approved lateral flow-based enzyme immonoassay (EIA) that detects anti-HCV antibodies (Ab) in whole blood or serum. The approved assay requires results be determined 20-40 minutes after test initiation; however, field observations suggest it may be possible to decrease read-time (RT) for viremic individuals (VIs).

Purpose: Our aim is to determine whether a RT prior to 20 minutes can be established for VIs that is non-inferior to the required 20-40 minutes RT.

Method: Blood samples from 46 HCV VIs and 11 long term resolvers (defined as clearing HCV >5 years prior) were tested with the OQ assay. Serial photos were taken for up to 20 minutes, and the time of first appearance of a positive band was recorded and confirmed by a second reader. Intensity ratio analysis was used to compare positive test bands at each time point to their final intensities. Negative controls included 6 uninfected subjects. Data collection is ongoing.

Results: By 5 minutes, 46/46 VIs had a positive result. The mean time to positivity was 2.6 minutes in VIs, compared to 7.4 minutes in the long-term resolvers ($p < 0.0001$). VIs were 65% male, median age of 59, median HCV RNA of 1.91x10^6 IU/ml, and 16 had cirrhosis. The long-term resolvers cleared the virus 5-14 years ago, following treatment, and all were cirrhotic. In contrast to the VIs, only 6 of 11 long-term resolvers were positive at 5 minutes. Based on these results, the probability of a VI testing positive by 5 minutes was 100% (95% CI, 92.3-100). Intensity analysis demonstrated that test bands from VI samples darken within 5 minutes to 52% (+/- 14%) of their final intensities, which is easily detectable (see figure). Kinetics of band intensity in viremic samples are shown in the figure, accompanied by a representative example.

Conclusion: Our results demonstrate that the OraQuick HCV Rapid Antibody test can reliably detect anti-HCV Abs by lateral flow in 5 minutes among viremic individuals. Although there may be value in documenting past HCV infection, the main goal of screening is to identify those infected. This shortened read time for testing may have important implications to improve engagement and linkage to care by facilitating follow-up HCV RNA in as little as 5 minutes.


Intensity Ratio x 100%
110
100
90
80
70
60
50
40
30
20
10
0
0 1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20
Healthy Serum Control Band (n=6)
Healthy Serum Test Band (n=6)
RNA+ Serum Control Band (n=20)
RNA+ Serum Test Band (n=20)
Control
Test
Representative
RNA positive
Time (minutes)

ID: 147

The population level cascades of care for HBV/HCV: A comparison of immigrant and long-term-residents in Ontario, Canada

Abdool Yasseen, University of Toronto**,** Jeff Kwong, ICES, Jordan Feld, University of Toronto, Morris Sherman, University Health Network, Lauren Lapointe-Shaw, University Health Network, Rafal Kustra, University of Toronto, Liane Macdonald, Public Health Ontario, Natasha Crowcroft, Public Health Ontario

Background: The global burden of hepatitis B and C viruses (HBV/HCV) is substantial, and monitoring infections across the diagnosis and treatment cascades is important for assessing the impact of interventions aimed at reducing this burden.

Purpose: To develop, characterize, and quantify the HBV/HCV cascades of care and identify disparities between domestic and migrant populations.

Methods: We used linked laboratory and health administrative records to describe the cascades of care for HBV/HCV in Ontario, Canada between January 1997 and December 2014. The HBV cascade was characterized into five distinct stages: 1) population prevalence, 2) diagnosis, 3) engagement with care, 4) treatment initiation, and 5) treatment adherence; and the HCV cascade was characterized into seven distinct stages: 1) population prevalence, 2) evidence of immunity, 3) nucleic acid testing, 4) viral RNA detection, 5) viral RNA genotyping, 6) treatment initiation, and 7) evidence of sustained virologic response (SVR). Lifetime prevalence of HBV/HCV infections were estimated from the first stage of each cascade and results were stratified by immigrant status and migrant subgroups, including those from HBV- and HCV-endemic countries, and compared to long-term-residents.

Results: There were 2,541,005 individuals (2,331,334 HBV and 1,007,251 for HCV) included in the study with an estimated lifetime prevalence of 102,011 (0.84%) for HBV and 160,093 (1.32%) HCV. HBV prevalence was highest among immigrants from HBV endemic countries (5.06%), whereas HCV prevalence was highest among long-term-residents (1.32%). For HBV, 67,328 (66.0%) were diagnosed, 38,758 (38.0%) were engaged with care, 10,397 (10.2%) initiated treatment, and 7,518 (7.4%) were adherent to treatment for at least 1 year. If they were diagnosed with HBV, migrants were more likely to be engaged with care (60.0% vs. 54.5%) but tended to initiate treatment less if they were engaged with care (24.6% vs. 35.7%) compared to long-term-residents. For HCV, 108,863 (68.0%) had evidence of HCV immunity, 85,592 (53.5%) were tested for HCV RNA, 57,838 (36.1%) had evidence of HCV RNA, 54,888 (34.3%) were genotyped, 14,010 (8.8%) had initiated treatment, and 3,520 (2.2%) had documented evidence of achieving SVR. Once migrants showed evidence of HCV immunity, they were more likely to be tested for HCV RNA (87.5% vs. 77.3%) but were less likely to have HCV RNA detected (57.2% vs. 69.4%) as compared to long-term-residents, however, those from HCV endemic countries showed comparable results (65.0%). Once diagnosed, migrants were more likely to initiate treatment (35.4% vs. 24.1%) and showed higher rates of SVR (40.5% vs. 21.9%) as compared to long-term-residents.

Conclusions: These findings provide HBV and HCV cascade of care estimates among the general and migrant populations prior to the introduction of direct acting antivirals. This information provides a population-based benchmark for future studies and highlight areas where public health officials should look for improvements

Participants list – Liste des participants

Michel Alary	CHU de Québec - Université Laval
Aslam Anis	University of British Columbia
Nathalie Bédard	CRCHUM
Neal Belluzzo	AMS Toronto
Alexandra Blair	Public Health Agency of Canada
Geneviève Boily-Larouche	CIHR III
Matthew Bonn	HepNS
Josh Booth	Toronto General Hospital
Magali Boudon	Dopamine
Julie Bruneau	Université de Montréal
Norma Choucha	CRCHUM
Karen Chow	Gilead Sciences Canada, Inc.
Simon Chrétien	Dopamine
Sophie Cousineau	McGill University
Thuy Dao	Hopital Maisonneuve Rosemont
Samuel Delisle-Reda	Centre de recherche du CHUM
Souleymane Diabaté	Laval Université
Linnea Doyle	Gilead Sciences Canada Inc.
Amanda Fletcher	Canadian Treatment Action Council
Lorraine Fradette	Centre de Recherche du CHUM
Alex Haines	Toronto Health Economic and Technology Assessment collaborative
Janet Hatcher Roberts	University of Ottawa
Rachel Hayes	McGill University
Lindsay Jennings	ASO
Aline Keyrouz	MUHC
John Kim	National HIV/AIDS Laboratories
Murray Krahn	University Health Network
Bruce Kreter	Gilead Sciences
Nadine Kronfli	McGill University
Stéphanie Laporte	Programme national de mentorat sur le VIH et les hépatites
John Law	University of Alberta
Sam Lee	University of Calgary
Sophie Lefevbre	Dopamine
Daryl Luster	Pacific Hepatitis C Network
Nimâ Machouf	Clinique de Médecine Urbaine du Quartier Latin
Sevil Marandi	Gilead Sciences Inc.
Dominic Martel	Centre hospitalier de l'Université de Montréal
Laurence Mersilian	Capahc
Martin Pagé	Dopamine
Tsvetelina Pantileeva	CRCHUM
Hansi Peiris	Research Institute of the MUHC
marjolaine pruvost	CAPAHC
Yasmine Rahal	AbbVie
Marylin Rheault	McGill University
Isabelle Robichaud	Research Institute of the MUHC
Carmine Rossi	BCCDC
Arvind Sandhu	Max Super Specialty Hospital
Deb Schmitz	Pacific Hepatitis C Network
Francine Tourangeau	CHRRimouski
Sarah Tran	CRCHUM
Chloé Trudeau	CHUM
D. Lorne Tyrrell	Li Ka Shing Institute of Virology - University of Alberta
Jennifer van Gennip	Action Hepatitis Canada
Sunil Varghese	West Ottawa Specialty Care
Virginie Verreault	CHUM
Sarey Wulf	Gilead Sciences Canada
Jim Young	McGill University
Ziba Aalamian	McGill University Health Centre
Mohamed Abdel-Hakeem	University of Pennsylvania
Mohamed Abdelnabi	CRCHUM-University of Montreal
Hiatem Abofayed	University of Alberta
Liza Abraham	St. Michael's Hospital
Fat'hiya Al Harthy	McMaster Children's Hospital
Amr Ali Hemeda	Future University In Egypt (FUE)
Karen Anand	Rx Infinity
Maria Ancheta-Schmit	GI Research Institute
Joanne Anderson	AbbVie Corporation
Dominica Anderson	Reseau ACCESS Network
Madanraj Appiya Santharam	Universite de Sherbrooke
Sandra Ardila	Université de Montréal
Andreea Adelina Artenie	Université de Montréal
Jacqueline Atkinson	Work
Berson Augustin	Mcgill University
Ceilia Bai	Gilead Sciences
Michael Bailey	CATIE
Nicole Ballantyne	CATIE Access Place
Patrick Barber	Gilead Sciences
Martin Baril	Gilead Sciences
Tamara Barnett	Cool Aid Community Health Centre
Tamara Barnett	Cool Aid Community Health Centre
Lisa Barrett	Dalhousie University
Ralf Bartenschlager	Universitätsklinikum Heidelberg, Molecular Virology

Sofia Bartlett	BC Centre for Disease Control/UBC
Shelley Beckstead	Street Health Centre
Francois Belanger	Lupin Pharma
Estelle Bene	Merck Canada
Anne Berberi	AbbVie Corporation
Michelle Bergeron	Gilead
Mamatha Bhat	University Health Network
Diane Bigras	Gilead Sciences
Marc Bilodeau	CHUM
Mia Biondi	Toronto Centre for Liver Disease
Cathy Bizruchak	AbbVie Corporation
Wendy Boivin	AbbVie Corporation
Sharon Bojarski	William Osler Health Sysem
Kouassi Edmond Diamanti Boka	SAVE THE LIFE NGO
Sergio Borgia	William Osler Health System
Brent Bostrom	AbbVie Corporation
Mathieu Boucher	AbbVie Corporation
Jean-Claude Boucher	Gilead Sciences
Josee Boulianne	Astellas Pharma Canada Inc
Catherine-Audrey Boutin	Udem-CHUM
Barb Bowditch	CATIE Access Place
Patricia Boyd	Positive Care Clinic Lakeridge Health
Ben Brenner	Gilead
Andrew Brett	CATIE
Josee Brisebois	Gilead Sciences Canada
Jennifer Broad	South Riverdale Community Health Centre
Heather Burt	Gilead Sciences
Carmen Cabral	PerCuro Clinical Research Ltd
Leanne Cadden	Salmon Arm Liver Clinic
Camelia Capraru	Toronto Centre for Liver Disease / VIRCAN
Christine Cash	Yukon Communicable Disease Control
Jasmin Chahal	McGill University
Michael Cheng	University of Toronto
Susan Christenson	Blood Tribe Department of Health
Geoffrey Christie	Gilead Sciences
Conan Chua	University Health Network
Sai Chung	University of Toronto
Carla Coffin	University of Calgary
Simon Collin	AbbVie Corporation
Sheilagh Commeford	Gilead
Brian Conway	Vancouver Infectious Diseases Centre
Curtis Cooper	University of Ottawa - The Ottawa Hospital
Shelley Crawford	Saskatchewan Health Authority
Angela Crawley	Ottawa Hospital Research Institute
Michelle Crosby	Island Health
Anna Cumaraswamy	Gilead Sciences Canada, Inc.
Leah Curnew	Memorial University
Cheryl Dale	Specialty Rx Solutions
Ecaterina Damian	CSIH
Karen Delina	Toronto Centre for Liver Disease/VIRCAN
Sylvie Denis	AbbVie Corporation
Linda Denis	Barrie/RXI
Anna DeWolff	Salmon Arm Liver Clinic
Melisa Dickie	CATIE
Lisa Douglas	Alberta Health Services
Anne Drost	Victoria Cool Aid Society
Kate Dunn	Alberta Health Services
Carol Dupasquier	Canadian Association of Hepatology Nurses
Camille Dussault	McGill Health Center University
Laurie Edmiston	CATIE
Stephanie Eiloart	RxInfinity Inc
Hashem El-Serag	Baylor College of Medicine
Art Epp	AbbVie Corporation
Aysegul Erman	University of Toronto
Patrick Ethier	AbbVie Corporation
Farah Faytrouni	BC CHILDREN'S HOSPITAL
Jeanette Feizi Farivar	GI Research Institute
Jordan Feld	University Health Network
Manuel Flores	CRCHUM
Andrea Forbes	Merck
Pam Ford	Regina Internal Medicine
Tanya Fournier	Alexion Pharma
Dennaye Fuchs	Saskatchewan Health Authority
Renee Gagnon	Correctional Services of Canada
Lesley Gallagher	Saskatchewan Infectious Disease Care Network
Rick Galli	bioLytical Laboratories, Inc.
Veeral Gandhi	AbbVie Corporation
Maryse Gauthier	Coverdale
Lisa Gauthier	Gilead Sciences
Julie German	Addiction Services Thames Valley
Peter Ghali	McGill
Arnaud Godin	McGill University
Corentine Goossens	CRCHUM-UdeM
judith goplen	cobblestone clinic
Sarah Gora	Lupin Pharma Canada
Shauna Granger	Penticton Hepatitis C Clinic
Jason Grebely	UNSW Sydney
Christina Greenaway	Jewish General Hospital

Zoë Greenwald	Jewish General Hospital
Pamela Gullo	Peterborough Clinic
Klaus Gutfreund	University of Alberta
Jodi Halsey-Brandt	Merck Canada
Nourdine Hamdane	Institute for Viral and Liver Disease
Sojung Han	University of Calgary
Sonja Hartz	PWNI
Michael Harvey	Merck
Wendy Hauck	Eisai Ltd
Saskia Hildebrandt	AIDS Committee of North Bay and Area
Stine Hoj	University of Montreal
Drew Hollingsworth	Merck
Tristan Holotnak	University of Calgary
Christopher Hoy	CATIE
Sarah Hughes	Island Health
Yong Gyu (Frank) Hyun	University of Toronto
Brendan Jacka	Centre de recherche du CHUM
Lynne Jamme	AbbVie Corporation
Naveed Janjua	BC Centre for Disease Control
Saumya Jayakumar	University of California, San Diego
Jean Jette	Coverdale
Jean Jetté	Coverdale
Carolina Jimenez	Children's Hospital of Eastern Ontario
Dan Johnson	Gilead Sciences
Christie Johnston	CATIE
Hsiao-Ming Jung	Albany Medical Liver Clinic
Mangyung Kandangwa	University of Saskatchewan
Kelly Karn	Specialty Rx
Susan Kelso	AbbVie Corporation
Dana Michelle Kennedy	AbbVie Corporation
MD Gulam Musawwir Khan	University of Sherbrooke
Grace Kim	AbbVie Corporation
Alexandra King	College of Medicine, UofS
Zak Knowles	CATIE
Hin Hin Ko	UBC
Beverley Kok	University of Alberta Hospital
Gillian Kolla	University of Toronto
Thomas Krahn	McGill University
Mel Krajden	BC Centre For Disease Control
Rasika Kunden	University of Saskatchewan
Hadi Kuriy	TGH-UHN
Rivka Kushner	CATIE
Martina Kusnir	Lupin Pharma Canada
Dimitriana Kuzyk-Bernier	Mount Carmel Clinic
Clémence Laforce	Coverdale Clinic
Douglas Laird	Hep C BC / AHC
Deki Dolma Lama	Nine
Kelly Lang	Regina General Hospital
Charlotte Laniece Delaunay	McGill University
Stephane Lassignardie	AbbVie Corporation
Jason Lau	Toronto Centre for Liver Disease
Frederick Lavigne	AbbVie Corporation
Regan Lavoie	Street Health Centre
Loretta Layton	AbbVie Corporation
Joachim Le Garrec	Alnylam Pharmaceuticals Canada
Elizabeth Lee	University Health Network- Toronto General Hospital
Kelly Leinster	Merck
Marise Lemieux	Gilead Sciences Canada Inc
Jennifer Leonard	Memorial University
Bernadette Lettner	South Riverdale Community Health Centre
Yiqiao Li	Johns Hopkins Bloomberg School of Public Health
Kristin Lichty	North Lambton Community Health Centre
Simon Ling	Hospital for Sick Children
Lewis Liu	University of Toronto
Jennifer Lowe	Public Health Agency of Canada
James Luyendyk	Michigan State University
Ann Ma	University of Toronto
Nancy MacDonald	McKesson Canada
Sonya MacParland	University of Toronto
Jood Madani	University of Ottawa
Iuliia Makarenko	McGill University
Kailash Makhejani	Toronto General Hospital
Lynette Manderson	Gilead Sciences Inc
Sarah Mansour	The Ottawa Hospital
Gayatri Marathe	McGill University
Alison Marshall	The Kirby Institute and the Centre for Social Research in Health, UNSW Sydney, Australia
Valérie Martel-Laferrière	CHUM
Steven Martin	Alberta Children's Hospital
Robert Martin	Gilead Canada
Kate Mason	South Riverdale Community Health Centre
Chelsea Masterman	SpecialtyRx Solutions
Sabrina Mazouz	CRCHUM
April Mazzuca	Cedar Project
Bruce McDonald	Merck
Keri McGuire-Trahan	AIDS Committee of North Bay and Area
Vanessa Meier-Stephenson	Universities of Calgary and Lethbridge
Andrew Mendlowitz	University of Toronto

Kerolous Messeha	University of Alberta
Sylvain Messier	Merck
France Mignault	Gilead Sciences Inc
Nanor Minoyan	University of Montreal / CRCHUM
Robert Mitchell	University of British Columbia
Aldo J. Montano-Loza	University of Alberta
Heidy Morales	CanHepC
Shafi Muhammad	CRCHUM, University of Montreal
Dylana Mumm	Gilead Sciences
Dana Mundil	Gilead Sciences
Adrienne Murdoch	Lupin Pharma Canada
Ali Murphy	CATIE
Blaise Myette	McKesson Canada
Patrick Nadeau	Lupin Pharma Canada
Catherine Nevin-Pike	HepCare/SpecialtyRx
Kate Newcombe	CUPS Health Clinic
Hugh Ngo	Gilead Sciences Canada
Henry Nguyen	NYU Langone Medical Center
Claudia Nigro	BC Hepatitis Program
Julia Oguzer	Hepatitis Outreach Society of Nova Scotia
Hayley Orlick	PerCuro Clinical Research Ltd
David Osorio Laverde	Université de Montréal
katia oteman	Gilead Sciences
Adam Palayew	McGill University
Amy Palumbo	Campbell River Hospital
Nick Pang	University of British Columbia
Hyejin Park	MUHC
Keyur Patel	UHN Toronto
Margo Pearce	BCCDC
Kevork Peltekian	Atlantic Hepatology
Diane Perreault	Coverdale
Christine Perreault	Coverdaleclinic
Cherie Perry	Cameron Street Clinic
Diederik Peters	AbbVie Corporation
Paul Plaisir	AbbVie Corporation
Kathryn Poldre	VIRCAN
Nashira Popovic	Public Health Agency of Canada
Mélanie Provost	Merck
Kelly Quinn	AbbVie Corporation
Sheikh Rahman	University of Western Ontario
Ismatul Rahman	McGill University
Alnoor Ramji	University of British Columbia
Norina Dean Ramos	GI Research Institute
Stuart Ray	Johns Hopkins Univ School of Medicine
Sonia Rayman	Gilead Sciences
Eve Roberts	University of Toronto
Marc Robitaille	AbbVie Corporation
Steven Roblin	Alnylam Pharmaceuticals Canada
Tim Rogers	CATIE
Marie-Claude Roy	AbbVie Corporation
Rod Russell	Memorial University
Matthew Sadler	University of Calgary
Yasmin Saeed	Leslie Dan Faculty of Pharmacy, University of Toronto
Sahar Saeed	Mcgill
Selena Sagan	McGill University
Maya Saleh	McGill University
Beate Sander	University Health Network
Naveen Sandhu	Alexion Pharma Canada
M Omair Sarfaraz	University of Toronto
Izza Sattar	University Health Network
Philippe Schinck	Gilead Sciences
Rick Schreiber	University of British Columbia
Giada Sebastiani	Mcgill University Health Centre
Hemant Shah	University of Toronto
Arezou Shahmoradi	University of Saskatchewan
Clinton Shard	AbbVie Corporation
Thomas Shaw-Stiffel	The Ottawa Hospital
Mohamed Shengir	McGill University
Naglaa Shoukry	CRCHUM
Lucy Smith	Memorial University
Hugo Soudeyns	Centre de recherche du CHU Sainte-Justine
Tara Stamos-Buesig	Eliminate Hepatitis C San Diego
Kimberly Stetsko	Lupin Pharma Canada
Mark Sulkowski	Johns Hopkins University
Hussain Syed	University of Alberta
Farzaneh Tamnanloo	Centre de recherche du CHUM (CRCHUM)
Julie Tan	McMaster University
Fozia Tanveer	CATIE
Sahid Tarawally	Sierra Liver Founda
Elaine Tattrie	Correctional Service of Canada
Shannon Taylor	CAHN
Norah Terrault	University of Southern California
Stephanie Tiffin	McKesson Canada
Stephanie Toigo	McGill University
Kristina Tomas	Public Health Agency of Canada
Marcel Tomaszewski	McGill University
Mario Trudel	Gilead Sciences
Keith Tsoi	McMaster University

Julia Uhanova	University of Manitoba
Marla Ullman	Coverdale Infusion Clinics
Robert Urbanic	Gilead Sciences Canada
Marie-Louise Vachon	CHU de Québec
Philippe Valois	Merck Canada inc.
Bhavesh Variya	Universite de Sherbrooke
Michel Vezina	AbbVie Corporation
Michel Vézina	Abbvie Canada Inc.
Paramvir Virdi	University of Manitoba
Adesh Vora	SpecialtyRx Solutions
Hannah Wallace	Memorial University
Jean-Philippe Wallach	University of British Columbia
Lori Lee Walston	Specialty Rx
Lingyan Wang	Memorial University of Newfoundland
Christopher Wang	University of Alberta
Rosalyn Weir	Saskatchewan Infectious Disease Care Network (SIDCN)
Bernard WILLEMS	Centre Hospitalier de l'Université de Montreal
Robert Wisniewski	Gilead Sciences Canada
William WL Wong	University of Waterloo
Kipp Wotherspoon	Gilead Sciences Canada Inc.
Colina Yim	Toronto Centre for Liver Disease
Eric Yoshida	University of British Columbia
Menisa Zaman	Weill Cornell
Xun Zhao	Université de Montréal
Blake Ziegler	Advanced Care Specialty Pharmacy
Donna Zukowski	CAHN

Sponsors – Commanditaires

Thank You To All Our Sponsors

And Partners

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