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# **Prenatal and Pediatric HBV and HCV: Room to Improve the Cascade of Care?**

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*PHO Microbiology Rounds*

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# Disclosures

## Relationships with commercial interests:

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AbbVie, Gilead

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McKesson, Omega Specialty Nurses, AbbVie, Gilead

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AbbVie, Gilead

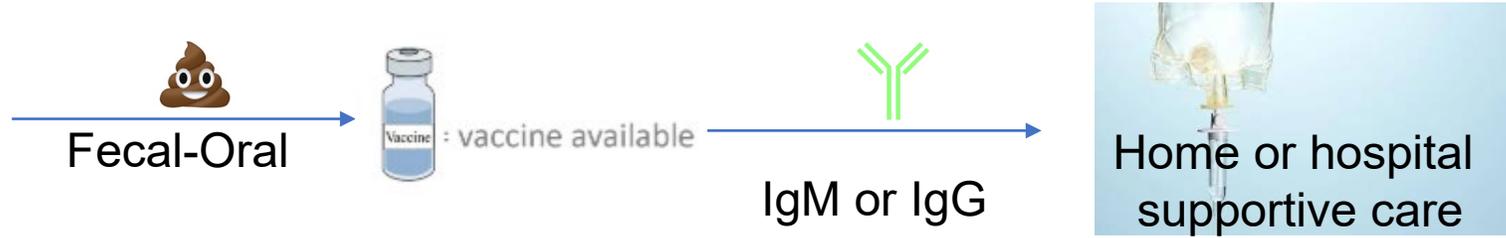
\*Some of my consulting fees pay for clinical and research program personnel and projects

# Objectives

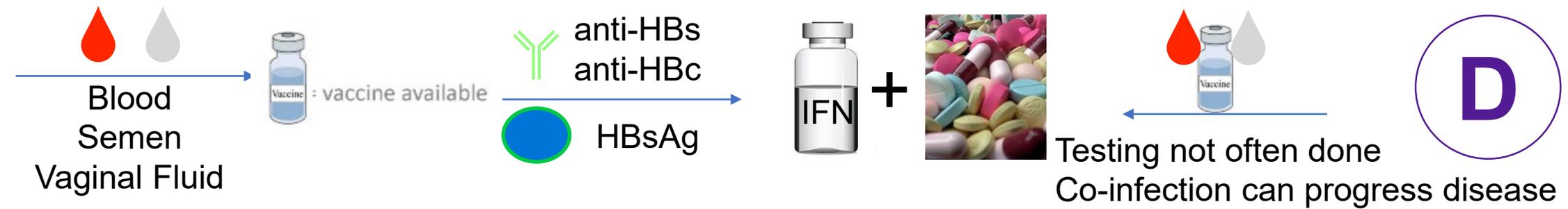
- 1) Understand the current practices for screening, linkage to care, and treatment for pregnant persons with hepatitis B and C
- 2) Understand the current practices in prevention of pediatric acquisition, as well as treatment for hepatitis B and C
- 3) Discuss areas for improved investment at the health system level such as prevention strategies, improvements in screening and testing algorithms, and better collection of administrative data

# Review of Viral Hepatitis

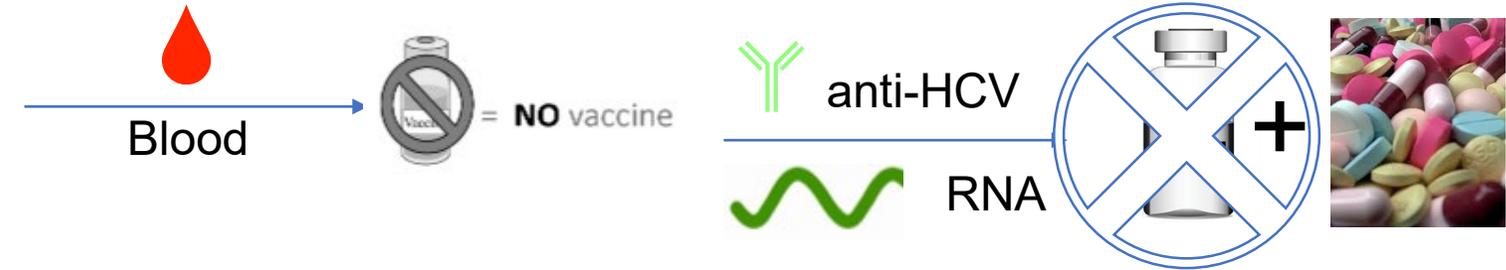
**A**



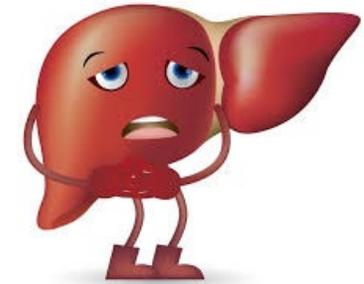
**B**



**C**



**E**



# WHO 2016: Elimination of Viral Hepatitis by 2030

2.24

~~viral hepatitis~~  
2030



NOhep



Canada made a promise to eliminate viral hepatitis as a public health threat by 2030.

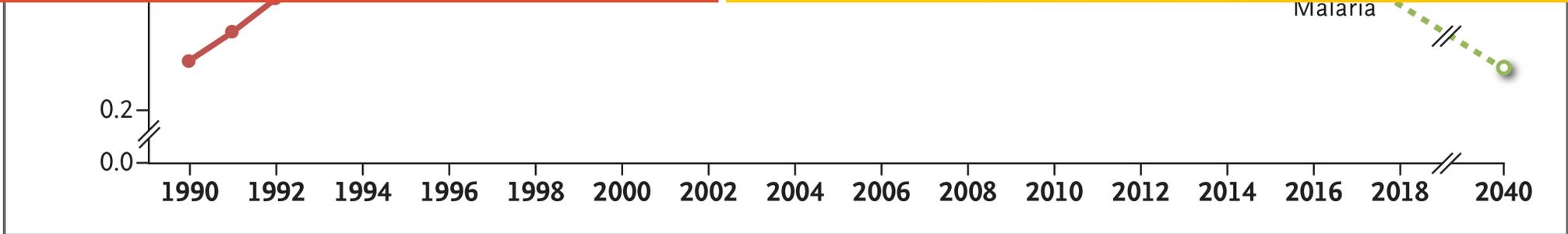
That's just 10 years away.

**So where's the urgency?**

#WorldHepatitisDay2020

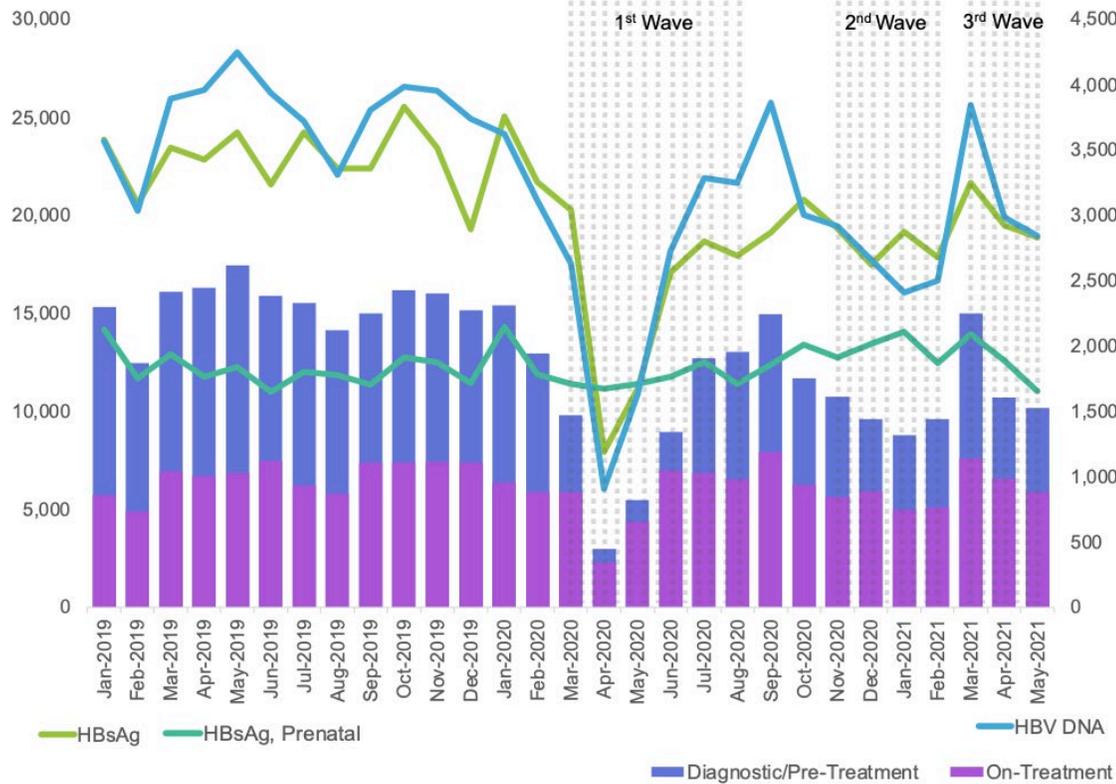
Visit [www.actionhepatitiscanada.ca](http://www.actionhepatitiscanada.ca) to take action.

ACTION HEPATITIS CANADA  
**AHC**  
ACTION HÉPATITES CANADA

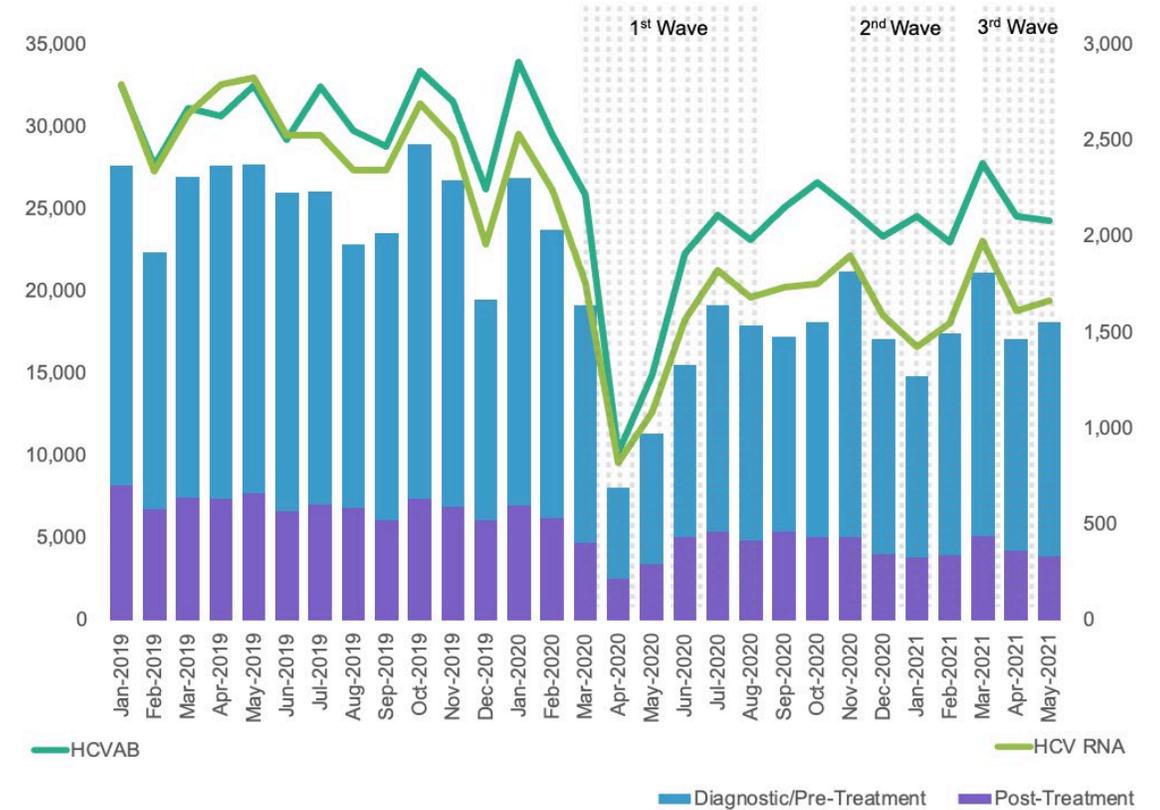


# Impact of COVID-19 on HBV and HCV Testing in Ontario

## HBV

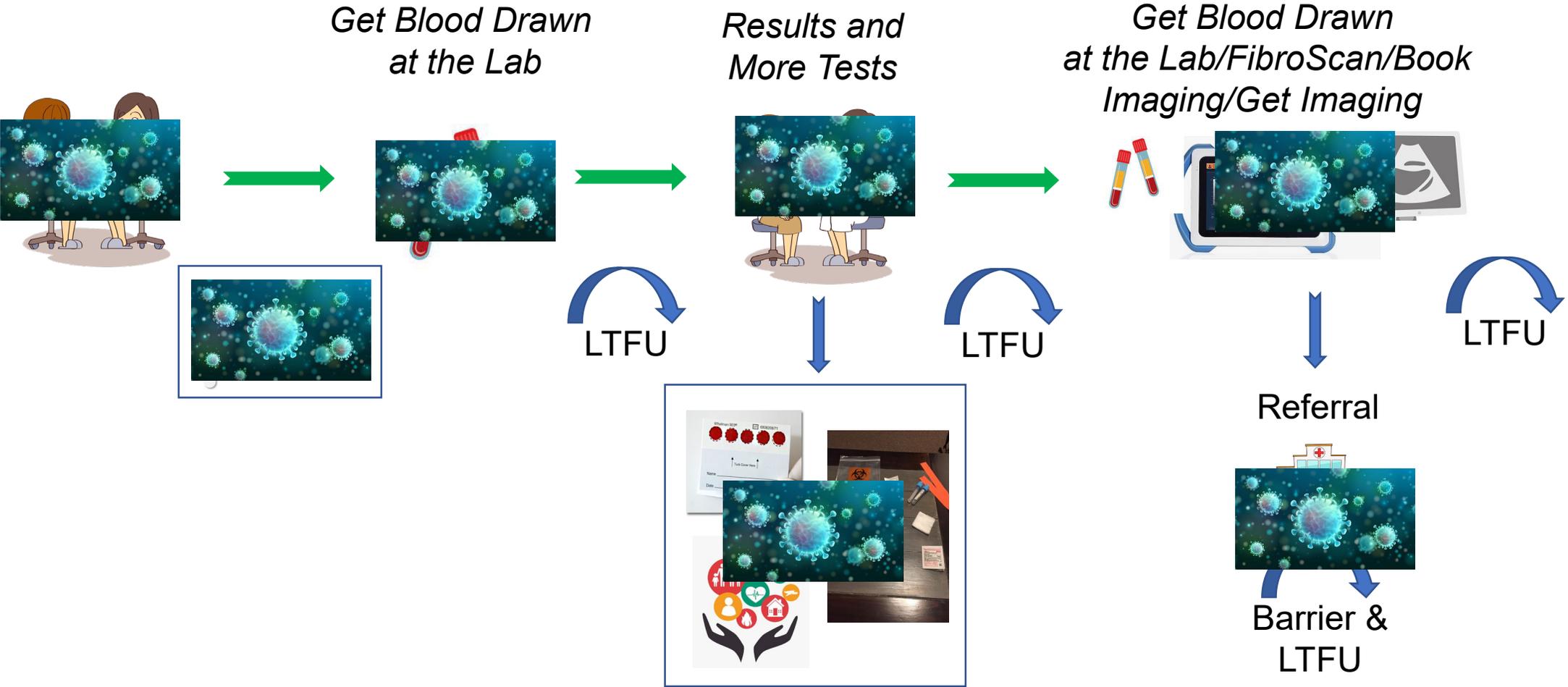


## HCV



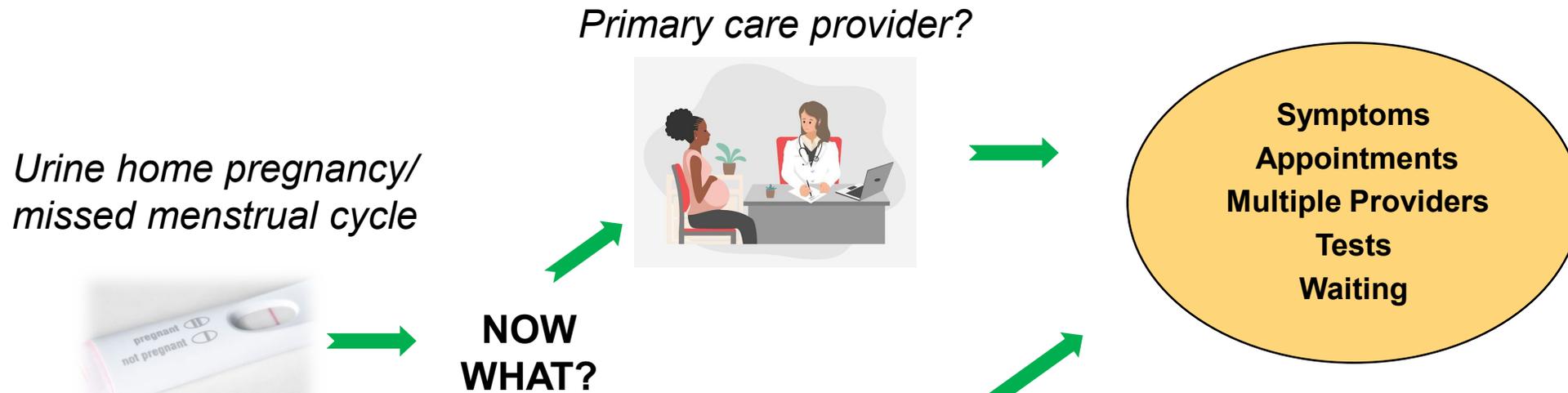
Mandel et al., 2021

# HBV/HCV Pre-Treatment Care Continuum





# Many Steps in Seeking Prenatal Care



*No primary care provider?  
How to even start?*

Some communities  
have self-referral OB

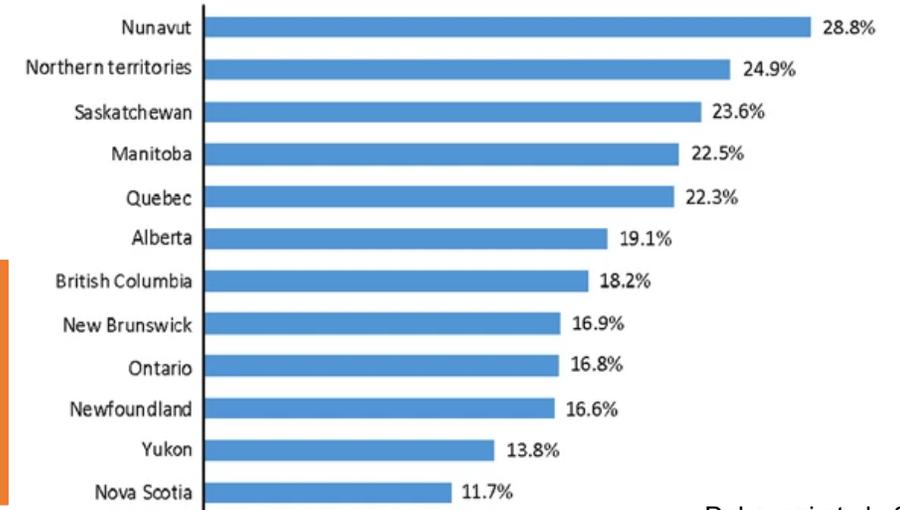
No prenatal care

Self-referral midwife  
requires confirmation

Walk-in for more  
testing & referral

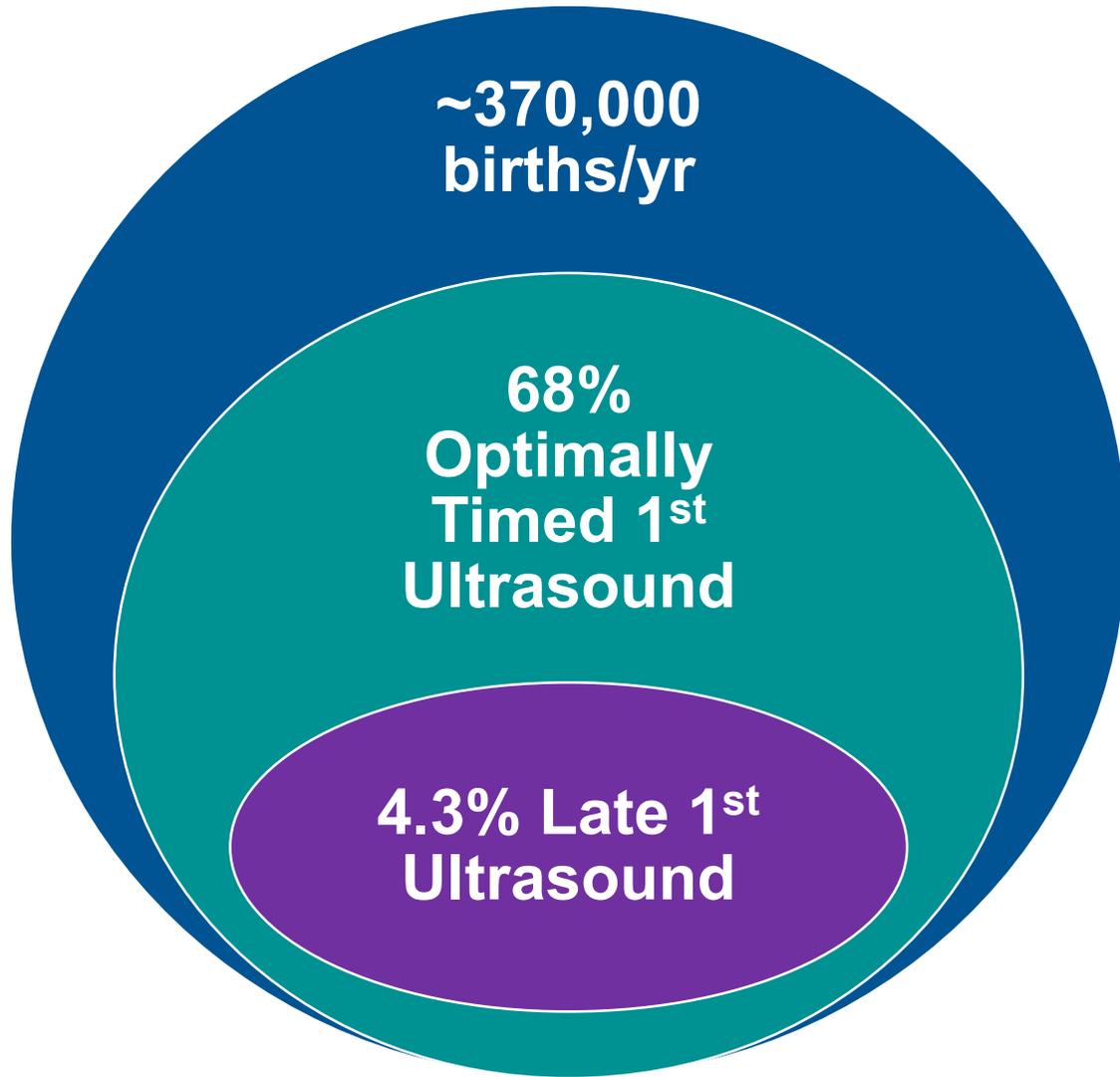
All more complicated  
when identifying as a  
newcomer, incarcerated,  
adolescent, other

*Inadequate prenatal care by province*



Debessai et al., 2016

# Barriers and Pregnant Persons Engagement



## *Motivators for vulnerable patients*

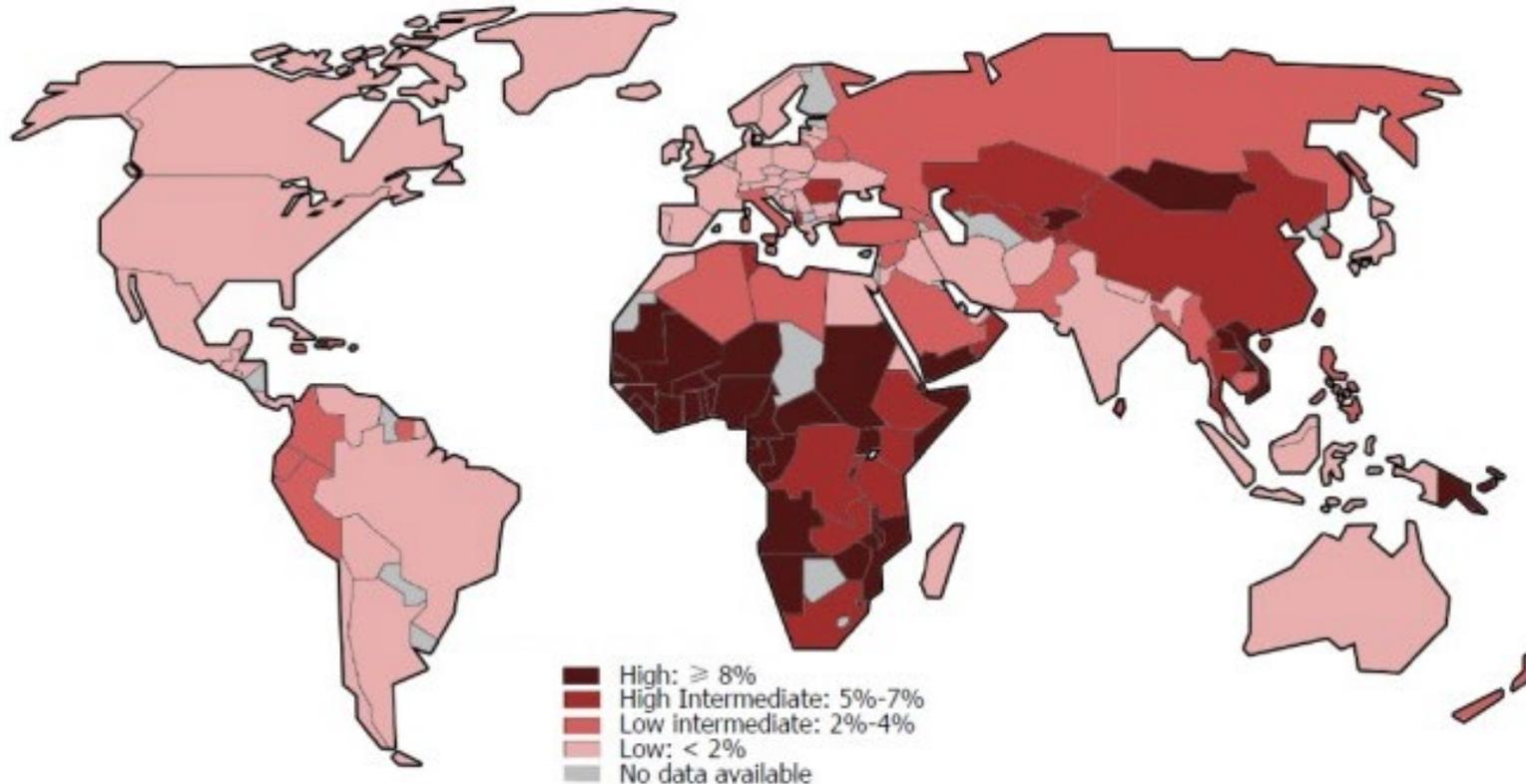
- Healthy pregnancy (both)
- Safety (both)
- Remaining with child following birth
- Support and assistance

## *Action*

- Seeking and attending prenatal appointments
- Seeking housing or housing upgrades
- Working with services to prepare (items)
- Addressing violence (verbal/physical/sexual)
- Recovery/trauma and opioid agonist programs (OAT)
- Restorative justice

Abdullah et al., 2019; Hubberstey et al., 2019

# HBV Global Epidemiology



## ***Rates, morbidity and mortality***

- In 2015, 257 million people were living with chronic hepatitis B infection (HBsAg+)
- In 2015, hepatitis B resulted in an estimated 887 000 deaths
  - cirrhosis and HCC
- In sub-Saharan Africa and East Asian countries predominantly transmitted *via* perinatal or horizontal route
- Developed countries most infections occur to young adults through injecting drug use or high-risk sexual behavior

World Health Organization, 2019

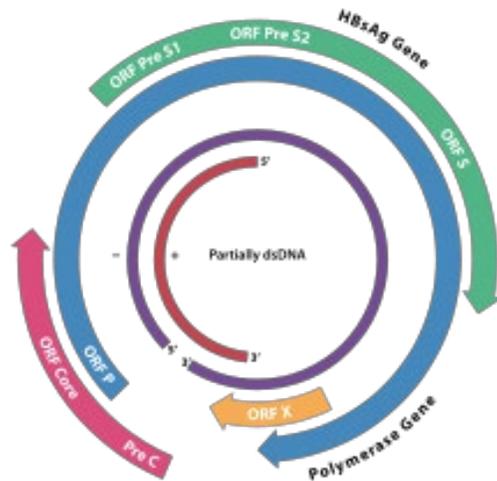
# HBV Virology

*ds-DNA virus*

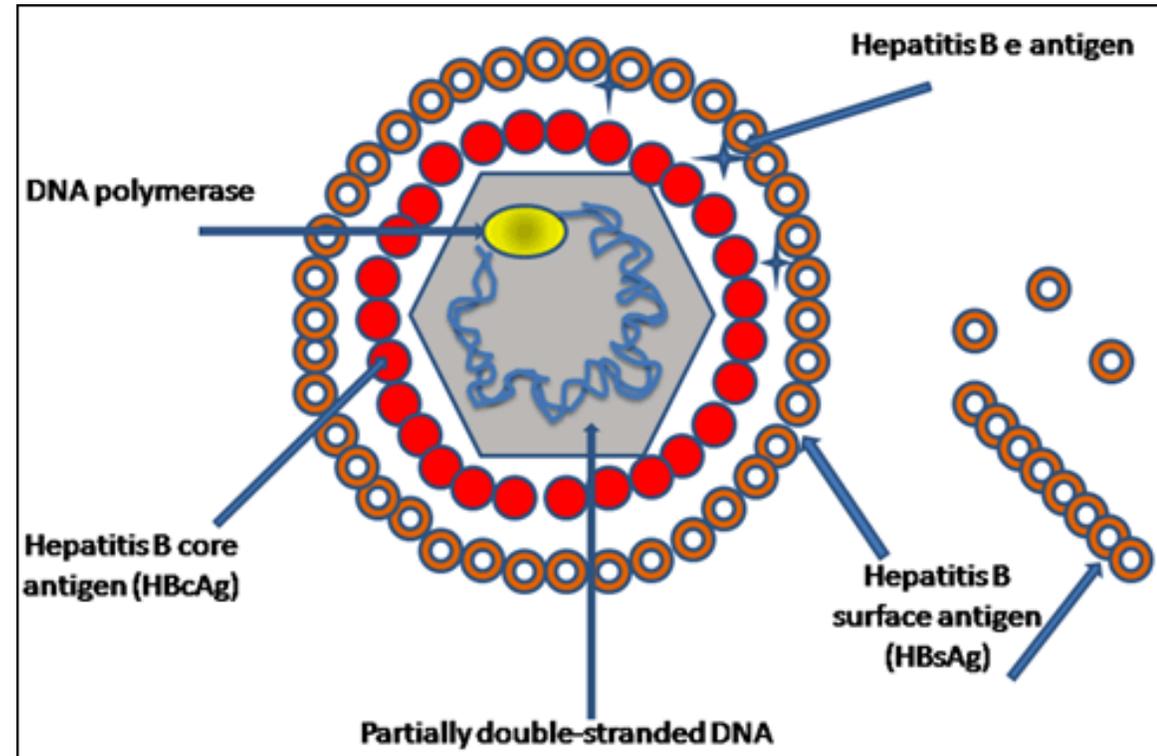
*Hepadnaviridae family*

*Circular genome*

*Thought to integrate into the host genome*



**Hepatitis B is VERY INFECTIOUS**



# HBV Screening

1. Born or resident in region where HBV is more common (Central, East, or South Asia; Australasia; Eastern Europe; South America; Sub-Saharan Africa; North Africa or Middle East)
2. Household contacts with HBV carriers (including unvaccinated persons whose parents were from HBV-endemic countries), especially children of HBV- positive mothers
3. Sexual contacts with HBV carriers, persons with multiple sexual partners
4. Illicit injection or intranasal drug use or shared drug paraphernalia (past or present)
5. Current or past incarceration
6. Patients with chronic renal failure who need dialysis Signs of liver disease (ie, abnormal liver enzyme tests) or other infectious diseases (ie, hepatitis C, HIV; hepatomegaly, splenomegaly, thrombocytopenia, and jaundice are late findings)
7. All pregnant women
8. Patients needing immune modulation therapy or those who will develop immunosuppression such as cancer chemotherapy

# Pediatric HBV Vaccination: Why Does Birth Dose Matter?

## *A quick review...*

Infection in childhood is associated with >90% chance of chronic hepatitis B  
There are multiple ways to prevent transmission of hepatitis B virus to infants and children

### Universal Hepatitis B Birth Dose Vaccination

In children born to HBsAg women:

Birth dose hepatitis B vaccination  
>90% effective to prevent transmission

Further reduced with passive  
prophylaxis at birth: HBIG

*No centralized database of women who  
are HBsAg matched to children  
receiving these interventions*

Would also prevent transmission from  
household & non-household contacts



### Universal Prenatal HBsAg Screening

SOGCs recommends universal  
prenatal HBsAg screening every  
pregnancy

*No evidence that this is occurring  
universally, but is a rationale as to why  
adolescent vaccination is acceptable*



### Follow-up Prenatal Testing and Antivirals

All positive prenatal HBsAg should be  
immediately followed by HBeAg and  
HBV DNA

Third trimester antivirals if viral load  
>200,000 IU/mL

*No linked database to ensure follow-  
up testing or antiviral initiation, falls to  
health units*



- WHO expanded BD recommendations to low-endemic countries like Canada in 2009
- Has decreased global prevalence from 5 to 1% in children under 5, 100+ countries have adopted

### ***5 provinces in Canada vaccinate in adolescence including Ontario***

- Assumptions:
  - If screening is being done universally prenatally, all children with HBsAg+ mom are getting vaccine x 3 and HBIG, children's only risk is sexual contact
  - Does not acknowledge horizontal transmission from non-household contacts
  - Canada is a destination country from endemic regions
  - Average age of those immigrating would have missed the newer vaccine programs
  - HBV is not screened for in the immigration medical

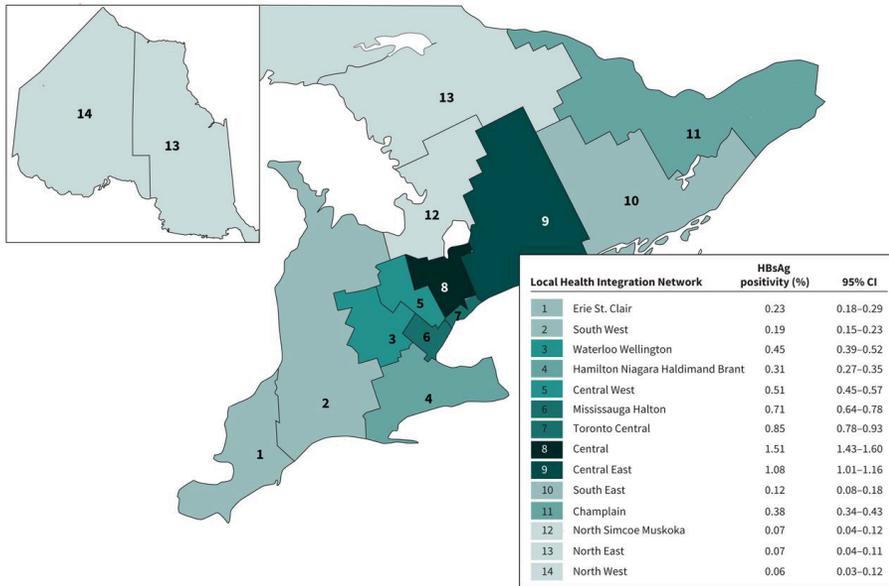
Created by M Biondi

# Burden of Prenatal HBV and Cascade in Ontario

## What do we know?

1

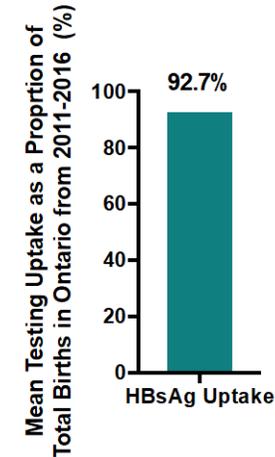
- Screening is nearly universal at 93%
- ON HBsAg prevalence 0.63%



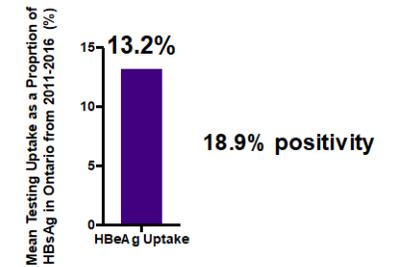
2

- Subsequent testing is poor

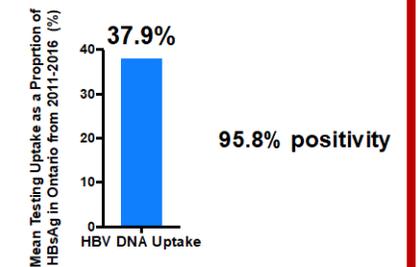
HBsAg Prenatal Screening



HBeAg Follow-up Testing



HBV DNA Follow-up Testing



Biondi et al., 2020

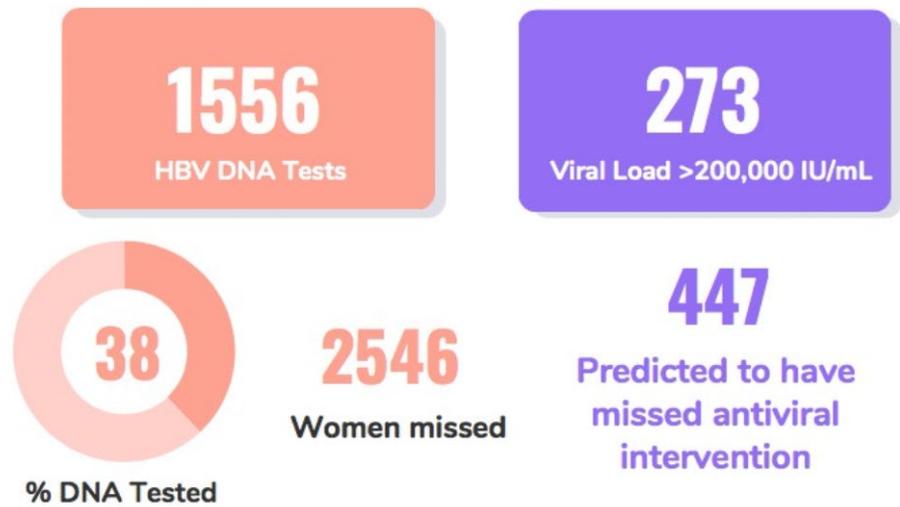
# HBV Prenatal Cascade in Ontario and Pediatric Rates

3

- If never getting HBV DNA, ~100/yr miss out on 3<sup>rd</sup> trimester antivirals

4

- ON children acquire HBV prior to vaccination
- Vaccination does not universally occur until adolescence (as in MB, SK, NS, NLFD), uptake only 70%



Age Groups (years)	Canadian-Born			Foreign-Born			Combined		
	Tested	Positive	Cases per 1,000	Tested	Positive	Cases per 1,000	Tested	Positive	Cases per 1,000
0-3	12,134	73	6	767	7	9	12,901	80	6
4-7	5,984	30	5	953	26	27	6,937	56	8
8-11	5,641	36	6	1,501	43	29	7,142	79	11
<b>Total</b>	<b>23,759</b>	<b>139</b>	<b>6</b>	<b>3,221</b>	<b>76</b>	<b>24</b>	<b>26,980</b>	<b>215</b>	<b>8</b>

Biondi et al., 2020

# Case: Horizontal Transmission Potential

Canadian born child, negative mom, positive dad

# Burden of Prenatal/Pediatric HBV and Cascade in Ontario

*What don't we know? And where public health and administrative data fails us...*

Prenatal	Transmission	Pediatric
<p>Why isn't subsequent testing done?</p> <ul style="list-style-type: none"> <li>Provider knowledge gap</li> <li>Referred but lost to follow-up</li> <li>Understand cascade</li> </ul>	# positive in household	Number of children who receive 3 x HBV vaccine in infancy (born to HBsAg+ person)
Number of eligible women who receive third trimester antivirals	# positive as a caregiver	Number of children who receive HBIG (born to HBsAg+ person)
	# positive daycare (regional)	Actual number of children living with HBV
<p><i>Immigration effect, estimates only, no testing during immigration medical</i></p>		

Biondi et al., 2020; Biondi et al., In Revision

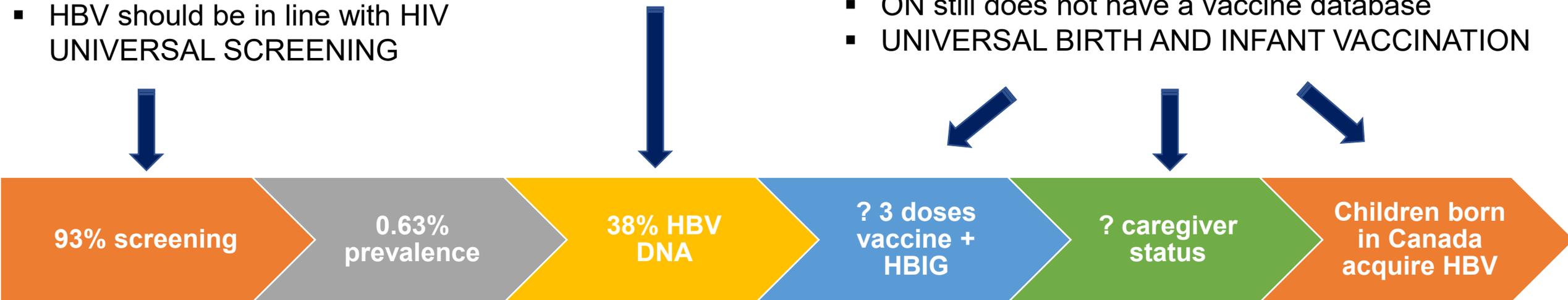
# How to Better Serve Pregnant Persons with HBV

## DECREASE/FULLY ELIMINATE VERTICAL TRANSMISSION OF HBV IN CANADA

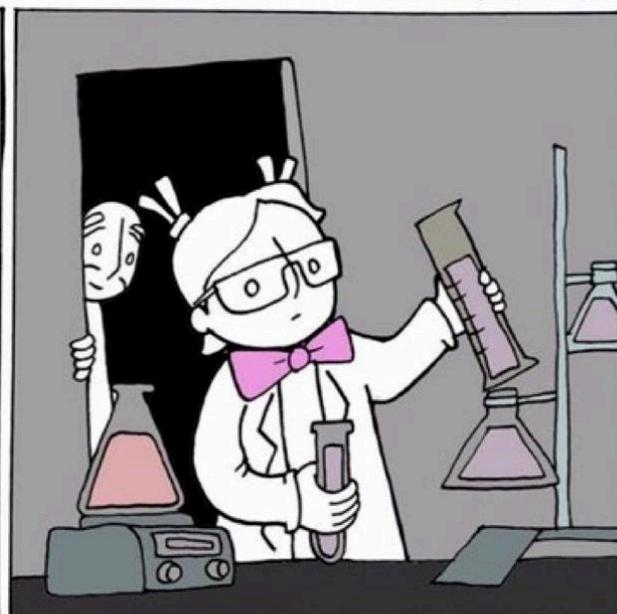
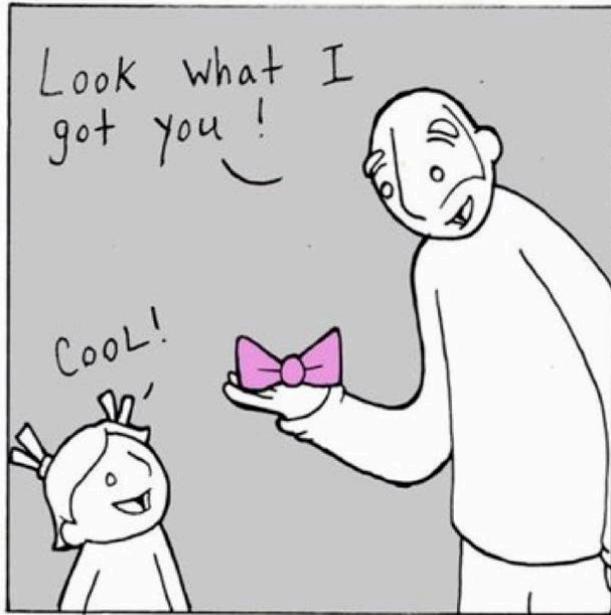
- Reflex HBeAg and DNA testing
- Better public health follow-up
- Understand the cascade
- Move to primary/OB care

- Infected persons should match HBIG given
- ON still does not have a vaccine database
- UNIVERSAL BIRTH AND INFANT VACCINATION

- HBV should be in line with HIV UNIVERSAL SCREENING

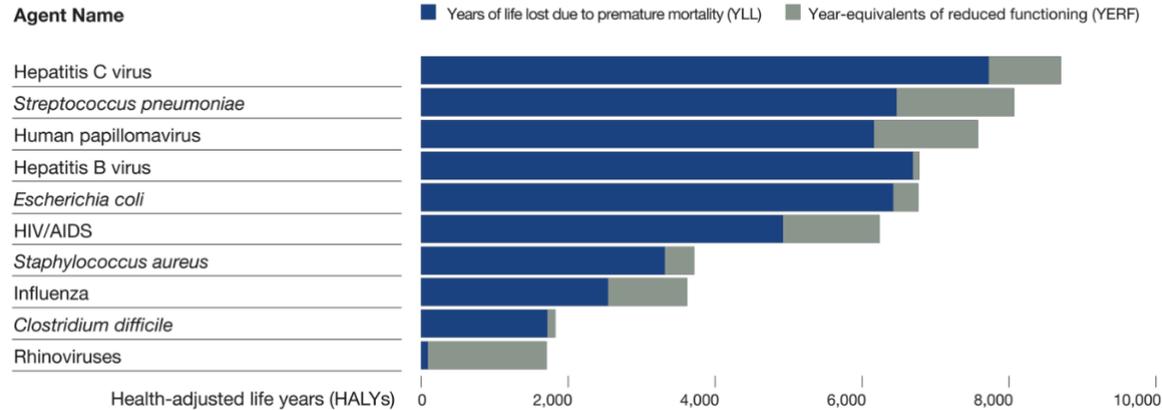


Biondi et al., 2020; Biondi et al., In Revision



# The Toll of HCV

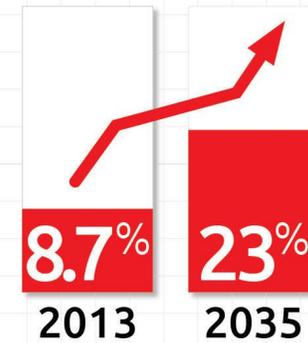
## The Most Important INFECTIOUS AGENTS in Ontario



OBIDS, 2010

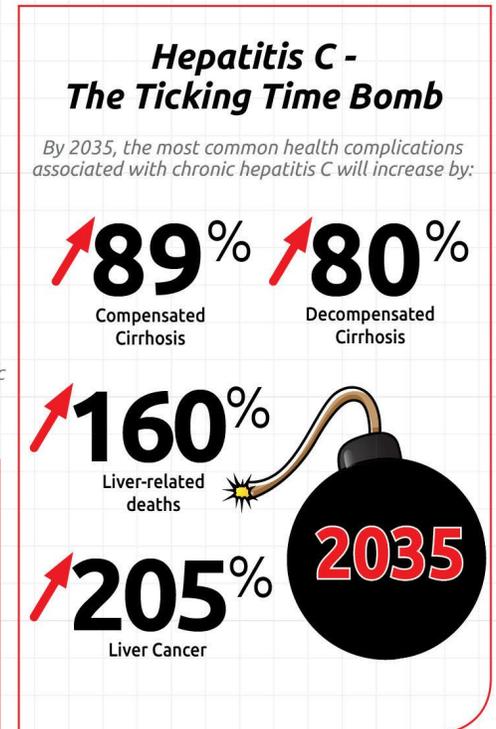
## Burden of Hepatitis C

## The Future Toll of Illness



The number of Canadians with chronic hepatitis C with cirrhosis and more advanced liver disease is on the rise.

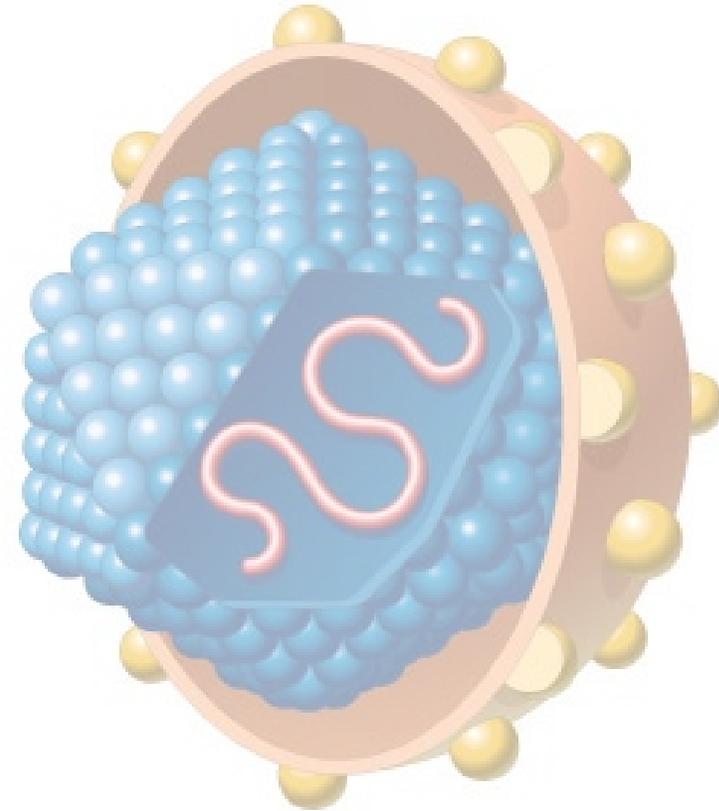
**75%**  
of hepatitis C patients have early-stage disease at any given time - an ideal opportunity to intervene with new antiviral therapy to avoid the future toll



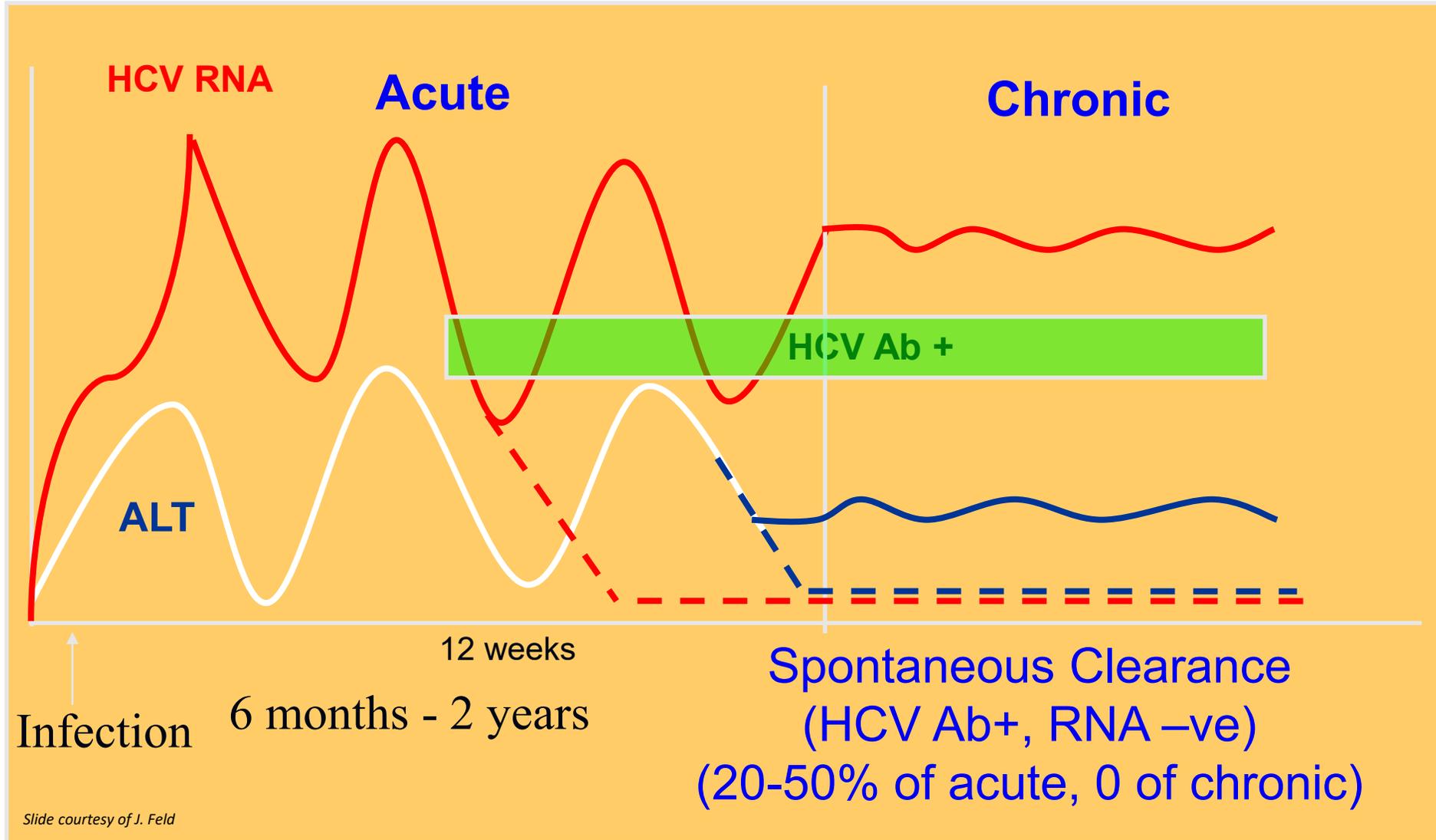
CLF, 2014

# HCV Virology

- Single-stranded (+)-sense
- RNA genome
- Enveloped
- *Flaviviridae* family
- *Hepacivirus* genus
- 7 known genotypes
  - Genotypes vary ~ 30% at nucleotide level
  - Subtypes vary ~ 20-25% at nucleotide level



# HCV Natural History



Slide courtesy of J Feld

# Who Should be Screened for HCV?

## *Risk Activity*

1. Past or present IDU (or any drug use?)
2. Past or present incarceration
3. Born to an HCV-infected mother\*
4. HIV+, in particular MSM
5. Sex/sharing person items with HCV+ person

## *Medical Risks*

6. Transfusion/products/transplant before 1992 in Canada
7. Chronic hemodialysis
8. Elevated ALT
9. Born in an endemic country, health care services

## *Cohort Screening*

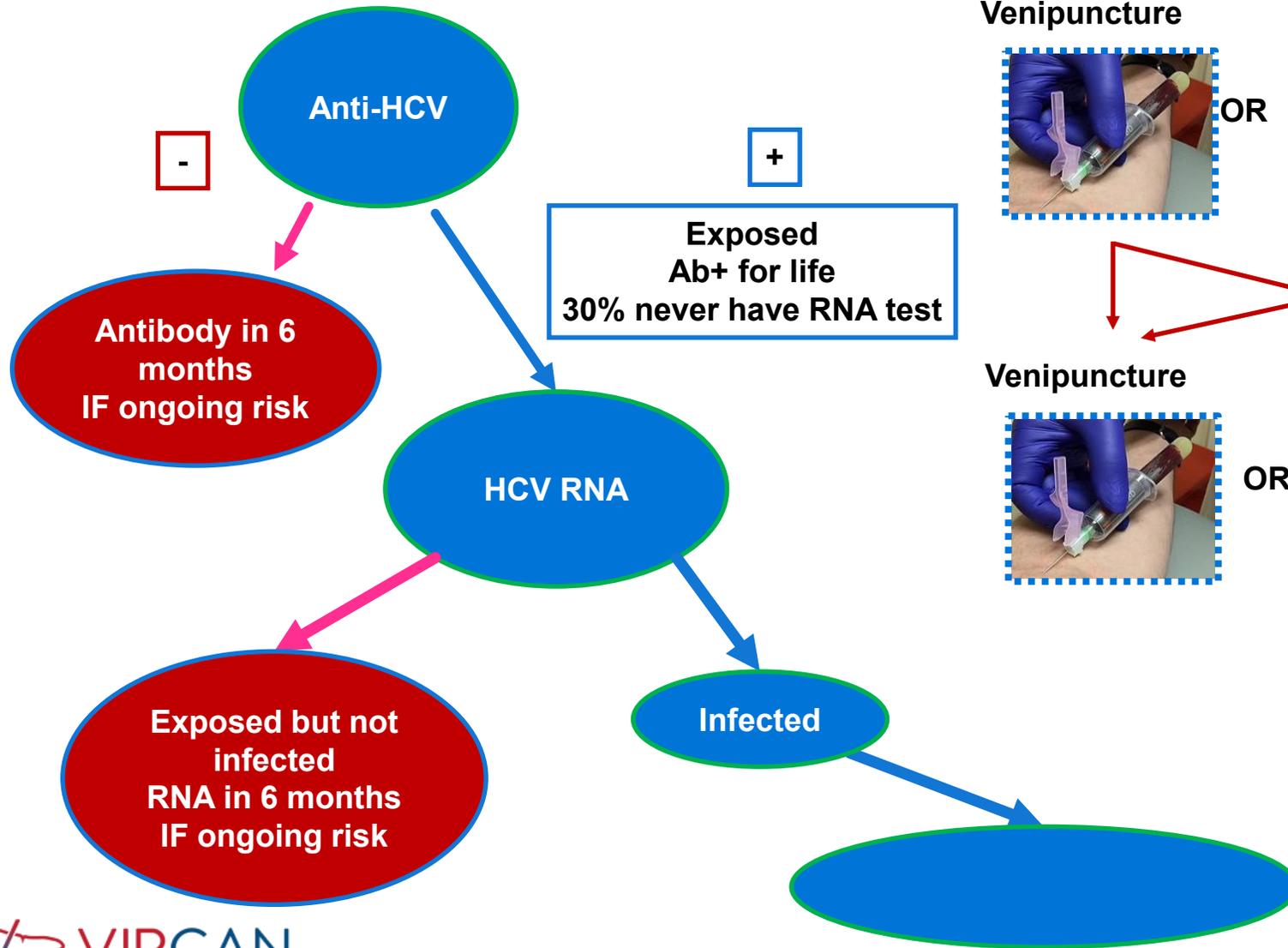
10. Born between 1945-1975

## *MISSED OPPORTUNITIES?*

- All adults
- All pregnant women

Shah et al. 2018

# HCV Testing Pathways



Venipuncture



OR

Rapid Finger-Prick



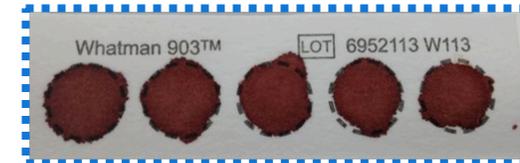
- High sensitivity
- VIRCAN 5-Minute Rule

Venipuncture



OR

Dried Blood Spot RNA



- PHOL since 2017

# Treatment in the Past

# Current Treatment – 95%+ Cure

Small numbers



Potential for large numbers

Advanced liver disease



Covered if no liver disease

Specialist prescriber/Extensive paperwork



Non-specialist MD/NP prescribers/Minimal paperwork

Complex drug regimens requiring teams



Simple drug regimens with solo providers

Frequent monitoring



Little or no monitoring

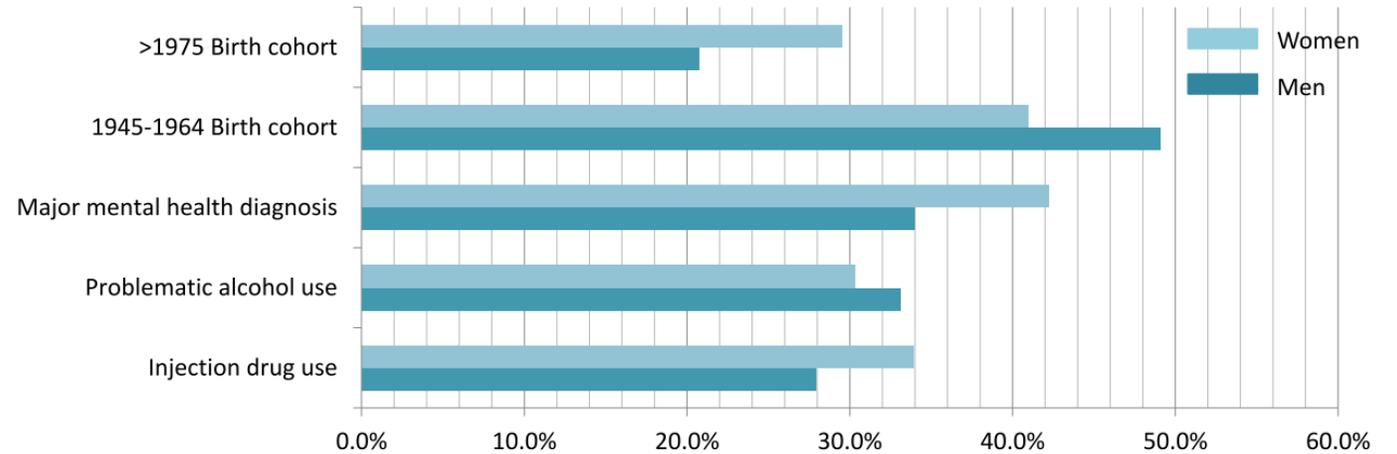
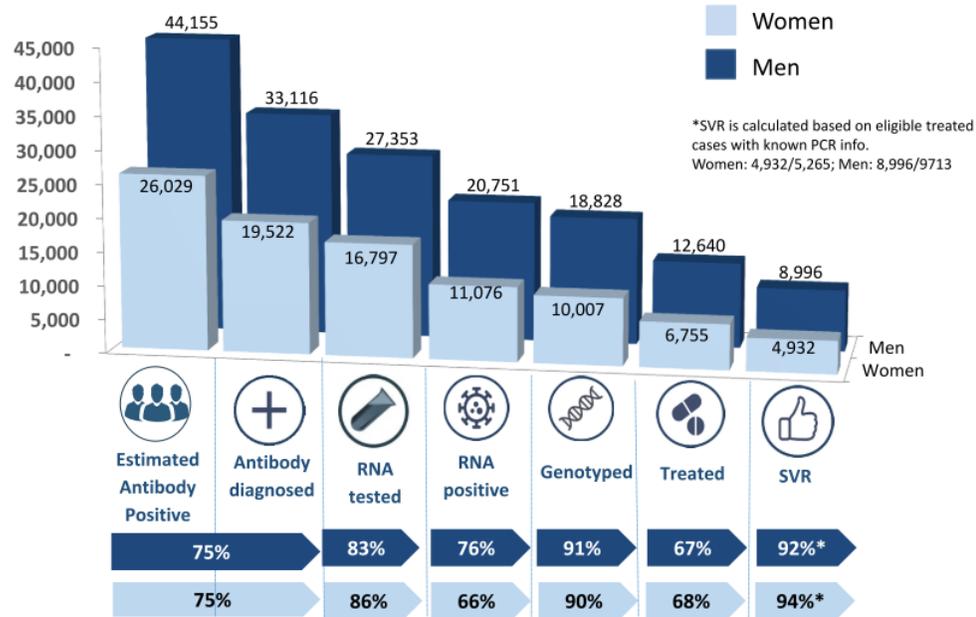
Response-guided therapy



Few on-treatment decisions

Biondi & Feld, CLJ, 2019

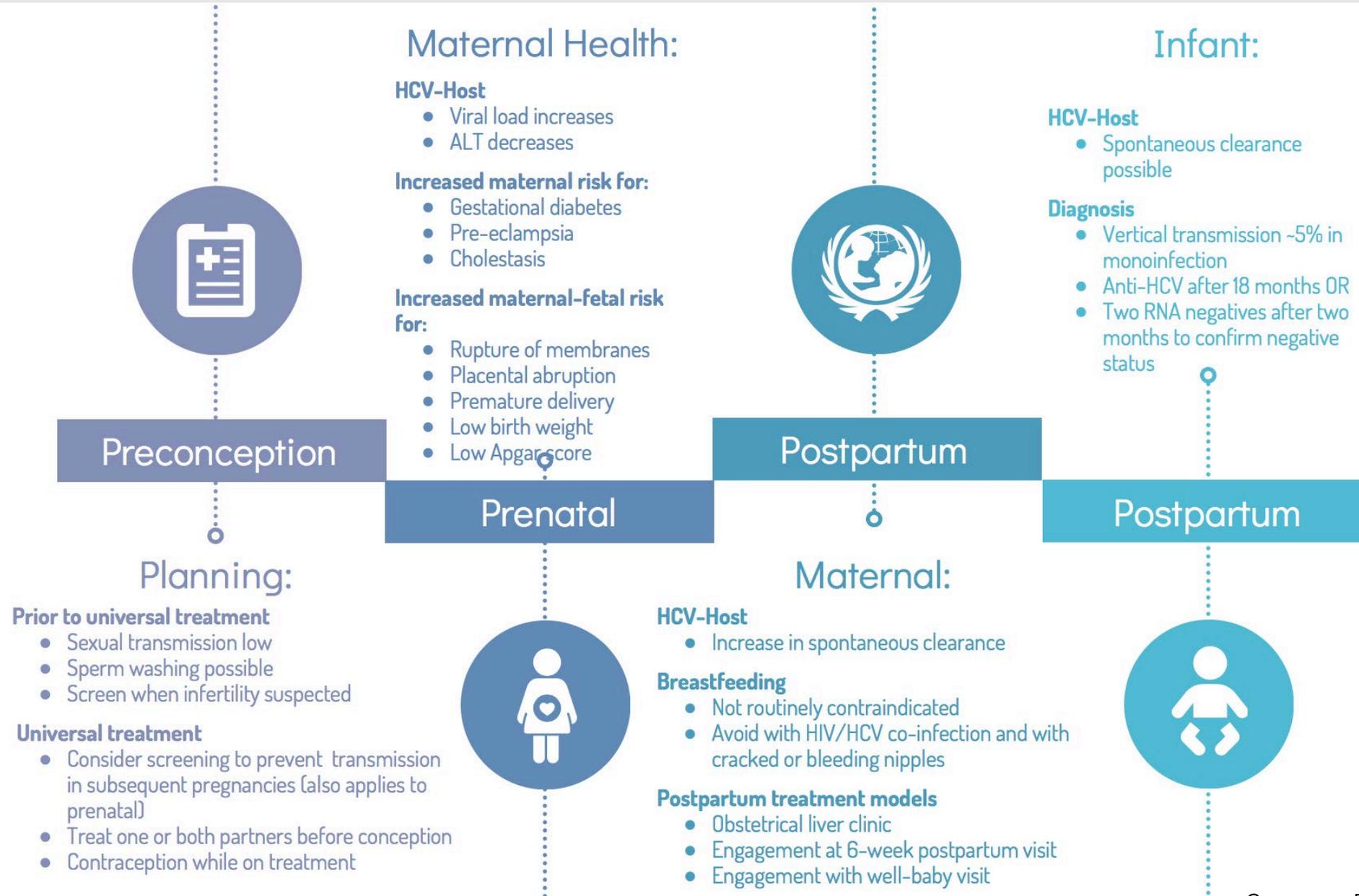
# Women of Childbearing Potential



**Rates are increasing among women of childbearing potential and disproportionately untreated**

Bartlett et al., Liver Int, 2019; Pearce et al., 2021

# HCV Maternal-Child Continuum



# Current Screening for Prenatal HCV

- Screening for HCV has traditionally focused on identifying those with risk factors for HCV acquisition
- Due to low screening rates, alternative approaches to screening such as birth cohort, and more recently prenatal screening have been adopted. In fact, over the last three years, the following US organizations now recommend universal screening in pregnancy: **CDC, AASLD, IDSA, ACOG**
- *The Society for Obstetrics and Gynecology Canada continues to recommend risk-based screening for prenatal HCV testing*
- However, women may not disclose their risk factors, may be unaware of them, or had risk factors but were not tested

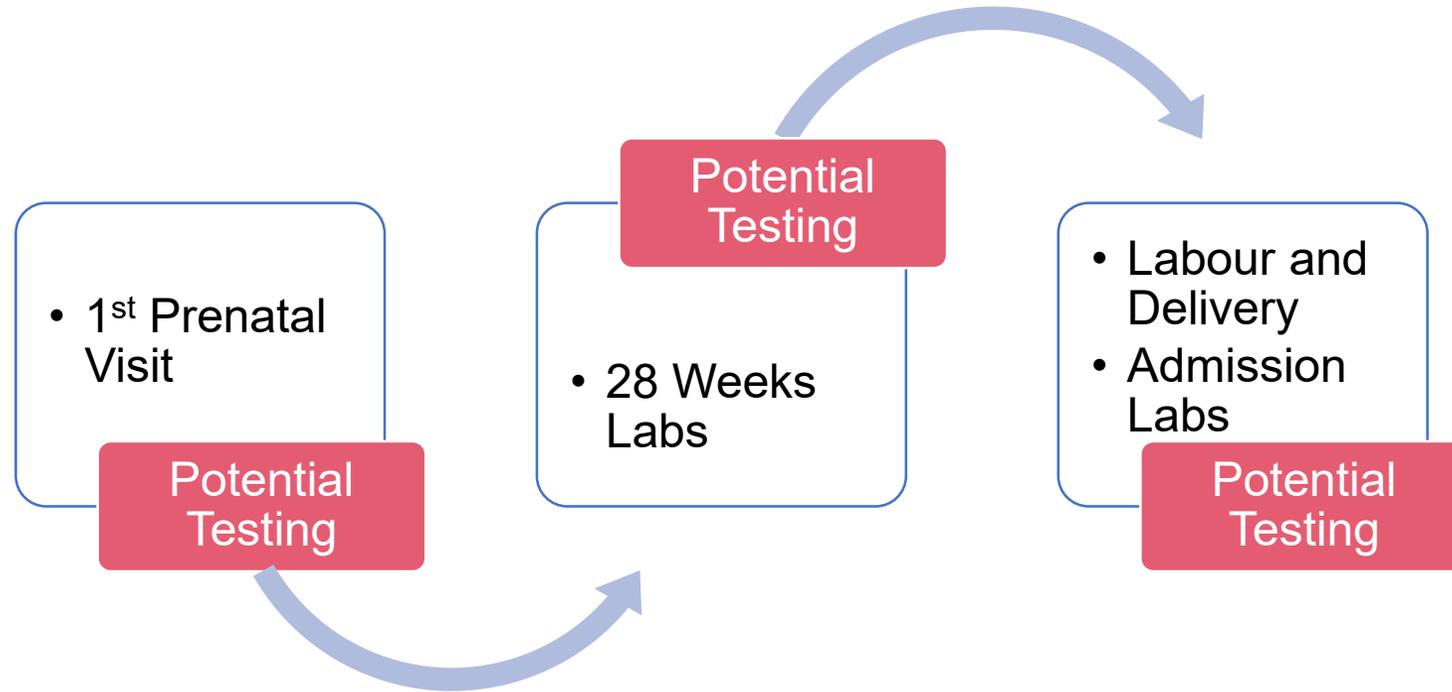
# Burden of Prenatal HCV – Rationale to Screen

- Identifying pregnant women with HCV is essential to:
  - Improve maternal health
  - Link women to care and treat postpartum
  - Test and treat the child

To date there is no formal analysis of universal screening of pregnant women in Ontario; Canada's most populated province.

***The objective of our study was to determine the prevalence of HCV antibody among pregnant women at LHSC as a QIP***

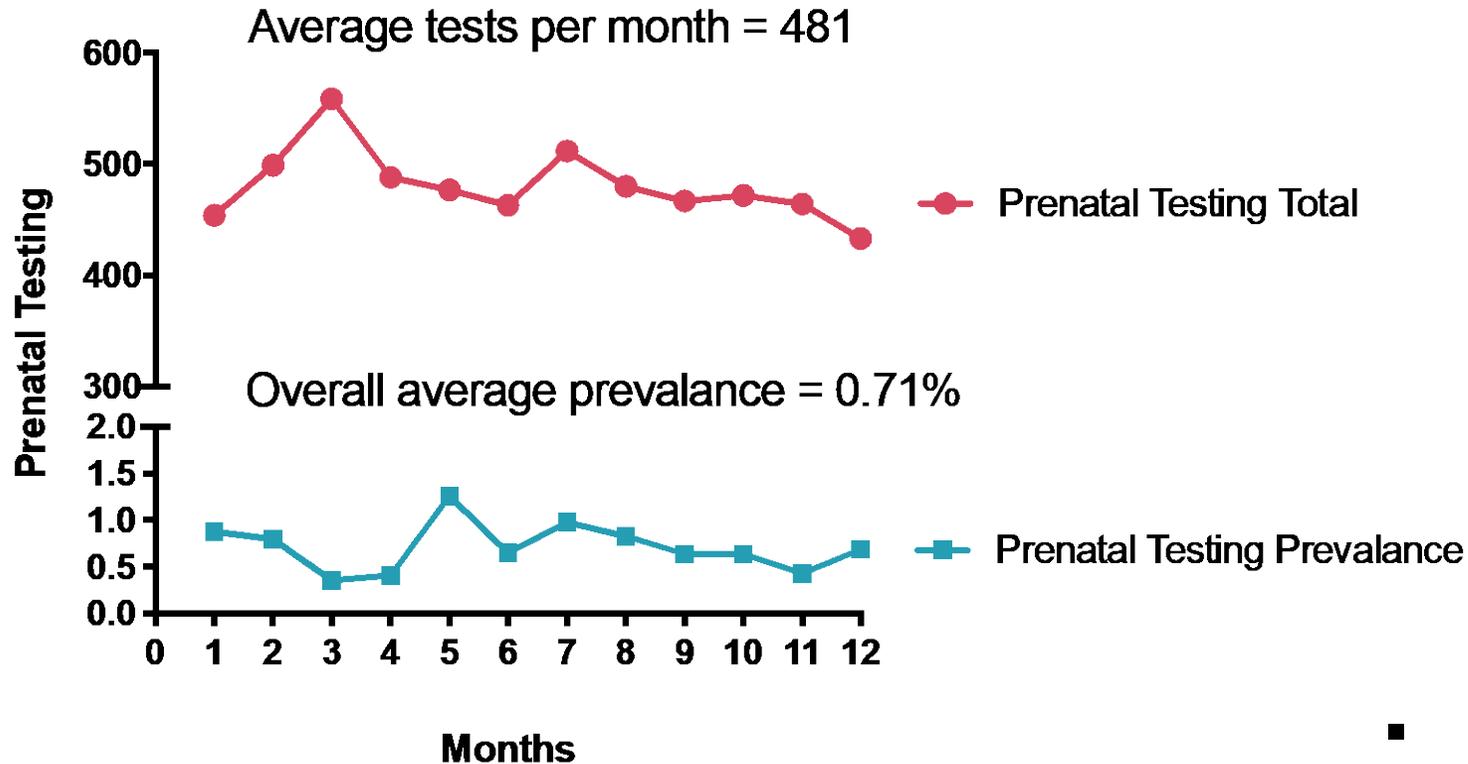
# Prospective Universal Antibody Screening in Major Obstetrical Program



**London Health Sciences Centre Prenatal Visits:  
Low- and High-Risk Pregnancies over 12 months.**

**Orders for duplicate testing within the same pregnancy were flagged and could be re-ordered should the clinician identify an indication to do so.**

# HCV Prevalence: QIP Results



- *This study provided real world evidence of the true prevalence of HCV Ab among pregnant women*
  - **At LHSC, prevalence was 0.71% (95%CI 0.51-0.96%)**
  - **Time for Canada to adopt universal screening??**
- **To come: In-depth analysis of co-infection, age, maternal postal code, and RNA testing, and linkage to care**

# Burden of Prenatal HCV and Cascade

## What do we know?

- Universal screening in only two provinces, issues with risk-based screening
- Risk-based prenatal screening ~20% uptake, true prevalence likely between 0.4-1%
- Screening and follow-up:

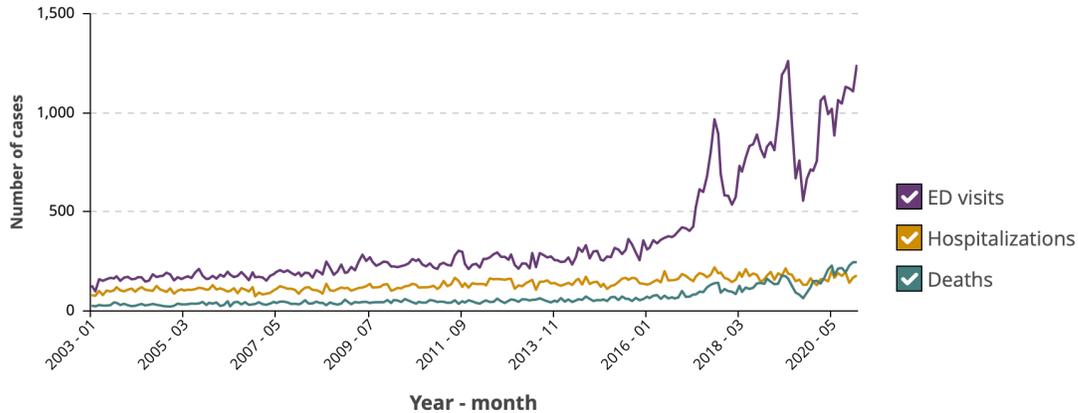
	Prenatal Screening Approach	Anti-HCV (%)	Age cohorts with highest prevalence	Subsequent Testing Rate (%)	RNA positivity (%)	Co-Infection with Positive Anti-HCV (%)		
						HIV	HBV	HIV/HBV
Saskatchewan (Provincial)	Universal	1.85	26-30	89.9	49.0	12.0	0.1	0.2
Ontario (Provincial)	Risk-Based	1.44	21-25	56.1	56.8	Data not available		
Ontario (Toronto)	Universal	0.40	31-35	Did not collect		0	4.2	0
Ontario (Southwestern)	Universal	0.71			In progress			

Biondi et al., 2022

# HCV Affects Vulnerable Women

2

## Opioid-Related Morbidity and Mortality 2003-2020 Ontario



3

- More likely to exchange sexual services for being injected by another individual
- Have multiple sexual and injection partners
- Little control over where drugs were acquired prepared, harm reduction
- Rates increasing among WOCBP, and less likely to be treated
- 16-fold increase in children being born to a person with OUD between 2002-2014

Wagner et al., 2013; Cedar Project, 2008; Puri et al., 2014; Lavalley et al., 2018; Pearce et al., 2021; PHO, 2021; Brogly et al. 2017; Camden et al., 2021

# Burden of Prenatal/Infant HCV and Cascade in Ontario

*Getting past the dogma of no interventions therefore no reason to test...*

4



Maternal & Infant Health  
Complications with HCV

5



Potentially poor follow-up postpartum (~10% treated)  
Consecutive pregnancies with HCV

6

Only 29% of  
children born to a  
positive mother  
screened

Greenaway et al. 2019; Bushman et al. 2021, Kushner et al., In Revision

# Questions Unanswered = Opportunities

## Prenatal

Why isn't subsequent testing done?

- Provider knowledge gap
- Referred but lost to follow-up



- Reflex testing
- Understand cascade

## Transmission

How does transmission occur?

- In utero vs L&D

## Pediatric

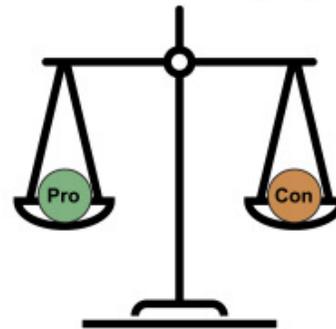
How many children (<18) have HCV

- ~1000?



- **Screening and linkage**
  - Screening in the right settings
  - Co-localization of care (well-baby)
  - Pediatric treaters in community

Treatment with DAAs during pregnancy



1. Maternal cure while engaged in pregnancy care
2. Possible decrease in MTCT
3. Maternal treatment while under insurance coverage
4. Decrease in community transmission
5. Potential decrease in HCV-associated adverse pregnancy outcomes?

1. Human safety in pregnancy not established
2. Safety during breastfeeding not established
3. More established data for treatment prior to pregnancy or children starting at age 3
4. Difficulty in accessing DAA therapy in time (prior to delivery)
5. Cost-effectiveness not established

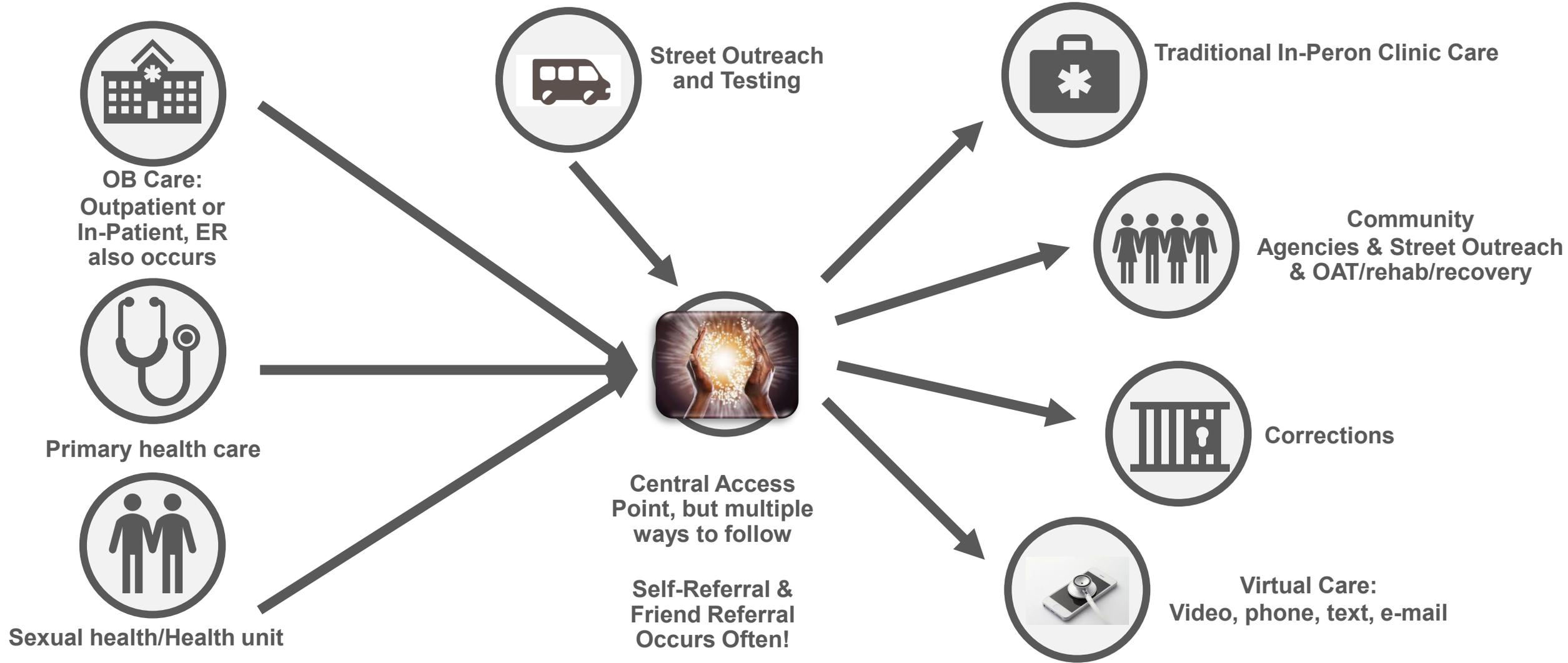
Kushner, Reau, 2020

# A Tale of 2 Cases

Viral load not "high enough to treat", preconception miss,  
but postpartum cure and pediatric testing

Corrections challenges, close contact required

# HCV Referral Pathway for Pregnant/Postpartum



# How to Better Serve Pregnant Persons with HCV

- **Vulnerable women have not been the focus of specialized programs towards HCV elimination**
  - More flexibility, trust building, peer models, don't give up!
- **Even when screened in pregnancy, follow-up poor**
  - Ask all women you treat if they have children?
    - Need HCV RNA reflex testing
- **An opportunity to prevent vertical transmission**
  - Universal screening and treatment in pregnancy? Prevents future transmission
  - Comprehensive and restorative: OAT, plans for postpartum period
- **We can eliminate pediatric HCV**
  - Improve screening – explain the rationale
  - Treat - ideally before the child ever aware

# Acknowledgements

*Thank you for your attention!*

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