HCV Debrief:
Global Hepatitis Summit 2023

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TORONTO CENTRE FOR LIVER DISEASE

Disclosures

- **Research:** Abbvie, Eiger, Gilead, GSK, Janssen, Vir, Wako/Fujifilm

- **Consulting:** Abbvie, Arbutus, GSK, Gilead, Janssen, Roche, Vir

Most important disclosure…

I can't cover the whole meeting in 30 minutes –
I had to leave out some great abstracts – sorry!

Thank you for sending slides!

Outline

- **Basic Science**
  - Virology
  - Immunology

- **Clinical**
  - Rare genotypes
  - Transplantation

- **Public Health**
  - Screening strategies
  - National cascades of care

Outline

- **Basic Science**
  - **Virology**
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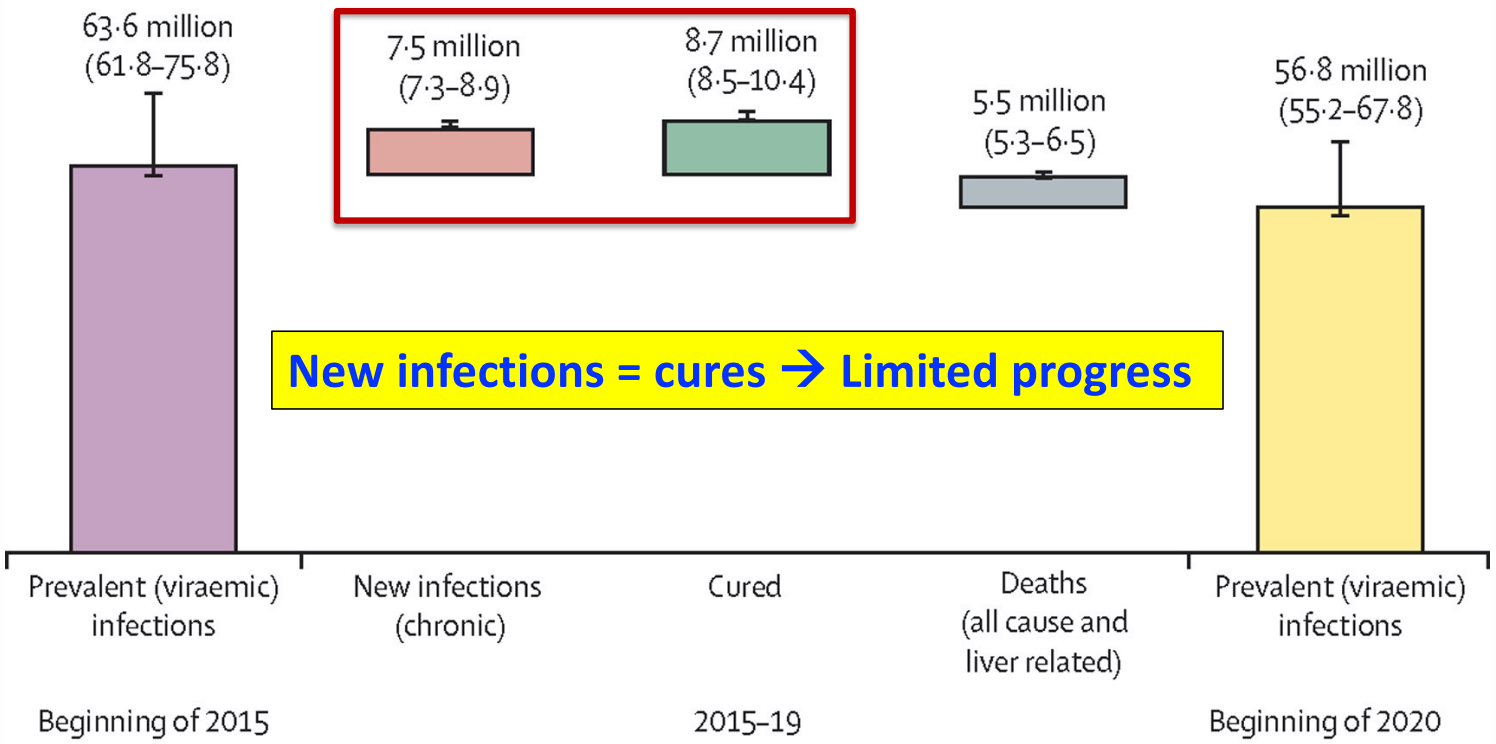
The Global Burden of HCV



New infections = cures → Limited progress

Need to 'turn off the tap' – we need a vaccine!

TORONTO CENTRE FOR LIVER DISEASE

HELMHOLTZ ZENTRUM FÜR INFEKTIONSFORSCHUNG

TWINCORE

A step-wise adaptation of hepatitis C virus leads to a high rate of infection in primary mouse hepatocytes

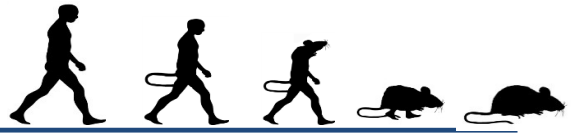
Julie Sheldon

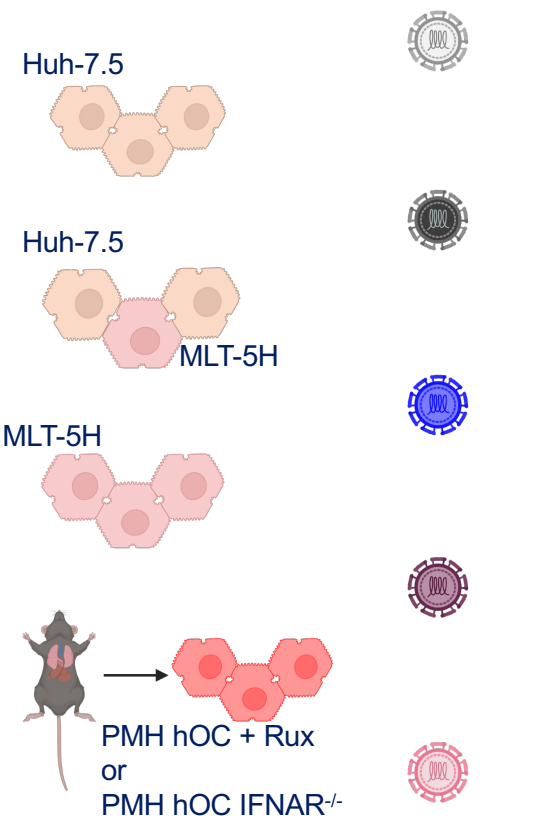
GLOBAL HEPATITIS SUMMIT 2023

PARIS FRANCE

April 25 - 28, 2023

HCV mouse model- Adaptation





Jc1

100 x passage in Huh7.5 cells

P100pop

15 x coculture passages in Huh7.5 and MLT-5H (mouse) cells
(MAVS$^{-/-}$ + 5 x HCV entry factors)

15℃C

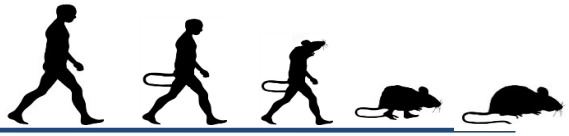
20 x passages in MLT-5H

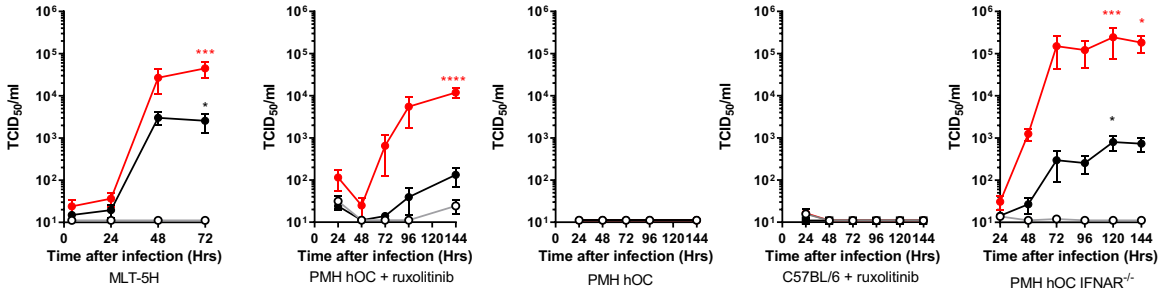
p20H

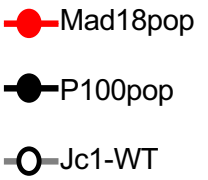
10 passages in PMHs from Mice with overexpression of **hO**ccludin/**C**D81 (hoc) and the presense of Ruxolitinib (JAK inhibitor) + 8 passages in PMHs from Mice with overexpression of hCD81/Occludin + IFNAR KO

MAD18pop

Adaptation of HCV-Jc1>Mad18

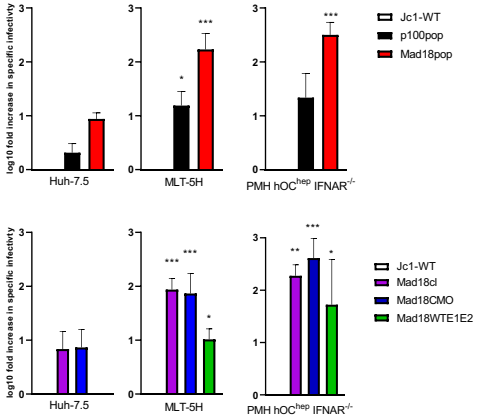




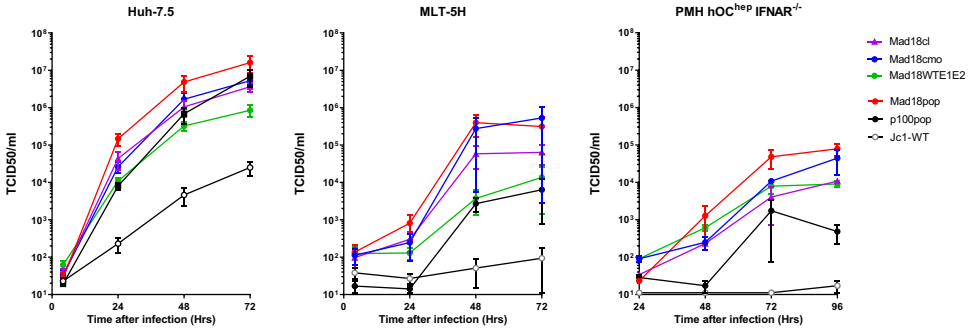


Mad18pop replicates better in **mouse cells**

Increased Specific infectivity



Clones replicate well in human and mouse cells



Next step:

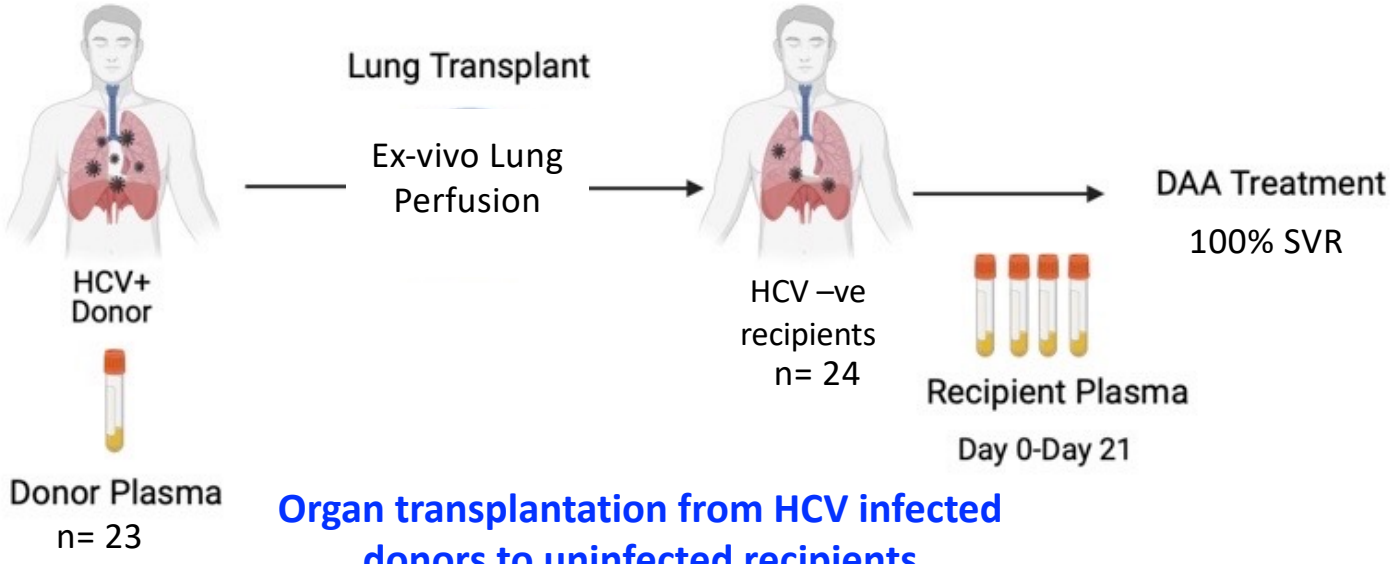
Infect mice!

Could be very useful immunocompetent small animal model

HELMHOLTZ ZENTRUM FÜR INFEKTIONSFORSCHUNG

TWINCORE

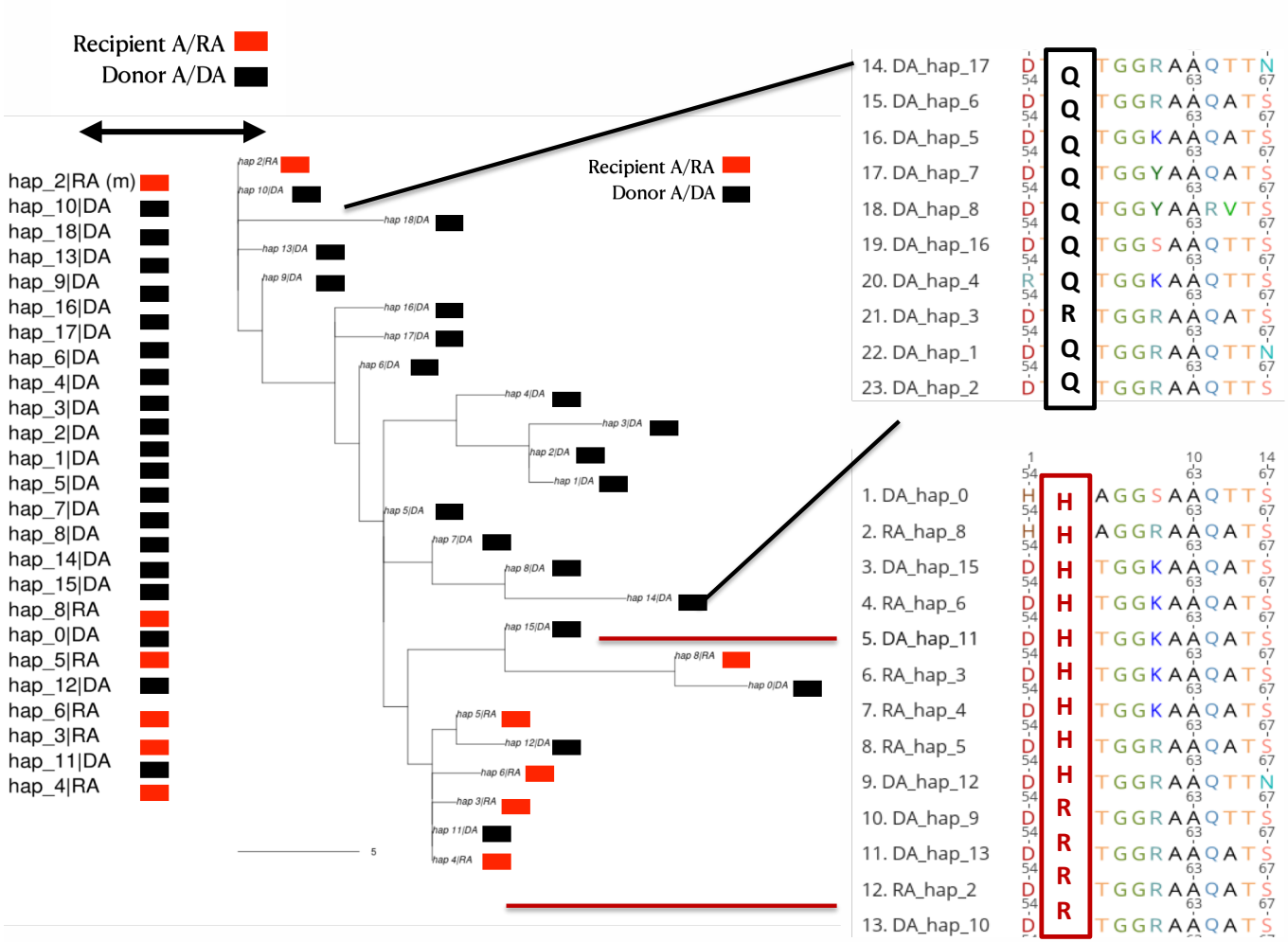
Observing Intentional Infection

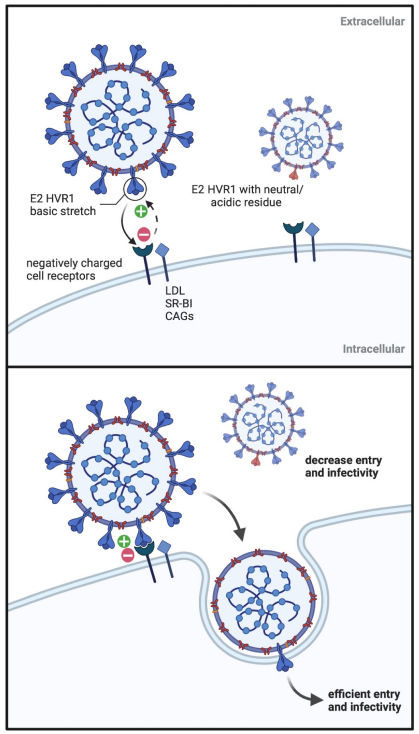


Organ transplantation from HCV infected donors to uninfected recipients

- Opportunity to 'observe' HCV infection
- Compare sequences from donor of Transmitted/Founders vs non-Founders
- Unique features of 'Founders' may narrow diversity required for vaccine

Cypel/Feld et al. Lancet Respiratory Medicine. (2019)





- Only variants with Basic residue (H/R) transmitted to recipients
- Associated with improved entry
- **Supports 'Founder concept'**

FadlelMawla GHS 2023, Callens,N et al.. J Virology ;2005. Penin,F et al. J Virology 2020.

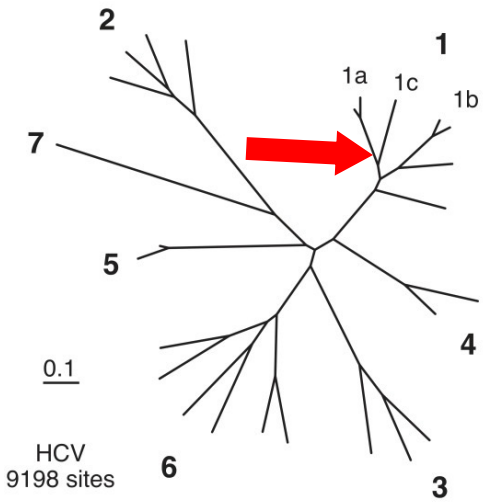
TORONTO CENTRE FOR LIVER DISEASE

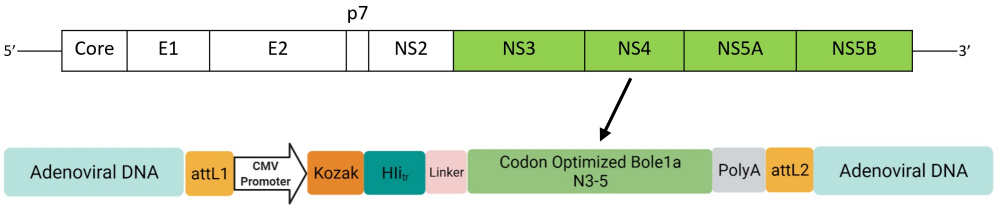
The Development Of A Pan-Genotypic Prophylactic Viral Vectored T Cell Vaccine Against Hepatitis C Virus

Rebecca Strain | Barnes Group

Strategies for a HCV T cell vaccine

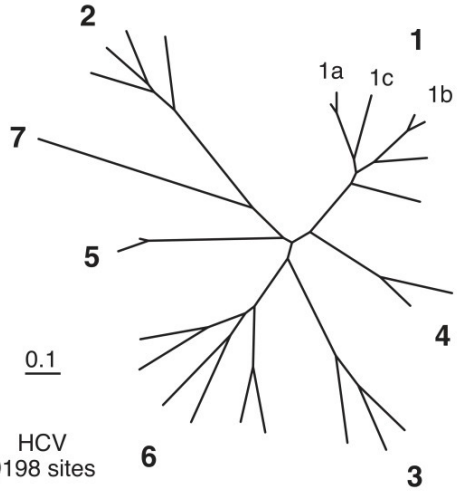
Ancestral sequence

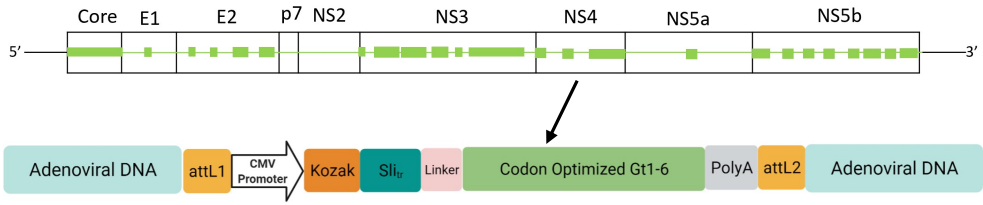




ChAd-Bole1a-NS

Conserved sequence





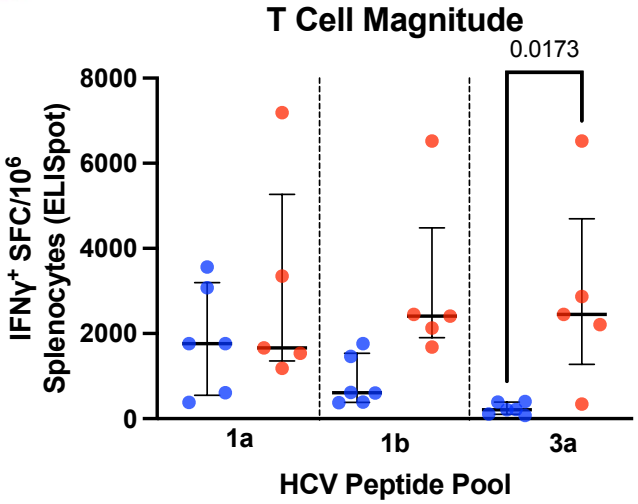
ChAd-Gt1-6

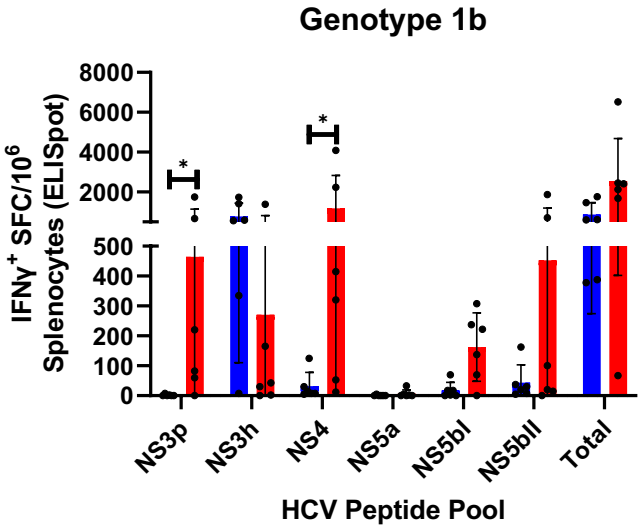
Munshaw, S. et al. (2012) Journal of virology; 86(10):5915–5921 | von Delft, A. *et al.* (2018) *Vaccine*; 36(2):313–321

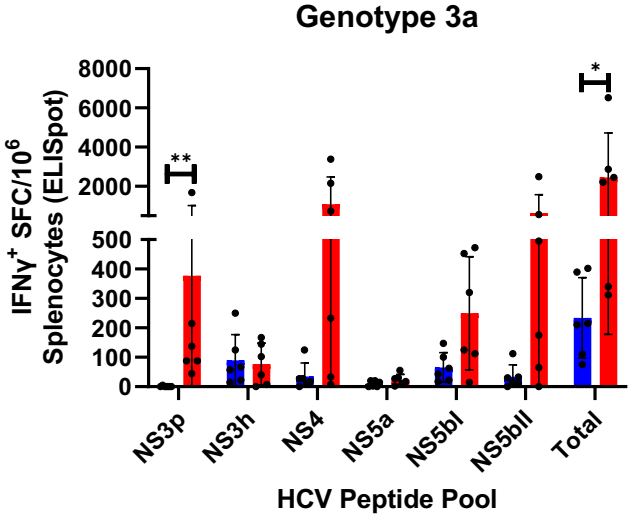
Which vaccine induces the highest magnitude T cell response targeting multiple genotypes?

= ChAd-Bole1a-NS

= ChAd-Gt1-6



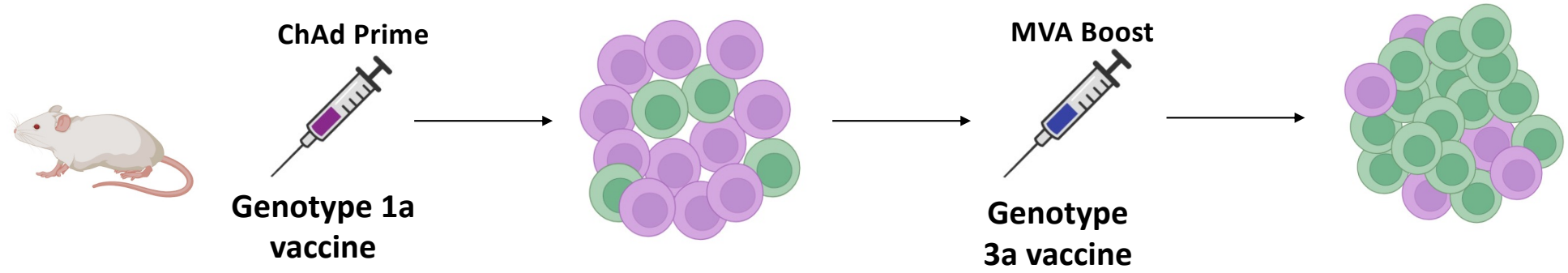




ChAd-Gt1-6 induces pan-genotypic T cell responses whereas the response to ChAd-Bole1a-NS is specific to genotype 1

Prime-boost regimen to induce pan-genotypic responses

Scenario 1:



T cell specific to genotype 1a

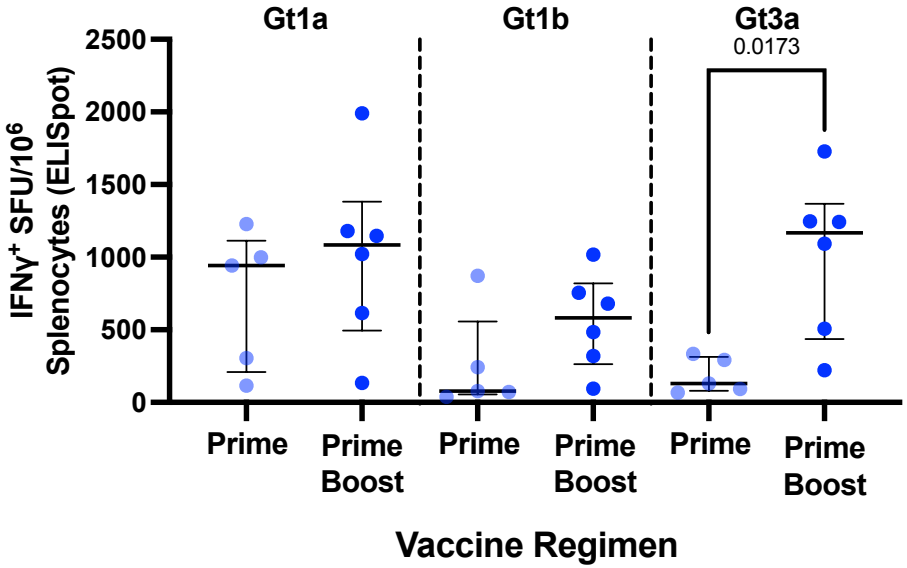
T cell specific to genotype 3a

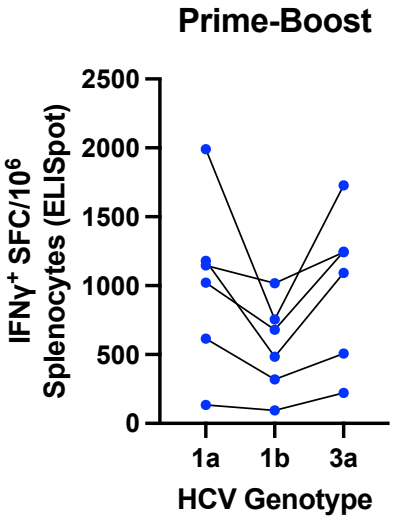
Cross reactive T cell

Does the prime-boost regimen induce a pan-genotypic T cell response?

Prime = ChAd-Bole1a-NS

Prime-Boost = ChAd-Bole1a-NS & MVA-Gt3a-NS





- **Viral vectors encoding different genotypes or conserved regions of G1-6 used in a prime boost approach generate T cell responses targeting multiple HCV genotypes**
- **Promising approach – next step – combine with B cell immunogen → bivalent viral vectors**

Summary

- Promising steps toward an immunocompetent mouse model for HCV infection

- Observed human infection supports ‘founder’ hypothesis – possibly narrowing diversity required for vaccine

- Viral vectors using a prime-boost strategy with different genotypes or conserved regions across genotypes generates T cell responses to multiple genotypes

Outline

- Basic Science
  - Virology
  - Immunology

- **Clinical**
  - **Rare genotypes**
  - **Transplantation**

- Public Health
  - Screening strategies
  - National cascades of care

Filling the final gaps in the guidelines…

EASL recommendations on treatment of hepatitis C: Final update of the series☆

European Association for the Study of the Liver*

Type of treatment	Genotype	Cirrhosis status	Prior treatment experience	Sofosbuvir/ velpatasvir	Glecaprevir/ pibrentasvir	Sofosbuvir/ velpatasvir/ voxilaprevir	Grazoprevir/ elbasvir
Genotype/subtype determination-based treatment	Genotype 1a, 1b, 2, 4, 5 and 6	No cirrhosis	Treatment-naïve	12 weeks	8 weeks	No	12 weeks (genotype 1b only)
			Treatment-experienced				
		Compensated (Child-Pugh A) cirrhosis)	Treatment-naïve		12 weeks		
			Treatment-experienced				
	Genotype 3	No cirrhosis	Treatment-naïve	12 weeks	8 weeks	No	No
			Treatment-experienced		12 weeks		No
		Compensated (Child-Pugh A) cirrhosis)	Treatment-naïve	12 weeks with weight-based ribavirin[a]	8-12 weeks[b]	12 weeks[a]	No
			Treatment-experienced		16 weeks		No
	Subtype 1l, 4r, 3b, 3g, 6u, 6v or any other subtype naturally harbouring one or several NS5A RASs[c]	No cirrhosis	Treatment-naïve	Unknown	Unknown	12 weeks	No
			Treatment-experienced				
		Compensated (Child-Pugh A) cirrhosis)	Treatment-naïve				
			Treatment-experienced				

EASL. J Hepatol 2020

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‘Unusual’ genotype 1 subtypes

640 patients who did not achieve SVR – French Reference Lab

284 (44.5%) G1
- 141 (22%) G1a, 96 (15%) G1b + **43 (7%) ‘Unusual’**

Parameters	N=43
Age, median (IQR)	61 (54-65)
Male sex, n/N (%)	22/43 (51.2%)
African birth, n/N (%)	37/40 (92.5%)
HIV-positive, n/N (%)	2/43 (4.7%)
Cirrhosis, n/N (%)	9/43 (20.9%)

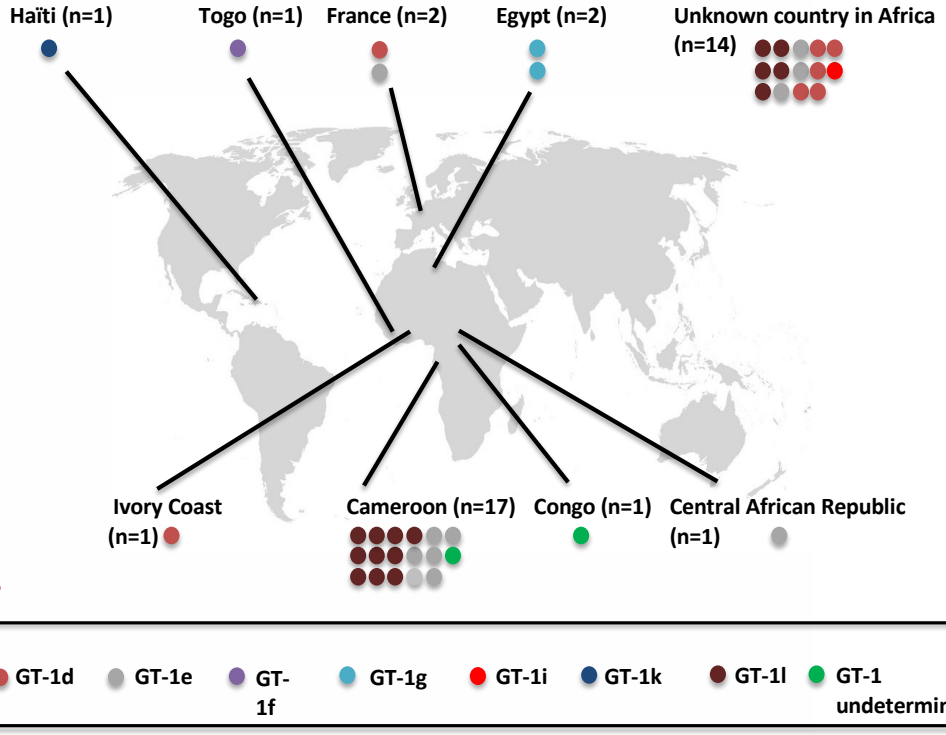
Prior Regimen

SOF + NS5A – 81% → **Failure with RAS at 31, 58, 93**

NS3 + NS5A - 14% → **Failure with RAS at 24, 28, 30, 31, 58, 92**

NS3 + NS5A + NS5B – 4.7%

Retreatment with G/P or triple regimen successful



- Over-represented among treatment failure – **likely due to ‘baseline’ resistance**
- Fortunately **retreatment with standard salvage regimens successful…no role for baseline RAS testing**

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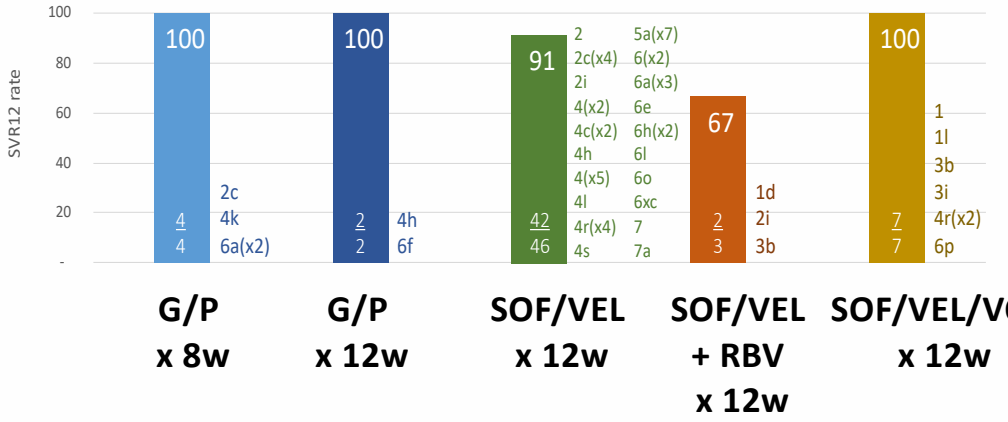
Treatment of rare subtypes with modern DAAs

Since 2014, **109 (13.1%)** of 829 treated had **rare HCV subtype** – outcome with DAAs Tx CHUM – Montreal

SVR12 rate with pangenotypic DAA regimen



Main characteristics of the 5 failures and RETREATMENT with 3 DAA-based regimen

Patient	Age	Genre	Cirrhosis (FS, kPa)	GT/ subtype	Initial treatment	RASs at treatment failure			Retreatment	Outcome
						NS3	NS5A	NS5B		
P1	59	M	No 4.0	3b	Sofosbuvir/velpatasvir PLUS RBV for 12w	No RAS	A30M L31M S62D	No RAS	Sofosbuvir/velpatasvir/voxilaprevir for 12w	SVR
P2	55	M	Yes 12.4	3i	Sofosbuvir/velpatasvir for 12w	No RAS	A30K S62M	No RAS	Sofosbuvir/velpatasvir/voxilaprevir for 12w	SVR
P3	69	M	Yes 15.2	6p	Sofosbuvir/velpatasvir for 12w	V361I S122T	Q24K F28V R30S T58P	No RAS	Sofosbuvir/velpatasvir/voxilaprevir for 12w	SVR
P4	62	M	No 8.2	4b	Sofosbuvir/velpatasvir for 12w	N/A	L28V L30S T58P	No RAS	---	Not treated
P5	64	F	No 6.1	4r	Sofosbuvir/velpatasvir for 12w	N/A	N/A	N/A	---	Not treated

- Overall **SVR 91%** → slightly reduced response ?lower SOF/NS5A due to **baseline NS5A RAS**
- **Multiple NS5A RAS at failure** but **responded to SOF/VEL/VOX x 12w**
- Similar conclusion → **no role for baseline RAS testing (or genotyping in non-cirrhotic)**
- **But further data – esp in LMIC would be helpful to optimize first-line therapy**

Murphy D, Ruiz I, *et al*, Canada, Abs. GHS2023-1211 Update, Fourati GHS 2023

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Implementation of the 'Toronto Protocol' – Glecaprevir/Pibrentasvir + Ezetimibe for Solid Organ Transplantation from HCV NAT+ Donors to HCV-uninfected recipients: Moving from Research to Standard of Care

Wesam Aleyadeh, Marcelo Cypel, Atul Humar, Ilona Bahinskaya, Jordan J Feld

Toronto Centre for Liver Disease & Multi-organ Transplant Program,
Toronto General Hospital, University Health Network, University of Toronto

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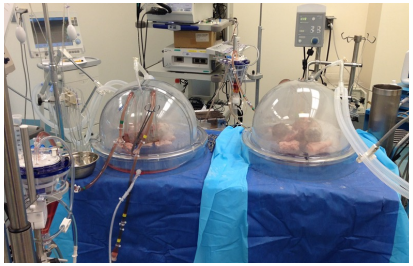
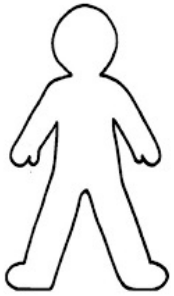
Extension of initial study to standard of care

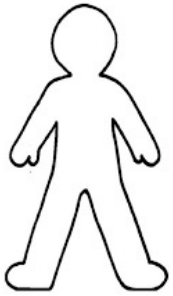
EVLP + UV – *(Lungs only)*
(reduce viral load & infectivity)



HCV NAT+ Donor



HCV-uninfected Recipient



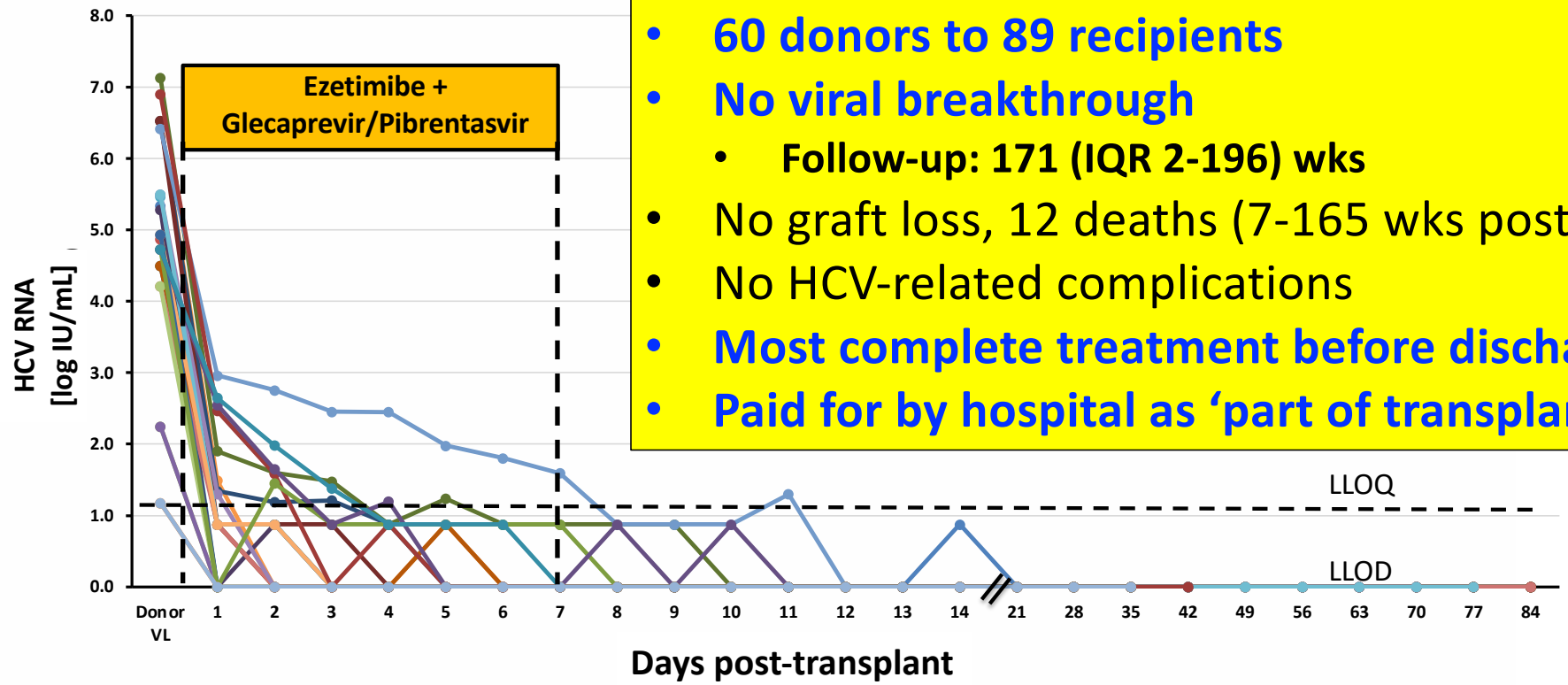
No EVLP
Lungs
Kidney
Heart
Pancreas

Pre-treatment
Ezetimibe + GLE/PIB x 1 dose
(prevent infection & replication)

Post-treatment
Ezetimibe +
GLE/PIB PO/NG x 7d

- **NAT (HBV, HIV, HCV) @ 2, 4, 24 and 4w**
- **HCV RNA @ 12w**
- **Hepatology at 12w**

Results



n=89 (30 study + 59 SOC)

- **60 donors to 89 recipients**
- **No viral breakthrough**
  - **Follow-up: 171 (IQR 2-196) wks**
- No graft loss, 12 deaths (7-165 wks post Tx)
- No HCV-related complications
- **Most complete treatment before discharge**
- **Paid for by hospital as 'part of transplant'**

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Summary

- 'Rare' HCV genotypes often have polymorphisms associated with NS5A (+/- NS3) resistance → over-represented among treatment failures
- But largely respond to retreatment
- Further data may help guide optimal first-line therapy in LMICs

- Very short-course therapy with G/P + ezetimibe is effective for transplant from HCV NAT+ donors to uninfected recipients

Outline

- **Basic Science**
  - Virology
  - Immunology

- **Clinical**
  - Rare genotypes
  - Transplantation

- **Public Health – Focus on Elimination**
  - **Screening strategies – the test, the setting**
  - **National cascades of care**

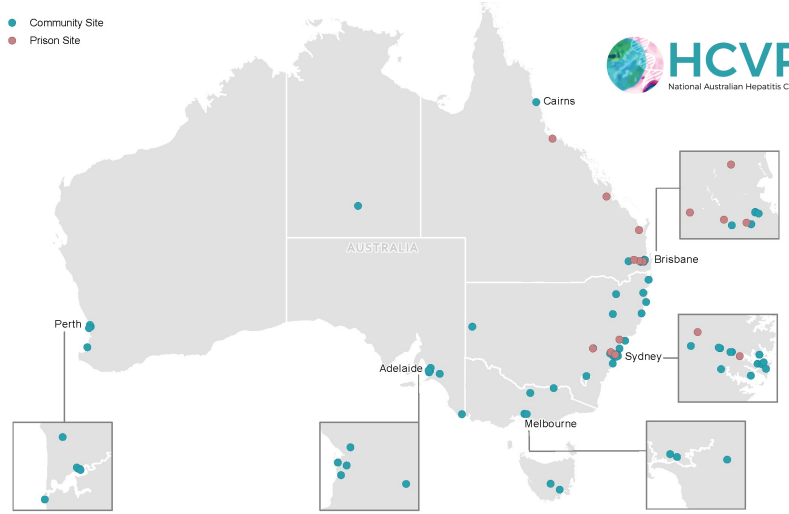
HCV elimination is a bit like being a Leafs fan

Insanity?
I like to think not…

Dogged optimism, aspirational thinking, new tools and hard work

TORONTO CENTRE FOR LIVER DISEASE

National Australian Hepatitis C Point-of-Care Testing Program



HCVPOCT
National Australian Hepatitis C Point-of-Care Testing Program

- 90 sites nationally with 50-60,000 people tested (2021-24)
- Drug treatment clinics, NSPs, prisons, mental health, mobile outreach models, homelessness services, Aboriginal Community Controlled Health Organisations
- Testing for anyone at risk of HCV or attending service
- Program includes:
    1) SOPs, logistics, deployment, and set-up
    2) Training
    3) Quality assurance program
    4) IT/connectivity
    5) Research and evaluation framework

National Australian Hepatitis C Point-of-Care Testing Program	
Program Duration	3 years
# Services	90 (200-300 testing sites/locations)
Specimens	Capillary finger-stick
Analytes	HCV antibody*, HCV RNA, HIV Ab/Ag, HBsAg
POC Device; Time to result	HCV Bioline*, 20 min (5 min pos); INSTI (1 min), Xpert, 60 min
Partners	Flinders University, Commonwealth Govt, State/Territory Govts, National and state community organisations

Grebely J, et al *Lancet Gastroenterology & Hepatology* 2023

National Australian Hepatitis C Point-of-Care Testing Program

- 66 sites are active across six states/territories (ACT, QLD, NSW, SA, TAS, WA)
- High-intensity testing campaigns at 11 prisons (QLD, n=8; NSW, n=1; and South Australia, n=2)
- 198 operators have received point-of-care testing training
- 9,326 HCV point-of-care tests (RNA: n=8,037; antibody: n=1,289)
  - Community: 2,752 (33%) received testing (11% prevalence)
  - Prisons: 5,575 (67%) received testing (16% prevalence)
- 1,192 people with current HCV infection
- **Treatment uptake: 77% overall**
  - **51% in community**
  - **87% in prison**

UNSW Kirby Institute

UNSW SYDNEY

HCVPOCT
National Australian Hepatitis C Point-of-Care Testing Program

Flinders UNIVERSITY | FHMRI FLINDERS HEALTH & MEDICAL RESEARCH INSTITUTE

Acknowledgements

This program is funded by the Australian Government Department of Health

FEASIBILITY OF HCV SELF-TESTING IN THE PRIMARY CARE SYSTEM: A REAL-WORLD STUDY INCLUDING 688 INDIVIDUALS FROM THE GENERAL POPULATION IN RIO DE JANEIRO (BRAZIL)

ABSTRACT NUMBER P151
Hugo Perazzo et al - INI/FIOCRUZ – Rio de Janeiro (Brazil)

Aim

To evaluate the usability and acceptability of oral fluid HCVST in general population in Brazil

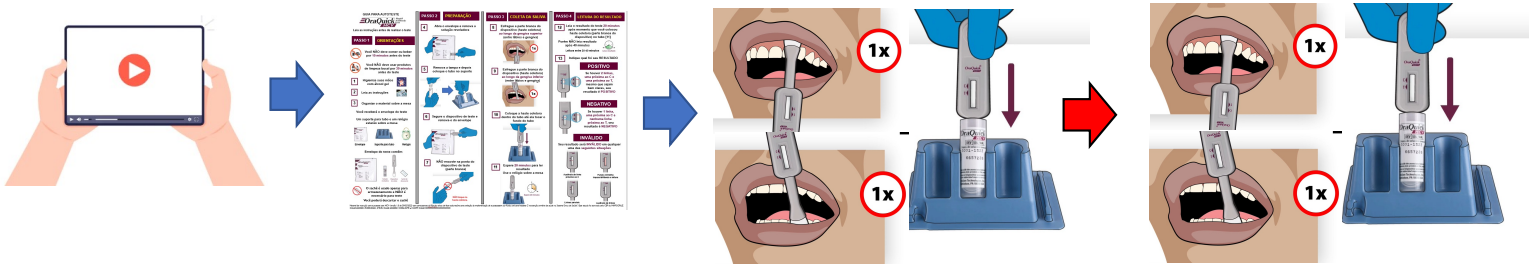
Study design and population

Cross-sectional study; **688 people from the general population** aged 18-79 years-old attending consultation at a Primary Health Care Unit (*Clinica da Família Felippe Cardoso*) at Rio de Janeiro (Brazil)

HCV self-testing

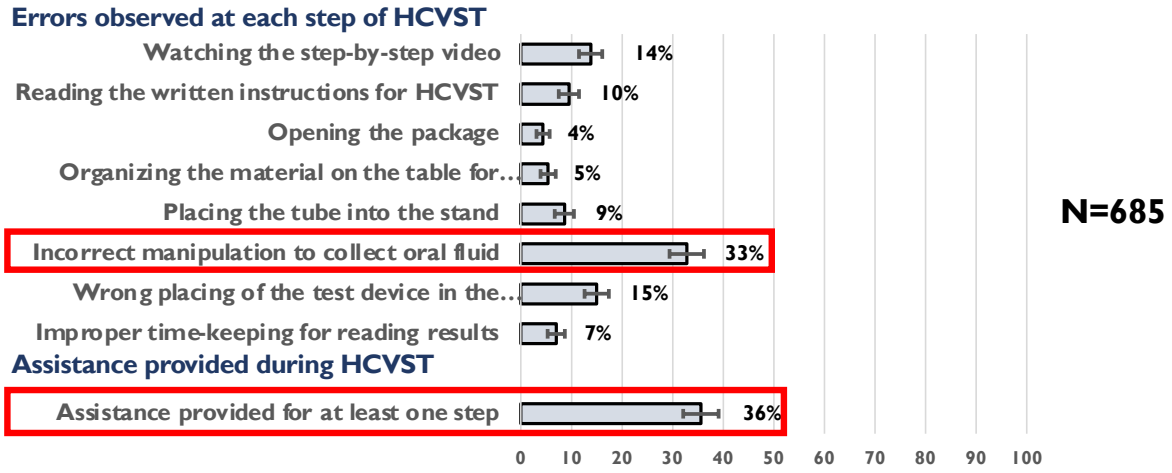
Oral fluid OraQuick® HCV Rapid Antibody Test observed by a healthcare worker

Video → **Written instructions** → **HCV ST** → **HCV test by HCW**



<u>If anti-HCV positive</u>:
HCV-RNA (GeneXpert)
Transient elastography (FibroScan)

Results



N=685

Concordance

Re-reading agreement

	Agreement	Cohen's kappa
All (n=682)	95.2%	0.56

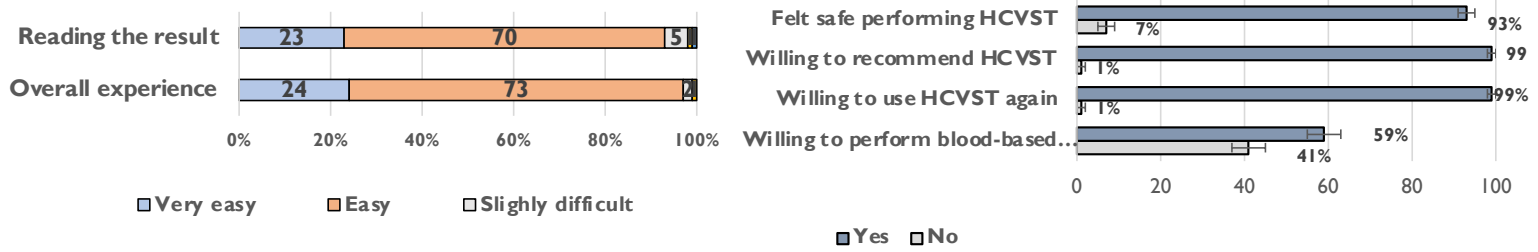
N=3 participants refused to inform HCVST result

Re-testing agreement

	Agreement	Cohen's kappa
All (n=626)	99.7%	0.67

Excluding invalid tests informed by participants (n=50) or by HCW (n=3); 3 participants refused to be tested by HCW

Post-testing evaluation



- Although some support required – **self-testing was acceptable & yielded relatively high quality results**
- **Self-testing in Pakistan also highly successful**
- Similar results with systematic review of self-testing for HCV (but limited data)

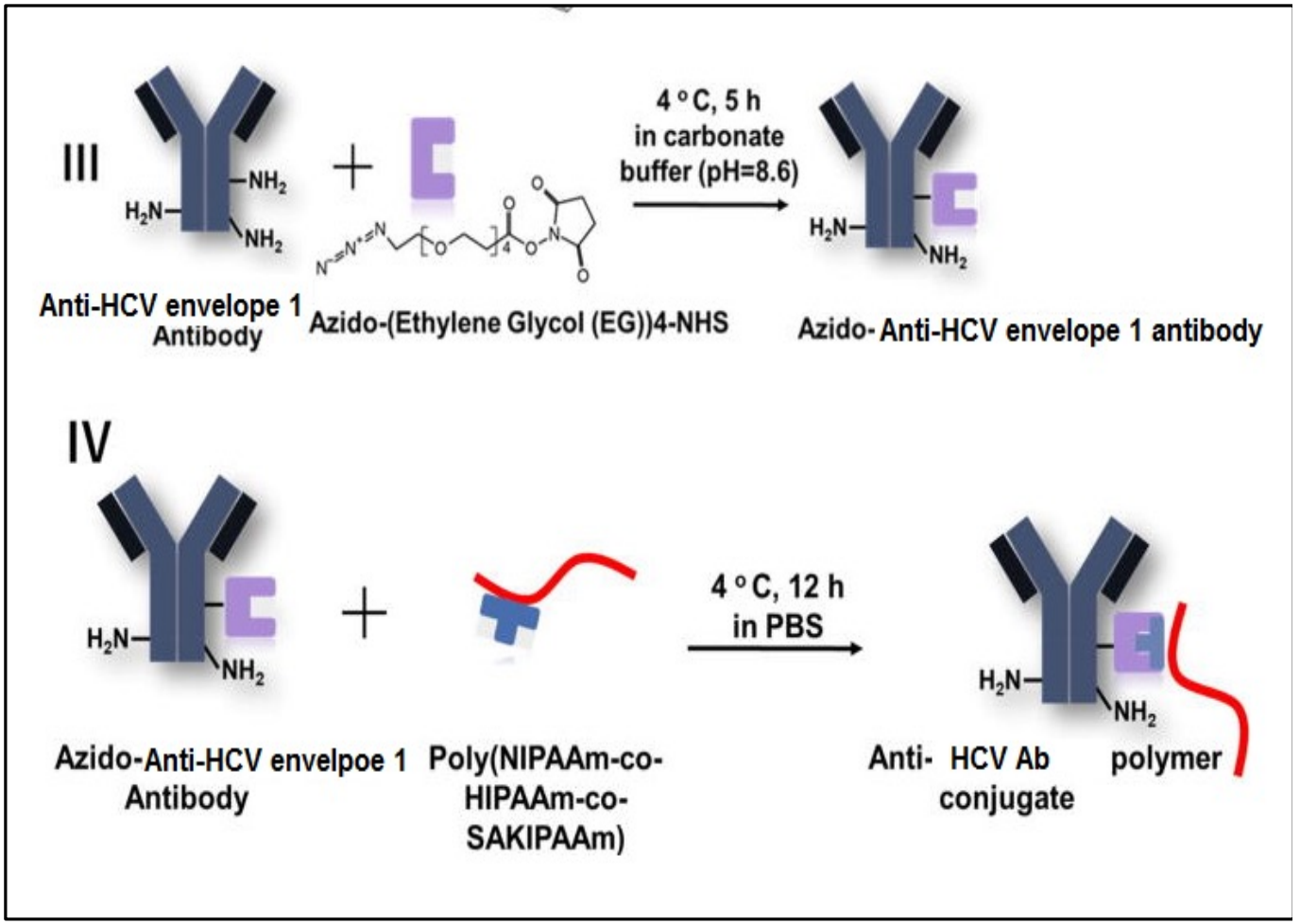
Perazzo et al GHS 2023, Hamid POCT Workshop 2023, Perazzo GHS 2023

A Novel Technology for diagnosis of HCV viremia using thermo-sensitive Smart Polymer: a pilot study of a point of care test of HCV compared to polymerase chain reaction (PCR)

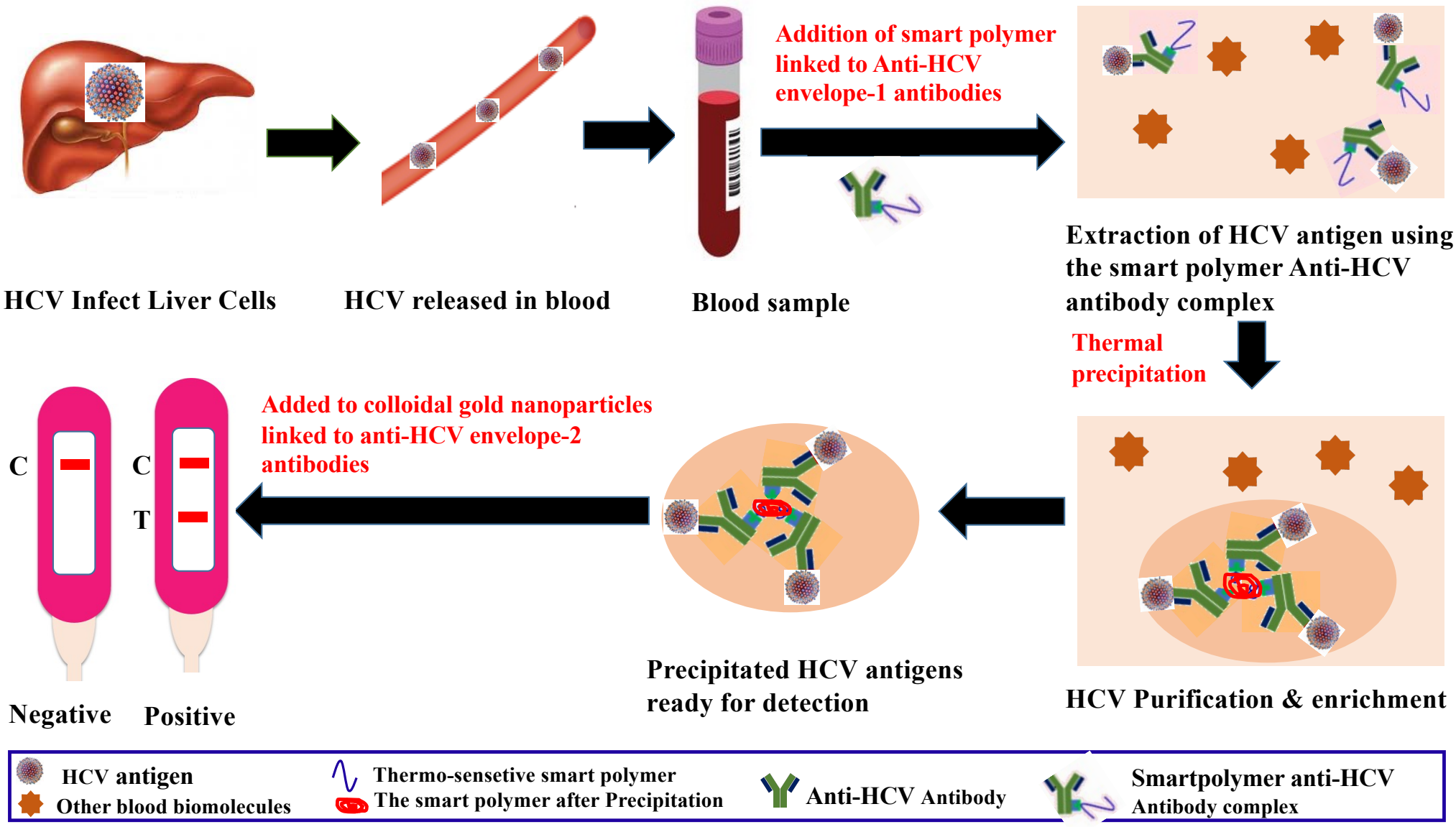
***Gamal Shiha*, Ahmed Nabil, Ayman Hassan, Reham Soliman, Mitsuhiro Ebara**

National Institute of material sciences (NIMS), Tsukuba University, Japan,
Egyptian Liver Research Institute And Hospital (ELRIAH) for Smart Biomaterials, Egypt

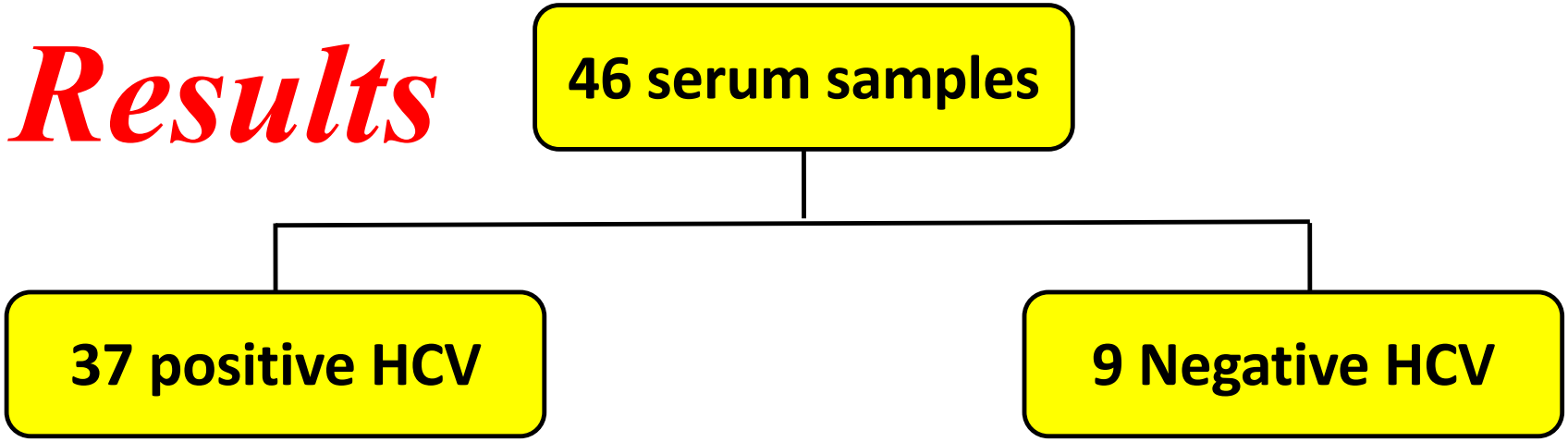
(III) Synthesis of azido-Anti- HCV envelope 1 Antibody.
(IV) Conjugation of azido- HCV envelope 1 Antibody with the temperature responsive P(NIPAAm-co-HIPAAm-co-SAKIPAAm) using click chemistry.



(*)Nabil A, Yoshihara E, Hironaka K, Hassan AA, Shiha G, Ebara M. Temperature responsive smart polymer for enabling affinity enrichment of current coronavirus (SARS-CoV-2) to improve its diagnostic sensitivity. Comput Struct Biotechnol J. 2021;19:3609-3617.


HCV Infect Liver Cells
HCV released in blood
Blood sample
Addition of smart polymer linked to Anti-HCV envelope-1 antibodies
Extraction of HCV antigen using the smart polymer Anti-HCV antibody complex
Thermal precipitation
HCV Purification & enrichment
Precipitated HCV antigens ready for detection
Added to colloidal gold nanoparticles linked to anti-HCV envelope-2 antibodies
C
C
T
Negative
Positive
HCV antigen
Other blood biomolecules
Thermo-sensetive smart polymer
The smart polymer after Precipitation
Anti-HCV Antibody
Smartpolymer anti-HCV
Antibody complex

Results



Parameter	Estimate	95% CI
Sensitivity	100%	90.59 – 100.0
Specificity	100%	70.08 – 100.0
Positive Predictive Value	100%	90.59 – 100.0
Negative Predictive Value	100%	70.08 – 100.0
Diagnostic Accuracy	100%	92.29 – 100.0

Exciting results – looking forward to seeing more….

What about the setting?

COMBINED COVID-19 VACCINATION AND HEPATITIS C VIRUS SCREENING INTERVENTION IN MARGINALISED POPULATIONS IN SPAIN

Jeffrey V. Lazarus[1-3], Marcela Villota-Rivas[1], Pablo Ryan[4-6], Maria Buti[7,8], Lara Grau-López[9-12], Guillermo Cuevas[4], José Luis Espada[13], William Morón[13], Raul Felipe Palma-Álvarez[9-12], Jordan J. Feld[15], Jorge Valencia[4,13,14]

[1]Barcelona Institute for Global Health (ISGlobal), Hospital Clínic, University of Barcelona, Barcelona, Spain, [2]Faculty of Medicine and Health Sciences, University of Barcelona, Barcelona, Spain, [3]CUNY Graduate School of Public Health and Health Policy, New York, NY, USA, [4]Department of Internal Medicine, Hospital Universitario Infanta Leonor, Madrid, Spain, [5]Faculty of Medicine, Complutense University of Madrid, Madrid, Spain, [6]Centro de Investigación Biomédica en Red en Enfermedades Infecciosas (CIBERINFEC), Madrid, Spain, [7]Department of Internal Medicine, Hospital Universitario Vall d'Hebron, Barcelona, Spain, [8]CIBERhd, Instituto de Salud Carlos III, Madrid, Spain, [9]Department of Psychiatry, Addiction and Dual Diagnosis Section, Hospital Universitari Vall d'Hebron, Barcelona, Spain, [10]Psychiatry Group, Mental Health and Addiction, Vall d'Hebron Research Institute (VHIR), Barcelona, Spain, [11]Biomedical Network Research Centre on Mental Health (CIBERSAM), Madrid, Spain, [12]Department of Psychiatry and Forensic Medicine, Autonomous University of Barcelona, Barcelona, Spain, [13]Harm reduction Unit "SMASD", Madrid, Spain, [14]Mobile testing unit, Madrid, Spain, [15]Toronto Centre for Liver Disease, University Health Network, Toronto, Canada

Professor Jeffrey V Lazarus [Jeffrey.Lazarus@ISGlobal.org]

Co-director of the Viral and Bacterial Infections Programme, ISGlobal, Hospital Clínic, Barcelona, Spain
Professor of Global Health, CUNY Graduate School of Public Health & Health Policy, New York, USA
Vice-chair, EASL International Liver Foundation

ISGlobal Barcelona Institute for Global Health | CLÍNIC BARCELONA Hospital Universitari | UNIVERSITAT DE BARCELONA | CUNY SPH GRADUATE SCHOOL OF PUBLIC HEALTH & HEALTH POLICY | Hospital Universitario Infanta Leonor SaludMadrid Comunidad de Madrid

GLOBAL HEPATITIS SUMMIT 2023

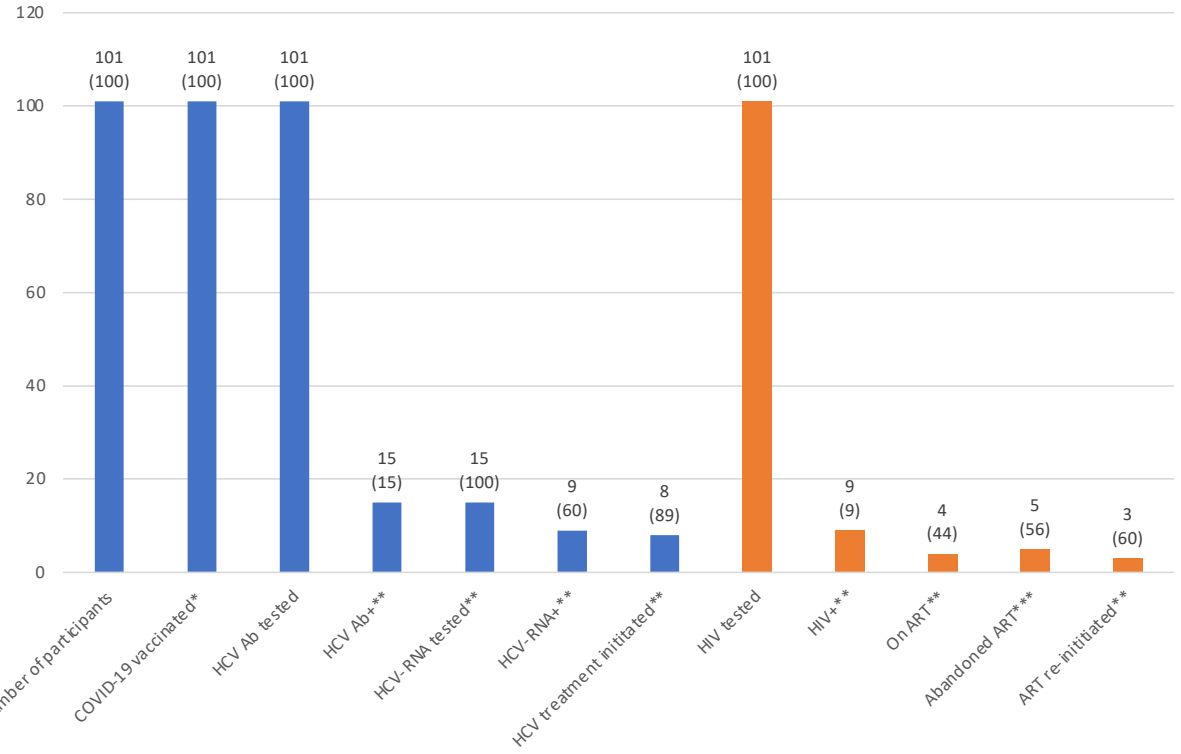
@JVLazarus
@Jorgeva60302987
@UCribado

Abstract #O19

RESULTS Mobile Testing Unit

- Of the 101 participants (mean age 36 [SD: 11]):
  - 69% male
  - 31% Spanish-born
  - 59% precarious living situation
  - 70% unemployed
  - 59% SUD
  - 30% incarceration history
  - 10% mental health disorders
  - 12% had a previous COVID-19 diagnosis
  - None had been vaccinated for COVID-19
- Of those HIV+:
  - None were new diagnoses
- Duration between positive HIV diagnosis and ART re-initiation was 103 days (25 - 138)
- Duration between **positive HCV-RNA diagnosis and treatment initiation was 83 days** (22 - 228)
- Duration of the **MTU intervention was 33 minutes** (25-75)

Analysis of the combined COVID-19 vaccination and HCV and HIV screening and linkage to care intervention at the mobile testing unit in Madrid, n (%)



@JVLazarus

UNIVERSITY of WASHINGTON

Feasibility and outcomes of a community pharmacist led program to treat hepatitis C virus among people who inject drugs in Seattle, WA

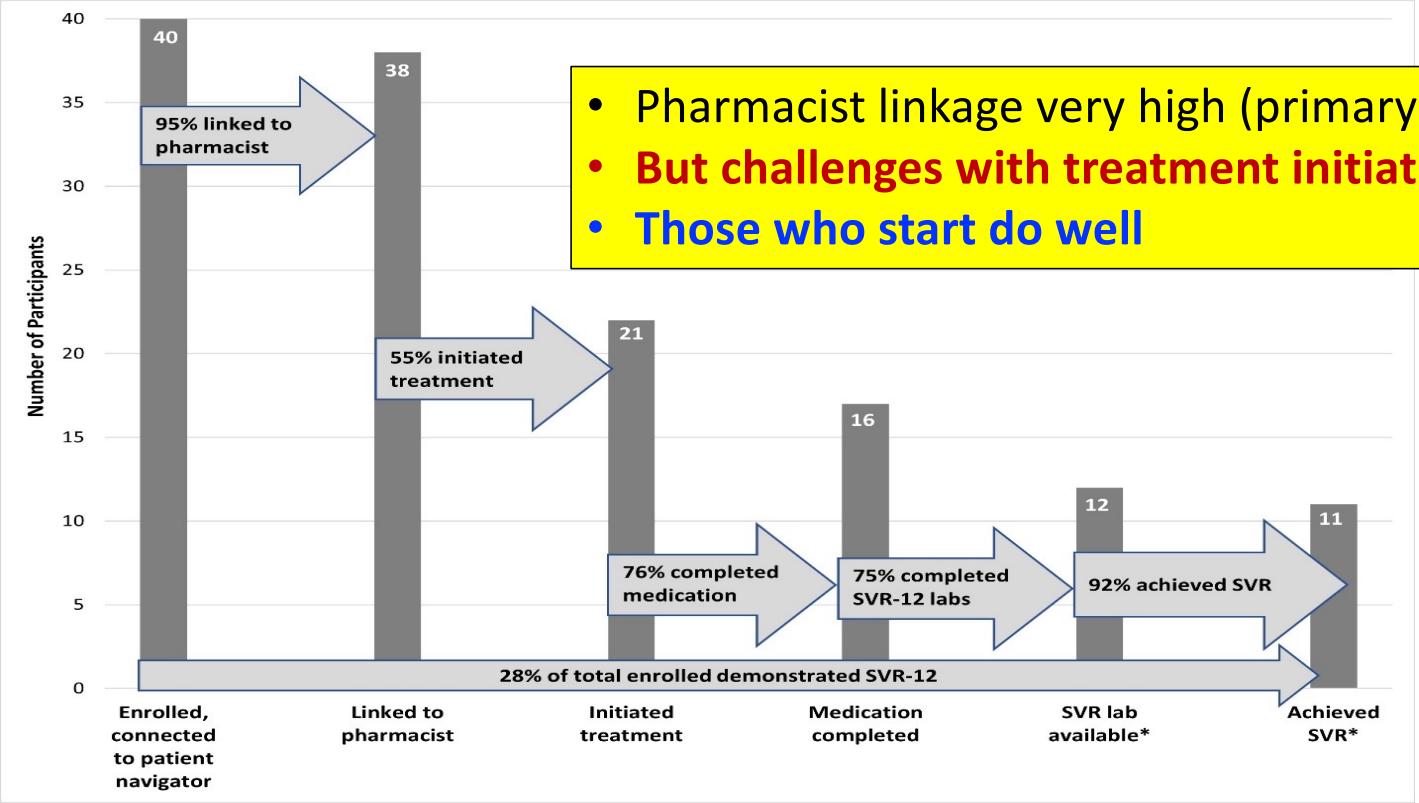
Tsui JI[1], Gojic AJ[1], Pierce KA[2], Tung EL[2,3], Connolly NC[1], Radick AC[1], Hunt RR[4], Sandvold R[5], Taber K[5], Kubiniec RH[6], Scott JD[8], Hansen RN[2,3,7], Stekler JD[8], Austin EJ[7], Williams EC[7,9], Glick SN[8,10]

[1] Department of Medicine, Division of General Internal Medicine University of Washington, Seattle WA, [2] Kelley-Ross Pharmacy Group, Seattle WA, [3] Department of Pharmacy, University of Washington, Seattle WA, [4] Des Moines University College of Osteopathic Medicine, Des Moines, IA, [5] Hepatitis Education Project, Seattle WA, [6] Evergreen Treatment Services, Seattle WA, [7] Department of Health Systems and Population Health, University of Washington, Seattle WA, [8] Department of Medicine, Division of Allergy and Infectious Diseases, University of Washington, Seattle WA , [9] Seattle-Denver Center of Innovation for Veteran-Centered and Value-Driven Care, Health Services Research & Development, VA Puget Sound, Seattle WA , [10] HIV/STD Program, Public Health - Seattle & King County, Seattle WA

Pharmacist, Physician, and Patient Navigator-Collaborative Care Model (PPP-CCM)

- **Aim**: To pilot and evaluate a pharmacist-driven program to treat hepatitis C among PWID seen in community sites.
- **Design**: Single-arm prospective observational study
  - Collaborative Practice Agreement (CPA) with detailed clinical protocols for HCV testing and treatment (also provision of naloxone, PrEP, vaccines and STI treatment)
  - **Primary outcome**: % successfully linked to the pharmacist for evaluation
  - **Secondary outcomes:** HCV tx outcomes (initiation, completion, and SVR12/cure), med adherence, substance use, HIV risk behaviors
- **Results**: 40 active PWID enrolled in Seattle, WA
  - Mean age 43.6 years, 12 (30%) female, 20 (50%) non-white and 15 (38%) homeless
  - Mainly heroin (80%) and methamphetamine users (68%); (38%) recent sharing

Results: HCV Care Cascade



- Pharmacist linkage very high (primary endpoint)
- **But challenges with treatment initiation**
- **Those who start do well**

* Includes n=5 participants who did not complete medication, due to either a treatment interruption or non-adherence.

Engagement in Hepatitis C Screening and Treatment Among Pregnant and Postpartum Individuals in Ontario Canada:

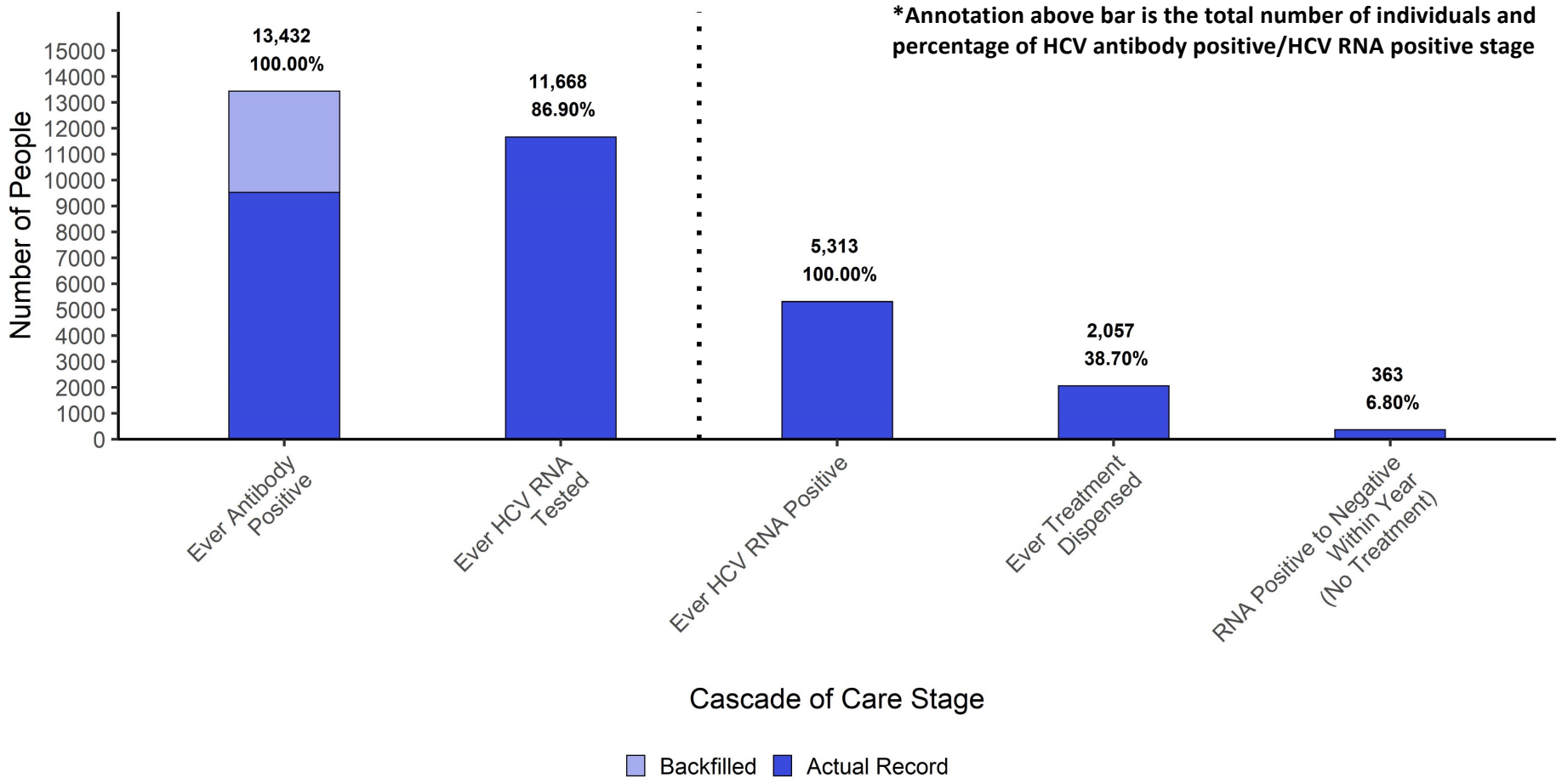
A Population-Based Retrospective Cohort Study

Andrew B. Mendlowitz, Jennifer A Flemming, Tatyana Kushner, William WL Wong, Zoe R Greenwald, Camelia Capraru, Jordan J Feld, Mia J Biondi

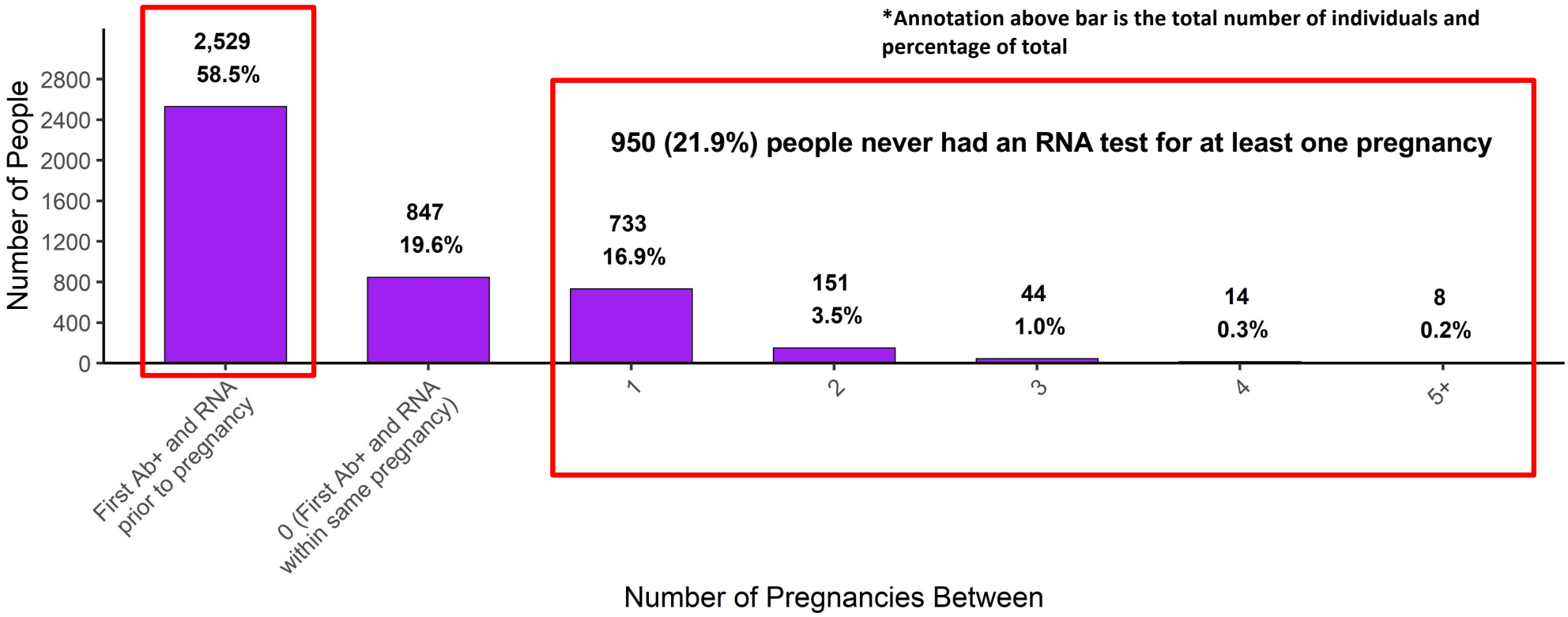
Global Hepatitis Summit
April 28, 2023

TORONTO CENTRE FOR LIVER DISEASE
CIHR IRSC
CanHepC Canadian Network on Hepatitis C Réseau Canadien sur l'Hépatite C
UHN Toronto General Toronto Western Princess Margaret Toronto Rehab
YORK UNIVERSITÉ UNIVERSITY
VIRCAN VIRAL HEPATITIS CARE NETWORK
IC/ES

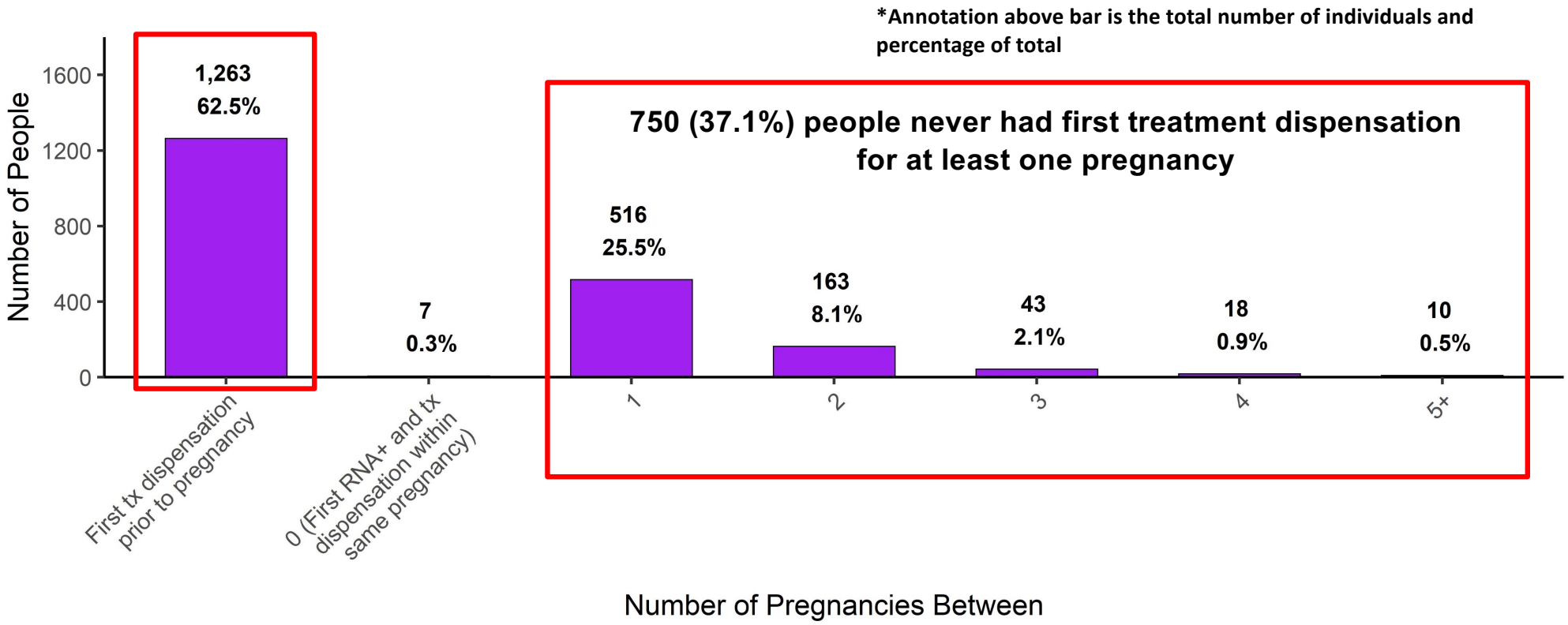
Results: *Overall Care Cascade from First HCV Ab+ to Dec 31, 2020*



Results: *Missed Chances for HCV RNA Testing*



Results: *Missed Chances for HCV Treatment*



Conclusions

- Large population-based study in an important and often overlooked population
- Reassuring Improvements in engagement in RNA testing and treatment initiation over time
- Important gaps in RNA testing and treatment initiation despite multiple pregnancies
- Hopefully new testing guidelines will improve testing and exploration of treatment in pregnancy holds some promise

High HCV Incidence is Associated with Social and Spatial Network Structures among People Who Inject Drugs in New Delhi

Steven J. Clipman, Shruti H. Mehta, Shobha Mohapatra, Aylur K. Srikrishnan, Katie JC. Zook, Shanmugam Saravanan, Paneerselvam Nandagopal, Muniratnam Suresh Kumar, Gregory M. Lucas, Carl A. Latkin, Sunil S. Solomon

Johns Hopkins University School of Medicine
Department of Medicine | Division of Infectious Diseases

2023 Global Hepatitis Summit, Paris, France
April 25, 2023

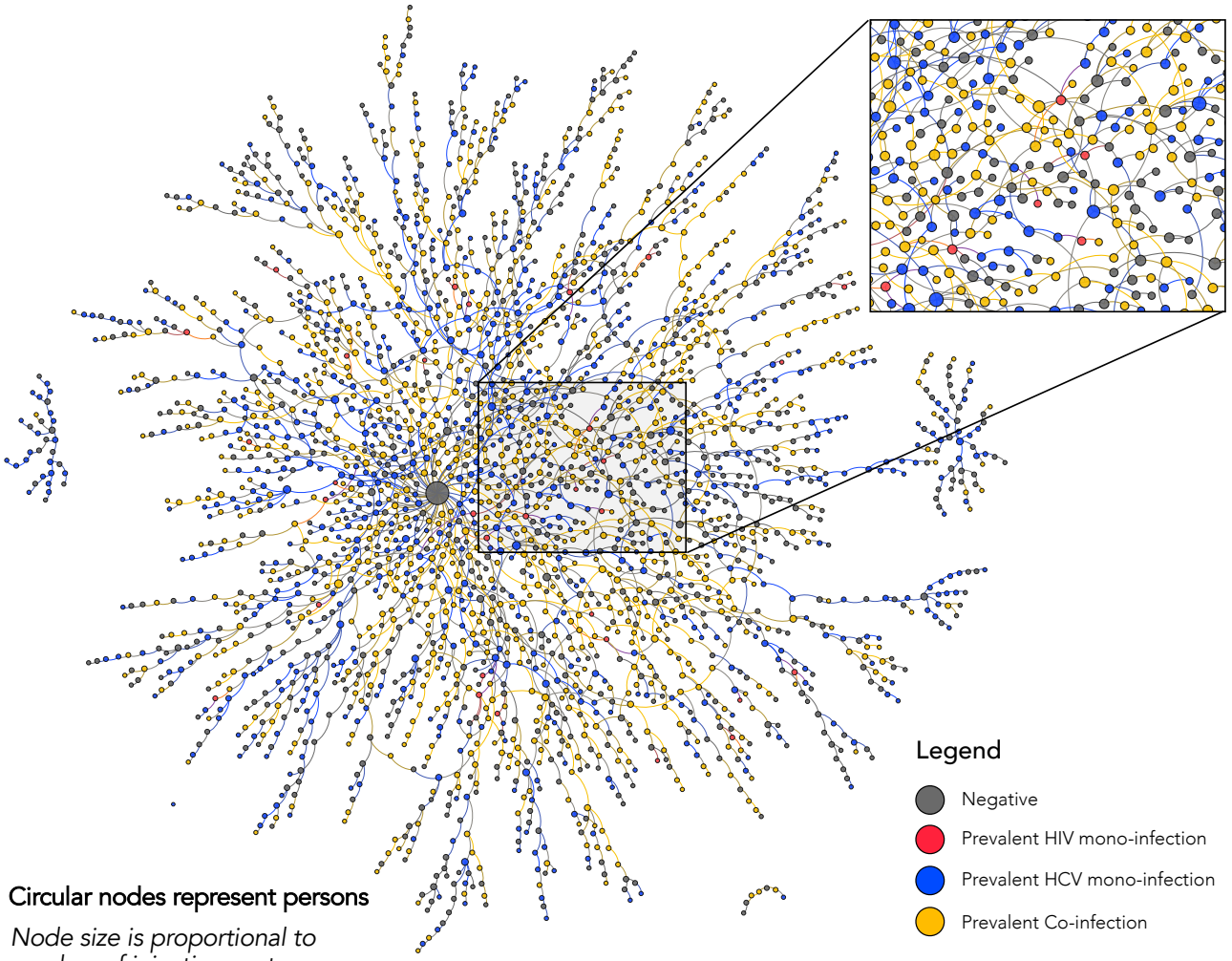
sclipman@jhmi.edu

Results

Baseline Disease Prevalence

HCV Antibody Prevalence:
65.1%
(1634/2512)
Proportion HCV RNA+: 79.6%

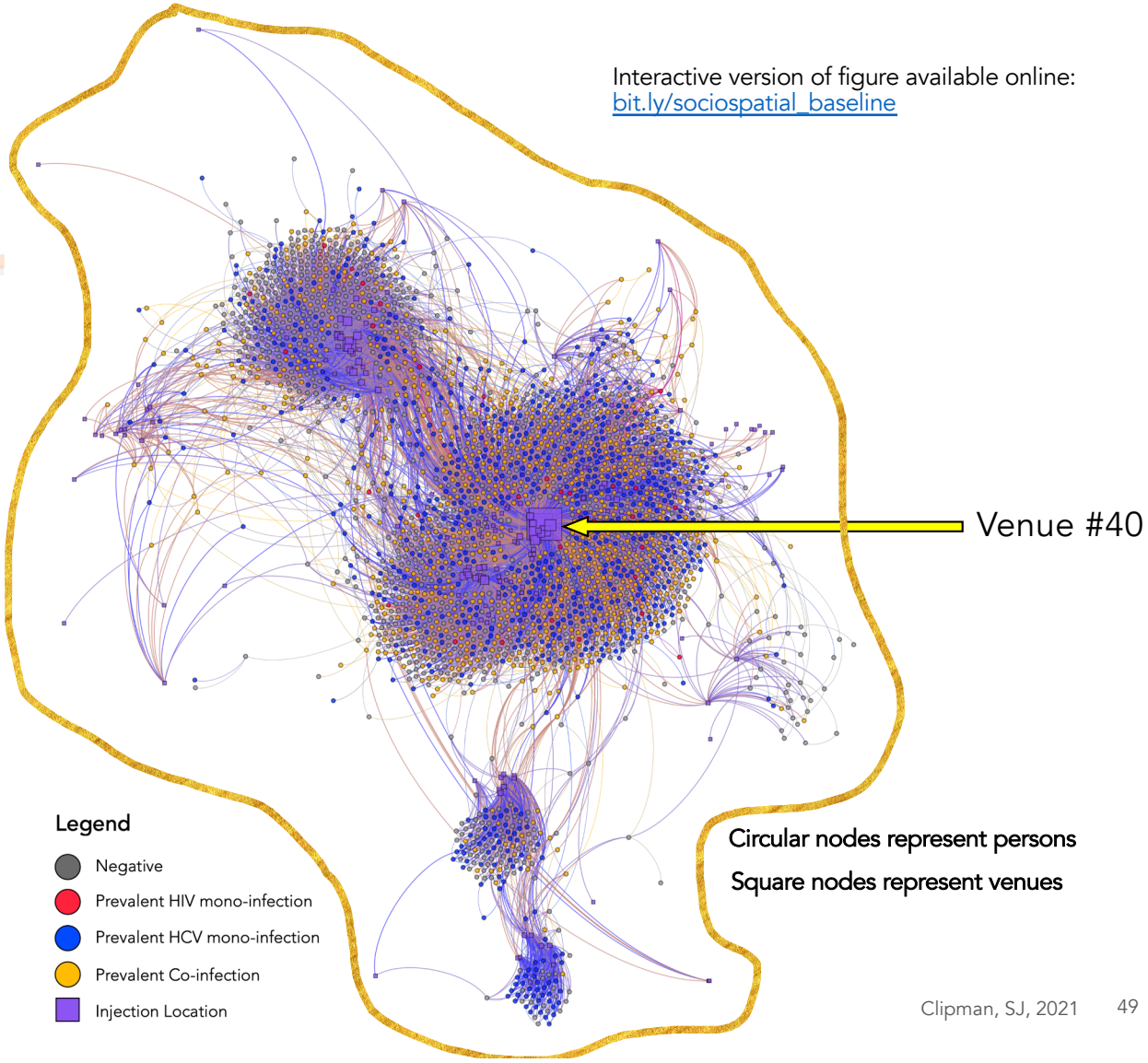
HIV Prevalence:
37.0%
(928/2506)
Proportion detectable RNA: 92.6%



Results

Spatial Data

- 181 unique injection locations
- Median number of injection sites per participant was 3 (IQR: 2 – 6)
- The 5 discrete sociometric networks representing injection partners merged into one large sociospatial network when accounting for injection venues



Results

HCV Incidence

Number HIV negative at baseline with follow-up	Person years of follow-up	Number of incident infections	Incidence rate (95% CI)
406	382.25	92	**24.1 (19.6 – 29.5)**

HIV Incidence

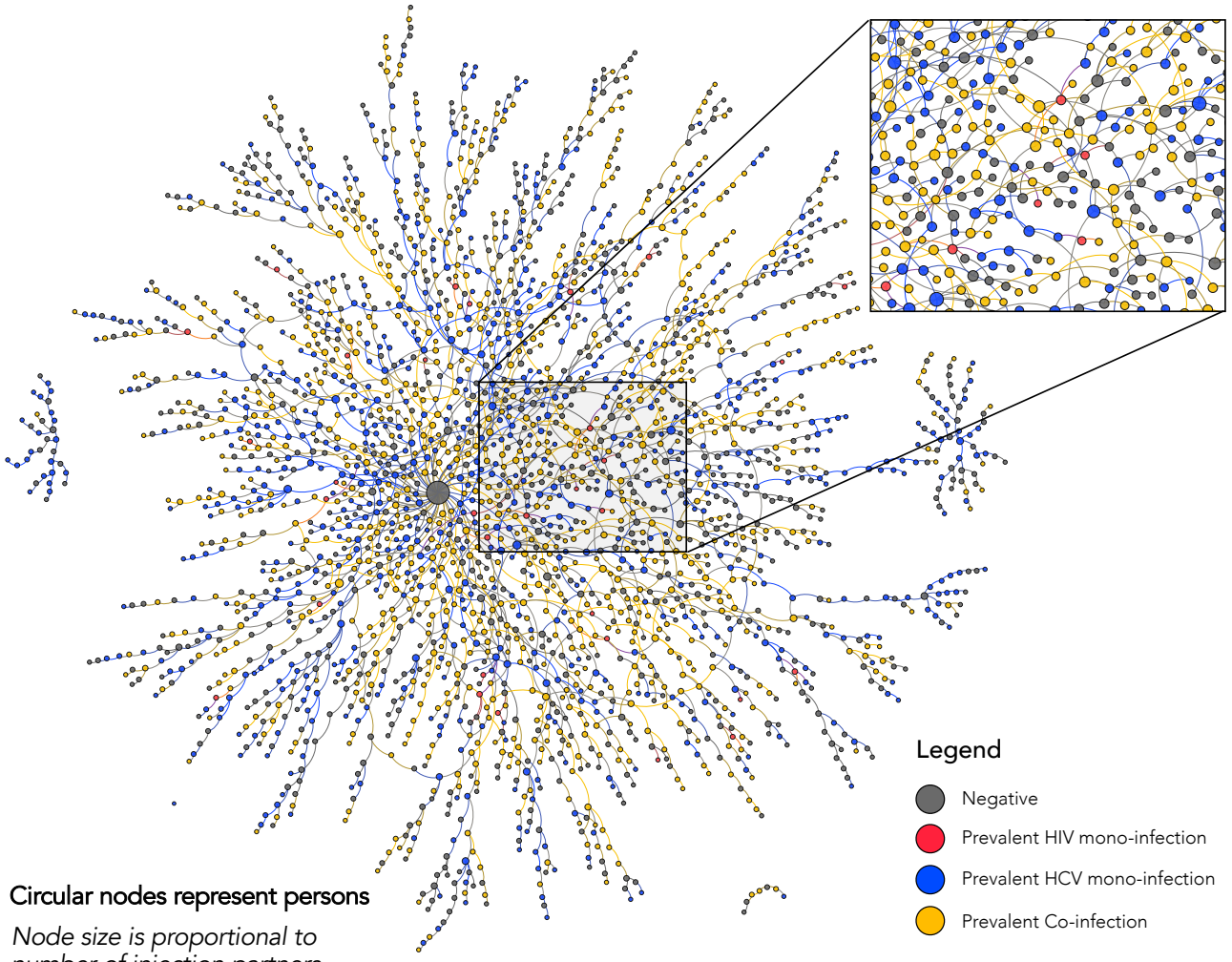
Number HIV negative at baseline with follow-up	Person years of follow-up	Number of incident infections	Incidence rate (95% CI)
782	747	159	**21.3 (18.2 – 24.9)**

Clipman SJ, 2022

Results

Network Structure

- Of the 92 incident HCV infections, 67% (62) were directly connected to at least one actively infected person (HCV RNA > 30 IU/mL)
- All 92 (100%) were within one degree of separation of an actively infected person



Results

Predictors of HCV Incidence

- Network-level factors remained highly significant even after adjusting for individual-level correlates
- Risk of incident HCV increased by 30% for each additional viremic alter
- Injecting at location #40 was associated with 2.5x greater risk
- Each step in social network distance from venue #40 decreased risk by 17%

Factors Associated with HCV Seroconversion	Univariable Model IRR (95% CI)	Multivariable Model 1 AIRR (95% CI)	Multivariable Model 2 AIRR (95% CI)	Multivariable Model 3 AIRR (95% CI)	Multivariable Model 4 AIRR (95% CI)	Multivariable Model 5 AIRR (95% CI)
Age (per 5-year increase)	0.74 (0.66 – 0.84)	0.78 (0.69 – 0.88)	0.77 (0.68 – 0.87)	0.77 (0.68 – 0.87)	0.75 (0.66 – 0.85)	0.76 (0.67 – 0.86)
Sexual Activity vaginal or anal sex in prior 6 months	0.48 (0.31 – 0.75)	0.56 (0.36 – 0.89)	0.58 (0.37 – 0.91)	0.58 (0.37 – 0.91)	0.62 (0.39 – 0.97)	0.59 (0.36 – 0.93)
Shared Syringes (prior 6 months)	3.72 (2.17 – 6.37)	2.38 (1.35 – 4.18)	2.49 (1.41 – 4.39)	2.46 (1.39 – 4.35)	2.22 (1.27 – 3.87)	2.35 (1.34 – 4.13)
Injection Frequency (per 50 injections in prior 6 months)	1.09 (1.06 – 1.12)	1.07 (1.04 – 1.11)	1.07 (1.04 – 1.11)	1.07 (1.03 – 1.11)	1.06 (1.03 – 1.10)	1.06 (1.03 – 1.10)
Number Actively Infected Injection Partners (HCV RNA-positive)	1.18 (0.93 – 1.50)	-	1.30 (1.02 – 1.66)	1.19 (0.85 – 1.67)	-	-
Network Distance from an Actively Infected Injection Partners (HCV RNA-positive)	0.78 (0.56 – 1.09)	-	-	0.85 (0.56 – 1.28)	0.77 (0.56 – 1.05)	0.82 (0.59 – 1.13)
Injecting at Venue #40	2.64 (1.75 – 3.98)	-	-	-	2.53 (1.66 – 3.85)	-
Network Distance from Venue #40	0.87 (0.77 – 0.99)	-	-	-	-	0.83 (0.73 – 0.94)

IRR: incidence rate ratio (univariable); AIRR: adjusted incidence rate ratio (multivariable)

Conclusions

- Networks can be leveraged to improve access to services
- To interrupt transmission, we need to look at epidemics from a larger lens – importance of achieving broad SVR
- Networks are more complicated than just direct inter-personal connections
- Spatial connections may be equally, if not more, important for intervention delivery – need to expand “treat a friend” approaches to key venues.

University of BRISTOL

Bristol Medical School

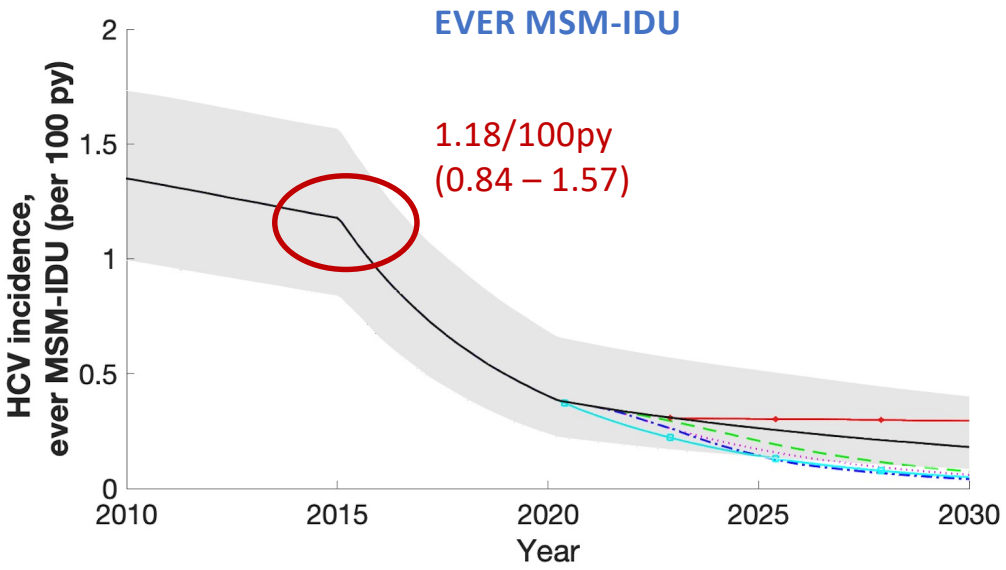
Impact of HCV testing and treatment on HCV transmission among men who have sex with men and who inject drugs in San Francisco: A modelling analysis

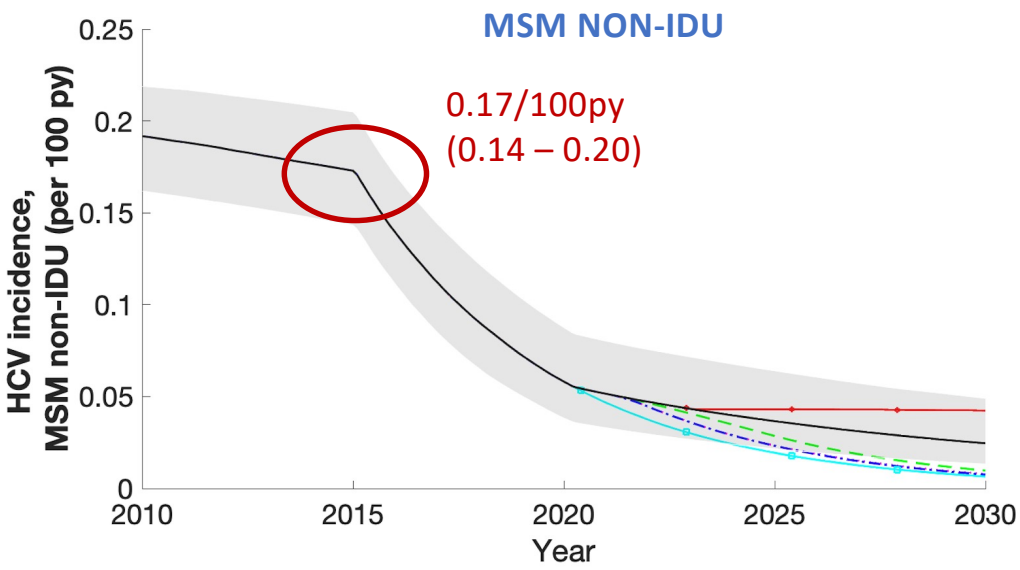
Global Hepatitis Summit

April 28th, 2023

Dr Adelina Artenie

Results: Projected HCV incidence over 2010-2030

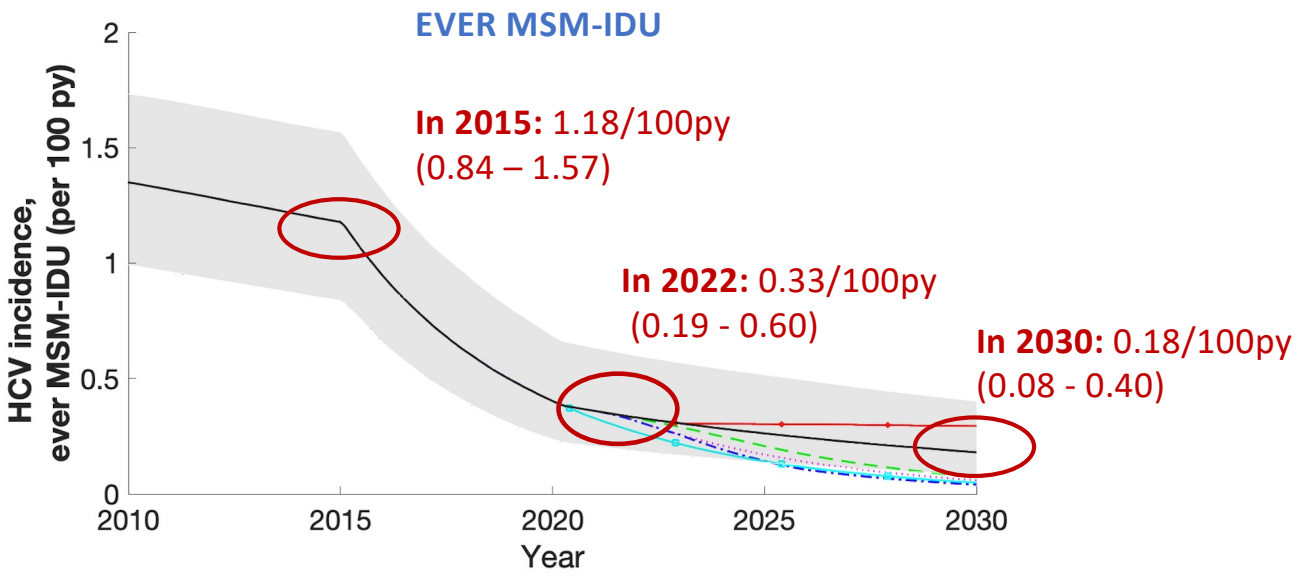




Population attributable fraction* (% new cases among all MSM attributed to IDU vs sexual transmission)

- **HCV: 43.3% (95%CrI: 33.8-51.8%) (even though minority of MSM – 13%)**
- HIV (for comparison): 2.8% (95%CrI: 1.8%-3.8%)

Results: Projected HCV incidence over 2015-2030 and estimated impact of HCV testing and treatment



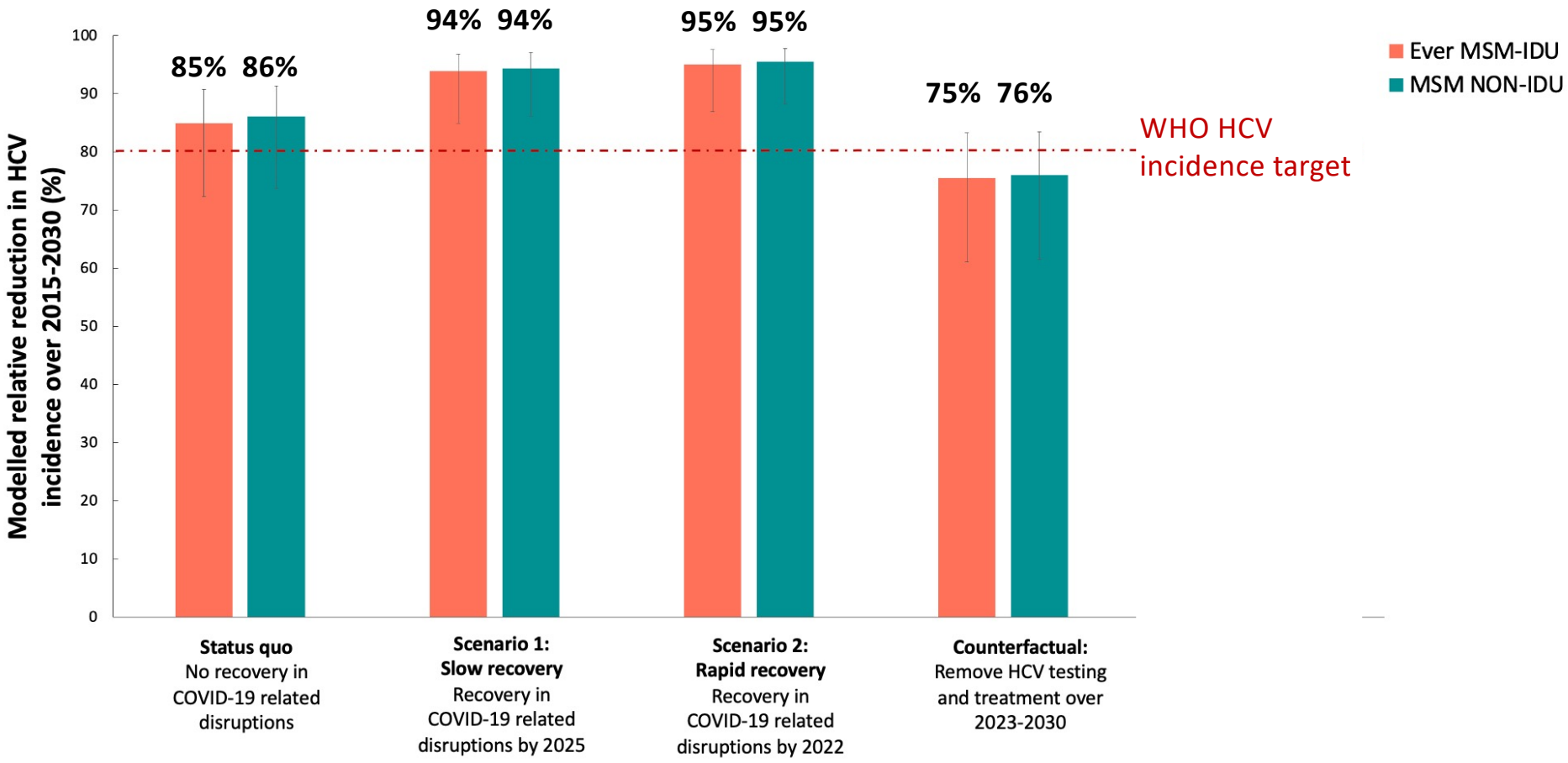
Status quo scenario (black line):
Assuming no recovery in COVID-19 disruptions until 2030:

% decrease in HCV incidence (95% CrI)

- **over 2015-2022: 72% (58% - 80%)**
- **over 2015-2030: 85% (72%-91%)**

Estimated contribution of HCV testing and treatment to the decline in HCV incidence over 2015-2030: 76% (95% CrI: 67% -90%)

Results: Modelled relative reduction in HCV incidence among ever MSM-IDU and MSM non-IDU in different scenarios over 2015-2030



Conclusions

- Modelling suggests that **HCV incidence has already decreased considerably (~70%) over 2015-2022 among ever MSM-IDU in San Francisco**, and the decline is largely attributed to the **high levels of testing and treatment** over this period

- Progress towards the WHO HCV incidence target seems modestly influenced by how fast disruptions in services recover following the COVID-19 pandemic

- **San Francisco is likely an outlier** - **unlikely to be representative of the wider MSM-IDU and MSM communities in the US**

BURDEN OF HEPATITIS C VIRUS INFECTION IN PUNJAB PROVINCE OF PAKISTAN: THE PUNJAB HEPATITIS SURVEY 2018

Objectives:

- To estimate the prevalence and risk factors for anti-HCV in the Punjab, Pakistan

Methods:

- Multi-stage stratified cluster survey of Punjab province. Clusters selected through stratified random sampling.
- 20 houses per cluster were selected using systematic sampling with random start.
- All household members of selected houses were interviewed for household characteristics, HCV risk factors and engagement with HCV care.
- Questionnaire and laboratory results were available for 14,305 participants.

Citation: Janjua NZ, Naveed A, Velásquez García HA, Huda S, Rasul S, Ahmad AM, Sarwar Z, Akhter S. Burden of hepatitis C virus infection in Punjab province of Pakistan: The Punjab Hepatitis Survey 2018. Abstract #: P100

Results

Overall prevalence of anti-HCV: **9.0%; translating into 7.96 million people**, slightly higher among females than males(9.2% vs 8.8%)

Of anti-HCV positive, 56% were positive for RNA. The prevalence of active infection was 5.0%, translating into **4.5 million infections**.

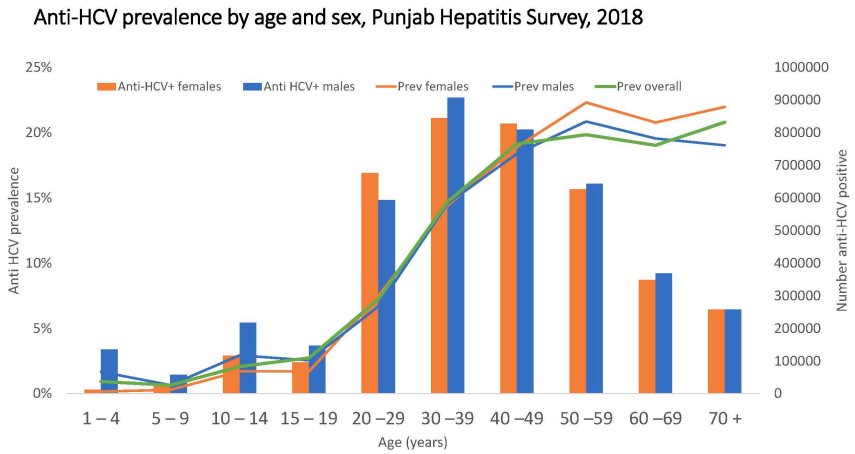


Table : Factors associated with anti-HCV positivity in Punjab Province, Pakistan by weighted multivariable logistic regression, overall and by sex

Variables	Adjusted odds ratio (95%CI)		
	Overall	Males	Females
Age (years; Ref: 20 – 29**)**			
01 - 04	0.12 (0.05-0.28)	0.23(0.09-0.61)	0.23(0.09-0.61)
05 - 09	0.05(0.03-0.09)	0.07(0.03-0.15)	0.07(0.03-0.15)
10 - 14	0.29(0.18-0.48)	0.38(0.22-0.68)	0.38(0.22-0.68)
15 - 19	0.29(0.2-0.4)	0.38(0.23-0.62)	0.38(0.23-0.62)
30 - 39	1.94(1.5-2.51)	2.09(1.42-3.09)	2.09(1.42-3.09)
40 - 49	2.53(1.95-3.28)	2.86(1.95-4.18)	2.86(1.95-4.18)
50 - 59	2.92(2.12-4.01)	3.26(2.19-4.83)	3.26(2.19-4.83)
60 - 69	2.62(1.89-3.63)	2.92(1.92-4.42)	2.92(1.92-4.42)
70+	2.57(1.84-3.58)	2.67(1.72-4.14)	2.67(1.72-4.14)
Sex, Female	0.94(0.83-1.06)		
Education (Ref: None)			
Primary	0.89(0.74-1.07)	1.04(0.79-1.37)	0.81(0.62-1.07)
Middle	0.77(0.62-0.96)	0.93(0.7-1.25)	0.65(0.44-0.96)
Matric	0.77(0.61-0.96)	0.88(0.66-1.18)	0.72(0.5-1.06)
Above Matric	0.45(0.32-0.62)	0.55(0.34-0.91)	0.39(0.26-0.59)
No. of injections received during past 3 months	**(Ref: 0)**		
1	1.08(0.77-1.53)	0.99(0.58-1.71)	1.13(0.74-1.72)
2	1.25(0.905-1.63)	0.97(0.59-1.61)	1.42(1.03-1.96)
3-4	1.73(1.27-2.36)	1.92(1.22-3.04)	1.57(1.05-2.33)
5 or more	1.36(1.1-1.69)	1.43(0.96-2.13)	1.34(0.98-1.83)
History of blood transfusion (Ref: No)	1.42(1.15-1.77)	1.19(0.78-1.8)	1.69(1.32-2.17)
Times received dental treatment in last 10 years	(Ref:0)		
2	1.47(1-2.15)	1.84(1-3.39)	1.25(0.68-2.32)
3	1.63(1-2.65)	2.26(1.19-4.29)	1.36(0.75-2.47)
4 or more	1.38(0.96-1.97)	1.43(0.93-2.2)	1.32(0.79-2.19)
Ever tattooed (Ref: No)	2.56(1.6-4.1)	2.65(1.18-5.99)	2.08(1.3-3.32)
Ever received a cut at Barber (Ref: 1)		1.32(1.03-1.73)	
Gravity (Ref: 0)			
1 to 2			0.77(0.5-1.19)
3 to 4			0.66(0.42-1.03)
5 to 6			0.68(0.41-1.15)
7 or more			0.58(0.32-1.05)

Risk factors for HCV positivity:

- Medical injection
- Dental treatment
- Blood transfusion
- Tatooing cut from barber
- Number of pregnancies

Hepatitis C Care Cascade and Progress Toward Elimination in the United States, 2021

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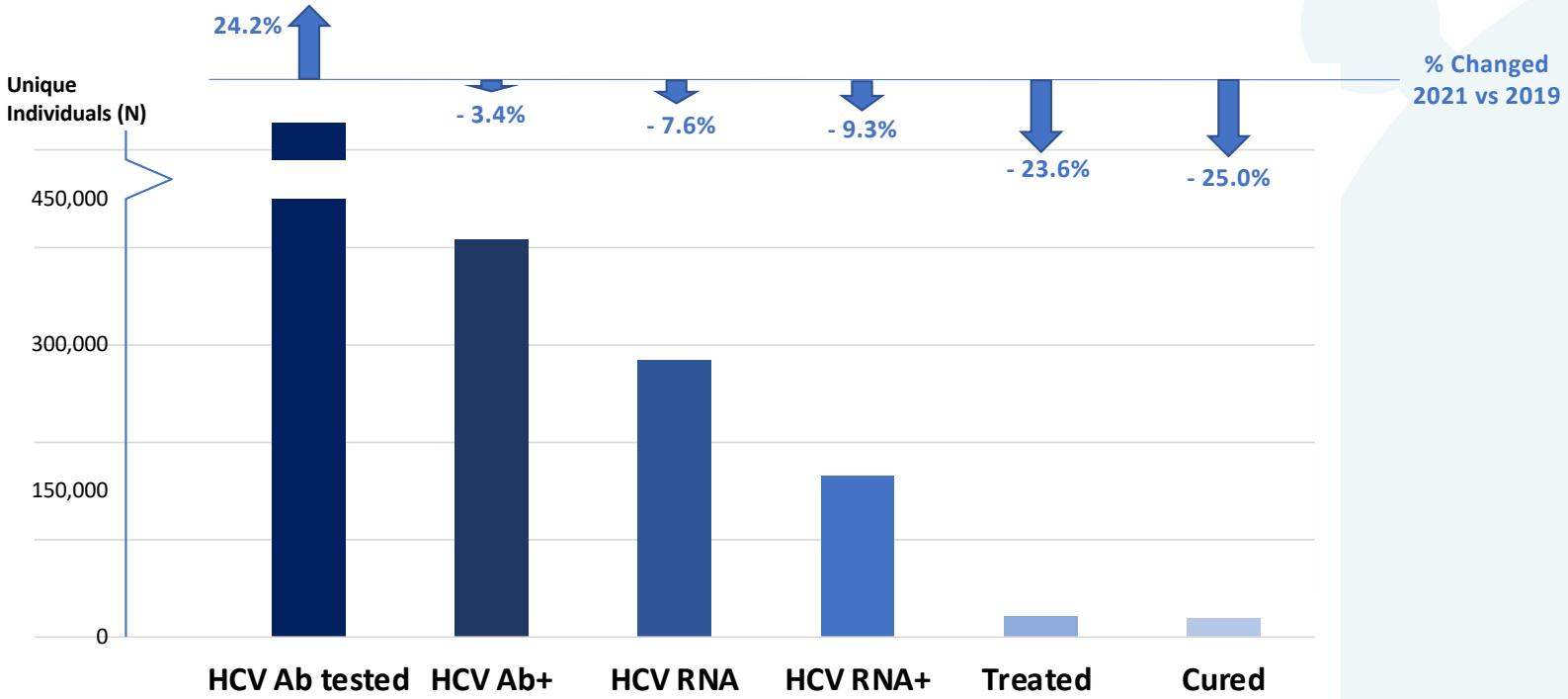
Changes in HCV Treatment and Cure, 2021 vs 2019



	HCV Ab tested	HCV Ab+	HCV RNA	HCV RNA+	Treated	Cured
Frequency (2021)	10,167,524	407,795	284,220	165,142	21,136	19,584
Proportion	100.0%	4.0% of Ab tested	100.0%	58.1% of RNA tested	12.8% of RNA+	92.7%* of treated

Figure is only showing HCV RNA tested, RNA+, treated (among those tested RNA+ in 2021), and cured individuals who had an Ab+ test in 2021.
HCV Treated and cured individuals were identified using validated imputation algorithms.
*Cure rate may be underestimated because patients diagnosed toward the end of 2021 may not have enough follow-up data to predict treatment initiation and cure.

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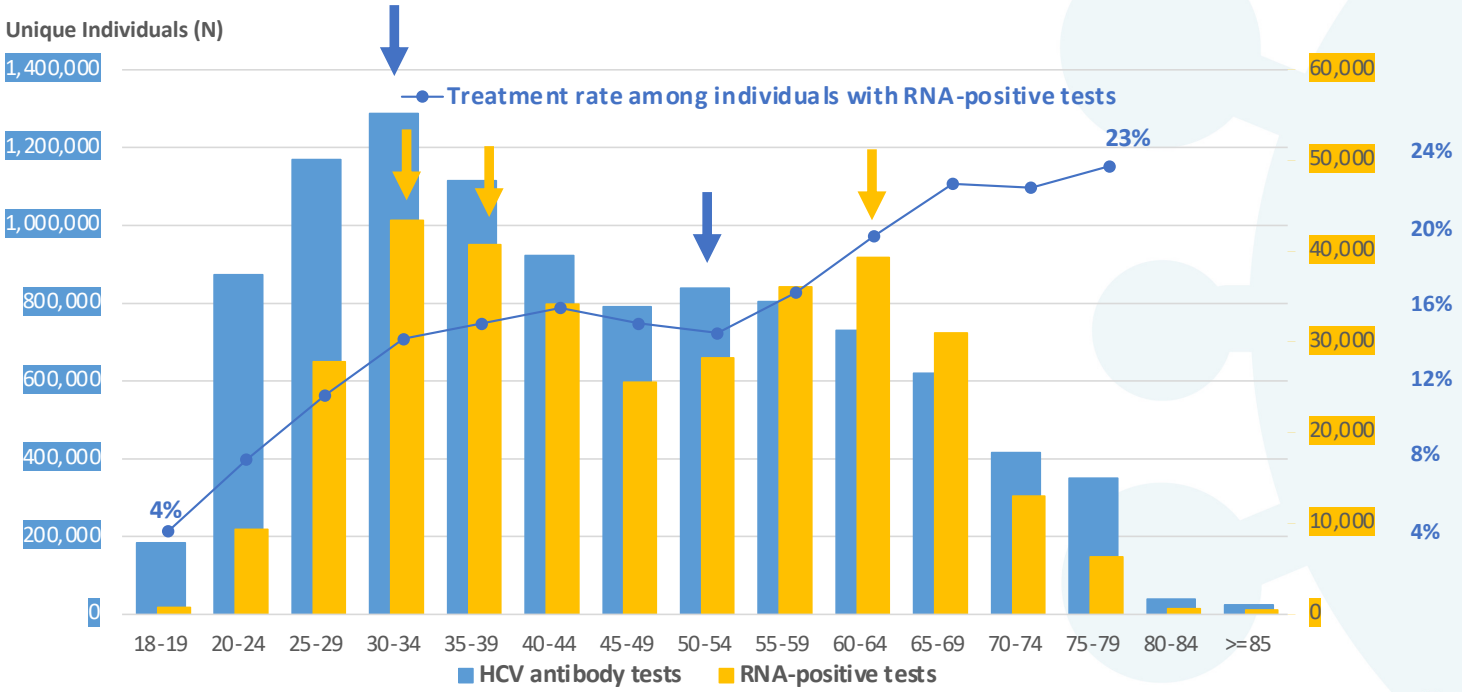
Age Distribution for Individuals with HCV Antibody Screening and RNA-Positive Tests Among Adults in the US in 2021



Receipt of treatment was determined based on a viral load decline of at least 1.2 × log10 units since the first positive HCV RNA test, indicating that treatment was initiated in the immediate period prior to the decline.

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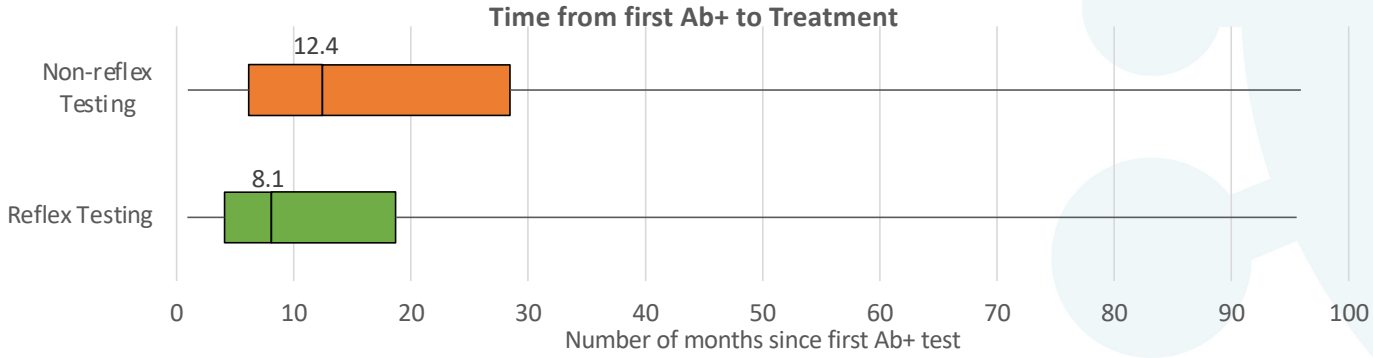
Association of Reflex Testing and Receipt of HCV Treatment, 2014-2021

- Received HCV treatment
  - 30% among persons having reflex HCV RNA testing
  - 8% among persons for whom HCV Ab and RNA testing were ordered separately

- Median time from first HCV Ab+ test to treatment
  - 8.1 mos. median, 14.5 mos. mean among persons having reflex HCV RNA
  - 12.4 mos. median, 19.9 mos. mean HCV Ab and RNA testing ordered separately



*Percent treated for individuals for whom Ab and RNA testing were ordered separately may be underestimated due to inclusion of those who may not have a confirmed RNA+ test result. Reflex testing (HCV Antibody with reflex to RNA test) was identified by matching the test date (date the specimen was drawn) of the Antibody test with that of the RNA test. Reflex testing analyses are only available with data from one large US national laboratory.

Receipt of treatment was determined based on a viral load decline of at least 1.2 × log10 units since the first positive HCV RNA test, indicating that treatment was initiated in the immediate period prior to the decline. Time to treatment analysis was limited to individuals with an Ab+ test at least 28 days prior to the viral load decline.

Conclusions

- The bimodal age distribution of HCV RNA+ tests supports the current policy for HCV testing of all adults.
- Reflex testing for HCV RNA is associated with higher rates of linkage to care and treatment initiation. Data suggest this should be implemented across laboratories.
- Treatment uptake across the U.S. remains low, suggesting continued barriers to initiation of therapy.
- Additional actions are needed to expand access to testing and treatment necessary to achieve the WHO HCV elimination goals by 2030 in the U.S.

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Summary

- Improved testing modalities important – POC HCV RNA at the national level, self-testing and a promising novel HCV Ag assay

- Opportunistic testing – COVID vaccination, pharmacies, pregnancy – effective strategy for reaching PWID
- But think about the bigger network including spatial aspects & provide supportive outreach care

- National cascade of care data critical to guide policy – risk factors, testing tools, populations to test and reach