Best of AASLD 2024: Hepatitis C

John D Scott MD MSc FIDSA
Professor, Medicine
University of Washington

Last Updated: February 5, 2025

Disclosures

In the last 2 years, I have served on data adjudication committees for the NIH and Novo Nordisk and the P&T Cmte for Premera

Thanks to Dr. McCrary for sharing slides from IDSA 2024 presentation.

Disclaimer

Funding for this presentation was made possible by 1 TR7HA53202-01-00 from the Human Resources and Services Administration HIV/AIDS Bureau. The views expressed do not necessarily reflect the official policies of the Department of Health and Human Services nor does mention of trade names, commercial practices, or organizations imply endorsement by the U.S. Government. *Any trade/brand names for products mentioned during this presentation are for training and identification purposes only.*

AETC AIDS Education & Training Center Program Mountain West

Outline

- HIV/HCV Coinfection
- Hep C Treatment Progress
- FDA approval of POC NAT test
- Treatment in Novel Settings
- Treatment in Pregnancy

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HIV/HCV Coinfection

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HIV/HCV Coinfection Background

- Approximately 2 M people worldwide are coinfected with HIV and HCV
- Patients with HIV/HCV coinfection have a more rapid progression to advanced fibrosis compared to HCV monoinfected patients, even in era of highly effective ART.
- Also lower spontaneous clearance of HCV if also HIV-infected
- Sustained virologic response to IFN and ribavirin was lower in coinfected patients; however, with newer directly acting antivirals (ie. Sofosbuvir/velpatasvir, glecaprevir/pibrentasvir) is the same as monoinfected patients
- With cleaner first line HIV regimens, there are much fewer drug-drug interactions but beware of a few: elvitegrevir/cobi and G/P, EFZ and sof/vel, boosted PI regimens. Due to limited experience, renal monitoring is recommended in patients taking tenofovir disoproxil fumarate and cobicistat or ritonavir with sofosbuvir/velpatasvir.

Chew, Kara W.; Bhattacharya, Debika. Virologic and immunologic aspects of HIV–hepatitis C virus coinfection. AIDS 30(16):p 2395-2404, October 23, 2016. | DOI: 10.1097/QAD.0000000000001203

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HCV Treatment Progress

CDC Study of HCV Treatment Patterns (2014-23)

Background

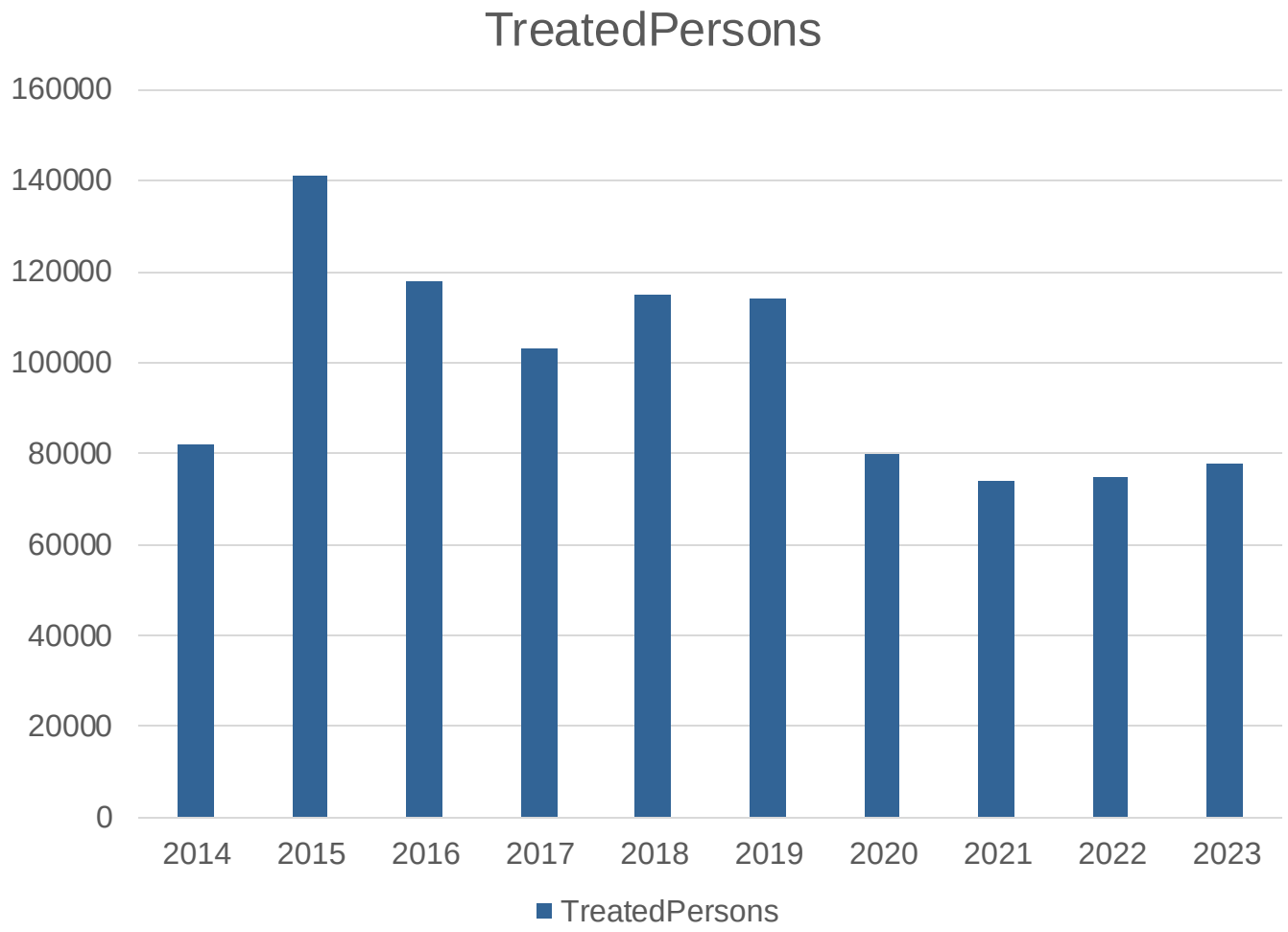
- As of 2020, 1.2 million Americans infected with HCV were treated
- Landscape has changed since then with fewer restrictions, simplified algorithm, and lower cost of tx

Data

- IQVIA pharmacy claims database
- Doesn’t include VA, carceral system, and managed care orgs; only has first paid claim

Results

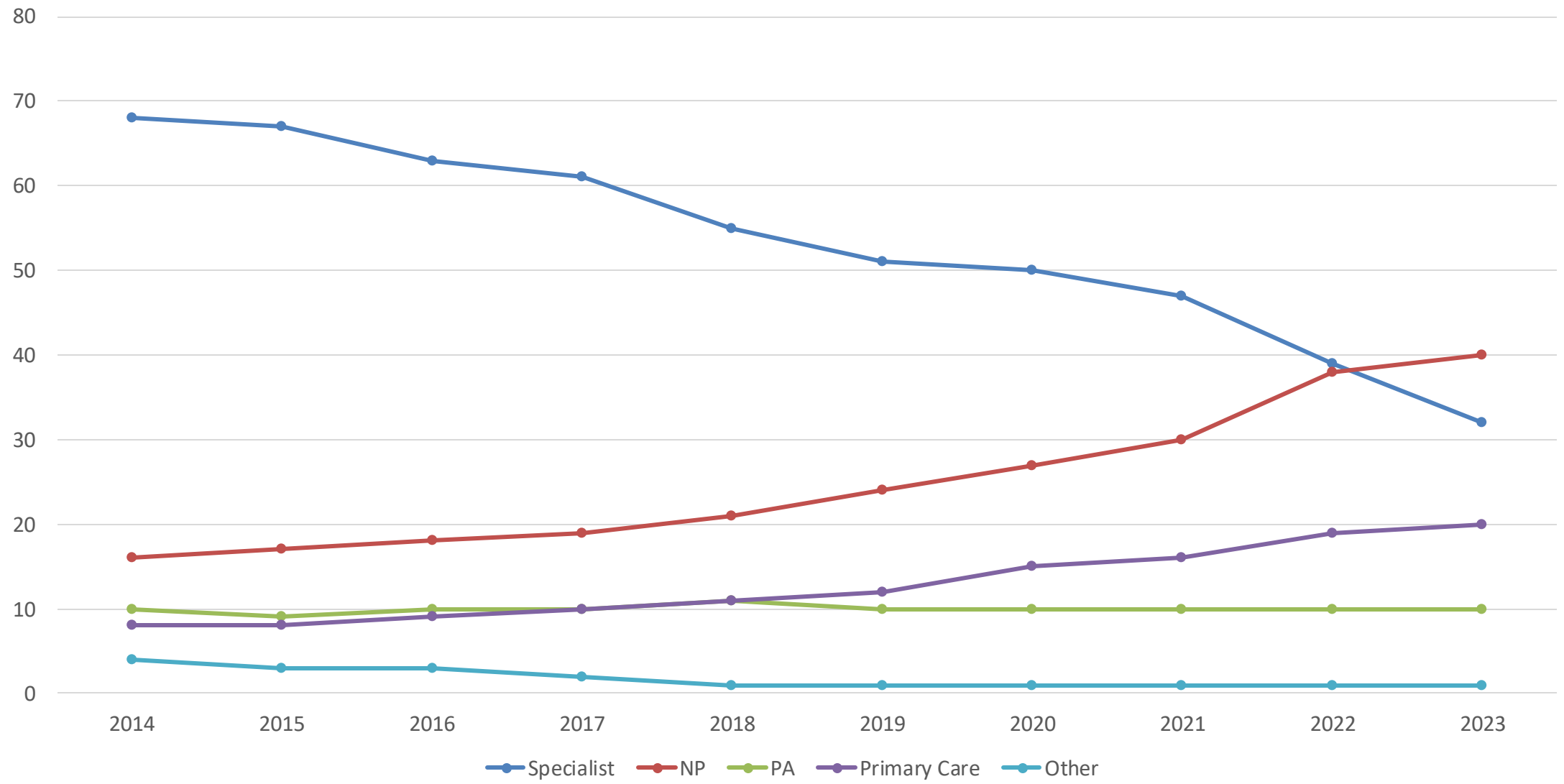
- Using IQVIA data, 980,062 persons were treated with DAAs
- Peak year was 2015
- Compared to peak, there were 48% fewer persons treated in 2023



Characteristics of Persons Treated with DAAs (2014-23)

- 69% white, 19% Black, 10% Hispanic
- Most common age group was 60+ yo but is declining and in last two years is 40-59 yo age group
- More men treated than women
- Commercial insurance was most common source of insurance, but Medicaid increasing quickly, accounted for 50% in 2023
- Top states: DC, LA, KY, AK, WV, MA, OR

Proportion of persons treated by provider type and year, United States, 2014-23



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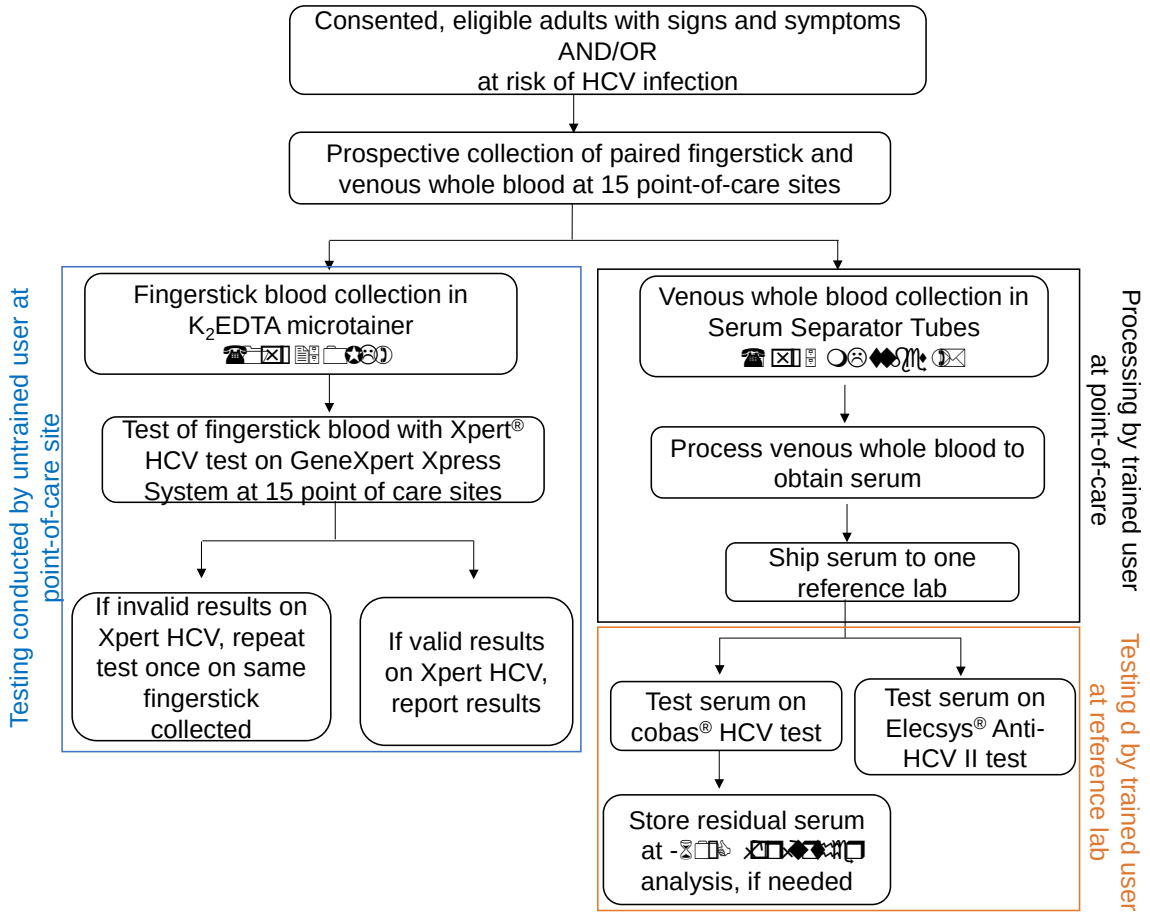
Cepheid Xpert for HCV RNA Detection

- First POC HCV RNA molecular test to receive de novo FDA approval and CLIA-waiver
- Detects HCV RNA through K-EDTA fingerstick whole blood sample
- Processing time <1 hr
- LOD is 35-136 IU/ml

Figure 1. Study Methodology and Workflow



Abstract 5051 Gail Louw, et al. The Liver Meeting, San Diego, CA 2024.

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Cepheid Xpert

Table 2. Agreement between Xpert HCV and Patient Infected Status (PIS)

		PIS[a]		
		HCV Positive[b]	HCV Negative[c]	Total
Xpert® HCV Test	HCV DETECTED	114	2	116
	HCV NOT DETECTED	8	861	869
	Total	122	863	985
PPA		93.4% (95% CI: 87.6 - 96.6)		
NPA		99.8% (95% CI: 99.2 - 99.9)		

[a] PIS categories defined as 1) active chronic infection based on reactive HCV antibody and "HCV Detected" cobas results; 2) past/resolved infection based on reactive HCV antibody and "HCV Not Detected" cobas results; 3) active acute infection based on non-reactive HCV antibody and "HCV Detected" cobas results and; 4) not infected based on HCV non-reactive HCV antibody and "HCV Not Detected" cobas results.

[b] Active chronic or acute infection

[c] Past/resolved infection or not infected

Sensitivity: 114/114+ 8 = 93.4%
Specificity: 861/861+ 2 = 99.8%
Positive Predictive Value: 114/116 = 98.2%
Negative Predictive Value: 861/869 = 99.1%

Machine costs $20k
Important to co-locate POC with access to treatment, harm reduction, vaccination

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Same Day and Next Day Treatment Starts

La Bodega Clinic (Buffalo, NY)

- Co-located hepatology and addiction medicine, integrated pharmacy support
- Referrals from prisons, STI clinics, primary care, street medicine, ED
- SW helps arrange transport or facilitate telemedicine
- Patients given red, yellow, green designation for needed level of support
- Has on-site POC testing

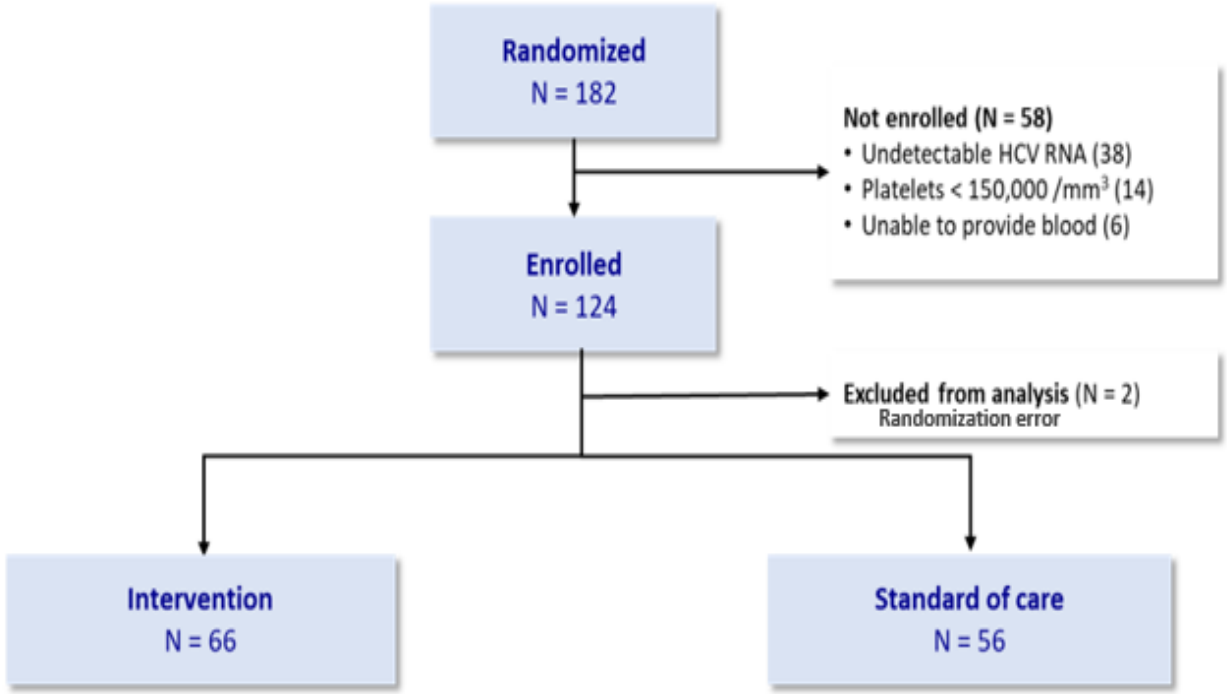
La Bodega Clinic

- Characteristics: 47% under 40 yo, 62% male, 7% had cirrhosis, 58% on MAT, 43% had active substance use, 83% on Medicaid
- 51% preferred shorter duration of therapy (younger and those on MAT especially)
- Overall full adherence was 59%
- Overall LTFU was 32%, esp. in telemedicine (acute detox setting)
- SVR12 97% (124/128)

RAPID HCV: rapid test and treat with peer support in opioid treatment programs

- Multicenter, open-label, randomized (1:1) trial
- Onsite HCV test and treat with peer support (RAPID HCV) vs standard of care referral to specialist HCV treatment (SOC)
- 5 OTPs in Baltimore, MD, Birmingham, AL, San Francisco, CA and Toronto, Canada
- HCV treatment with glecaprevir/pibrentasvir
- Primary outcome: HCV treatment initiation within 12 weeks of randomization
- Secondary outcomes: Time to treatment initiation, Sustained virologic response at 12 weeks
- Safety: Grade 3 or higher adverse events

Figure 1: Study Flow

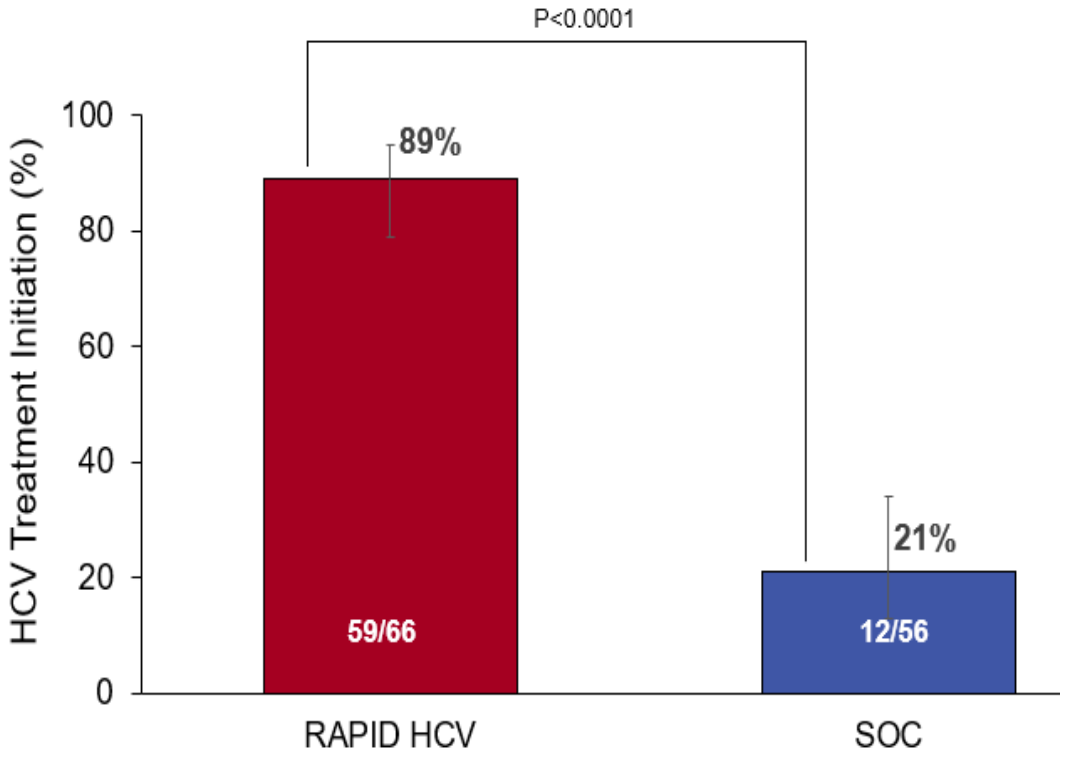


RAPID HCV: Results

Table 1: Study participant demographics

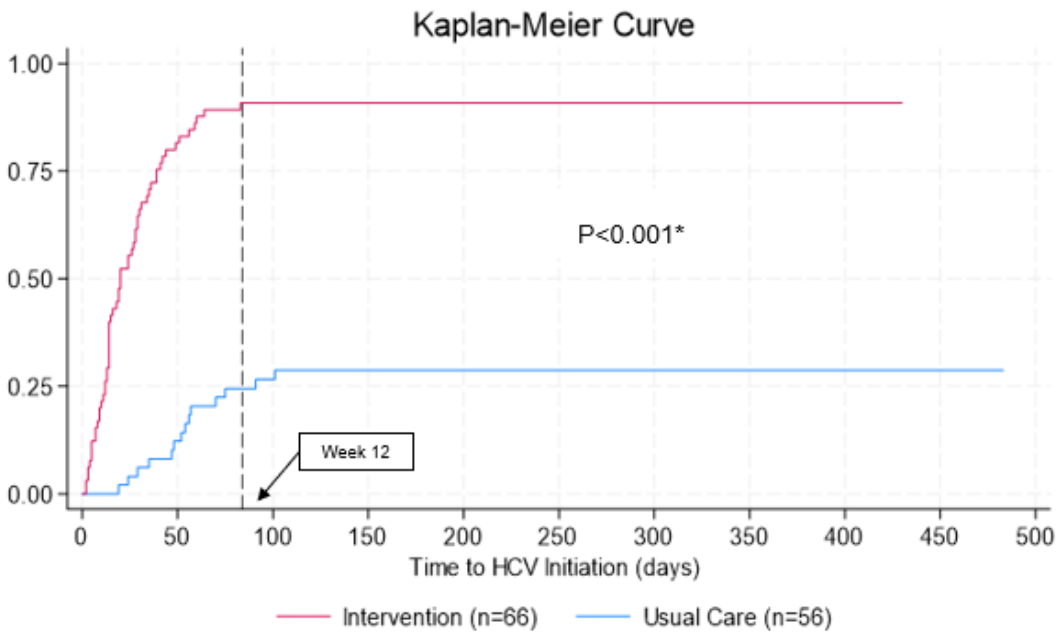
Characteristic	Total (N=122)	RAPID HCV (N=66)	SOC (N=56)	P-value
Mean age, m (SD), years	48.0 (11.8)	48.3 (11.5)	47.5 (12.3)	0.72
Male, n (%)	73 (59.8)	36 (54.5)	37 (66.1)	0.20
Race, n(%)				
White	71 (58.2)	37 (56.1)	34 (60.7)	0.76
Black	45 (36.9)	25 (37.9)	20 (35.7)	
Homeless in prior 6 months	38 (31.1)	21 (31.8)	17 (30.4)	1.00
Substance detected in urine	82 (67.2)	41 (62.1)	41 (73.2)	0.25
Fentanyl	64 (52.5)	37 (56.1)	27 (48.2)	0.51
Cocaine	56 (45.9)	29 (43.9)	27 (48.2)	0.29

Figure 2: HCV treatment initiation by randomization arm



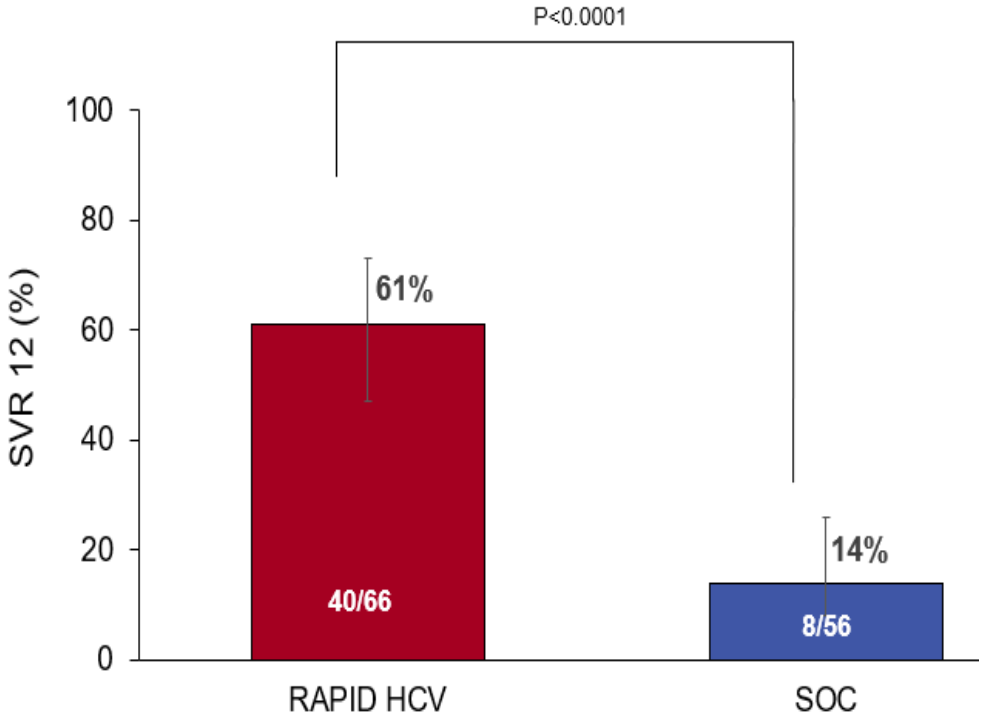
RAPID HCV: Results

Figure 3: Time to treatment initiation



	RAPID HCV	SOC	P-value
Median (IQR) days	19 (11-34)	53 (35-70)	<0.001

Figure 4: SVR12 by randomization arm among randomized participants



RAPID HCV: Conclusions

Table 2: Reasons for not achieving SVR 12

Patients, n (%)	RAPID HCV n=66	SOC n=56
SVR12	40(61)	8(14)
Did not initiate treatment	7(11)	44(79)
Recurrent HCV viremia*	11(17)	1(2)
Unable to get blood draw due to poor venous access	2(3)	(0)
Did not return for SVR 12 assessment	6(9)	3(5)

*Recurrent viremia does not distinguish viral relapse and HCV reinfection

Safety: No drug related grade 3 or higher or serious adverse events reported

- On site HCV test and treat with peer support at OTPs was associated with significantly higher rates of HCV treatment initiation and SVR compared to offsite referral for specialist HCV treatment
- HCV treatment integration into OTPs has potential to advance HCV elimination efforts among PWUD

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HCV Treatment in Pregnancy: Interim Analysis of STORC Study

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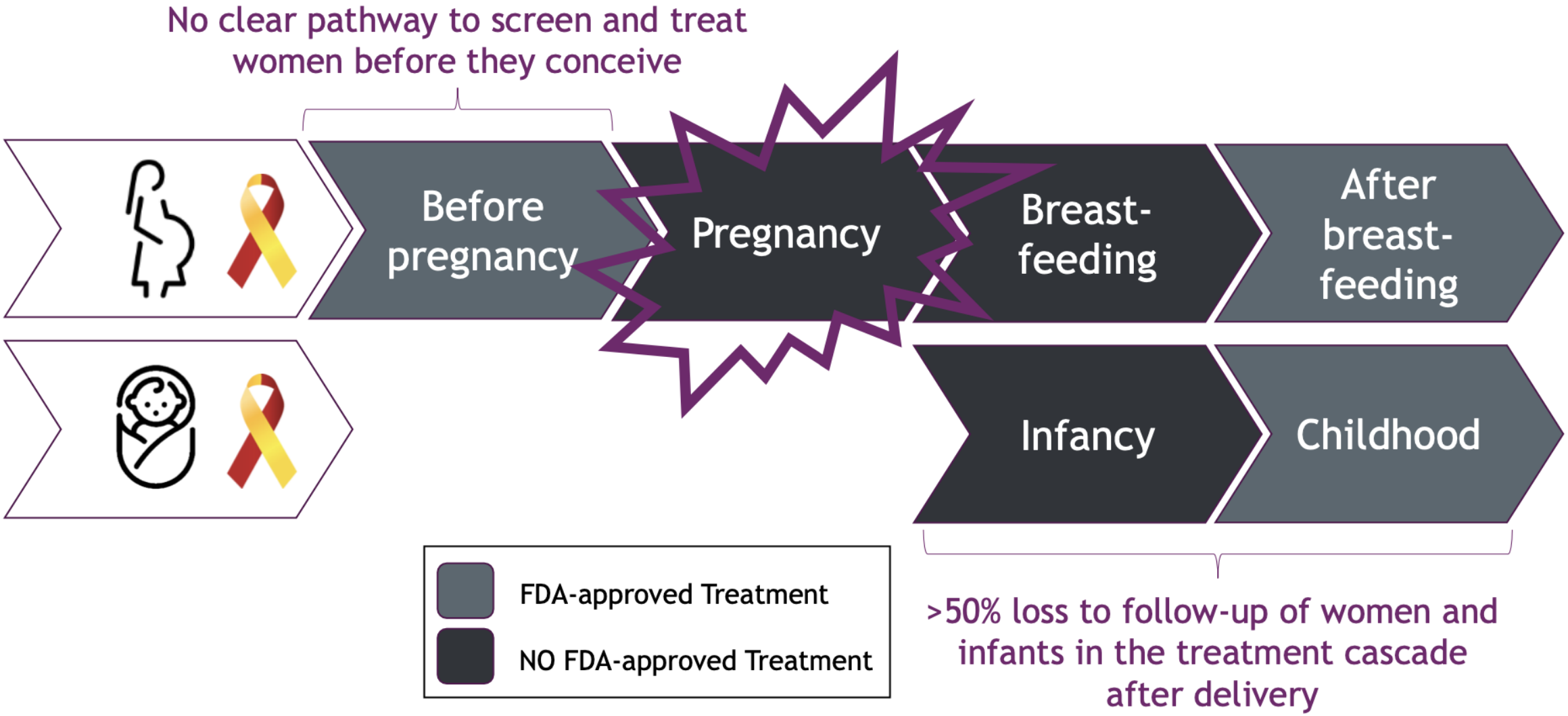
HCV Treatment Availability for Pregnant People and Children



Kushner T, et al. Hepatol Commun. 2018;2(11):1306-1310.

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HCV Treatment During Pregnancy?

Potential Benefits of Treatment

- Maternal cure during a time of high health care engagement/insurance coverage (antenatal care) with unique motivation (fetal benefit).
  - Reduced community transmission
  - Reduction of HCV-associate morbidity
  - Psychological benefit to HCV cure
- Reduction of HCV-associated pregnancy risk (cholestasis, fetal growth restriction, preterm birth)
- Reduction of perinatal HCV transmission

Potential Risks of Treatment

- Limited safety data DAAs in pregnancy and breastfeeding

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Why not just wait until post-partum?

This approach is NOT working.

> Obstet Gynecol. 2022 May 1;139(5):916-918. doi: 10.1097/AOG.0000000000004760. Epub 2022 Apr 5.

Postpartum Follow-up Care for Pregnant Persons With Opioid Use Disorder and Hepatitis C Virus Infection

Marian Jarlenski [1], Qingwen Chen, Katherine A Ahrens, Lindsay Allen, Anna E Austin, Catherine Chappell, Julie M Donohue, Lindsay Hammerslag, Paul Lanier, Mary Joan McDuffie, Jeffrey Talbert, Lu Tang, Elizabeth E Krans;
Medicaid Outcomes Distributed Research Network (MODRN)

> Hepatol Commun. 2021 Sep;5(9):1543-1554. doi: 10.1002/hep4.1748. Epub 2021 Jul 1.

Enhancing Linkage to Hepatitis C Virus Treatment Following Pregnancy in Women Identified During Perinatal Care

Rachel L Epstein [1 2], Carole Moloney [2], Jacob Garfinkel [3], Kelley Saia [4], Elisha M Wachman [5], Sara Lodi [6], Stephen J Pelton [2]

> J Am Pharm Assoc (2003). 2022 May-Jun;62(3):864-869. doi: 10.1016/j.japh.2021.12.006 Epub 2021 Dec 18.

Quality improvement to evaluate and provide treatment for chronic hepatitis C postpartum

Casey Behnke, Oriel Nissim, Whitney Simerlein, Kristin Beeker, Jessica L Tarleton, Gweneth B Lazenby

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It is also not working for exposed infants…

2023 pediatric recommendations – screen with HCV RNA 2-6 months

Study from Tennessee examining testing for HCV in infants exposed during pregnancy

- >3,000 HCV-exposed infants
- **Only 26% with any HCV screening**
- **Significant differences** by race/ethnicity
- **51 infants with confirmed/probable HCV**

CM Thomas, et al. *Open Forum Infectious Diseases*, Volume 12, Issue Supplement_1, February 2025, ofae631.1180, https://doi.org/10.1093/ofid/ofae631.1180

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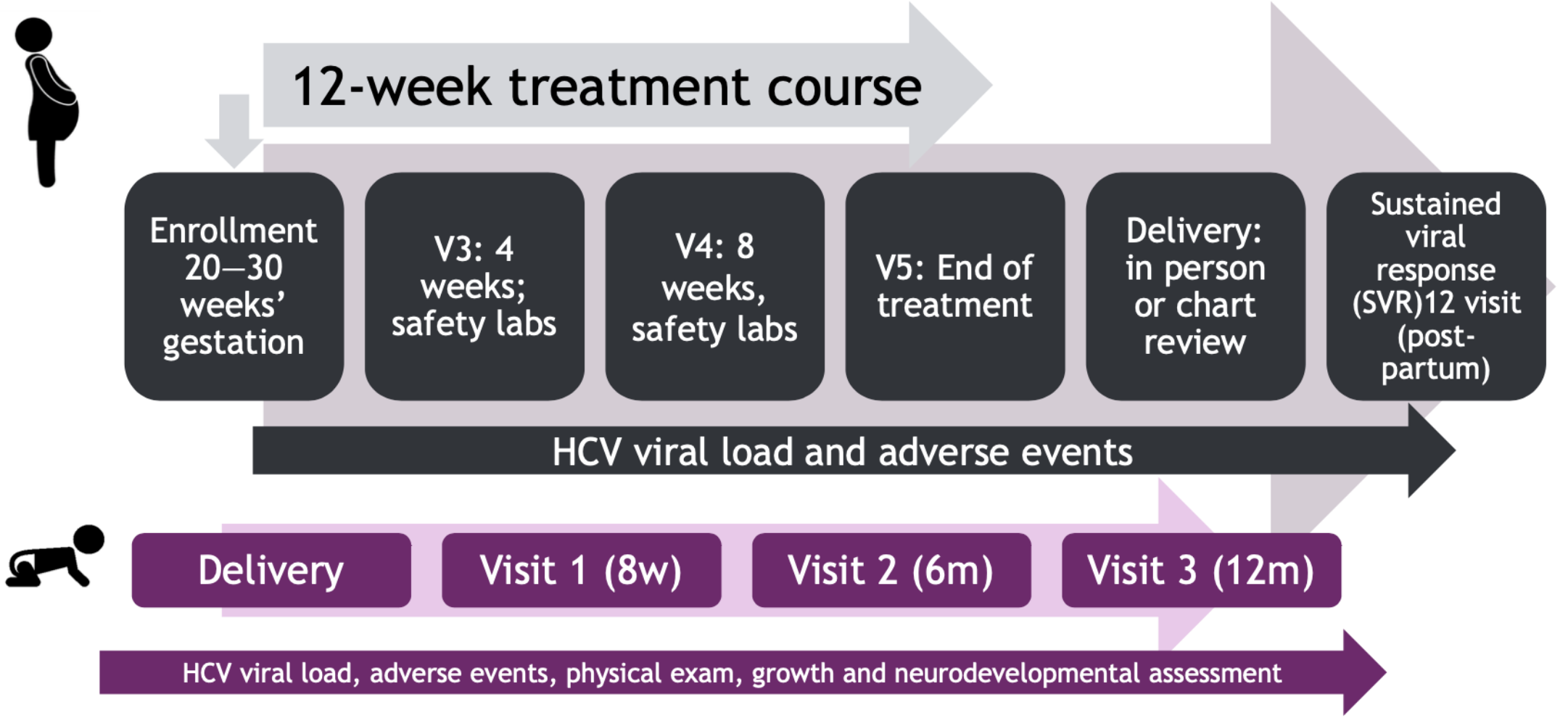
STORC Study Design



Study Design

- Open label, prospective clinical trial of sof/vel in pregnant women
- International study: 6 US sites, 3 Canadian

Inclusion Criteria	Exclusion Criteria
Age 18-45 yo	Previous DAA tx
RNA detectable	Contraindicated medications
Chronic, not acute HCV	History of cirrhosis
20-30 wks of pregnancy	Confirmed chromosomal abn
Nl 20 wk ultrasound	Clinically significant drug use
Neg HBsAg	Significant abnl screening labs
If HIV+, on ART and undetectable	If HIV+, CD4 ct <200 c/ml in last 6 mos
If taking antacids, willing to modify for sof/vel tx	

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Study Flow (as of October 28, 2024)

61 patients screened

50 enrolled

46 delivered meds, 44 completed study med

1 had vomiting,
1 withdrew
consent

35 completed SVR assessment

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Demographics and Clinical Characteristics (n=50)

- Median age: 31 (18-40 yo)
- 84% public insurance, 16% private insurance
- 92% had FIB-4 <1.45, 8% indeterminate
- 84% white, 6% multiracial, 4% Asian, 2% Black, 2% Native American
- 80% smokers, 80% IDU hx
- 46 previous children exposed to HCV
- 28% previous children tested for HCV (no MTCT)
- 24% hx of pre-term birth

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Pregnancy Outcomes from 44 Deliveries

Outcomes	N (%) or Median	# Participants
Gestational Age at Delivery	38 + 0 wks	44
Pre-term birth	6 (14%)	44
Cholestasis	0 (0%)	44
SVR12	35 (100%)	35
Perinatal HCV Transmission	0 (0%)	26

Preterm Birth Clinical Circumstances

- 36+4 wks premature rupture of membranes
- 36+4 wks premature rupture of membranes
- 36+2 wks premature rupture of membranes
- 36+2 wks spontaneous preterm labor
- 33+5 wks spontaneous preterm labor, breech presentation
- 33+4 wks marginal placental abruption

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Maternal and Infant Safety Data

Maternal (N=40)

- Nausea/vomiting (18)
- GERD (7)
- Fatigue (7)
- Headache (5)
- Elevated CK (1)
- Light sensitivity (1)
- Numbness fingers (1)
- Arthralgias (1)
- Insomnia (1)

Infant (N=4)

- Hirschprung's Disease
- Retrognathia
- Pyloric stenosis
- Pre-auricular skin tag

None of the maternal or infant SAEs were deemed related to SOF/VEL

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Key Points

- Sof/vel is well-tolerated in pregnancy
- High effectiveness in cure in women and preventing MTCT
- Benefit of lowering risk of cholestasis of pregnancy
- More GI side effects
- Key window of opportunity to treat
- Who should treat HCV in pregnancy?

Summary

- Peak HCV Tx was 2015, patients are increasingly younger and on Medicaid
- POC NAT may help expedite tx
- New treatment paradigms are needed to treat current patients, rapid starts with support appear successful
- Sof/vel is safe and effective in pregnant women; who should treat them?
- G/P is safe and effective in acute hep C, use 8 wks

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Acknowledgment

This Mountain West AIDS Education and Training (MWAETC) program is supported by the Health Resources and Services Administration (HRSA) of the U.S. Department of Health and Human Services (HHS) as part of award 1 TR7HA53202-01-00 totaling $2,982,063 with 0% financed with non-governmental sources.

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