HEPATITIS C TREATMENT IN THE NEW DAA ERA :

Frontline implications

PRESENTED BY

Rivka Kushner, Moderator

Dr. Hemant Shah,

Rachael Edwards,

Elaine Polflit,

Lisa Toner

June 29, 2018

CATIE

Canada's source for HIV and hepatitis C information

Webinar Agenda (1.5 hours)

- Overview of DAA treatment

  Dr. Hemant Shah, 25 minutes
- Reflections on how DAA treatment has changed frontline work

  Rachael Edwards, 10 minutes

  Elaine Polflit, 10 minutes

  Lisa Toner, 10 minutes
- Q & A

  30 minutes

Dr. Hemant Shah

Clinic and Education Direction, Francis Family Liver Clinic

Dr. Hemant Shah is an Assistant Professor, Staff Hepatologist and Clinician-Educator at the Francis Family Liver Clinic at the University of Toronto, Ontario, Canada. He presently serves as the clinical and education director of the liver program. His clinical focus is viral liver disease and he maintains a busy teaching practice. In addition to clinical care, Dr. Shah is actively engaged in projects to develop innovative models of care for viral hepatitis, progress interprofessional collaboration and improve knowledge levels amongst primary care and specialty providers. Dr. Shah also holds several national education leadership positions and is a co-principal author of the Canadian Consensus Guidelines on Hepatitis C. Dr. Shah has graduate training in Health Practitioner Education.

Hepatitis C Treatment in the New DAA Era: Frontline Implications

Hemant Shah MD MScCH HPTE
Clinical Practice Director, Francis Family Liver Clinic
University of Toronto
@hepatoMD

Name: Dr. Hemant Shah

Disclosures

(over past 24 months)

	Speaker	Advisory	Research	Consultant
Abbvie	√	√		√
Boehringer-Ingelheim			√	
BMS	√			√
Gilead		√	√	√
Intercept		√		√
Lupin	√	√		√
Merck	√	√		√

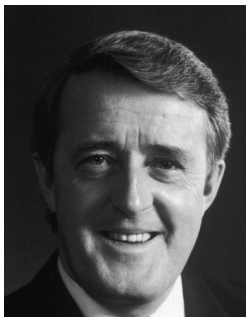
Outline

- A Brief History
- Benefits of Treatment
- Treatment Options Today
- Hep C as a Public Health Problem

HCV Milestones

- 1975: Description of non-A, non-B hepatitis
- 1989: Identification of HCV
- *1991: First interferon studies for Hepatitis C Treatment*
- 1993: HCV genome organization and polyprotein processing delineated
- 1997: First HCV clone constructed
- 1998: First use of IFN-α and Ribavirin therapy
- 2003: First clinical studies of HCV protease inhibitor
- 2005: Production of recombinant HCV in tissue culture

What else happened in 1991?



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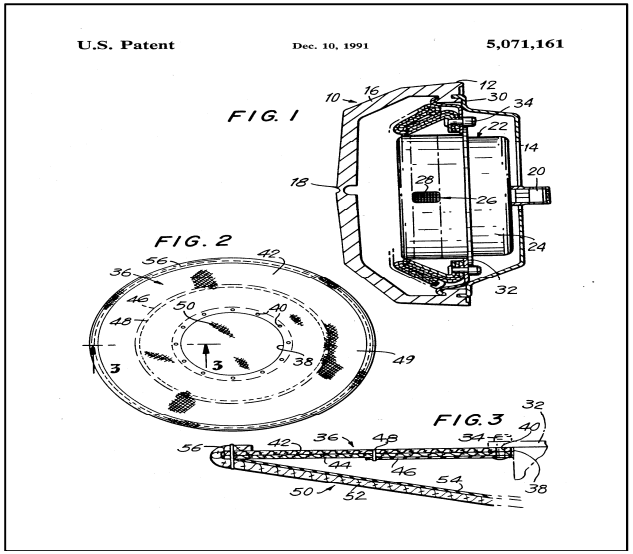
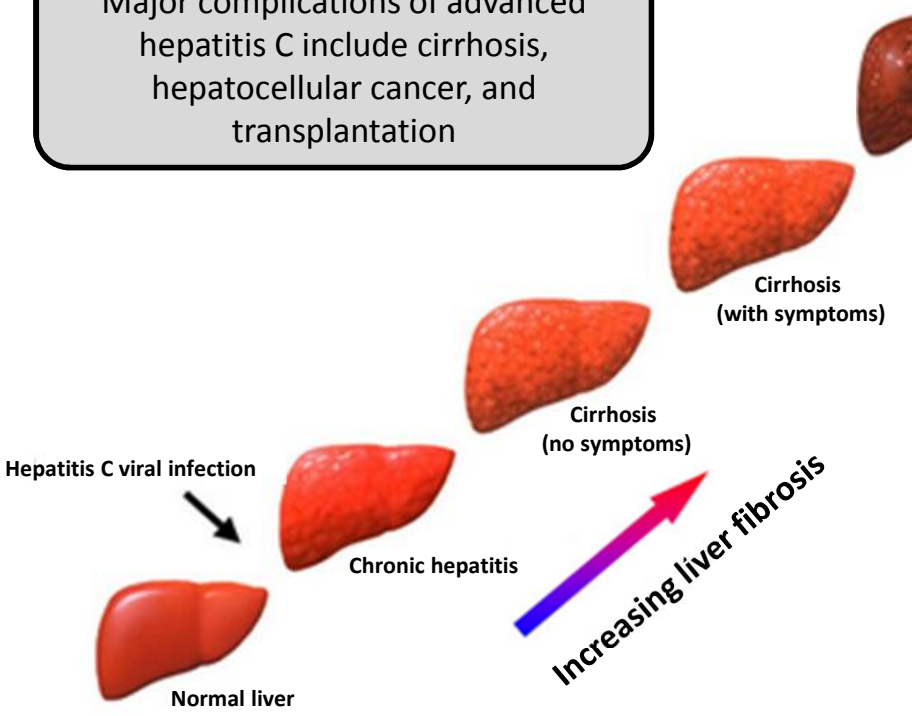


What Are the Complications Associated with Hepatitis C?

Major complications of advanced hepatitis C include cirrhosis, hepatocellular cancer, and transplantation



HCC, hepatocellular carcinoma.
Myers R, et al. *Can J Gastroenterol Hepatol.* 2014; 28(5):243-50.

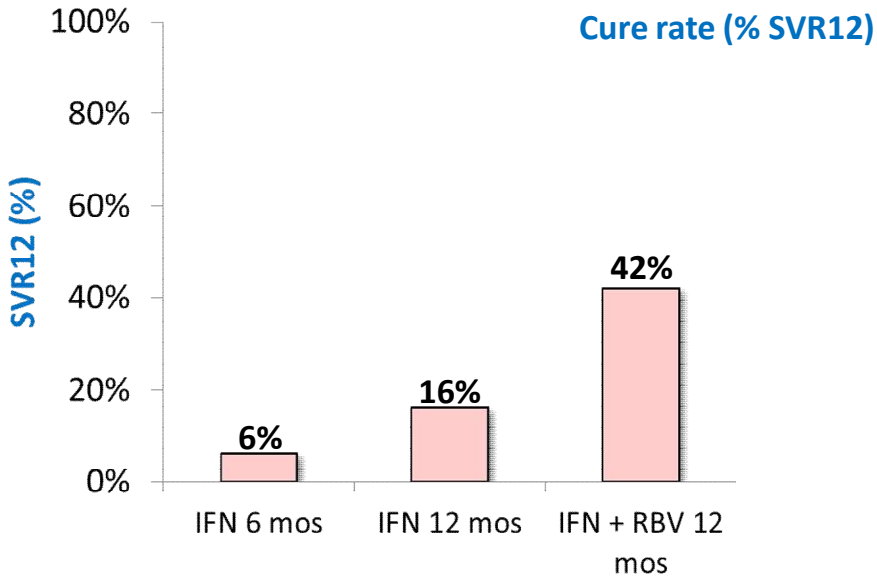
Severity of disease fibrosis F scores

Score	Description
F4	Cirrhosis
F3	Severe fibrosis
F2	Moderate fibrosis
F1	Mild fibrosis
F0	No fibrosis

Patients cured after they already have cirrhosis need lifelong monitoring

Circa 2011…HCV Treatment Efficacy

Up to 2011
IFN- & RBV-based,
up to 1 year Tx



DAA, direct-acting antiviral; IFN, interferon; mos, months; PegIFN, pegylated interferon; PI, protease inhibitor; RBV, ribavirin; Tx, treatment.

Strader DB, et al. *Hepatology.* 2004; 39(4):1147-71; Vertex Pharmaceuticals Incorporated. Incivek Product Monograph; Jacobsson I, et al. Presented at EASL 2013, Poster #1425; Manns M, et al. Presented at EASL 2013, Oral presentation #1413; Lawitz E, et al. Presented at APASL 2013, Oral presentation #LB-02; Afdhal N, *et al. N Engl J Med.* 2014; 370(20):1889-98; Kowdley KV, et al. *N Engl J Med.* 2014; 370(20):1879-88.

Circa 2011…Side Effects of HCV Treatment

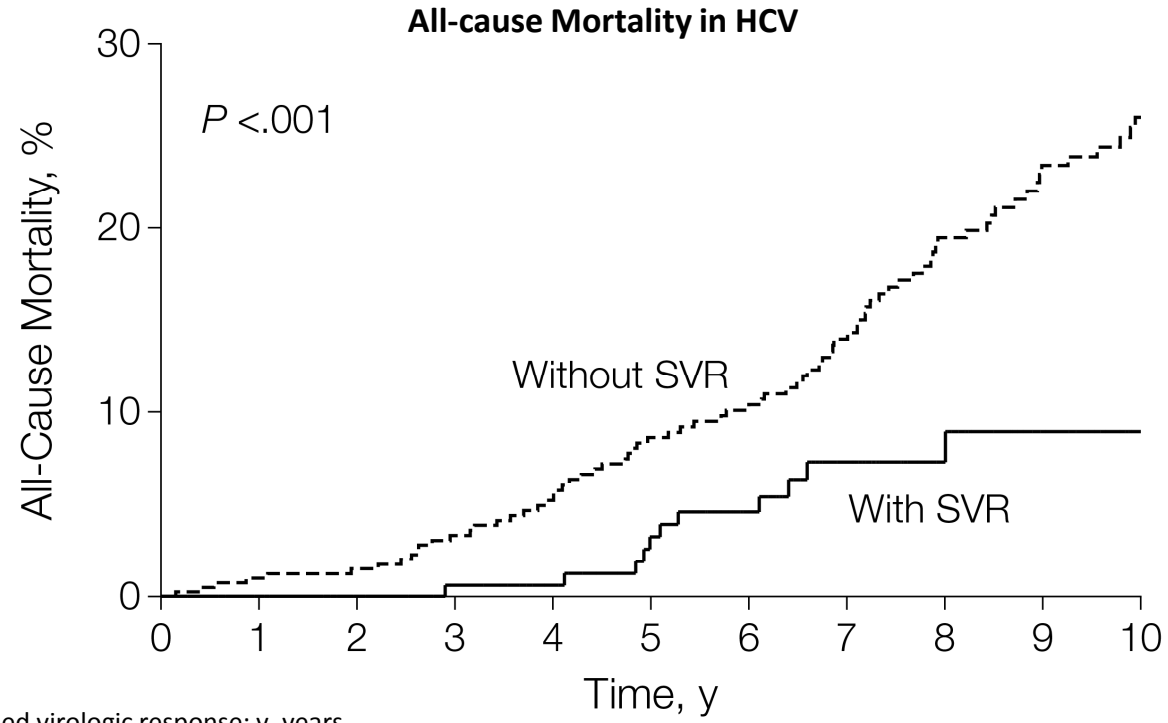
- Flu-like symptoms
  - Headache
  - Fatigue or asthenia
  - Myalgia, arthralgia
  - Fever, chills
- Nausea
- Anorexia
- Diarrhoea
- Psychiatric symptoms
  - Depression
  - Insomnia
- Alopecia
- Injection-site reaction
- Leukopenia
- Thyroiditis
- Autoimmunity
- Thrombocytopenia
- Hemolytic Anemia

INTRON® A. *PDR*. 56th ed. 2002. ROFERON®-A. *PDR*. 56th ed. 2002.

Populations that were challenging to treat

- PWUD/Substance Abuse – Excluded from all trials
- Co-infection – Longer duration for all HIV/HCV infected persons
- Renal failure – Use the lowest dose of ribavirin and a lot of side effects
- Decompensated cirrhosis – Rarely treated, and with a lot of side effects
- Post-transplant HCV recurrence – Drugs increased risk of organ rejection, only treated after liver damage in the new organ
- Anyone with minimal fibrosis – Drugs simply not approved

Curing Hepatitis C Saves Lives

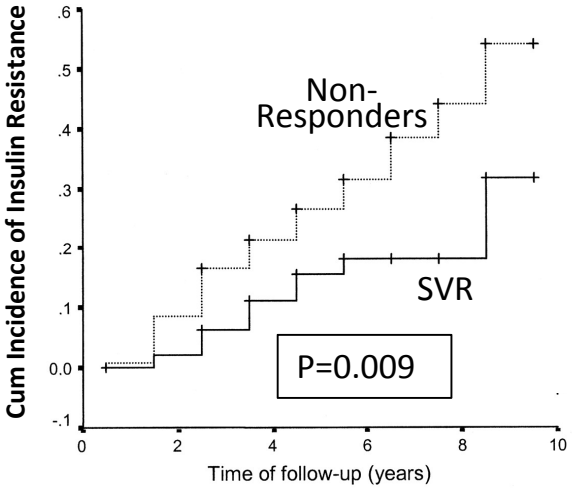


SVR, sustained virologic response; y, years.

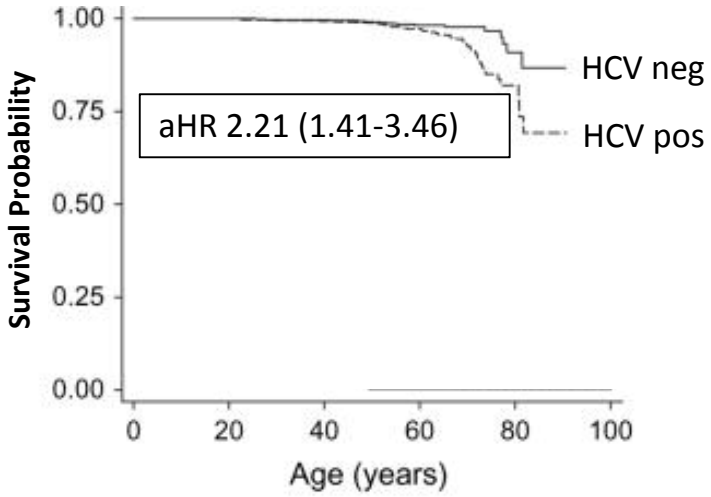
Adapted from van der Meer AJ, et al. *JAMA.* 2012; 308(24):2584-93.

Benefits beyond the liver

Risk of Insulin Resistance/DM



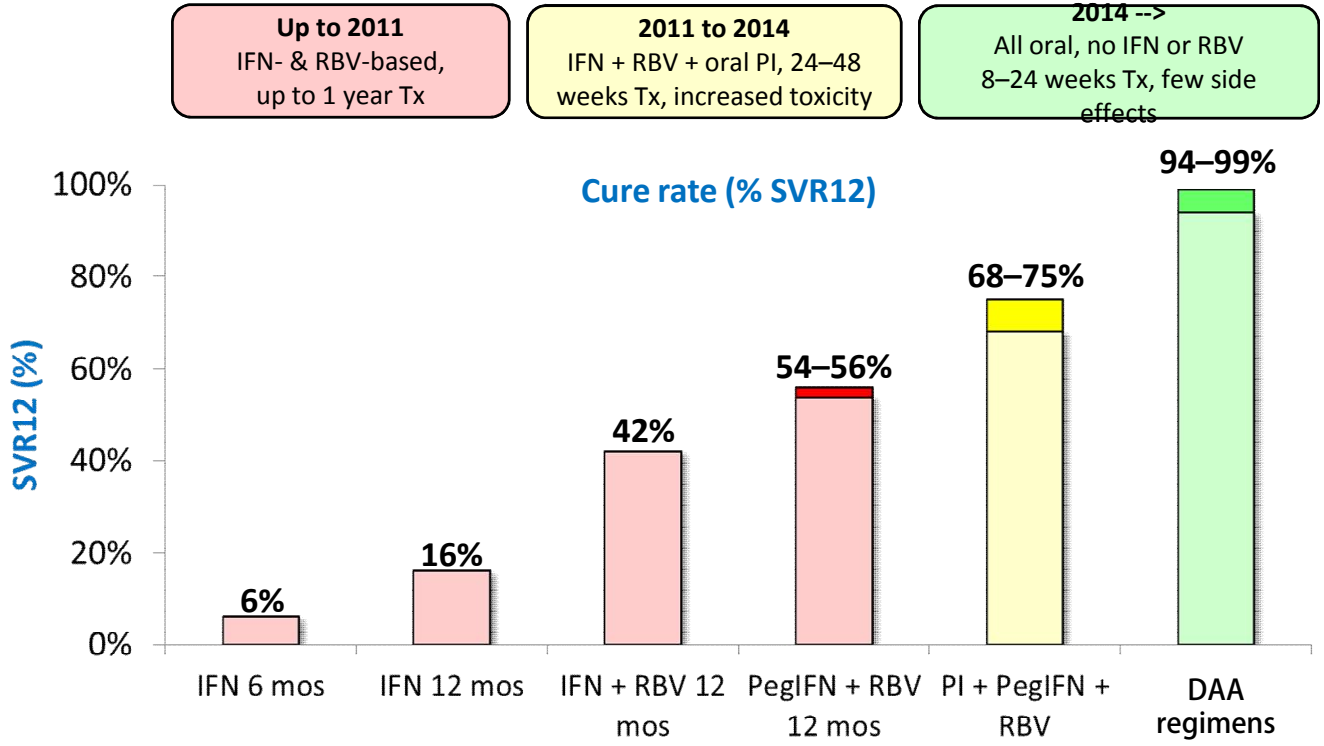
Cardiovascular Disease



SVR may reduce diabetes and heart disease

Simo Diabetes Care 2006
Guiltinan Am J Epi 2008

Rapid improvements in HCV Treatment Efficacy



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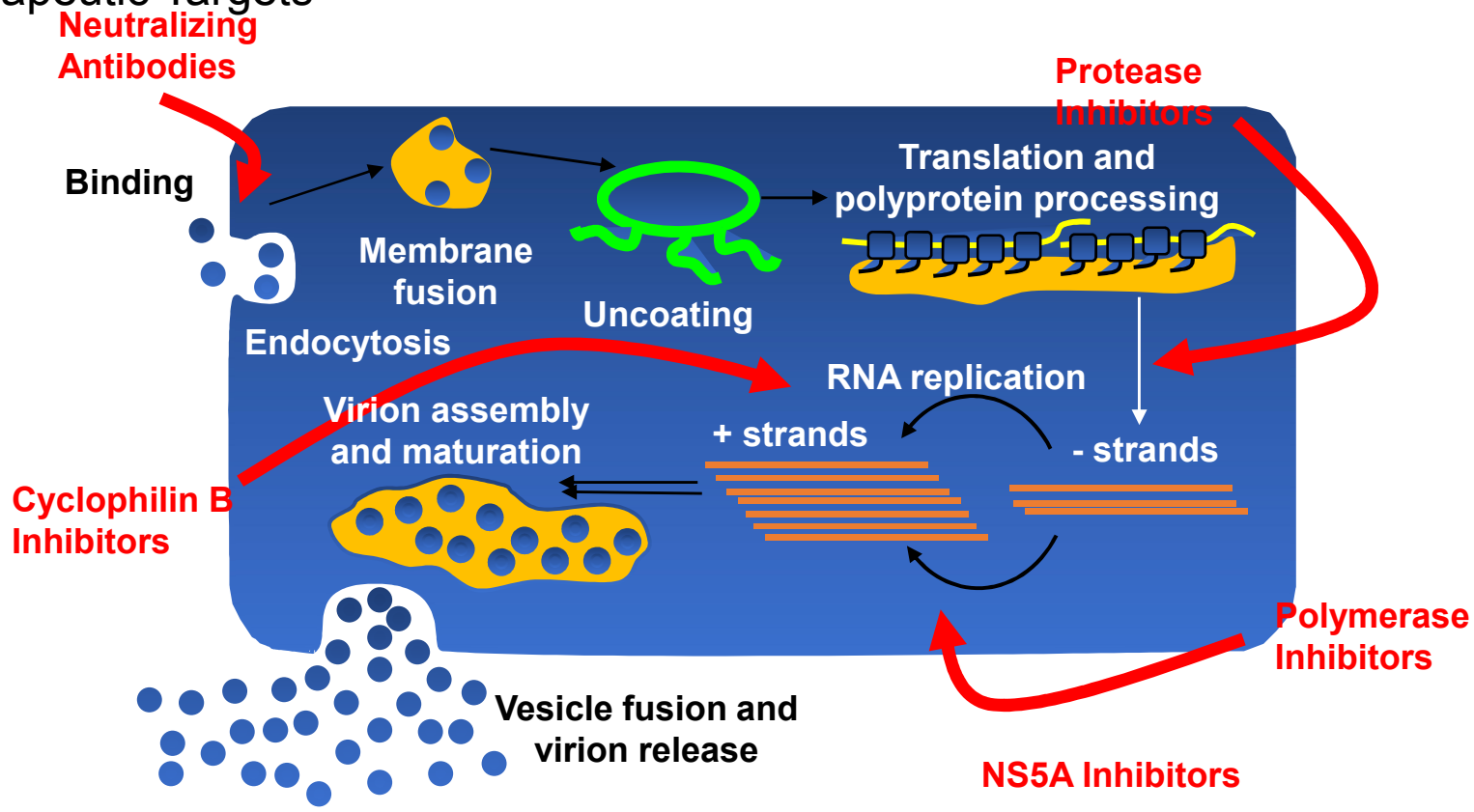
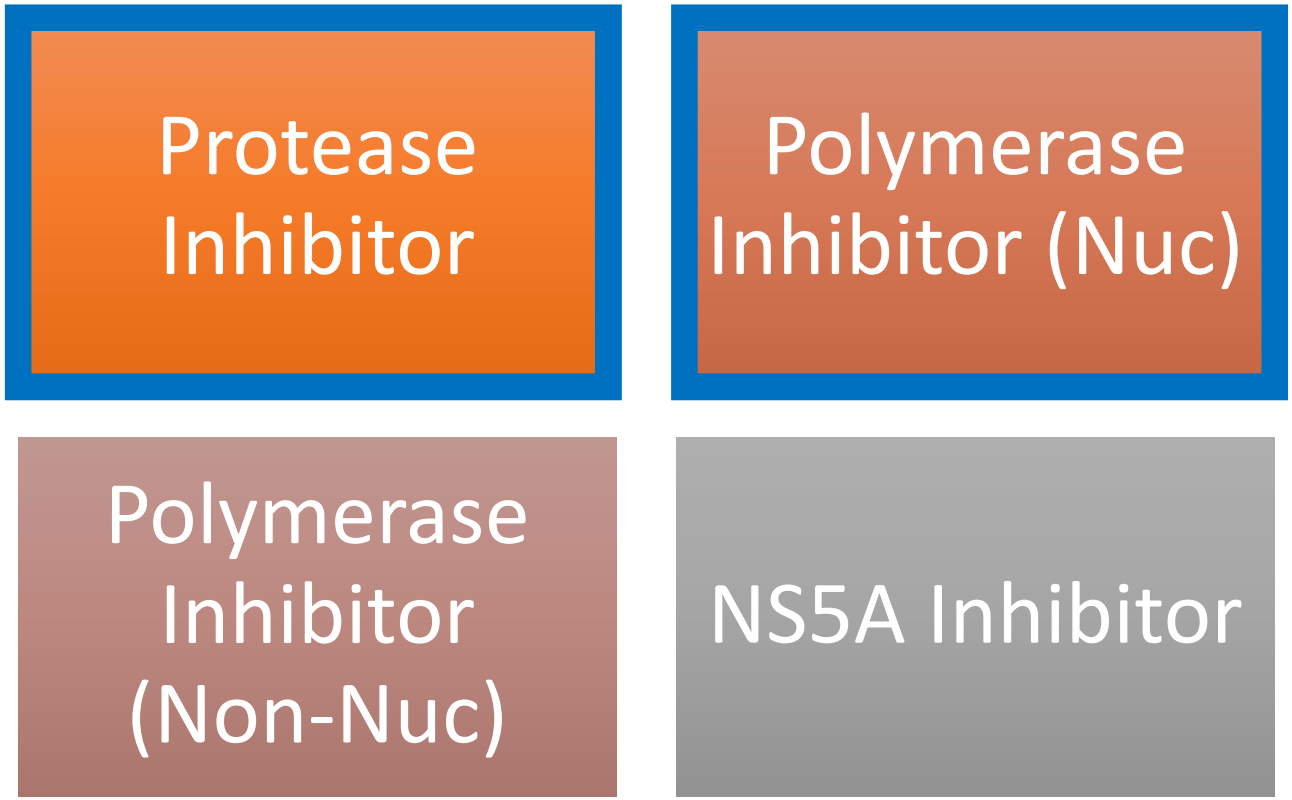
HCV Therapeutic Targets



Davis et al. *Semin Liver Dis*. 1999 (suppl 1).

Current Therapeutic Classes/Options – Used in Combo



Approved Regimens in Canada

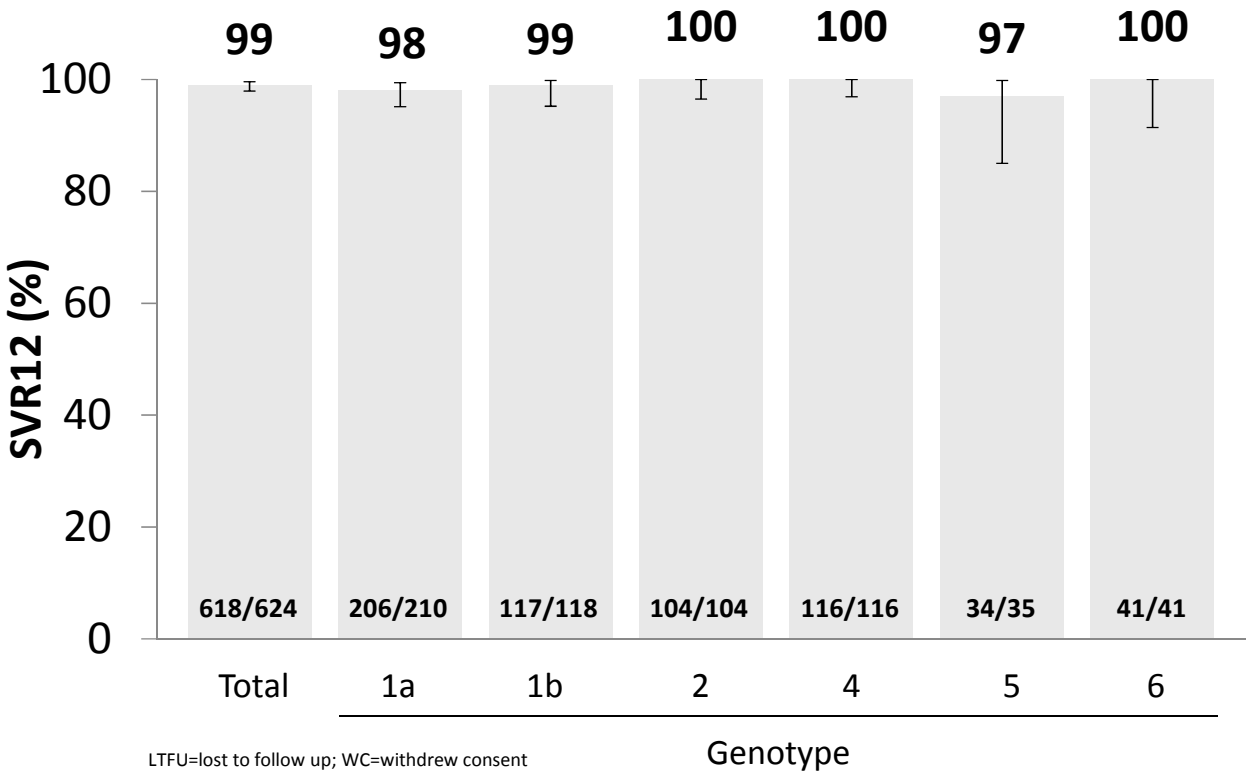
Regimen	HCV genotype						
	1a	1b	2	3	4	5	6
Ledipasvir/sofosbuvir (Harvoni)	8–12 wk†	8–12 wk†	NR	+ ribavirin 12 wk	12 wk	12 wk	12 wk
Elbasvir/grazoprevir (Zepatier)	12–16 wk ± ribavirin‡	8–12 wk§	NR	+ sofosbuvir x 12 wk	12 wk	NR	NR
Paritaprevir/ritonavir/ombitasvir + dasabuvir (Holkira Pak)	+ ribavirin 12 wk	12 wk	NR	NR	Paritaprevir/ ritonavir/ ombitasvir + ribavirin 12 wk	NR	NR
Sofosbuvir + daclatasvir (Sovaldi + Daklinza)	12 wk	12 wk	12 wk	12 wk	NR	NR	NR
Sofosbuvir/velpatasvir (Epclusa)	12 wk	12 wk	12 wk	12 wk	12 wk	12 wk	12 wk
Glecaprevir/pibrentasvir (Maviret)	8 wk	8 wk	8 wk	8 wk	8 wk	8 wk	8 wk
Sofosbuvir/velpatasvir/ voxilarevir (Vosevi)¶	NR	NR	NR	NR	NR	NR	NR

Note: HCV = hepatitis C virus, HIV = human immunodeficiency virus, NR = not recommended.
*Where indicated, to be dosed according to weight: ≤ 75 kg: 1000 mg daily; ≥ 75 kg: 1200 mg daily. See Appendix 1 for reference supporting recommendations.
†In individuals without cirrhosis and without HIV with a viral load < 6 million IU/mL, an 8-week regimen of ledipasvir/sofosbuvir may be considered.
‡Resistance testing suggested for people with genotype 1a infection before treatment with elbasvir/grazoprevir. If resistance to nonstructural 5A (NS5A) inhibitors is present, treatment should be extended to 16 weeks with the addition of weight-based ribavirin.
§Eight weeks recommended in treatment-naive patients with fibrosis stages F0–F2. For those with F3 or F4, 12 weeks of therapy should be given.
¶Reserved for individuals who have been treated previously with direct-acting antiviral agents.

Hemant Shah et al. CMAJ 2018;190:E677-E687

ASTRAL-1: SOF/VEL STR for 12 Weeks in GT 1, 2, 4, 5, 6 HCV-Infected Patients ‡

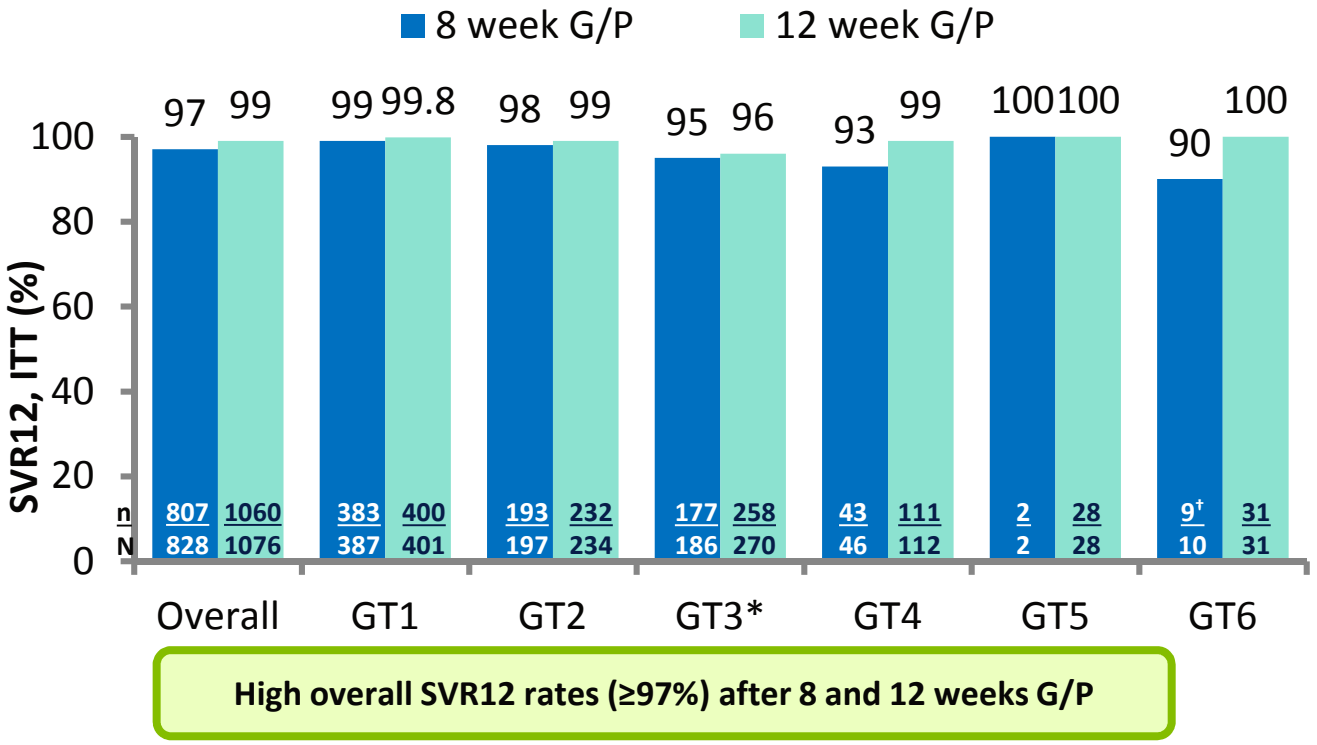
Treatment is Highly Effective



LTFU=lost to follow up; WC=withdrew consent

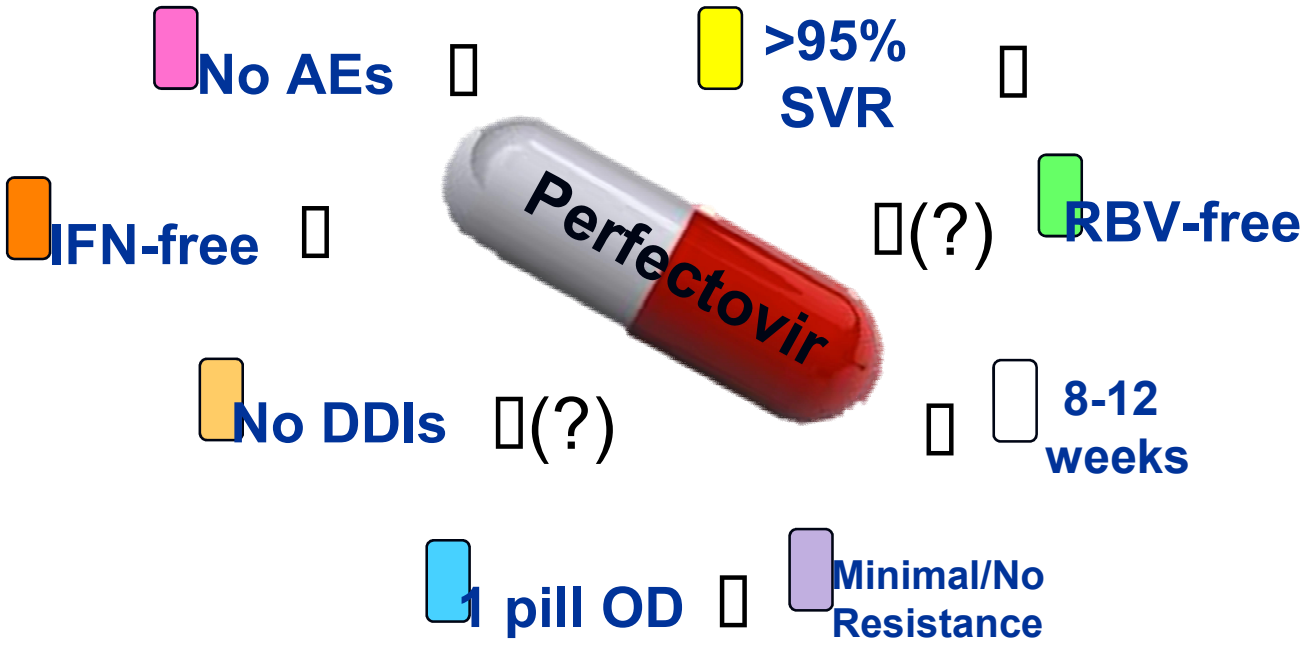
Feld, AASLD, 2015, LB-2. Feld JJ, et al. *N Engl J Med*. 2015. DOI: 10.1056/NEJMoa1512610

Treatment is Highly Effective



- Puoti M, *et al. J Hepatol* 2017; **66**:S721 (poster presentation SAT-233).

Treatment is Pretty Close to ”Perfectovir"



Treatment is Effective in Challenging Populations

- PWUDs – Lots of data demonstrating treatment is tolerated, it works, and patients are adherent
- Co-infection – Most HIV/HCV patient groups in studies do better (!) than monoinfected
- Renal failure – Several good treatment options that work
- Decompensated Cirrhosis - Still a bit of a challenge but a lot of progress has been made
- Post-transplant – Drugs work as well as pre-transplant

Post-treatment Follow Up: Recommendations

- Patient achieves SVR and does not have advanced fibrosis (F1-2):
  - Follow up same as if never infected; no need for repeat HCV testing
  - Considered cured, but not immune against new HCV infection if ongoing high risk behaviours
  - If ongoing risk for HCV or unexplained hepatic dysfunction, assess for recurrence/reinfection with HCV RNA testing
- Patient achieves SVR and has advanced fibrosis (F3 on non-invasive fibrosis testing or liver biopsy):
  - Surveillance for HCC with twice-yearly ultrasound
  - If cirrhosis, screen for esophageal varices with endoscopy
  - If persistently abnormal LFT, assess for other causes of liver disease
- ***There is no immunity and reinfection is possible***

AASLD IDSA Recommendations: hcvguidelines.org

5g of diamonds

25 1-carat ($1900 each)

Cost = $48,000

5g of daclatasvir

12 weeks of treatment, 60mg/day

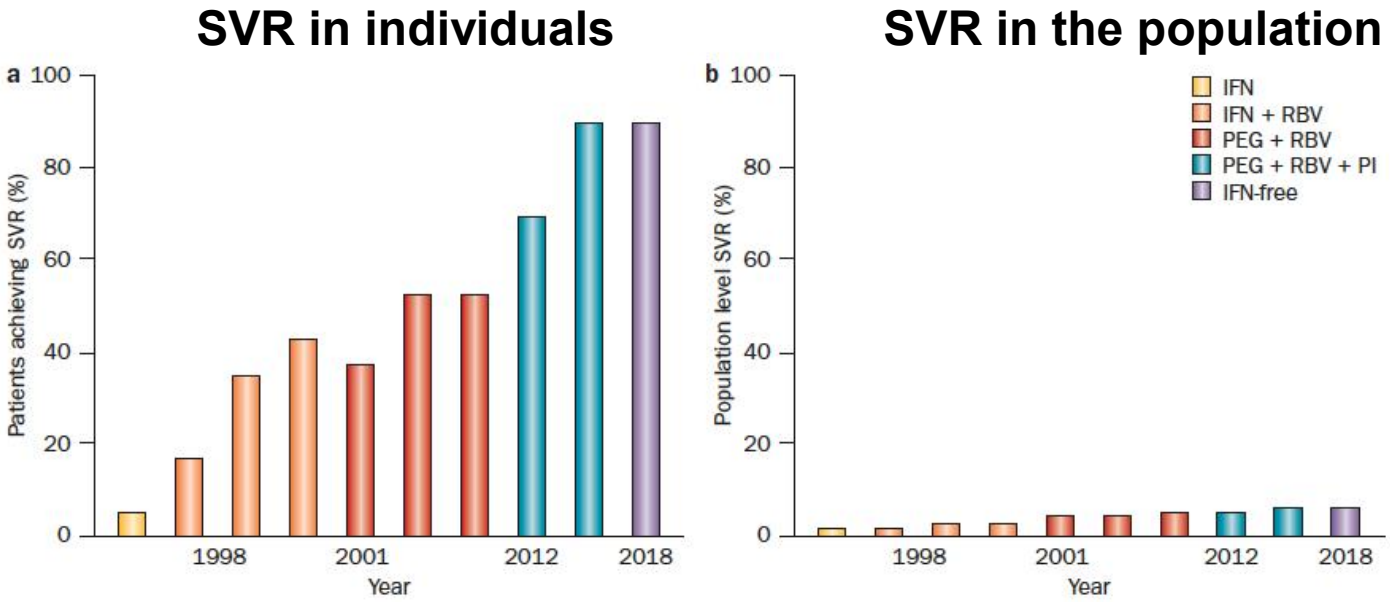
Cost = $53,000 (UK price)

Andrew Hill, 2nd International HIV/Viral

However…2018 a Banner Year!

- Provinces/Territories that have lifted treatment access criteria:
  - Alberta
  - BC
  - Ontario
  - Quebec
  - Saskatchewan
  - Manitoba
  - Yukon
  - PEI (Aim to eliminate HCV)
- Maybe more that I don’t know of!

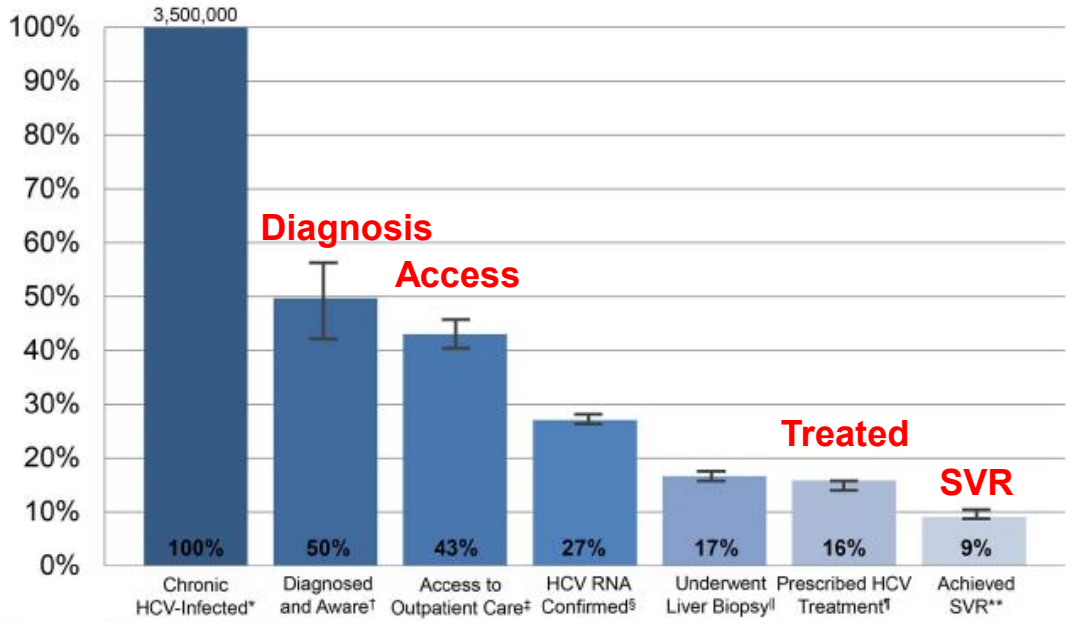
Treatment uptake more important than SVR rate



Improved access more important than improved therapy

GOAL: Improving the cascade of care

Modeled data for non-VA US population



Yehia PLoS One 2014

Future Challenges

- HCV elimination will require a coordinated strategy amongst various stakeholders, government and providers
- Tools to achieve elimination exist, we just have to apply them.


THANK YOU FOR YOUR ATTENTION
ASK HARD QUESTIONS TO GOOGLE

Rachael Edwards

CAMPP Coordinator, Hepatitis Nurse Specialist, CUPS Calgary

Rachael graduated from Mt. Royal University as a registered nurse in 2010. Rachael's passion is to provide quality nursing care in primary care and community settings to individuals who use drugs and alcohol, and experience homelessness and structural vulnerability. She has worked for CUPS since 2006 with vulnerable and marginalized individuals living in poverty. The Liver Clinic at CUPS has been in operation since 1999 and has touched thousands of lives. For the last six years, Rachael has worked treating people for HCV through the inferferon/ribavirin regime, triple therapy and now the new era of DAAs. In 2016, she started the Calgary Allied Mobile Palliative Program (CAMPP) to help homeless individuals access palliative and end-of-life care and to provide comfort and dignity to this very vulnerable population.

CUPS Liver Clinic, Calgary AB

Rachael Edwards RN BN presenting to CATIE June 29 2018

CUPS
Engage. Motivate. Achieve.

Helping low-income individuals and families overcome poverty through:

- **Health**
- **Education**
- **Housing**

CUPS Health Clinic

Primary Care
Women's Health
Prenatal
Obstetrics
Pediatrics
Mental Health
Liver Clinic
On-site lab

Outreach Clinics
Dental Clinic
Optometry
Dietician
Foot Care
Visiting Specialists

Over 5000 unique patients per year
Over 28,000 visits in 2016-17

CUPS HEALTH

CUPS Liver Team

Dr. Gisela Macphail MD, MPH Infectious Disease

Rachael Edwards RNBN Palliative & Hepatitis Care

Kate Newcombe RNBN Harm Reduction

CUPS Liver Clinic

- Providing treatment and care for marginalized individuals with Hepatitis C for 19 years
- Provides wrap-around, low-threshold services
- On site and outreach fibroscans
- Onsite and outreach lab services by RNs
- Offers screening, education, support, vaccines, treatment, and follow-up for people with or at risk of Hepatitis C, in clinic and outreach setting
- Offers support for complex social determinants of health including access to harm reduction supplies and education, Opiate Agonist Therapy, mental health supports, detox and addiction treatment, housing, food and clothing

Treatment is more than just medication

Definition

"Management and care of a person [during] the combating of disease or disorder"

Dorland's Medical Dictionary

Shifts in the DAA era

- More people are eligible for treatment
- More tolerable side effect profile compared to interferon/ribavirin
- More accessible to people using a harm reduction philosophy of care
- Team engages in more research on engaging the whole person over a shorter duration of treatment
- Cascade of care is more important that ever as we work toward eliminating HCV by 2030
- Treating more people with no change in resources
- Since people do not become as fatigued or unwell on treatment they are not as able obtain income
- People may continue to use drugs or alcohol during treatment
- People do not require the intensive case management provided by liver team therefore do not build as strong a relationship with the team

Role of nursing in the DAA era

- Nurse led team embedded in an interdisciplinary primary care clinic
- Focus on capacity building for other nurses and prescribers in DAA era
- Focus on cascade of care to identify where people are falling off
- Same resources available since interferon era
- People pursing HCV treatment are cued with people from primary care clinic to access mental health supports, dietician, social work

Caring for the whole person

- Client readiness. If a person shows up and wants treatment the CUPS liver team will cue them up for treatment. This includes booking diagnostic screening, counselling regarding treatment, harm reduction, reducing risk of re-infection, how to apply for medication coverage, completing insurance forms for medication coverage, referrals and advocacy for housing and/or primary care.
- Weekly in clinic visits with RN while on treatment. Weekly phone calls to those who have mobility or transportation limitations and those who are maintaining employment.
- Medication delivery to clinic so people do not have to also go to pharmacy to pick up meds
- Daily overserved dosing available as needed
- Post treatment reminders re HCC screening, post treatment fibroscan, reminder phone calls re post treatment labs (12 week post tx PCR)
- Peer outreach workers and peer support group offered for all participants before, during, and after treatment

Elaine Polflit

Chief Administrator, SIS program, CIUSSS Centre-Sud-de-L'Île-de-Montréal

Ms. Elaine Polflit holds a Bachelor's degree in Psychology and is currently completing a Master's degree in Public Administration. She has been working in the field of addiction and urban health in Montreal for the past 15 years. She is currently the Program Manager for the Supervised Injection Services (SIS) at the CIUSSS Centre-Sud-de-l'Ile-de-Montréal where she coordinates the nursing activities. In recent years, Ms. Polflit has managed the Cran’s Relais Low-Threshold Clinic, which provides opioid agonist therapy services to a vulnerable population who do not receive appropriate care through traditional services. As part of her work, she structured the services offered on site to include, among other things, psychiatric assessment services and access to hepatitis C treatment.

INTEGRATING HCV TREATMENT IN A LOW THRESHOLD SETTING

Elaine Polflit, Adminstration chief for the Supervised Injection Sites, CIUSSS Centre-Sud-de-l'Ile-de-Montréal

PLUS FORT AVEC VOUS

Centre intégré universitaire de santé et de services sociaux du Centre-Sud-de-l'Île-de-Montréal
Québec

THE RELAIS LOW THRESHOLD OST CLINIC MODEL

The strengh of integrated services and wrap-around care

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et de services sociaux
du Centre-Sud-
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Québec

Relais low threshold OST clinic

- Offers OST (methadone, suboxone, kadian)
- Ease of access
- Multidisciplinary team
- Outreach work
- Global health services

HOW WE GOT THERE

The long hard road to integrating HCV treatment in the service offer

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HCV treatment in Quebec pre DAA

- **What were the hurdles?**
  - Treatment offered in specialized clinics or institutionnal setting
  - High threshold structure
  - New team, new rules
  - Disintegrated multisites service offer
- **Who had access?**
  - Very organised patients
  - Abstinent
- **What happens?**
  - Patients lost to follow up
  - Discouragement

Why was it so hard?

- Memories of the Interferon treatment era
- Fear of being overloaded
- Offering treatment to active IV users
- Lack of trained clinicians
- Cost of treatment vs fear of reinfection
- Treatment already available in other clinics

Slow and steady wins the race

- Specialized training for nurses and social workers
- Mentorship for GP
- New intake questionnaires integrating HCV status and follow up
- Pharma support

ELIMINATING THE VIRUS OR CURING THE DISEASE

'I always used to say we eliminate the virus but we also cure the patients, which are two different things and the new treatments will carry on eliminating the virus but may not cure the patient, and I think we have to look into how we replace that role, and that is going to be difficult.' (London Hepatologist)

Source: Harris, M. & Rhodes, T. (forthcoming). From the social relations of care to the pharmaceuticalisation of treatment: Transitions in treating hepatitis C. Health

What changed for the best?

- Increased access
- No specific level of fibrosis requirement for treatment
- Stabilizing effect of treatment
- Offered to active PWID
- Younger and more vulnerable patients
- Shifting model of care

The pharmaceuticalization of HCV treatment

- Limiting the concept of treatment to access to the molecule
- Taking psychosocial support out of the equation
- Underestimating the effects and impacts of treatment on patients
- Not taking into consideration the life changing aspects of treatment

WHAT'S NEXT?

HCV treatment in the SIS setting

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Québec

First steps towards an HCV treatment offer

- Nurses training
- Connecting with services already offered in community organizations (peer navigators, psychosocial support…)
- Increased offer of HCV screening
- Evaluating the need by consulting people using the services
- Putting in place a nurse led practice
- Possibly offering HCV treatment on site

MERCI!

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Québec

Lisa Toner

Community Outreach Coordinator, Réseau ACCESS Network

As the Community Outreach Coordinator at Réseau ACCESS Network –HIV/Hepatitis Health and Social Services, Lisa Toner has ten years' experience on the frontline collaborating with marginalized people, community-based organizations and healthcare providers to coordinate and deliver supportive and educational programs related to HIV, Hepatitis C and Harm Reduction alongside a multidisciplinary clinical team. Lisa is an advocate for those living with, affected by, and/or at risk of Hepatitis C and HIV as well as struggling with challenges of problematic substance use and mental illness. She has helped carry out several initiatives of benefit to those accessing services in Greater Sudbury and across the region, including HCV prevention outreach, connecting those requiring Hepatitis C treatment and support services, overdose prevention education and advocacy, naloxone distribution and continually advocating at a Provincial level to address the needs of Northern Ontario through the Ontario Harm Reduction Advisory Committee.

Locally, Lisa coordinates with partnering organizations to promote, develop and improve harm reduction services in our Northern Ontario community. As co-chair of the AIDS Bereavement and Resiliency Program of Ontario Lisa consults and liaises with members to drive the direction of the organization to meet the bereavement needs of organizations working in a drug poisoning crisis.

Hepatitis C Treatment in the new DAA era: frontline implications

Lisa Toner
Community Outreach Coordinator of the HCV Treatment Team
Réseau ACCESS Network – HIV/Hepatitis Health and Social Services
Sudbury, Ontario

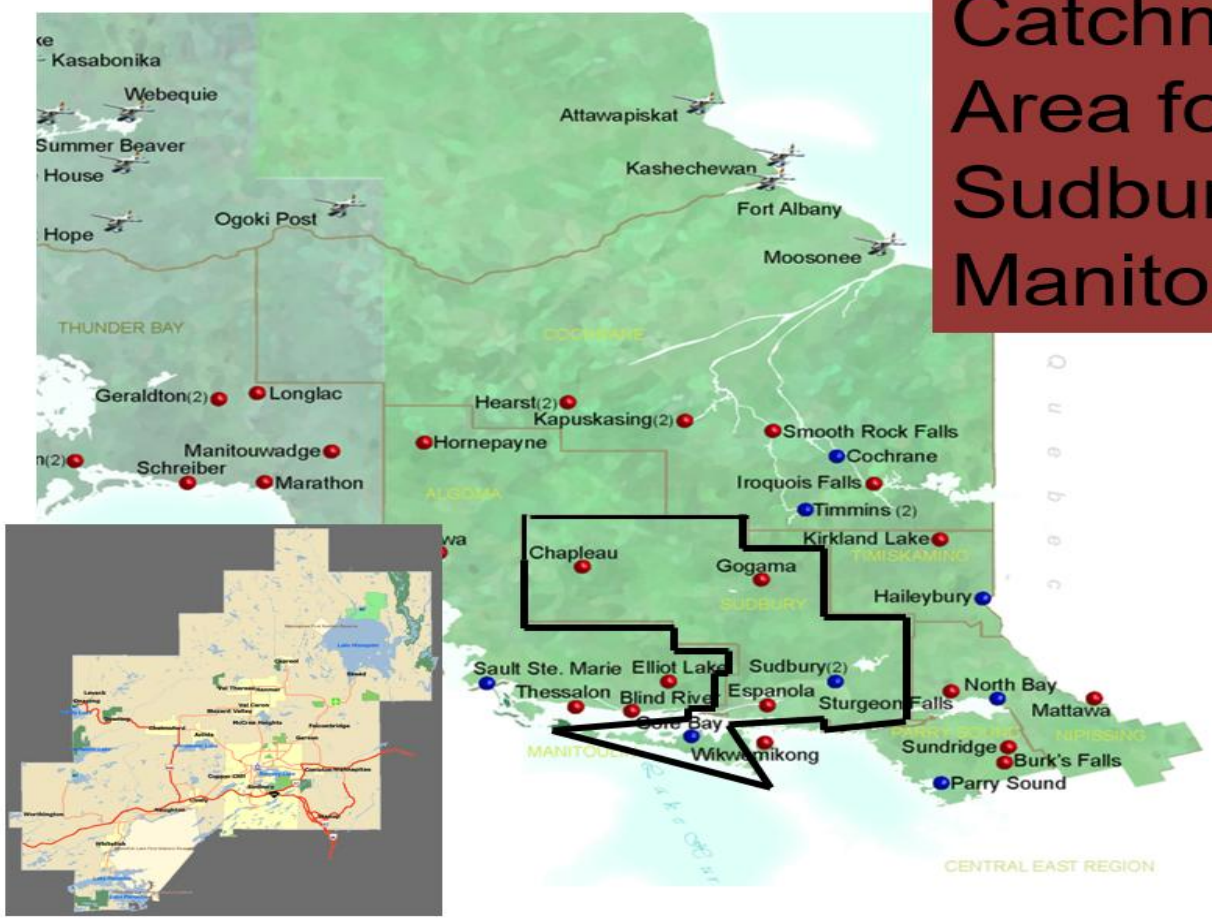
Réseau ACCESS Network

HIV/Hepatitis Health and Social Services

- Non-profit, community-based charitable organization
- Committed to promoting wellness, harm and risk reduction and education
- Supports individuals and serves the whole community in a comprehensive/holistic approach to HIV/AIDS, Hep C and related health issues

Striving to improve the quality of life of people living with, or at risk of, HIV & Hep C, and leading our community in the elimination of all barriers, including stigma and discrimination

Catchment Area for Sudbury-Manitoulin



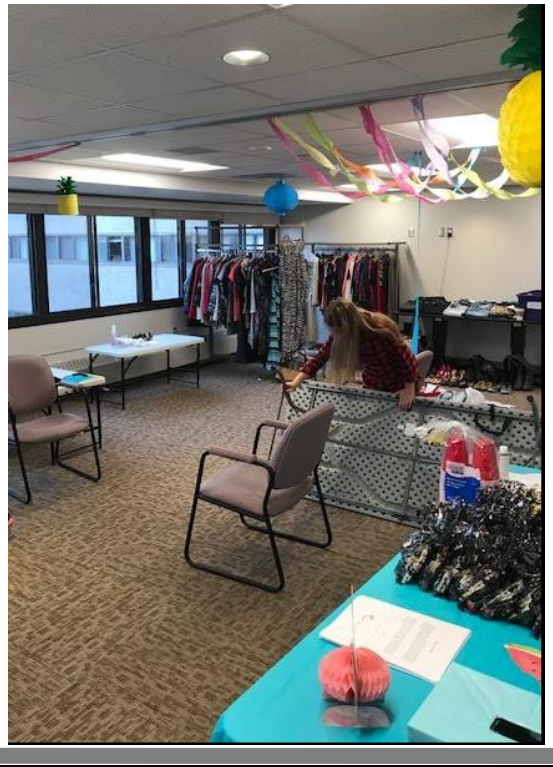
The population we serve

- 100% of the HCV caseload is experiencing mental health challenges and/or substance use
- In our region PWUD have the highest risk level and highest transmission rate of those at risk and living with HCV
- 70% of our caseload is referred to our in office psychiatric services
- 15% of the caseload is already connected to outside psychiatric services
- 10% refuse to attend psychiatric referral/not interested
- We work with the most marginalized and vulnerable members of our community

Significant Shifts

- Open access, length of treatment, < side affects, increased adherence, increased clearance rates
- Psychiatric service shift
- Micro elimination
- Priority population events

Significant Shifts



Program/Role Changes

- Testing event locations
- Engagement between RNA's

Groups

Socials

In house events

Pop ups

Outreach

Food bank

Peer involvement - honoraria

Community Member Support

Before, during and after treatment

BEFORE

- RNA's chronic HCV
- Manage mental illness
- Stabilization

Income

Housing

Social supports

- Harm reduction
- Referrals
- Primary care

Community Member Support

Before, during and after treatment

DURING

- Blood work, primary care needs as it relates to HCV tx
- One on one counselling, groups
- Med dispense planning
- Managing side affects

AFTER

- Harm reduction
- RNA – 6 months
- Peer work

Questions?

Please type your question or comment into the chat box.

Thank You

PRESENTED BY

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CATIE

Canada's source for HIV and hepatitis C information