The liver & beyond – impacts of chronic hepatitis C infection

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Land Acknowledgement

PHSA & BCCDC serve communities across British Columbia, on the territories of many distinct First Nations.

We are grateful to all the First Nations who have cared for and nurtured the lands and waters around us for all time, including the xʷməθkʷəy̓əm (Musqueam), Sḵwx̱wú7mesh Úxwumixw (Squamish Nation), səlilwətaɬ (Tsleil-Waututh), and S'ólh Téméxw (Stó:lō) Nations, on whose unceded and ancestral territory our offices are located and where many of us work and live.

Whether we are located in this area or in another territory across the land colonially known as Canada, we acknowledge these homelands and recognize and respect Indigenous people as the original peoples of these lands.

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Disclaimer

All inferences, opinions, and conclusions drawn in this presentation are those of the author(s), and do not reflect the opinions or policies of the BC Ministry of Health or Data Steward(s).

Acknowledgements

Thank you to the people who have lived & living experience of hepatitis C infection whose data has been included in the analyses presented here, and for whom it is intended to benefit.

BCCDC Teams

Clinical Prevention Services

Data & Analytic Services

BC HTC British Columbia Hepatitis Testers Cohort

Data Stewards

BC Centre for Disease Control
Provincial Health Services Authority

British Columbia Ministry of Health

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Outline

1. Role of the liver & how hepatitis C virus infection impacts the liver
2. Extrahepatic manifestations of hepatitis C infection
3. Overview of hepatitis C treatment & follow-up
4. Hepatitis C care cascades

Role of the liver & how hepatitis C virus infection impacts the liver

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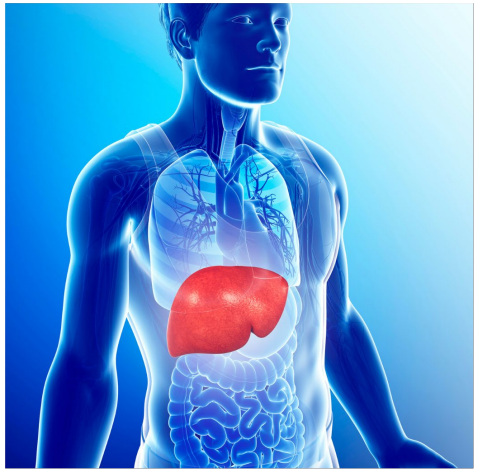
How the liver works



Normal liver

Cirrhotic liver

- The liver is an essential organ in our bodies
- It processes things we consume, like food & liquids, and converts them in to forms our body can use
- It also ‘cleans up’ our blood by destroying old red blood cells
- It helps eliminate waste from our body

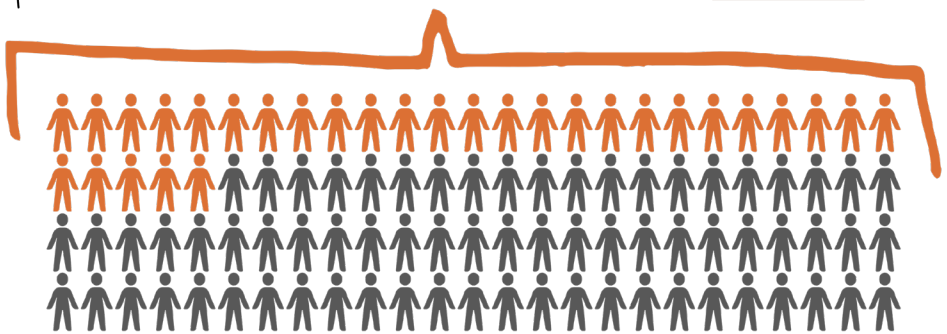
Image credits

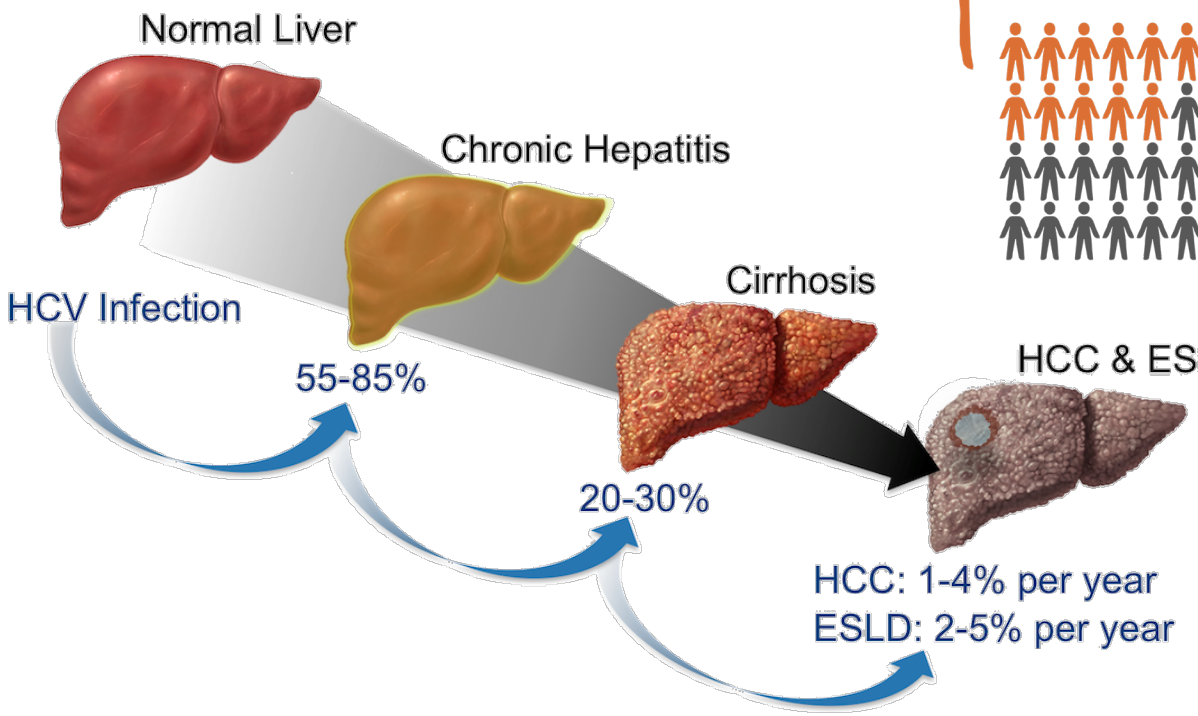
https://en.wikipedia.org/wiki/SpongeBob_SquarePants_%28character%29

Among people who have a hepatitis C infection;

70% develop chronic hepatitis C infection, which will not clear without treatment.

For every 100 people with chronic hepatitis C infection, 30 people develop scarring on their liver, which causes impaired liver function, and is known as cirrhosis:





Among those 30 people with cirrhosis, 1 will develop hepatocelluar carcinoma (liver cancer) and 2 will develop End Stage Liver Disease (liver failure) each year.

https://www.hepatitis.va.gov/hcv/background/natural-history.asp

Extrahepatic manifestations of chronic hepatitis C infection

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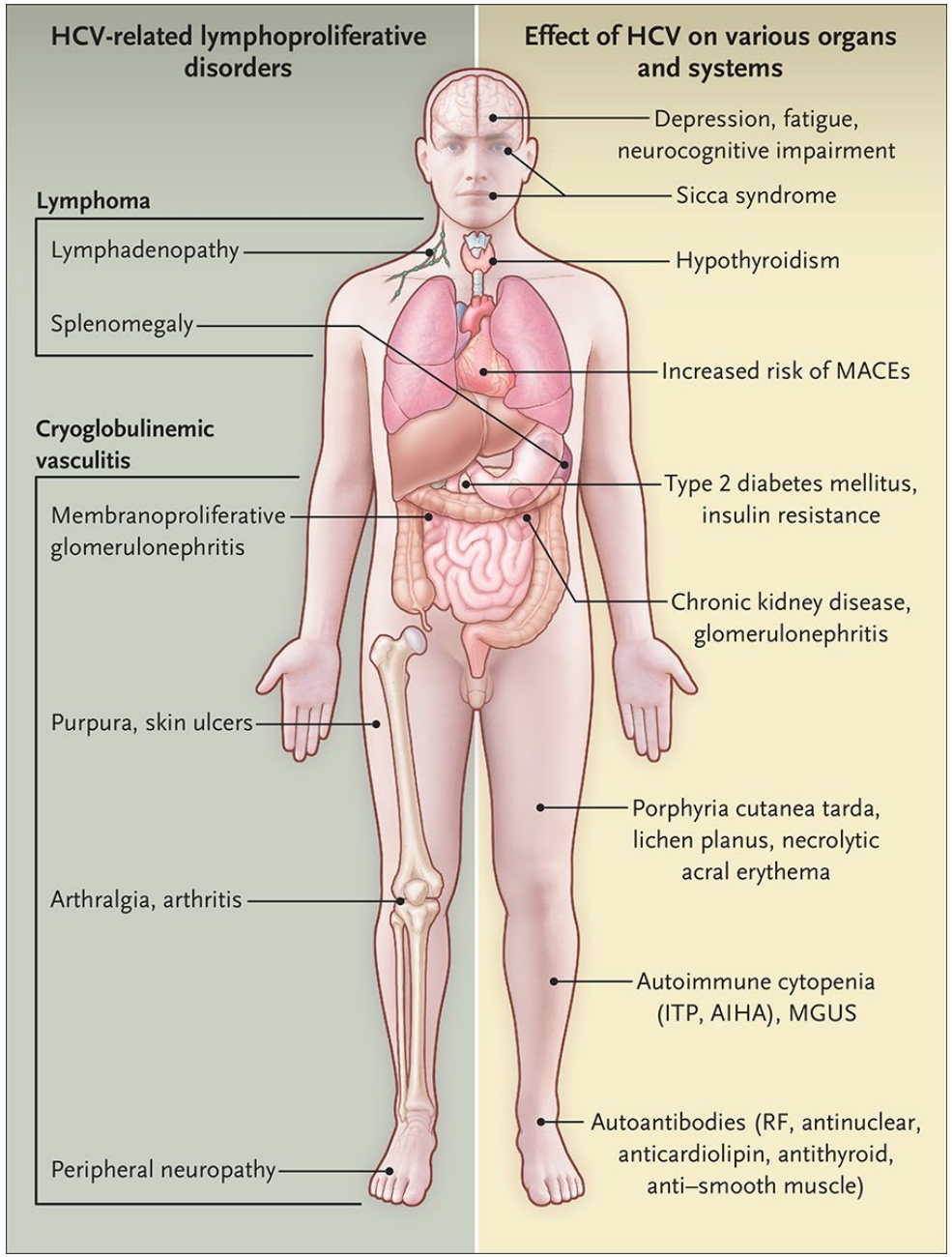
Cancer of the lymphatic system, swollen lymph nodes, enlargement of the spleen

Kidney damage; decreased kidney function, chronic kidney disease, kidney failure

Bleeding from blood vessels under the skin

Swollen, tender, stiff & painful joints

Damage to nerves; weakness, numbness and pain, usually in the hands and feet



Decreased mental function, low mood/energy

Dry eyes and mouth

Underactive thyroid function

Heart attack, stroke, congestive heart failure, ischemic heart disease, peripheral arterial disease, coronary artery disease, cardiac arrest

Type 2 diabetes

Dermatological disorders; Lichen planus (itchy skin, rash, painful sores), photosensitivity (painful, blistering lesions on sun-exposed areas of the skin)

Low blood cell count

Autoimmune diseases; rheumatoid arthritis, lupus, scleroderma, Sjögren's syndrome, polymyositis, dermatomyositis, Graves' disease, Hashimoto's thyroiditis, etc.

Cacoub, Patrice & Saadoun, David. (2021). Extrahepatic Manifestations of Chronic HCV Infection. *New England Journal of Medicine*, *384*, 1038-1052. https://doi.org/10.1056/NEJMra2033539

Risk of hep C for extrahepatic manifestations

- Higher incidence of extrahepatic cancers; anal, oesophagus, lung, oral, bile duct, pancreatic
- Higher incidence of autoimmune disease
- Higher incidence of type II diabetes
- Higher incidence of cardiovascular disease
- Higher incidence of kidney disease

BUT: HCV treatment reduces these risks almost back to zero for *most* people!

1. https://www.frontiersin.org/journals/oncology/articles/10.3389/fonc.2022.983238/full
2. https://drc.bmj.com/content/9/1/e002145.abstract
3. Jeong, Dahn, et al. "EFFECT OF DAA TREATMENT ON EXTRAHEPATIC MANIFESTATIONS INCIDENCE: A POPULATION-BASED STUDY IN BRITISH COLUMBIA, CANADA." *HEPATOLOGY*. Vol. 76. 2022

Hepatitis C treatment & follow-up

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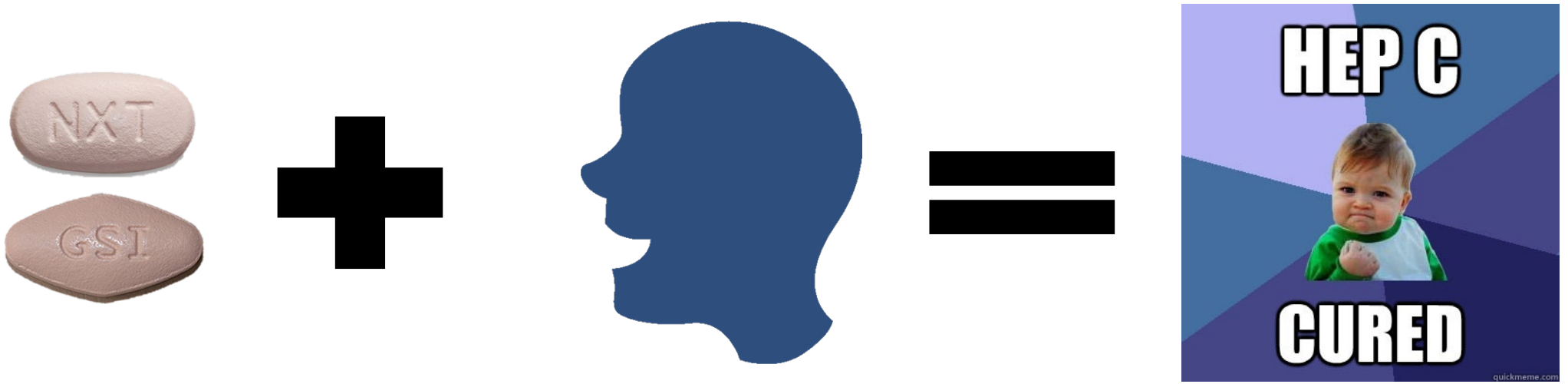
Hepatitis C is the only curable chronic viral infection in medical history!

Hep C treatment is also very simple



HCV treatment is:

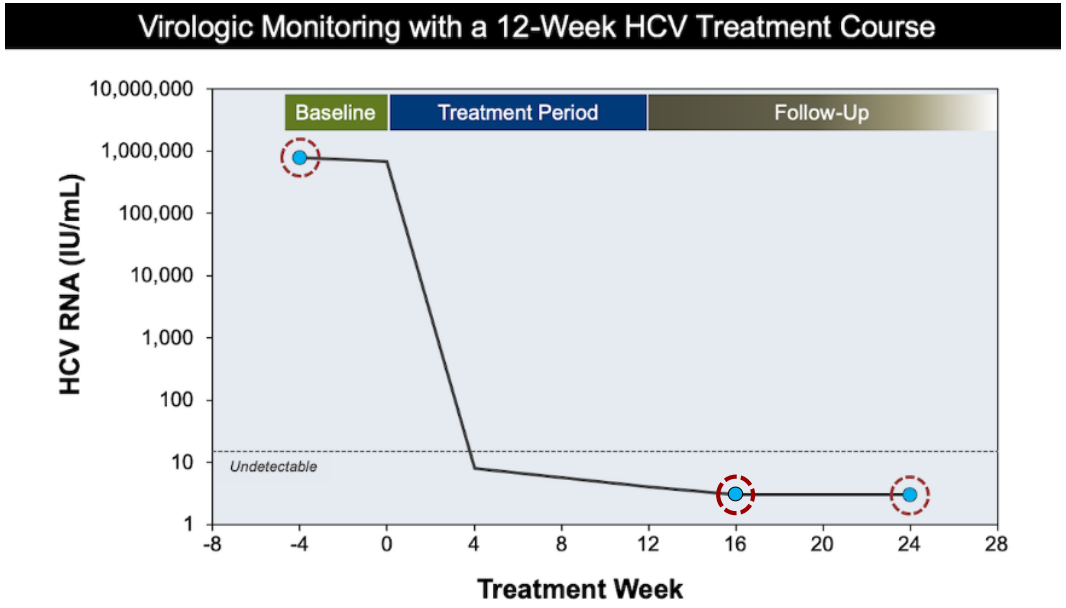
- *Covered by BC PharmaCare for <u>all</u> people with HCV infection*
- *1 or 3 tablets, once per day, for just **8-12 weeks***
- *The medications have minimal side effects*
- *Close to 99% of people who complete the treatment are 'cured'*

Citations:

1. https://www.hepatitisc.uw.edu/go/treatment-infection
2. http://www.quickmeme.com/meme/3ubhso

Assessment of Sustained Virological Response (SVR) after completion of HCV treatment

Successful viral eradication (cure) of HCV infection is defined as undetectable plasma or whole-blood HCV RNA using a highly sensitive PCR assay at least 12 weeks after completion of DAA therapy (SVR12)[1]



- Data suggest there is a very high correlation between SVR4 (undetectable plasma or whole-blood HCV RNA using a highly sensitive PCR assay 4 weeks after completion of DAA therapy) and SVR12[2]
- Therefore, opportunistic testing of HCV RNA at any time **beyond 4 weeks after treatment completion** is adequate, especially when there is concern about subsequent loss to follow-up.

Image credit: https://www.hepatitisc.uw.edu/go/treatment-infection/monitoring/core-concept/all#monitoring-after-receiving-hcv-therapy

References

1. https://www.hcvguidelines.org/evaluate/monitoring
2. https://onlinelibrary.wiley.com/doi/10.1111/jvh.13600

Why is DAA treatment sometimes unsuccessful?

- Non-completion of treatment -> if entire medication course is not completed as prescribed (because of forgetting tablets, having side effects, losing tablets, etc.) it is possible the treatment will not be successful

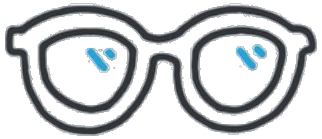
- Liver cirrhosis -> the ‘sponge’ is blocked, making it difficult for the drug to get to every single infected hepatocyte, so the virus is able to ‘escape’ and mutate

- Rare viral strains/genotypes -> some people are living with a less common strain of hep C and the DAA medications don’t work as well against some of these

Why post treatment ‘SVR’ testing is important

Individual perspective

- To know our hep C status- HCV RNA undetectable means we can’t transmit the virus anymore
- To check if we might need to do another course of treatment, in order to cure the virus and reduce risk of further complications



Care provider perspective

- Ensure patient gets appropriate follow-up care if additional treatment course is required
- If patient has on-going risks for hep C re-infection, getting an SVR result is important in order to determine if a subsequent detectable HCV RNA result is a reinfection or a treatment relapse/failure

Public health perspective

- Determine if virus is being eliminated from population
- Monitor areas where further support for providers or patients may be needed

Surveillance perspective

- Determine if hep C cure is equitably being achieved among all populations
- Track progress towards hep C elimination targets

If 1st DAA treatment is unsuccessful

- Aall adult patients in BC who do not have end stage liver disease are able to be re-treated again if the 1st DAA treatment is unsuccessful
- If an HCV re-infection is able to be confirmed; a 1st line DAA regimen;
  - sofosbuvir-velpatasvir (Epclusa™) for genotype 1 to 6 for ~12 weeks
  - glecaprevir-pibrentasvir (Maviret™) genotype 1 to 6 for ~8-16 weeks
  - ledipasvir-sofosbuvir (Harvoni®) for genotype 1 for ~8-24 weeks
- If HCV re-infection is not able to be confirmed, or it is determined that the 1st line DAA treatment failed, then treatment will be with a 'salvage' regimen;
  - sofosbuvir-velpatasvir-voxilaprevir (Vosevi™) genotype 1 to 6 for ~12 weeks
  - glecaprevir-pribentasvir (Maviret™) for genotype 1 for ~12-16 weeks
- **Re-treatment after 1st line DAA treatment failure is successful in 96-97% of cases**

https://www2.gov.bc.ca/assets/gov/health/practitioner-pro/special-authority/prescriber_info_hep_c.pdf

Post-treatment follow up

- Everyone with cirrhosis requires on-going monitoring (blood tests and/or ultrasound every 6 months to monitor for progression of liver disease (cancer and decompensation)
  - Even if cirrhosis ‘regresses’ (goes away), on-going monitoring for cancer is still required, because the damage to the DNA in the liver cells could already have occurred
- Everyone with on-going potential re-exposure to hep C should be tested for HCV RNA again every 12 months to monitor for re-infection

Hepatitis C care cascades

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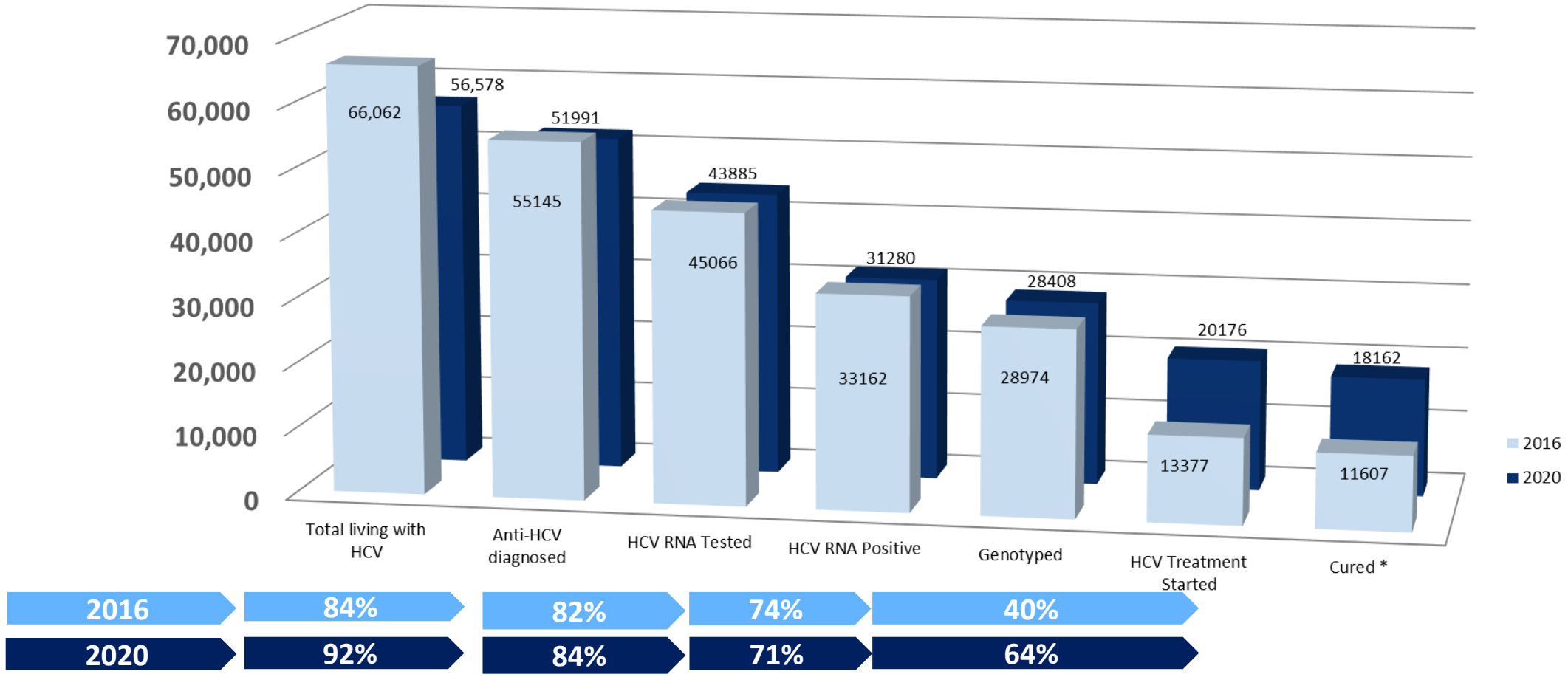
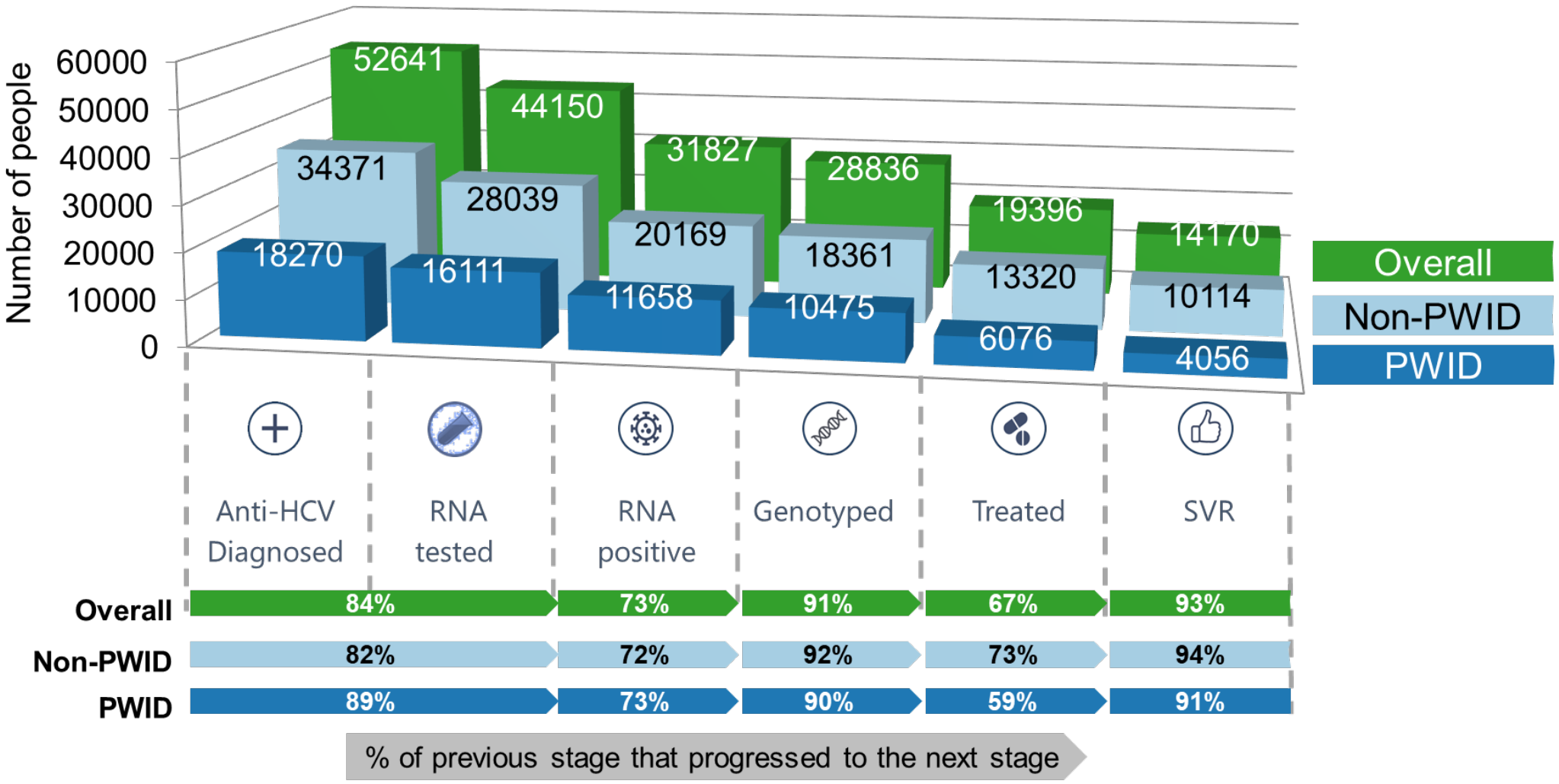
Hepatitis C care cascade in BC as of 2020



*Cure = SVR yes + SVR unknown + SVR missing

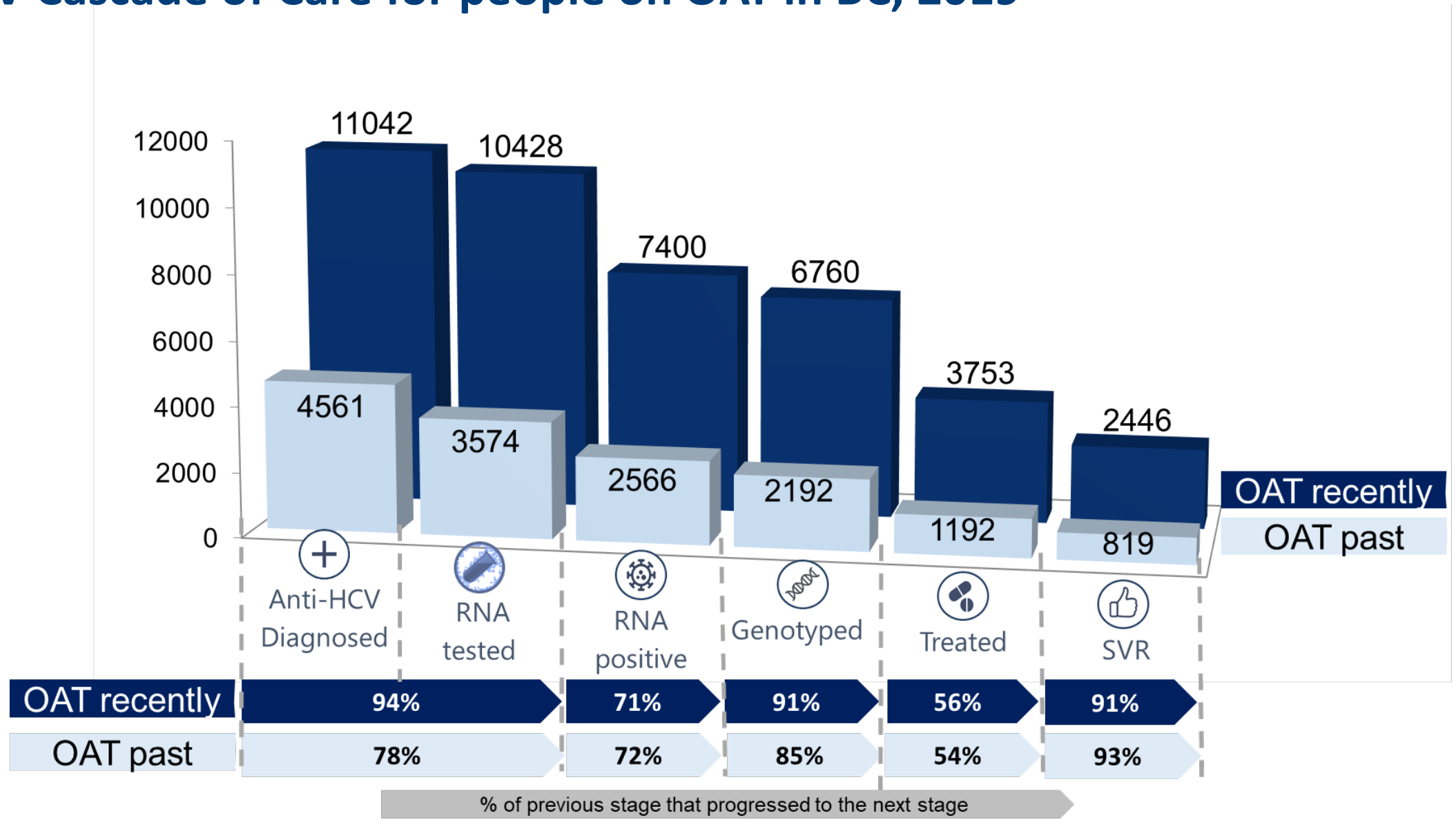
Data Sources:
https://bchtc.med.ubc.ca/hepatitis-c-cascade-of-care-in-bc/

HCV Cascade of Care for PWID in BC, 2019

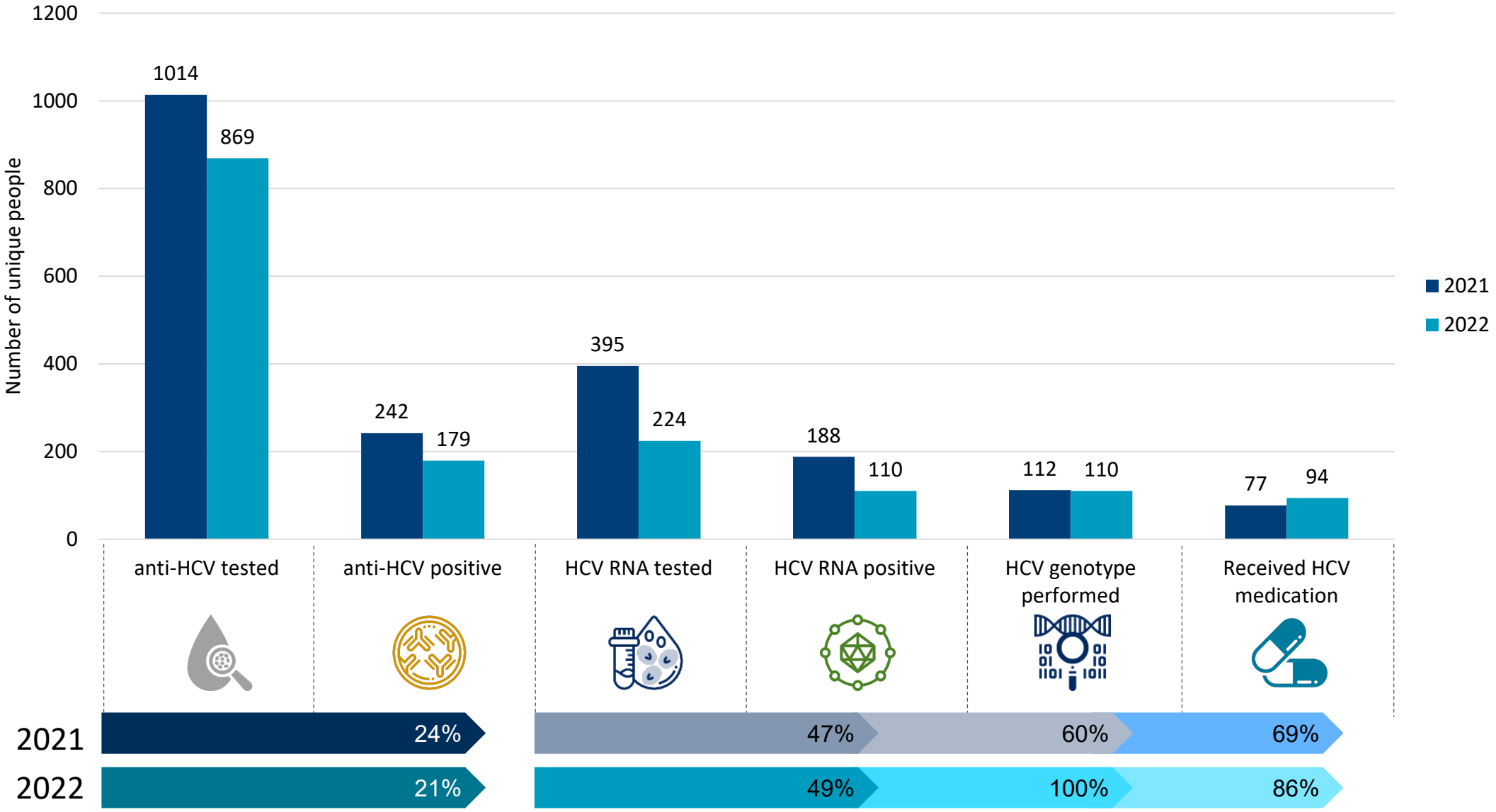


Reference: Bartlett SR et al. 'Continued inequities in the hepatitis C cascade of care experienced by people who inject drugs in British Columbia in 2019: A population-level linked data study', *2020 AASLD Liver Meeting*, Virtual. DOI: 10.1002/hep.30941

HCV Cascade of Care for people on OAT in BC, 2019

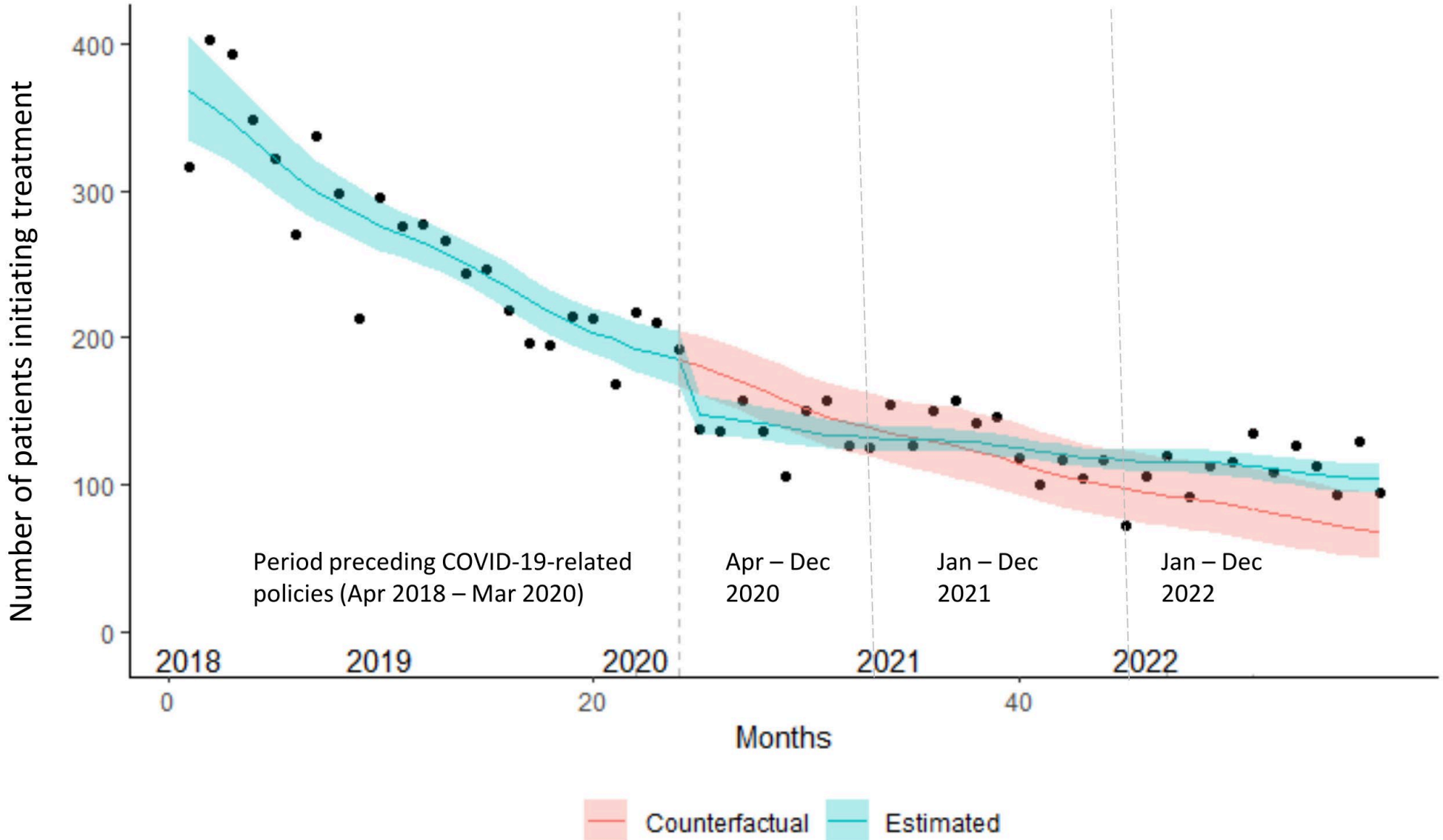


HCV care cascade among people incarcerated in BC, 2021- 2022



Reference: Bartlett SR et al. Canadian Liver Meeting, Halifax, February 2023

Figure 1. Number of individuals initiating HCV treatment in BC following the start of COVID-19-related policies (estimated vs counterfactual based on pre-policy trend)



Morrow et. Al. 2023

Questions?

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Hepatitis C Reports

The Clinical Prevention Services Epidemiology & Surveillance team reports on new diagnosis of, risk factors and treatment for hepatitis C.

CPS monthly surveillance reports

The CPS monthly surveillance reports provide the most current information on new diagnoses and testing for hepatitis C.

- Monthly Surveillance Report - August 2022

Annual Hepatitis C reports

- Hepatitis C Annual Report 2000-2019

British Columbia Hepatitis Testers Cohort (BC-HTC)

The purpose of the BC-HTC is to monitor disease burden related to hepatitis and associated infections and social conditions, evaluate impact of interventions, and monitor hepatitis program progress to inform policy and programming in British Columbia and Canada.

http://www.bccdc.ca/health-professionals/data-reports/hepatitis-c-reports

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