Reaching the undiagnosed: Advances in hepatitis C testing

November 23, 2022

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

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Today's Panelists

- **Jordan Feld**
  MD, Hepatologist, University Health Network
- **Olivia Dawson**
  Program Manager, International Network on Health and Hepatitis in Substance Users (INHSU)
- **Kate Dunn**
  Community Engagement, Alberta ECHO
- **Kristin Lichty**
  Hepatitis C Treatment Registered Nurse, North Lambton Community Health Centre
- **Kellie Guarasci**
  Clinical Nurse Lead, Cool Aid Community Health Centre
- **Stephen MacInnis**
  Peer Outreach Worker, Cool Aid Community Health Centre

Today's Agenda

1. **Overview: hepatitis C testing in Canada**
   Jordan Feld, MD

1. **INHSU HCV Intervention Toolkit**
   Olivia Dawson

2. **Panel discussion: strategies to help reach the undiagnosed**

3. **Questions**

Reaching the Undiagnosed: Advances in hepatitis C testing

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Disclosures

- **Research:** Abbvie, Cepheid, Eiger, Enanta, Gilead, Janssen

- **Consulting:** Abbvie, Gilead, Janssen

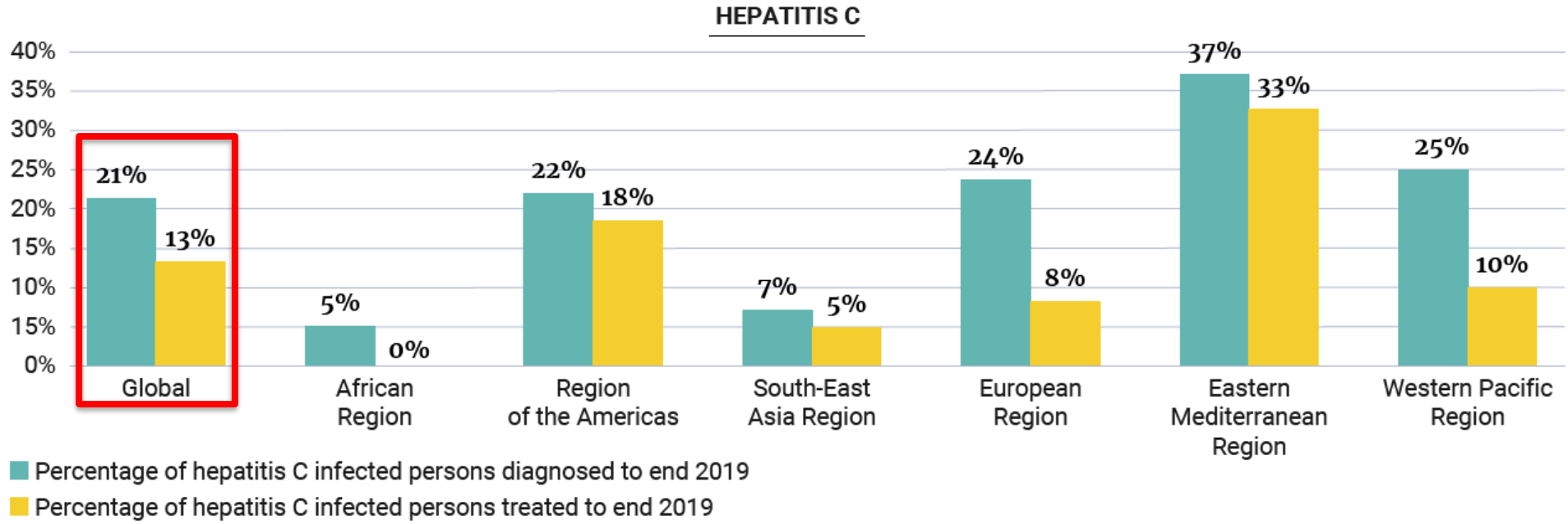
Land Acknowledgement

- I would like to acknowledge the traditional custodians of the land where I live and work
  - Mississaugas of the Credit
  - Anishnabeg
  - Chippewa
  - Haudenosaunee
  - Wendat
  - Many diverse First Nations, Inuit and Métis peoples
- We express our gratitude to the community and Elders past and present

Learning Objectives

- Recognize the key role that testing plays in supporting people with hepatitis C to access care and treatment
- Appreciate the landscape of hepatitis C testing in Canada including types of tests and how tests are integrated into health systems
- Understand recommendations in the *Blueprint* related to testing and its importance in advancing progress towards hepatitis C elimination in Canada
- Understand the impact of the COVID-19 pandemic on HCV testing and where opportunities may exist to improve testing strategies

Lots of work to do!



- By end of 2019 – **9.4 M people treated but only 21% diagnosed globally!**
- **We cannot cure those we have not yet diagnosed**

WHO Global Progress Report HIV, Hepatitis and STIs 2021

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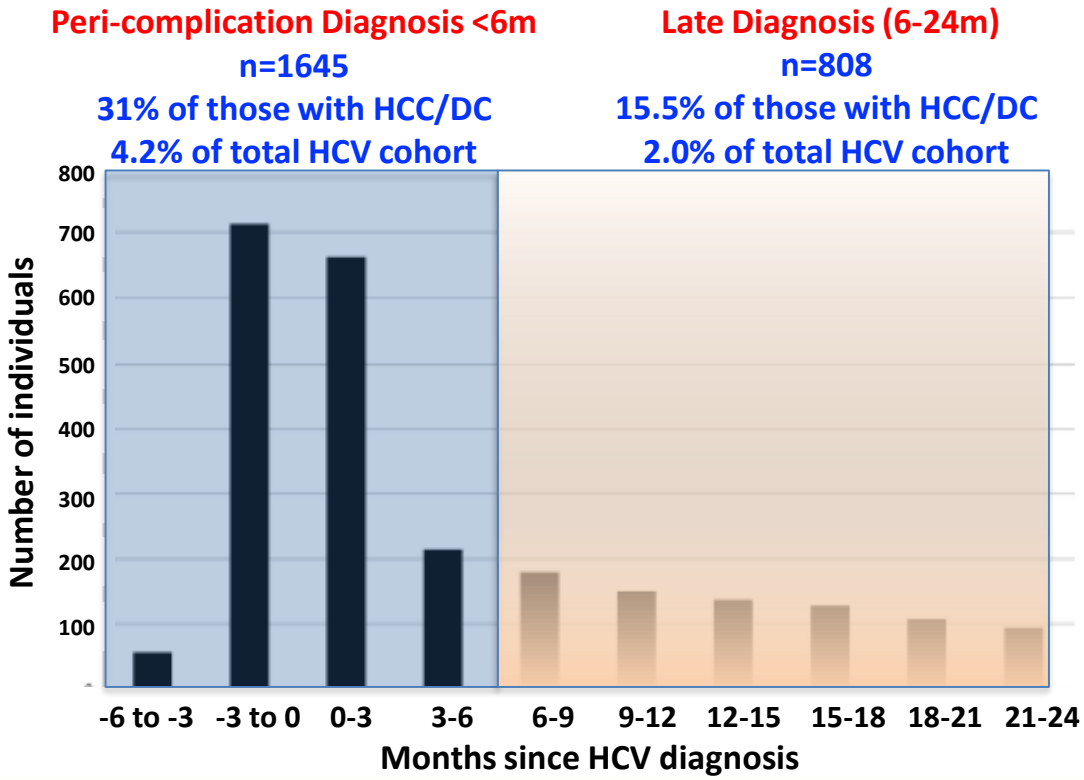
Consequences of late diagnosis

Time from diagnosis of HCV until first presentation of HCC or DC n=39,515



Outcome	@1 yr Hospitalized	Died
Peri-complication	51%**	34%**
All others	11.5%.	2.0%
Transmission	??	??

**p<0.0001

Increased risk for late diagnosis

- Increasing age
- Alcohol use
- Co-morbidities
- Fewer MD & ER visits

Reduced risk for late diagnosis

- IDU or mental health dx
- Immigrants

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Who is diagnosed late?

- **Connection with the system**
  - Older
  - Alcohol use (no work-up done)
  - Few medical visits

Risk-based screening inadequate

Need to find connections

- **Low risk for late diagnosis**
  - IDU
  - Mental health issues
  - Immigrants

Risk-based screening is helping

Moorman Hepatology 2015, Samji J Hep 2017, Alavi J Hep 2016, Lapointe—Shaw Liver Int 2020

Strategies

US

- **Screening recommendations**

  USPSTF & CDC

  – Onetime screening all adults

  – Should help with diagnosis – need to ensure followed by linkage to care

  – ***EMR reminders & quality measure for PCPs to make it actually happen***

- **Removing remaining barriers**

  – Still Medicaid/care restrictions

Canada

- **Screening recommendations**

  – Canada still entirely risk-based screening

  – Risk-based screening required but clearly not enough

- **Low barrier testing**

  – POC testing not reimbursed in Canada

  – Reflex testing not available in many Provinces

  – EMR reminders (but need to see a doctor!)

  – ER screening, screening in the community

- **Awareness**

  – Population level awareness – it works – e.g.PWID awareness fairly high

  – Self-referral – not widely available

USPSTF 2020, CDC 2020

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Screening Approaches

- **Risk-based**
  - Identify and test only those with risk factors
- **Pros:**
  - High yield
  - Cheaper
- **Cons:**
  - Contact w/ health system
  - Must know, acknowledge & discuss risk factors
  - Test may be stigmatized
  - Miss those without RFs

Not mutually exclusive

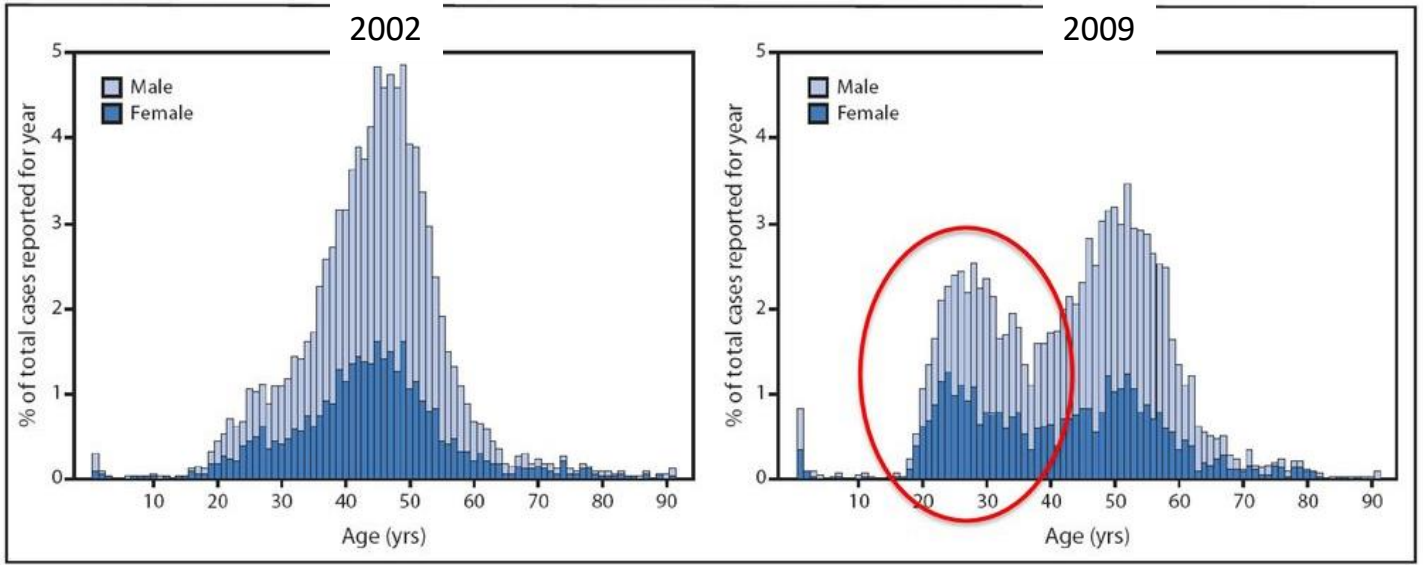
Clearly need both approaches!

- **Population-based**
  - Test a segment of the population eg. baby boomers, immigrants
- **Pros:**
  - High coverage rate
  - Easy to implement
- **Cons:**
  - Need to choose the pop'n
  - Low yield, expensive
  - May be stigmatizing to pop'n – eg. immigrants

Did we miss the boat on baby boomer screening?

Should we be moving to 1 time screening of all adults?
I'm not sure – but we should be exploring this…quickly!

Changing epidemiology of HCV



- Fueled by opioid epidemic – rising incidence & prevalence in younger cohorts
- **US – now recommends screening one-time HCV screening all adults >18 yo**
- **And screening in every pregnancy…should we be doing the same?**

MMWR 2014, CDC USPSTF 2020

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And if we screen…how should we screen & diagnose?

HCV diagnosis needs simplification

Step 1
See the doctor

Loss to F/U

Step 2
To the lab
for HCV Ab

Loss to F/U

Step 3
See the doctor
for result

Loss to F/U

Step 4
To the lab
for HCV RNA

Loss to F/U

Step 5
See the doctor
for result

Loss to F/U

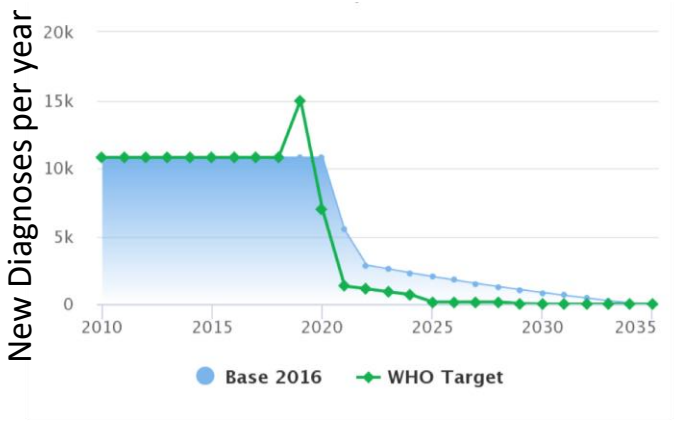
Step 6
Start DAA therapy
(may be additional steps:
fibrosis assessment,
approvals etc)

Additional challenges:
- Phlebotomy
- Turn around time
- Provider awareness

Lots of places to 'get lost'…particularly if HCV not a priority ***& COVID made it worse!***

Screening gets harder over time

Australia



Numbers the same…
Much harder in 2025 than 2018

- Will need very active case-finding
- All steps in continuum likely harder with time…**especially screening & diagnosis!**
  - **Harder to find, Harder to engage, Harder to cure (?)**

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Progress toward elimination in Canada

Province	Anticipated year of achieving HCV elimination				Annual treatments needed over 2021–2030 for HCV elimination by 2030 (%)	Incident cases of ESLD averted by elimination by 2030	HCV-related deaths averted by elimination by 2030	Year of achieving cost savings of HCV elimination by 2030	Cost savings of HCV elimination by 2030, CAD million
	Base case (0% reduction †)	10% reduction	20% reduction †	10% increase †					
Alberta	2029	2034	‡	2027	§	§	§	§	§
BC	2028	2033	‡	2027	§	§	§	§	§
Manitoba	2036	‡	‡	2031	540 (8.8%)	19	10	2028	10.6
New Brunswick	2027	2028	2047	2026	§	§	§	§	§
NFLD & Labrador	2024	2024	2024	2023	§	§	§	§	§
Nova Scotia	2025	2026	2027	2025	§	§	§	§	§
Ontario	2035	‡	‡	2030	7,700 (8.7%)	210	110	2028	114.5
PEI	2023	2023	2023	2023	§	§	§	§	§
Québec	2037	‡	‡	2031	2,800 (8.8%)	90	50	2029	31.2
Saskatchewan	2024	2024	2024	2024	§	§	§	§	§

If they don't come to you…go to them

A converted shuttle bus was converted to perform HCV screening in a number of settings

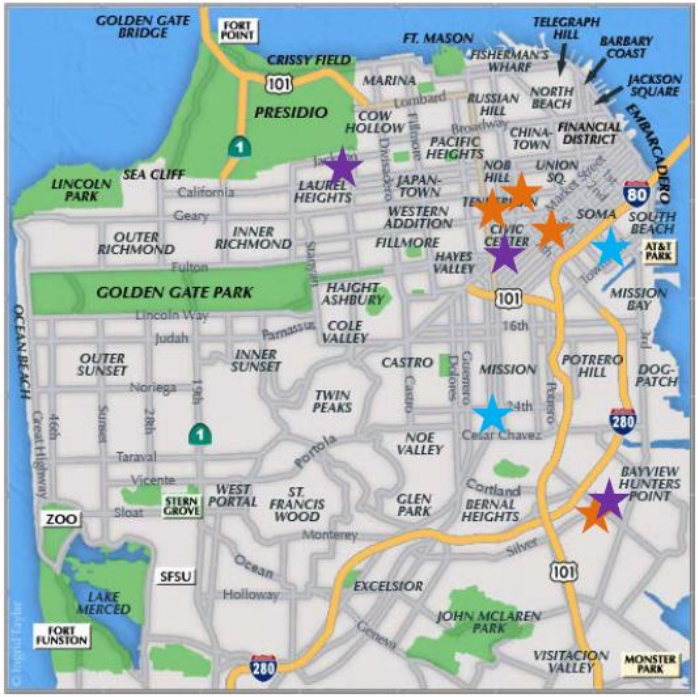
HCV Ab+ patients were offered confirmatory HCV RNA, GT, FibroScan, counselling and linkage to HCV care

Screening settings:

1)Street outreach ★

2)Community events ★

3)Methadone programs ★



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This is what it could look like

Finger Prick

Anti-HCV POCT

5-20 min

POC HCV RNA/Ag

<15 min

POC APRI/FIB4/TE Exclude cirrhosis

<15 min

Start treatment

Diagnosed, assessed and ready to start in 30 minutes or less with only a finger prick!

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Important improvements required to improve HCV testing in Canada

Technology

1. Reflex HCV RNA (or core Ag) testing for all positive Ab tests
2. Access to FUNDED point-of-care (POC) Ab tests
3. Access to FUNDED point-of-care (POC) HCV RNA tests
4. Access to FUNDED Dried Blood Spot (DBS) testing

Policy

1. Updated screening guidelines – beyond risk–based
2. Data linkage and sharing to guide policy
3. Funding of active screening efforts – (e.g. Ontario HCV Teams)

Ensuring Equity in Elimination Efforts

Community readiness

Active engagement

Peer involvement

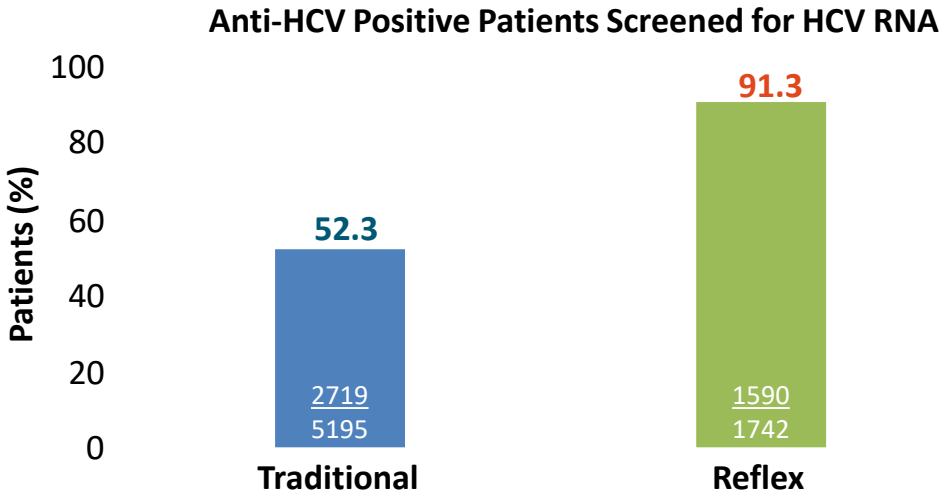
Advocacy

Reflection

Revision

Impact of reflex HCV RNA testing

HCV RNA reflex testing of anti-HCV positive patients in Spain, 2015-2018



Some efficiencies to help:

1. Avoid repeat Ab testing in positives
2. Drop confirmatory Ab testing

Reflex testing is very effective – increasingly **but not universally available**

Lopez-Martínez. J Clin Microbiol. 2020

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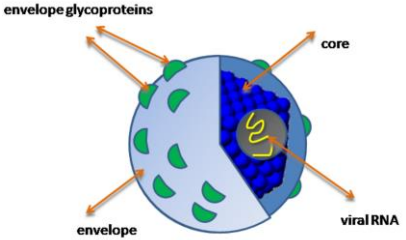
Alternative to RNA

- Learning from COVID-19
- **POC Antigen testing** – confirm active infection
  - SARS-CoV-2 Ag tests – 5' and $5/test! → **cheap enough to skip Ab screen**

- **HCV Core Ag**
  - Correlates well with HCV RNA but less sensitive
  - Can be done on the same sample as used for Ab test
  - Cheaper – 15-25% cost of HCV RNA (a bit arbitrary)
  - Fully automated (**but requires central lab**)
  - **Will be difficult to make 'POC'** – lysis of sample, dissociation from Abs and signal amplification for sensitivity all required…challenging!

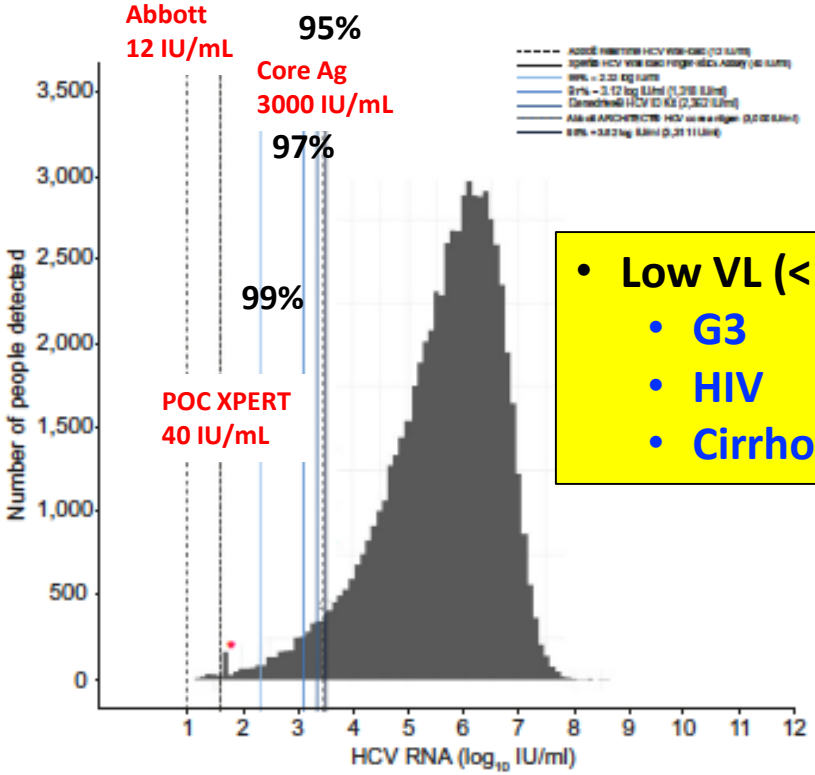


Is HCV core Ag good enough?

- 62,000 samples from around the world
- Different genotypes
- HIV
- **97%>1000 IU/mL**

- **With current tests <1% miss rate, if increase threshold to 1000 IU/mL ~3% miss rate for chronic HCV**

EASL now recommends HCV RNA with threshold of 1000 IU/mL



- **Low VL (<1000)**
  - **G3**
  - **HIV**
  - **Cirrhosis**

Freiman J Hep 2019, EASL HCV Clinical Practice Guidelines

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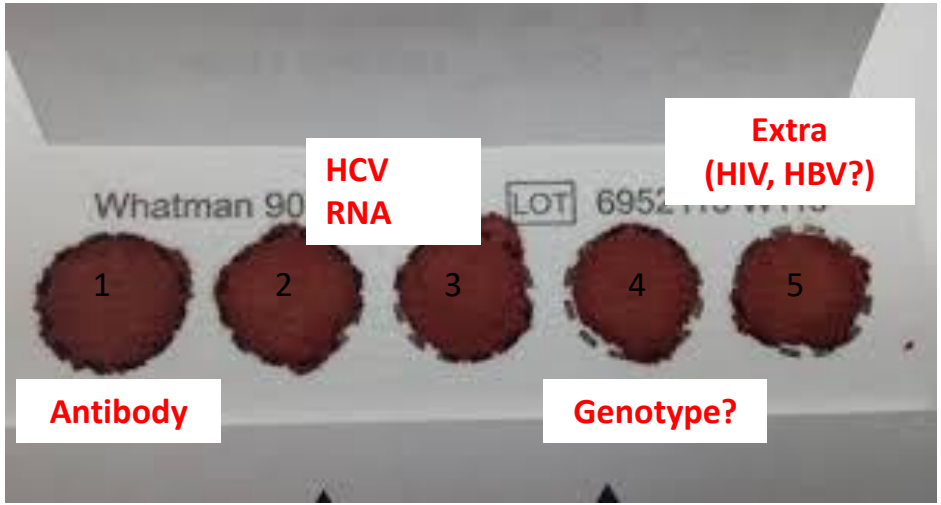
Issues with Core Ag

- Sensitivity good but probably not good enough (**yet!**)
- Particularly given that false negatives more likely in those we cannot miss (cirrhosis, HIV, G3)
- Performs less well for confirmation of SVR – false + and false -
- Not PoC – significant technical challenges

- For now…as a sole test, only option would be **Combined Ag/Ab test with HCV RNA done for Ab+/Ag-** → would reduce HCV RNA testing but not a panacea…
- But – **an improved Core Ag test – sensitivity/PoC could be a major step forward**

Not just the test, but the collection method

Dried Blood Spot (DBS) Testing

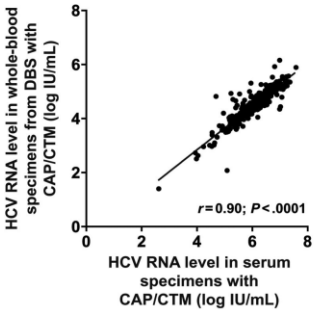


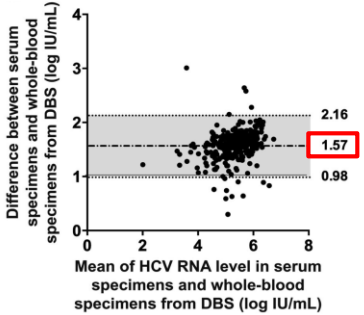
Pros:
- No blood draw (screening drives, PWID)
- Peer testing
- Easy storage → mail to lab
- No need for 2nd visit for confirmatory RNA test

Cons:
- Smaller volume – may need multiple pricks – better with capillary
- Lower HCV RNA titre
- No immediate result

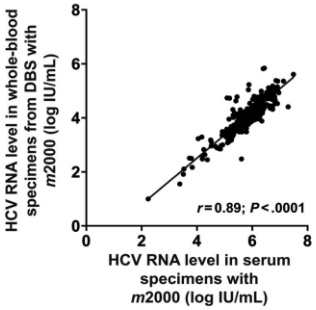
HCV RNA off DBS

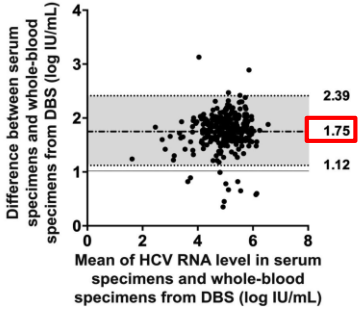
CAP/CTM (Roche)





*m*2000 (Abbott)





- Predictably **lower HCV RNA titre** - ~1.5-2 log IU/mL
- Rarely goes from positive to negative – particularly for diagnosis

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DBS in remote settings

- High burden of HCV in Canadian Indigenous populations
- Very remote communities → no road access
- Very limited resources

- **HCV Screening**
  - Community leaders (Chief & council) support
  - **Peer screeners → DBS**
  - Peer & RN counseling
  - Screen >1/3 adult pop'n 3d
- **Linkage to care**
  - Local MD/RN – treatment with ECHO model
  - OAT clinics

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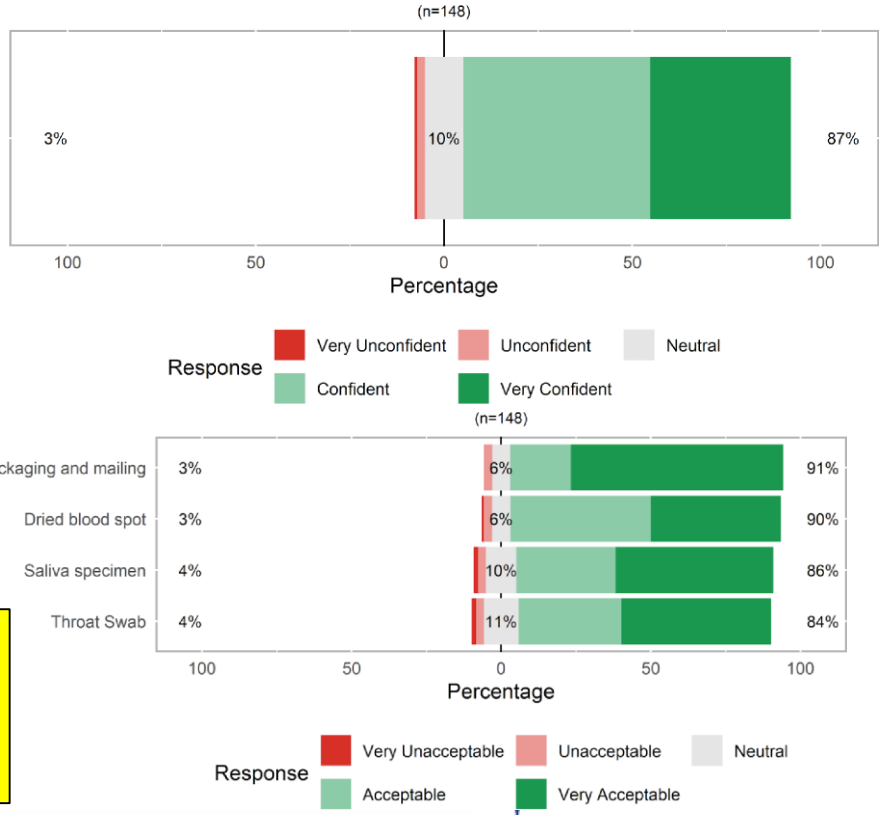
DBS Self collection



- Has been evaluated in HIV & SARS-CoV-2
- High acceptability, comfort and performance
- **Worked for COVID – why not HCV?**

Valentine-Graves PLoS One 2020, Takano BMC ID 2018

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But still not point of care…

Rapid antibody tests

- Meta-analysis
- >13,000 individuals included in 18 studies (11 in LMIC) between 1992 and 2012

Specimen	Specificity	Sensitivity
Whole blood POCTs	99.5%	98.9%
Serum & Plasma POCTs	99.7%	98.9%
Serum & Plasma RDTs	98.6%	98.4%
Saliva POCTs	98.2%	97.1%

Other issues: Co-infection, accuracy across genotypes

Shivkumar Ann Int Med 2012

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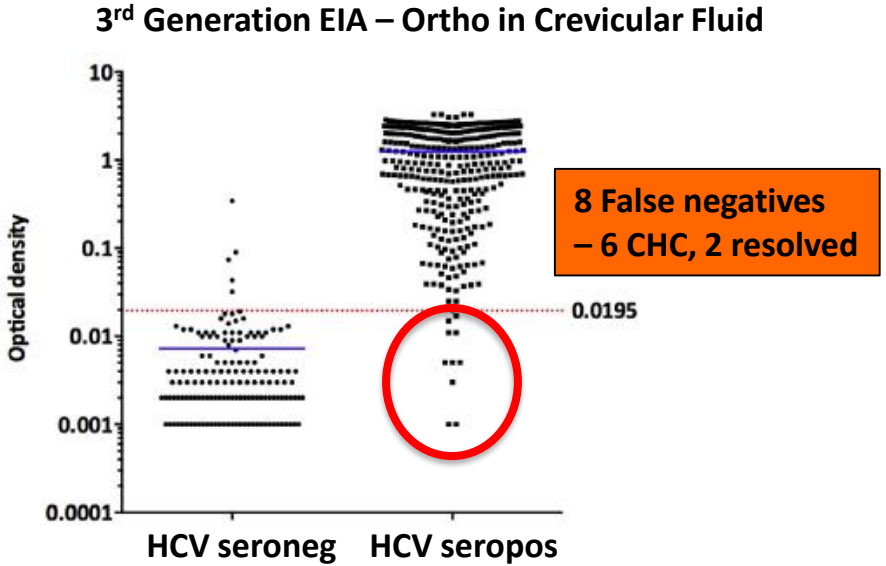
Oral Fluid (saliva)

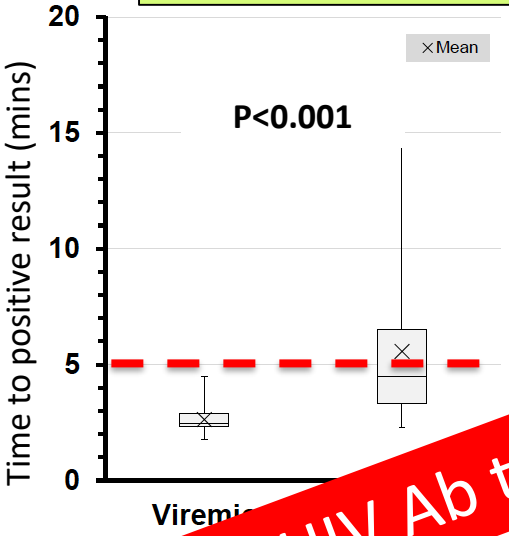
OraQuick test crevicular fluid – 513 patients – **Specificity 100%, Sensitivity 97.6%**



- Despite excellent performance – **not FDA/HC approved** but approved in UK & Europe
- Significant advantages for screening in certain settings

Making OraQuick quicker

Can we take advantage of the fact that Ab titers wane with time?



OraQuick HCV Ab	Viremic		Predictive Values
Positive at 5 min		113	PPV 66.8% (95% CI 0.62-0.72)
Negati	0	70	NPV 100.0% (95% CI 0.95-1.00)

Sensitivity: 100% (95% CI 0.98-1.00) **Specificity: 38.3** (95% CI 0.32-0.42)

bioLytical HIV Ab test → <2' to result – PoC has to be fast!

- atients positive within 5 minutes (clinic + real-world validation cohort)
- **negative, not viremic** (reduces number of RNA tests that need to be done)
  - if positive immediate RNA by DBS/venipuncture or POC RNA **still required**
- Only need to engage for 5 minutes

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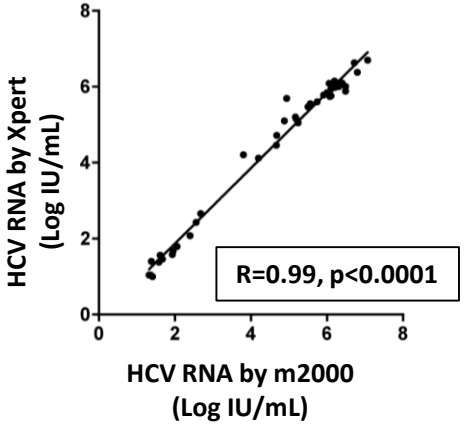
Rapid HCV RNA – almost PoC

Serum/plasma sample (1mL)

Cartridge to reader

~100 mins



- Relatively easy-to-use rapid HCV RNA test
- All genotypes → **60' to result**
- High correlation with standard PCR assays – analytical performance r=0.99
- Real-world performance very good **(but not FDA/HC approved!)**
  - **Venipuncture - Sens 100%, Spec 99.1%**
  - **Finger-prick – Sens 95.5%, Spec 98.1%**
- Positive results - **<40' but negative result requires 57'**

McHugh J Clin Micro 2017, Grebely Lancet Gastro Hep 2017, Grebely JID 2020

In the right setting…RNA can be your first test

- **Offering HCV testing in KeepSIX SCS**
  - Xpert HCV RNA at entry – high uptake
  - 54/124 (**43%**) positive @ BL + 10 in f/u
  - 43/64 (**67%**) linked to care
  - 29/43 (**67%**) treated
  - 25/29 (**86%**) SVR

- Similar program Melbourne, Australia
  - Prevalence 28% → 89% treated
  - Including 13 on day of positive test!

Testing practices by Canadian province

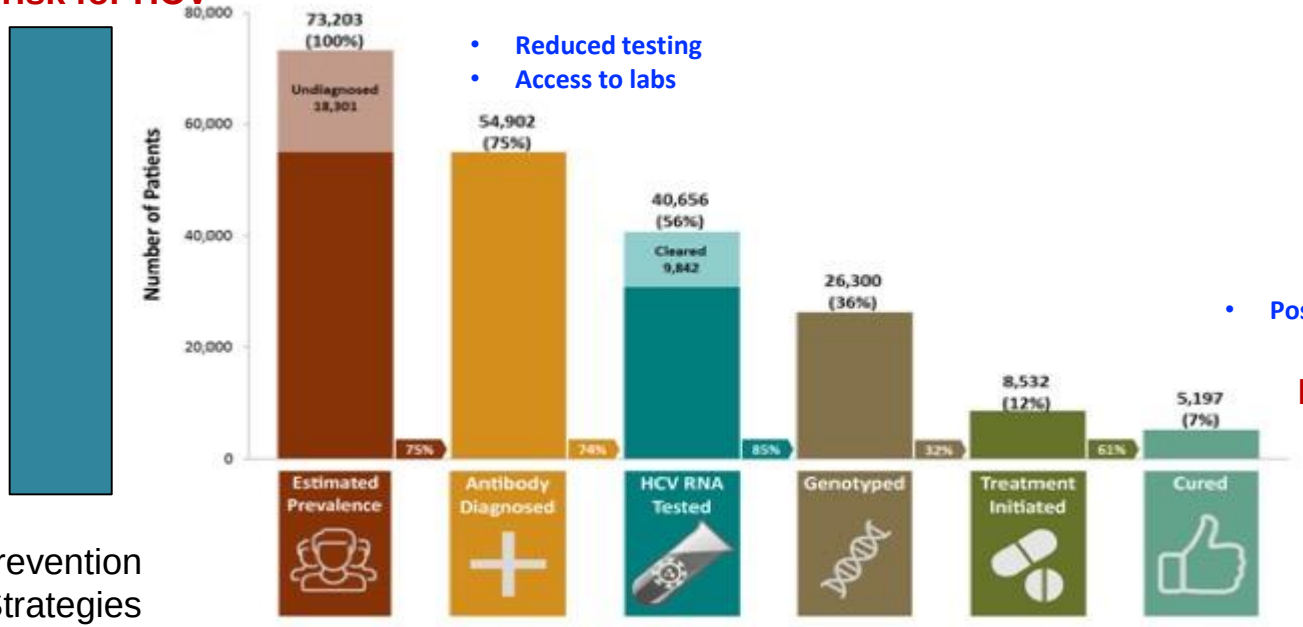
Testing	BC	AB	SK	MB	ON	QC	NB	NS	PEI	NL
Central laboratory Ab	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓
Community/hospital laboratory Ab that is not a provincial central lab	✓	✓	✓	X	✓	✓	✓	X	X	X
Reflex antigen testing	X	X	✓	✓	X	X	X	X	X	X
Reflex RNA testing	✓	✓	X	✓	X	X	✓	✓	✓[1]	✓
POC testing	✓	✓	✓	✓	✓	✓	✓	✓	✓	Not used
POC testing require provincial oversight	X	X	✓	X	X	X	X	X	✓	N/A
Ab repeated after POC testing before RNA*	✓	✓	✓	✓	✓	✓	✓	X	✓	N/A
DBS testing	Pilot/NML	Pilot/NML	Pilot/NML	Pilot/NML	✓	X	Pilot/NML	Pilot/NML	Pilot/NML	Pilot/NML

[1]Antibody positive samples sent to Nova Scotia for RNA testing

*NML, National Microbiology Laboratory

COVID-19 affects all aspects of the cascade

At risk for HCV



- Reduced testing
- Access to labs

- Postpone follow up care

Post-treatment outcomes

Prevention Strategies

Long-term Follow-up

- Reduced harm reduction
- Increased use

- Deferral of treatment

Adapted Janjua et al eBiomed 2016

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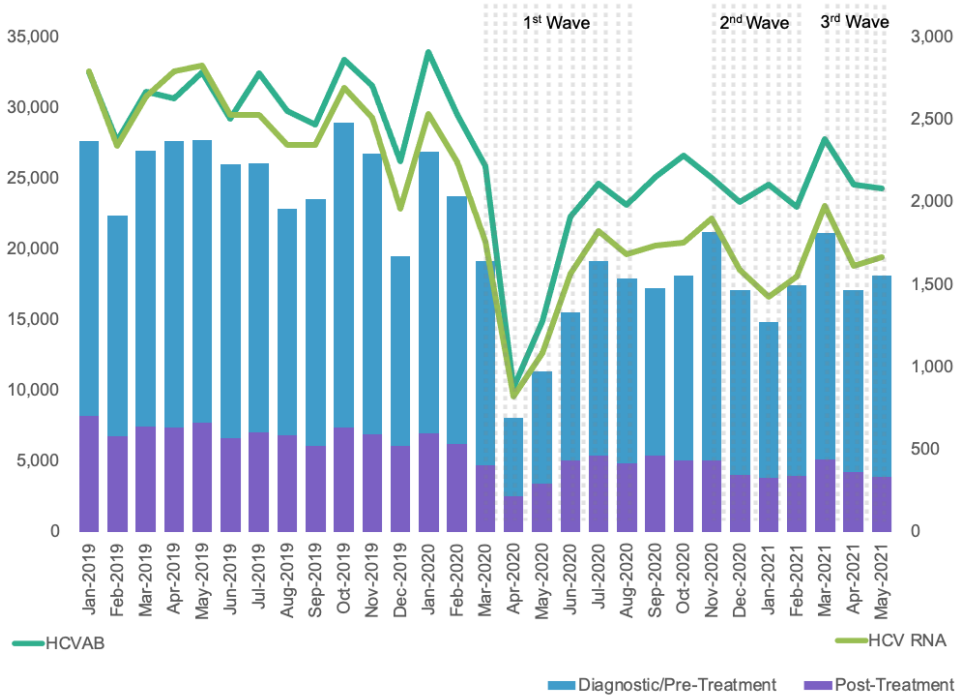
Impacts of COVID-19 Pandemic on HCV Testing in Ontario



- Significant declines with each wave
- **Rebound to below pre-pandemic levels**

Mandel E et al J Viral Hepatitis 2022

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Are there silver linings?

- **New technologies** – rapid, cheap POC diagnostics (some of the same platforms…)
- **Integrated NATIONAL data sharing** → up to the minute dashboards! Rapid linkage to administrative data → track elimination and identify the gaps!
- **Approaches to 'reach' the 'hard to reach'** – test for HCV (and HIV) too!
- **Self-testing 'the norm'**
- **DBS self-collection for Ab responses**

Match the test to the situation

- Considerations
  - **Population** – likelihood of follow-up, prevalence of HCV
  - **Sample type** – need for phlebotomy vs finger-prick (vs saliva)
  - **Urgency for treatment** – need for PoC
  - **Geography** – access to care provider – self-collection (DBS)
  - **Cost** – test type, prevalence
- Was done fairly well for COVID-19
  - RDT vs PCR used fairly effectively – need to consider a public health approach - balance individual vs population…
  - **Elimination requires a public health approach**

Don’t let perfect get in the way of very very good

PoC not suitable for all settings

No impact to ER flow
No cost to the department

Rapid testing is not always ‘rapid’ – pre and post-test counseling + linkage

Matching the test to the setting

- **Current model** (Ab then RNA or Ab reflex RNA)
  - Boomer/all adult screening, prenatal (?), OAT clinics (?) → **Reliable F/U**
- **PoC Ab + PoC RNA/DBS**
  - Screening drives/outreach, prison, inpatient screening
- **PoC saliva + PoC RNA/DBS**
  - Screening drives, opportunistic screening (ER, prison) – **where blood/sharps or time is an issue (accept lower sensitivity of saliva)**
- **PoC RNA (or Core Ag)**
  - Very high prevalence population – active PWID (SIS), prison (?), OAT (?)
- **DBS**
  - Rural remote (no lab), hard-to-reach, self-collection, time issues (ER)

Summary

- Diagnostics are a critical tool for HCV elimination – have not kept pace with therapeutics
- **Use the tests we have well → do not let perfect get in the way of very very good**
- Critical to match the testing paradigm to the clinical situation
  - Time to diagnosis is *not always* the biggest issue
  - Using our current tests more efficiently would help – e.g. the 5' rule
  - Need to focus on a public health approach to testing – beyond risk-based
  - Requirements outlined in the *Blueprint* & the *Roadmap* → **implementation required!**
- PoC tests (Ab and RNA) need to be faster & funded! – true PoC <5'
- ***Hopefully the rapid innovation for COVID-19 will spill over to HCV to lead to diagnostics that accelerate elimination!***

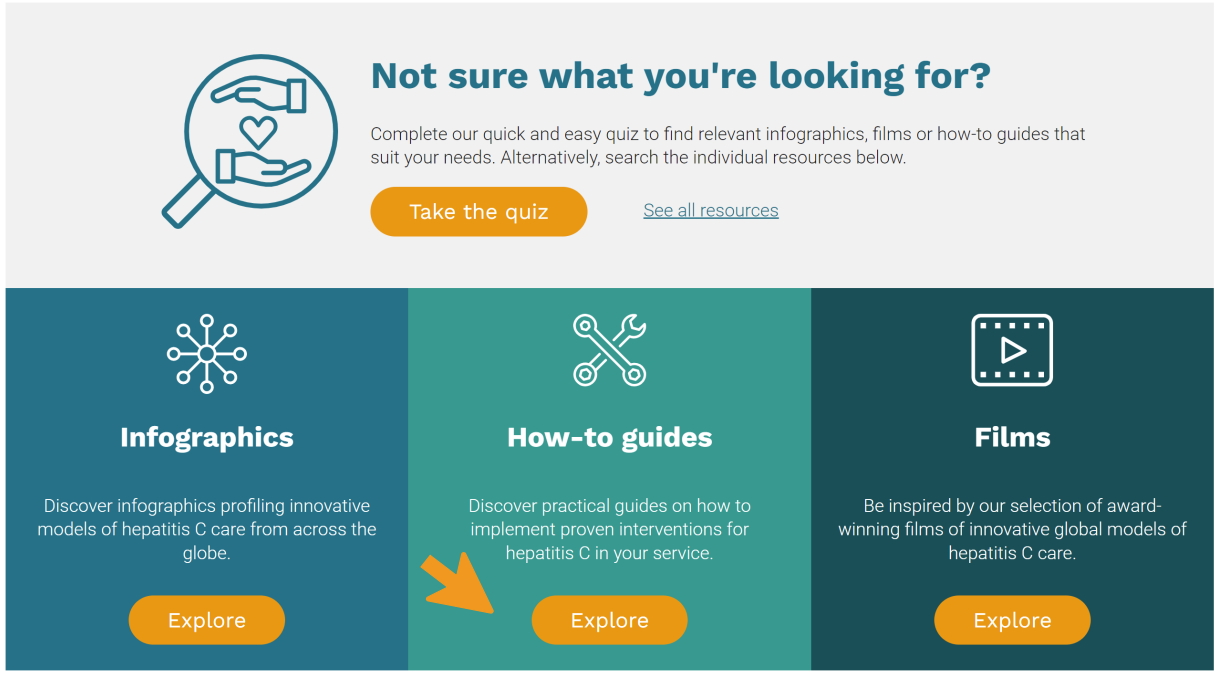
Hepatitis C Intervention Toolkit

Practical how-to guides for setting up interventions in your service to enhance the HCV care cascade

INHSU

Hepatitis C Intervention Toolkit - Overview

An online digital interactive toolkit profiling a range of evidence-based interventions to enhance the HCV care cascade.



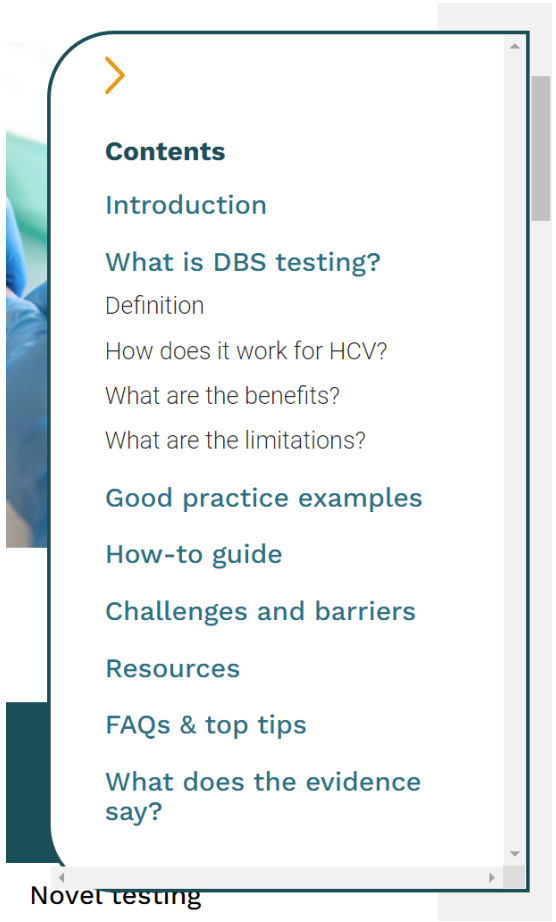
How-To Guides on:

1. Dried blood spot testing
2. HCV Point-of-care antibody testing
3. HCV Point-of-care RNA testing
4. Peer support
5. Patient navigation
6. EMR Audit & case finding

The Intervention Toolkit, infographics and films, are all filterable though an interactive quiz, which allows you to refine your search and find resources profiling best practice models of hepatitis C care from across the INHSU network and beyond.

INHSU www.inhsu.org/what-we-do/global-knowledge-exchange/hepatitis-c-intervention-toolkit

Hepatitis C Intervention Toolkit



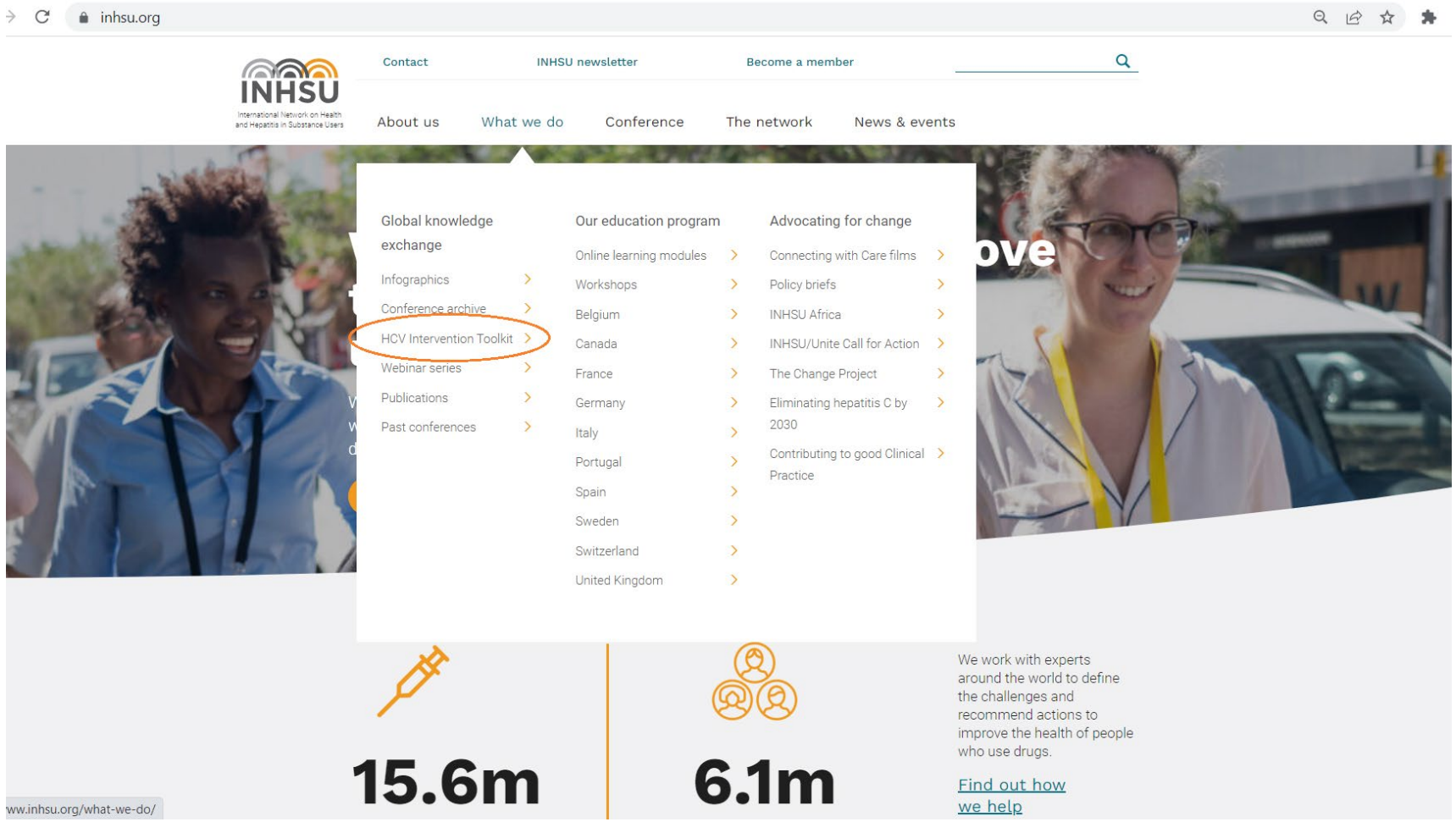
Each how-to guide provides practical guidance on how to set up the intervention in your service, resources to help you, as well as challenges and barriers you might encounter and how to overcome them.

Interventions launched include HCV POC RNA testing, HCV POC Antibody testing, dried blood spot testing and peer support

Next intervention: Patient Navigation

INHSU www.inhsu.org/what-we-do/global-knowledge-exchange/hepatitis-c-intervention-toolkit

Hepatitis C Intervention Toolkit



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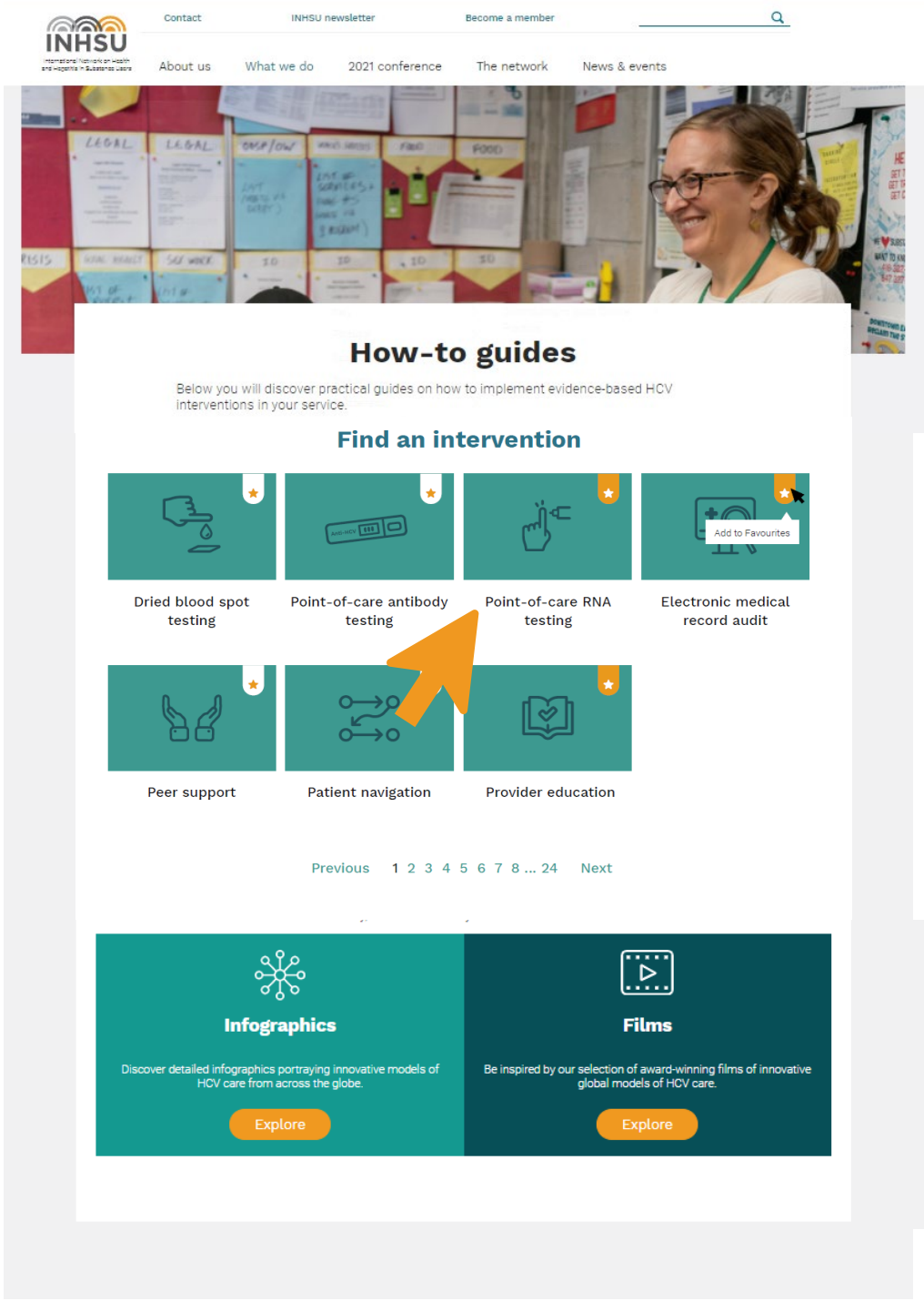
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How-to guides
Below you will discover practical guides on how to implement evidence-based HCV interventions in your service.
Find an intervention
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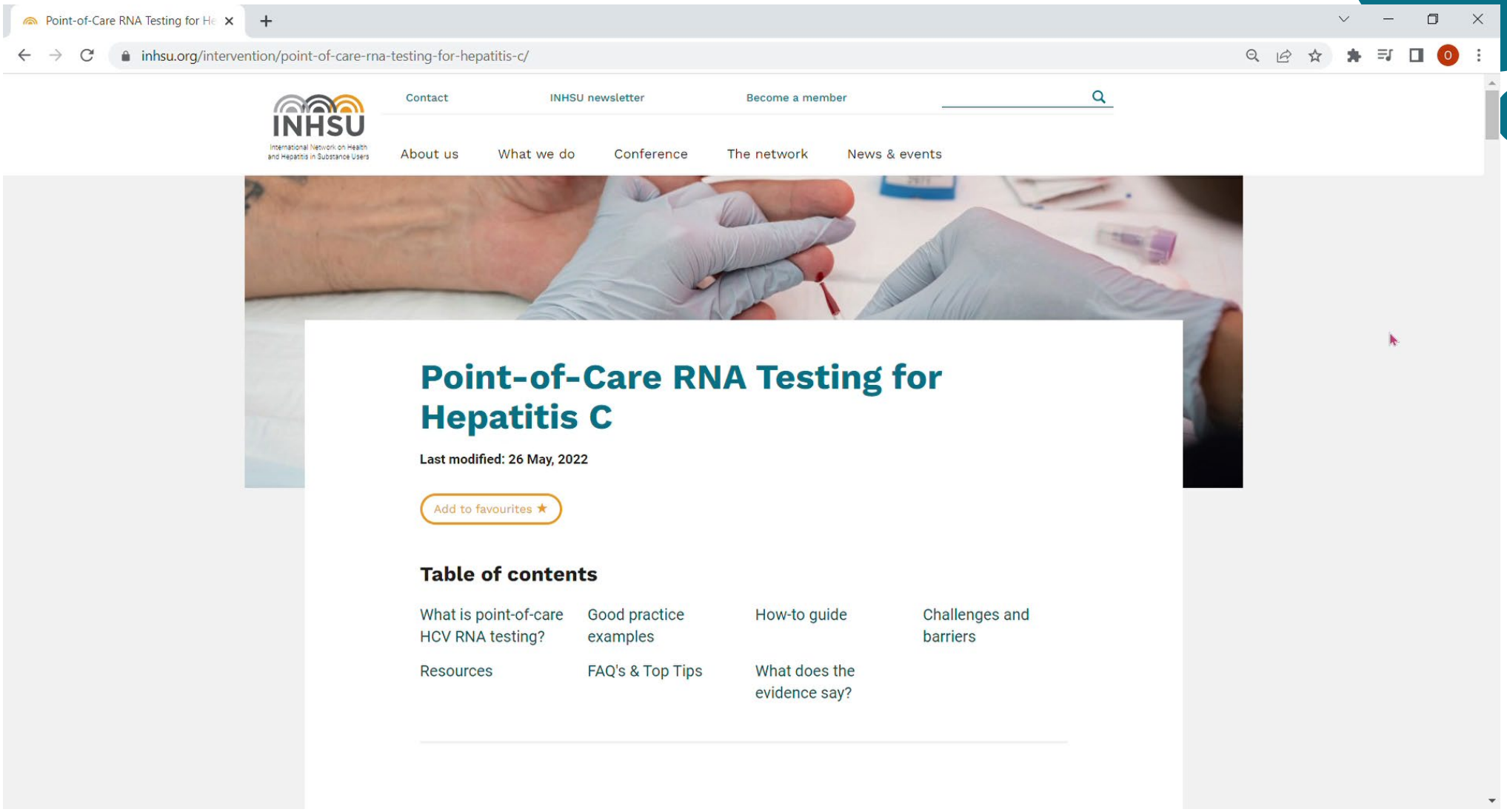
Dried blood spot testing
Point-of-care antibody testing
Point-of-care RNA testing
Electronic medical record audit
Peer support
Patient navigation
Provider education
Previous 1 2 3 4 5 6 7 8 ... 24 Next
Infographics
Discover detailed infographics portraying innovative models of HCV care from across the globe.
Explore
Films
Be inspired by our selection of award-winning films of innovative global models of HCV care.
Explore


Point-of-Care RNA Testing for He
inhsu.org/intervention/point-of-care-rna-testing-for-hepatitis-c/
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Point-of-Care RNA Testing for Hepatitis C
Last modified: 26 May, 2022
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Table of contents
What is point-of-care HCV RNA testing?
Good practice examples
How-to guide
Challenges and barriers
Resources
FAQ's & Top Tips
What does the evidence say?

Hepatitis C Intervention Toolkit

- Sign up to receive communications about the toolkit
- Questions?

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DRIED BLOOD SPOT TESTING

IN LOW BARRIER HEP C CARE

North Lambton
Community Health Centre

WHY DO WE USE DRIED BLOOD TESTING?

- Task shifting to increase access to testing
- Reduces barrier of blood draw
- Easy to perform in non-clinical settings

- DBS in addition to other strategies that facilitate low barrier hepatitis C care

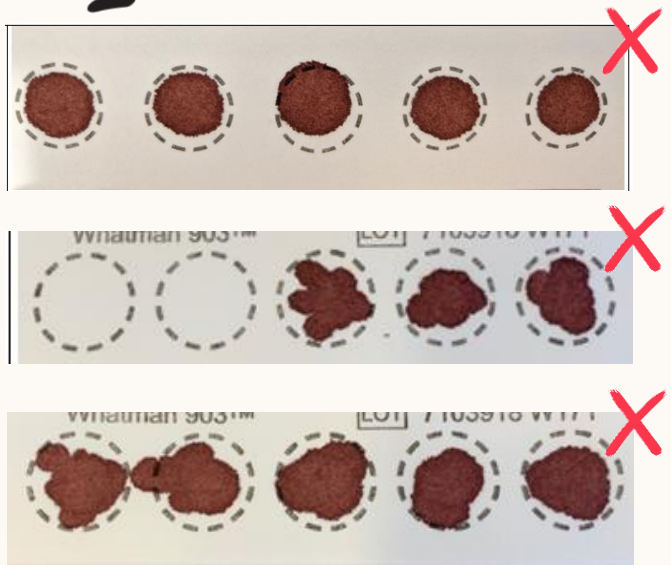
North Lambton Community Health Centre

DRIED BLOOD SPOT COLLECTION

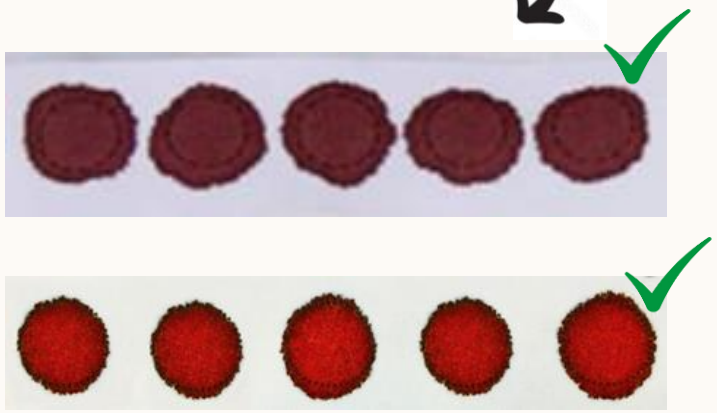
North Lambton Community Health Centre

WHAT DOES A SAMPLE LOOK LIKE?

UNACCEPTABLE SAMPLE



ACCEPTABLE SAMPLE



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HELPFUL HINTS

PUBLIC HEALTH LAB

- Let lab know your plan to submit DBS for HCV viral load testing and your reasons for doing so

CLIENT CHOICE

- DBS samples are less sensitive than traditional venous samples

PROBLEM SOLVING

- Cold hands can made finger poke blood collection difficult – keep hand warmer bags in kit

THANK YOU

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- Treatment access in remote & Indigenous communities
- Engagement on a community specific capacity
- Supporting awareness resources
  - Language
  - Visuals
  - Wellness Story