



# Direct-acting antiviral therapy: Have we reached perfectovir for PWID?

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## Disclosures

I have received grants, honoraria, consultant fees and travel support from AbbVie, Gilead & Merck.



# What is PERFECTOVIR?



**Biological PERFECTOVIR:** optimal efficacy of HCV therapy when administered to a target population (PWID) under controlled conditions.



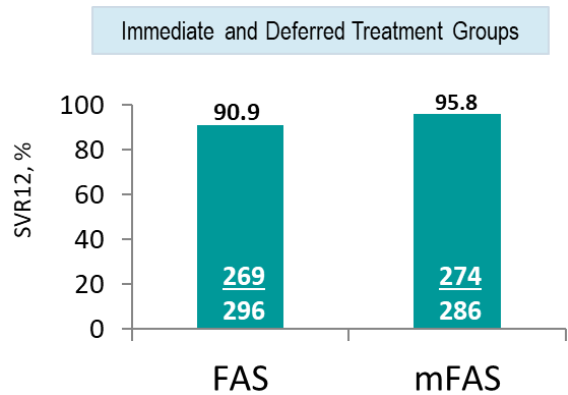
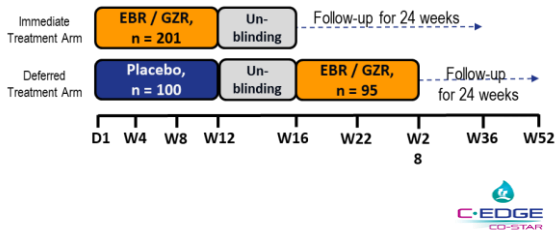
**Functional PERFECTOVIR:** optimal efficacy of HCV therapy when administered to a target population (PWID) under "real life" conditions, usually in settings where HCV therapy was previously administered to members of the target population.



**Societal PERFECTOVIR:** optimal efficacy of HCV therapy when administered to unselected members of the target population (PWID) under uncontrolled conditions.

# BIOLOGICAL PERFECTOVIR

C-EDGE CO-STAR – 25% active PWID during treatment

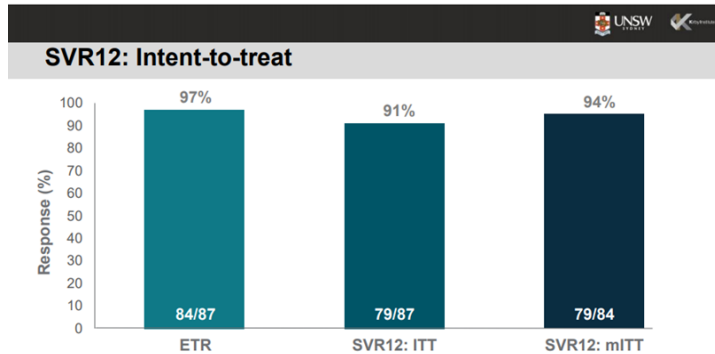


Dore GJ, et al. Ann Intern Med 2016



# BIOLOGICAL PERFECTOVIR

D3FEAT – 57% injecting in last 6 months



- 3 people lost to follow-up between ETR and SVR12
- 2 cases of viral relapse/reinfection (undergoing sequencing to distinguish)

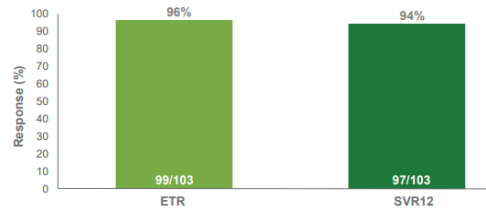
Conway B, et al. INHSU 2017, New York, United States, September 6-8, 2017



# BIOLOGICAL PERFECTOVIR

SIMPLIFY – 100% injecting in last 6 months, 74% in last 30 days

- DAA treatment-naïve patients with GT1-6 chronic HCV infection (F0-4)
- People with recent injecting drug use (past six months)
- Participants with HIV and decompensated liver disease excluded
- Electronic blister packs to monitor adherence



- 3 people lost to follow-up between ETR and SVR12 (no virological failure or viral relapse)
- 1 case of reinfection (1a-1a, % nucleotide: NSSA, 10.1%; NSSB, 4.6%, Core-E2, 12.0%)

Grebely, et al. Lancet 2018

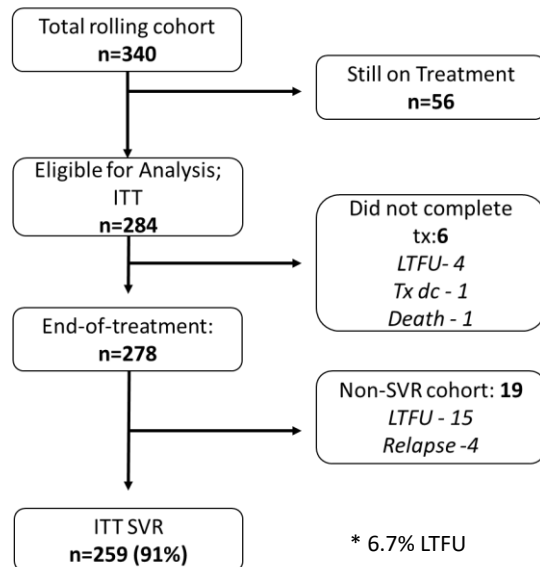
## BIOLOGICAL PERFECTOVIR

Under clinical trial conditions, SVR12 rates that exceed 90% can be achieved with currently available, simple, well tolerated all oral therapy directed against HCV infection.

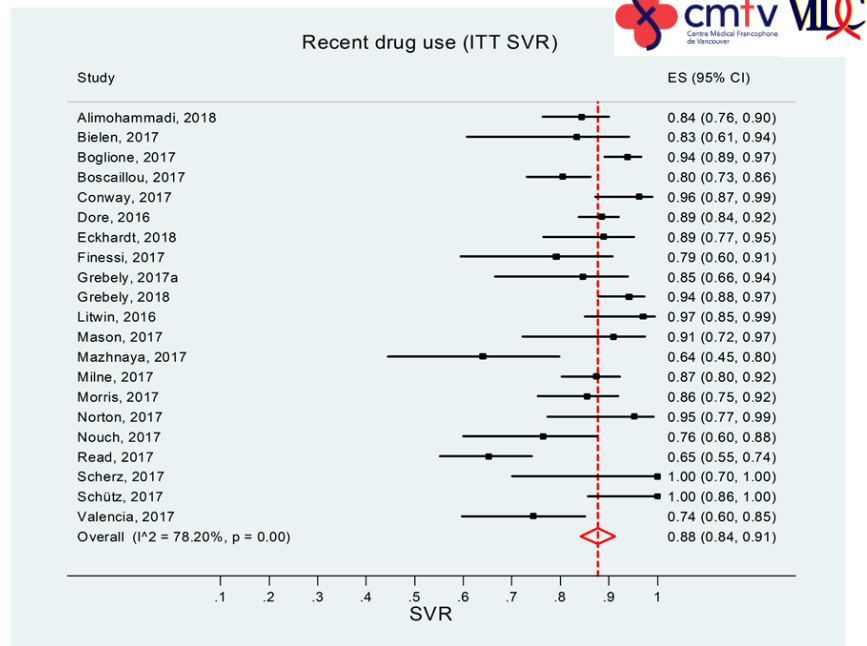


## FUNCTIONAL PERFECTOVIR

Time frame : May 2014 – Aug 2018



FUNCTIONAL  
PERFECTOVR



Hajarizadeh B et al. (2018) (in press)

FUNCTIONAL  
PERFECTOVR



## Prospective observation study of HCV treatment starts in four main tertiary centres in South Australia (Feb/16 – Mar/17)

N = 1,909 (90% treatment starts)

SVR12 (PP): 95.7%

SVR12 (ITT): 80.4%

**14.2% LTFU**

Haridy et al. 2018. J Viral Hep.

## FUNCTIONAL PERFECTOVIR

Decrease in treatment starts  
from 1251 to 668 in the  
latter 6 months of study

“Our findings highlight the need  
to explore additional strategies  
to identify, treat and follow-up  
patients in order to achieve  
elimination targets”

Haridy et al. 2018. J Viral Hep.

## FUNCTIONAL PERFECTOVIR

Under experienced real life  
conditions, SVR12 rates that exceed  
90% can be achieved with currently  
available, simple, well tolerated all  
oral therapy directed against HCV  
infection **AS LONG AS PATIENTS ARE  
ABLE TO COMPLETE TREATMENT  
AND FOLLOW UP AND TREATMENT  
STARTS CAN BE MAINTAINED.**

## FUNCTIONAL PERFECTOVIR

Re-infection/recurrent viremia

D3FEAT/SIMPLIFY: 4.8/100 py

Recent PWID (BCHTC): 3.1/100 py

Only occurs in active PWID

Holeksa et al (INHSU 2018)

SVR12 117/122 (PP, active PWID)

4 cases of recurrent viremia, all among 14 individuals who did not attend SVR12 visit.

Haridy et al. 2018. J Viral Hep.

## SOCIETAL PERFECTOVIR



WHO Goals: 90% reduction in *new* cases of chronic HCV, 80% of treatment eligible persons with chronic HCV treated, 65% reduction in HCV-related deaths by 2030



Globally approx. 71 million people have HCV [1]



Of those, 6.6 million are PWID with chronic viremia [2]



Likely less than 10% have been treated and cured [3]



ONLY 6 MILLION LEFT TO GO!!!!

Grebely J, Dore GJ. Antiviral Res 2014;104:62–72  
 Hicks, INHSU 2018  
 Grebely J, IJDP 47 (2017) 26–33

## EASL Recommendations on Treatment of Hepatitis C 2018



“TREATMENT SHOULD BE CONSIDERED WITHOUT DELAY IN PATIENTS...AT RISK OF TRANSMITTING HCV(PWID)”



“DAA-BASED THERAPIES ARE SAFE AND EFFECTIVE IN HCV-INFECTED PATIENTS RECEIVING OST, THOSE WITH A HISTORY OF INJECTING DRUG USE, AND THOSE WHO RECENTLY INJECTED DRUGS”



“IT IS THUS CRITICAL THAT HCV CARE IN PWIDS BE INTEGRATED WITHIN A FRAMEWORK THAT ADDRESSES DRUG-RELATED HARMS, PREVENTS OVERDOSE MORTALITY, ADDRESSES SOCIAL INEQUALITIES, AND IMPROVES DRUG USER HEALTH”

Vancouver's  
Downtown  
Eastside  
(DTES)



- Home to approximately 18,000 residents
- 80% self identify as PWUD
- 25% active PWID (estimate)
- FINANCIAL & HOUSING INSECURITY THE NORM

PWID: people who inject drugs; PWUD: people who use drugs

Conway B. Personal communication



# HCV prevalence

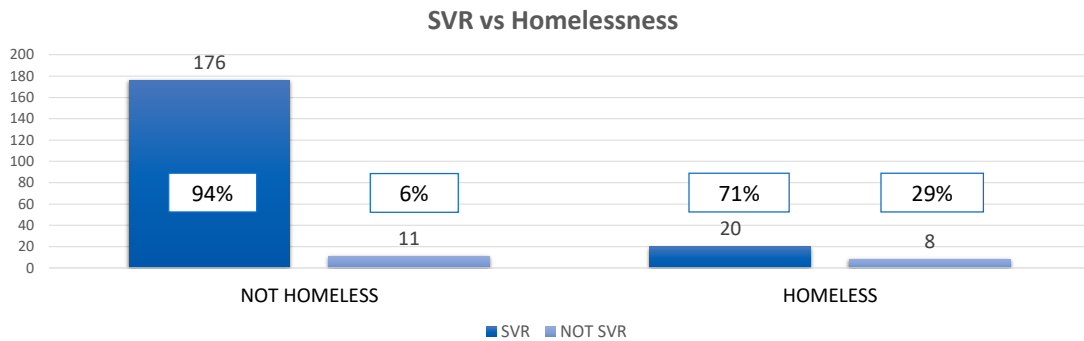
- **~300,000** Canadians are infected with HCV
- **80,000** of these cases are in British Columbia
- As many as **10,000** may be within or near(ish) Vancouver's DTES



BC-CfE. Fact Sheet: Hepatitis C (HCV). Retrieved from: <http://www.cfenet.ubc.ca/sites/default/files/uploads/HCV%20Fact%20Sheet.pdf>  
 UHRI. (2013). Drug Situation in Vancouver. Retrieved from: [http://www.cfenet.ubc.ca/sites/default/files/uploads/news/releases/war\\_on\\_drugs\\_failing\\_to\\_limit\\_drug\\_use.pdf](http://www.cfenet.ubc.ca/sites/default/files/uploads/news/releases/war_on_drugs_failing_to_limit_drug_use.pdf)



## Effect of Homelessness on HCV Treatment outcome at VIDC



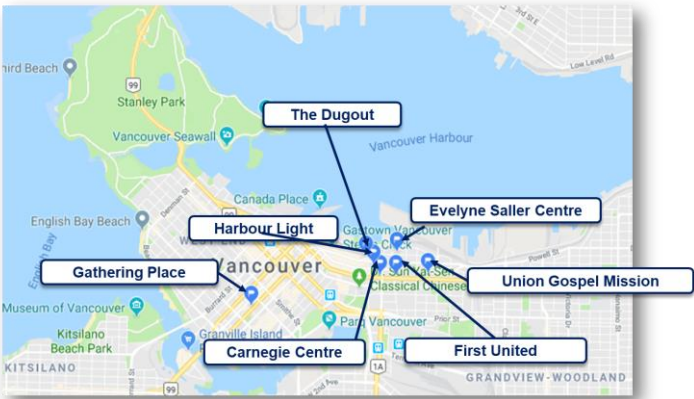
Thiam A. Personal Correspondence.

# The ENTENTE program

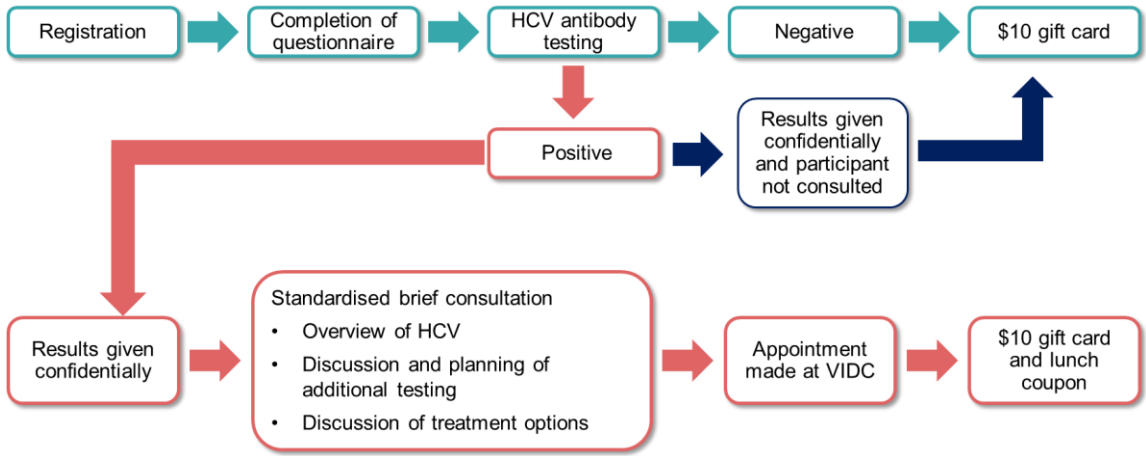
- Using the medical system as a tool to promote social change
- The main issue relates to lack of engagement



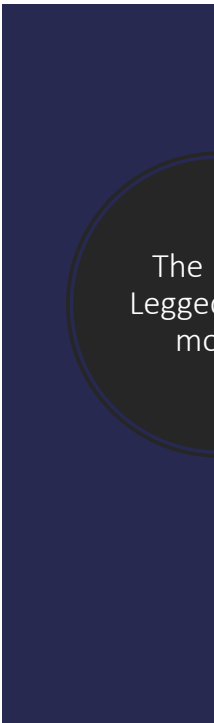
# Community Pop-up Clinic Locations



# A Typical Community Pop-up Clinic



Alimohammadi A, et al. Can Liver J. 2018 doi:10.3138/canlivj.1.2.002



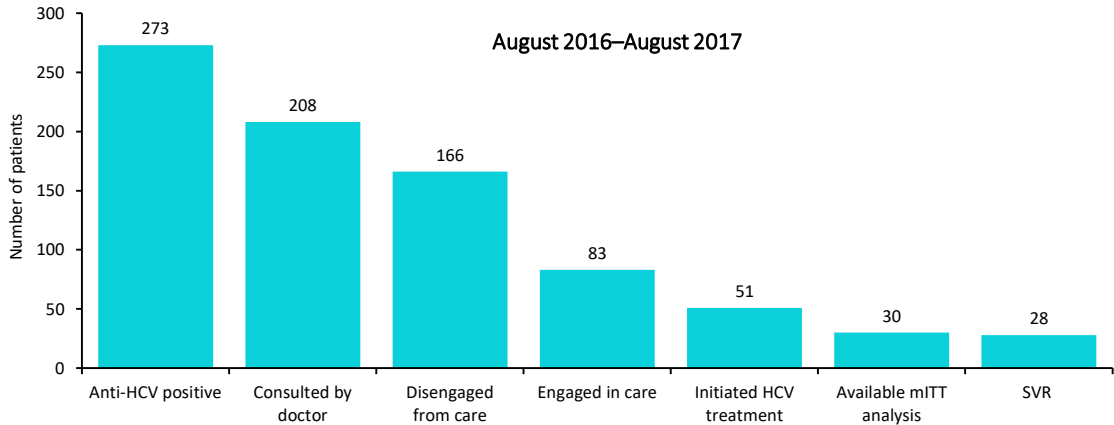
## The Four-Legged Chair model

- Holistic medical care delivered through a multidisciplinary programme



COPD: chronic obstructive pulmonary disorder; GERD, gastroesophageal reflux disease; MD: doctor of medicine

# Community pop-up clinics: 3 hours/week, 5 HCV cases, 4 consulted, 2 treated



Conway B. Unpublished data

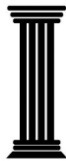
SVR: sustained virological response

## Initial engagement



- Weekly CPCs to provide rapid HCV & HIV POC tests in Vancouver’s DTES
- Immediate consultation with healthcare provider
  - Immediate design of multidisciplinary plan of care

## Multi-disciplinarity



- All needs addressed
- Flexibility of goals
- Flexibility of modalities of interaction
- Accountability

## Durability

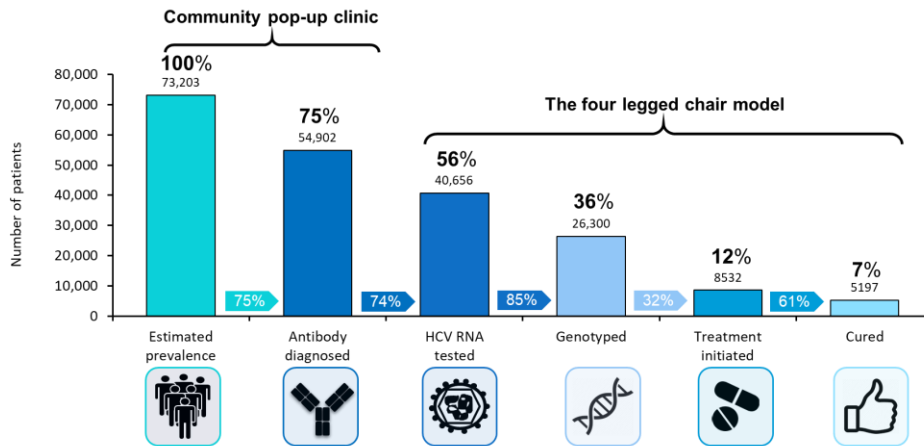


- Ongoing low-threshold care
- LTFU strategy
- Weekly HCV Support Group

Vancouver Infectious Diseases Centre – the three pillars

CPC: community pop-up clinic; LTFU: lost to follow-up; POC: point of care

The BC Hepatitis Testers Cohort (BC-HTC):  
Cascade of care — where our interventions work



Janjua NZ, et al. Ebiomedicine 2016;12:189–95.

The VIDC Team



- Brian Conway
- David Truong
- Letitia Chu
- Victor Chiang
- Caitlin Eisen
- Julie Holeksa
- Billy Ma
- Rukhsana Omer
- Robyn Parsons
- Ussanee Prabakaran
- Kitty Poon
- Dorothy Rhee
- Priya Sian
- Astou Thiam
- Jamie Tongco
- Deanna Woo
- Leo Yamamoto
- Rossitta Yung



Anchorage Daily News, August 5, 2018.

## THINK BIG – I PROMISE SCHOOL

- GED courses and job placement help for parents/guardians – “family wraparound” approach
- Programs that help children develop skills to deal with the trauma they may see in their lives
- Teachers also have access to psychological services so that they can better support the students
- Long school day – 9-5, longer school year – July-May
- Keep kids occupied, less chances to be bored and get into trouble
- STEM-based summer camp
- Free breakfast, lunch, snacks, access to food pantry for families
- Free bike, free uniforms, tablet
- Free tuition for students who graduate to University of Akron





FIND AND ENGAGE PWID IN CARE



DESIGN PLAN OF MULTIDISCIPLINARY CARE, INCLUDING HCV THERAPY



DESIGN A PLAN OF LONG-TERM ENGAGEMENT IN CARE (DURABILITY)



DESIGN A PLAN OF SOCIAL INTEGRATION



# SOCIETAL PERFECTOVIR



Have we achieved PERFECTOVIR?



**Biological PERFECTOVIR:** This was the purview of clinical trials and has clearly been achieved.



**Functional PERFECTOVIR:** This is the purview of dedicated, committed partnerships between teams of individuals and the community they serve and has been achieved in a meaningful and impactful way.



**Societal PERFECTOVIR:** This is a societal project

**POLICY & PARTNERSHIPS**





# SOCIETAL PERFECTOVIR



WE ARE NOT THERE YET,  
BUT WE WILL GET THERE IF  
WE ACCEPT THE CHALLENGE  
BEFORE US, A CALL TO BE  
GREAT AND TO THINK BIG



SOCIETAL PERFECTOVIR  
AMONG PWID WILL ONLY BE  
ACHIEVED IF WE LEARN TO  
USE THE HEALTHCARE  
SYSTEM AS AN AGENT OF  
SOCIAL CHANGE