2020 GI AND LIVER SYMPOSIUM

Annenberg Center For Health Sciences at Eisenhower
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Southern California Society of Gastroenterology

Update: Hepatitis C: Abstracts from AASLD/EASL

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Disclosures

Speaker Bureau:	AbbVie, BMS, Eisai, Exelixis, Gilead, Intercept, Salix, Mallinckrodt
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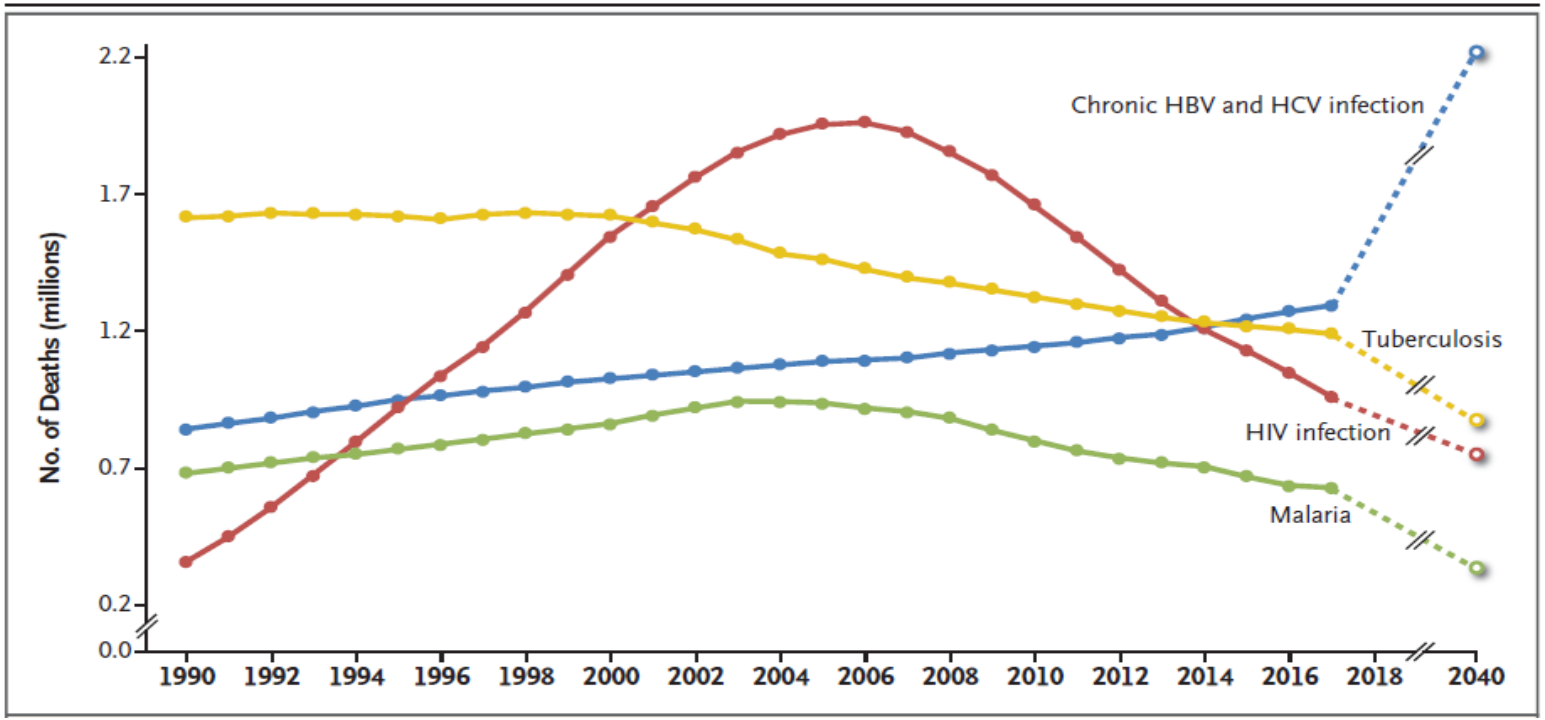
Aims

- Demonstrate how the natural history and relative contribution to liver diseases have been altered by hepatitis C treatment
- Describe novel techniques to improve linkage of care and extend therapy to vulnerable populations infected with hepatitis C
- Clarify milestones needed for hepatitis C elimination

Worldwide Deaths From Chronic Viral Hepatitis as Compared with Deaths from Tuberculosis, HIV, and Malaria

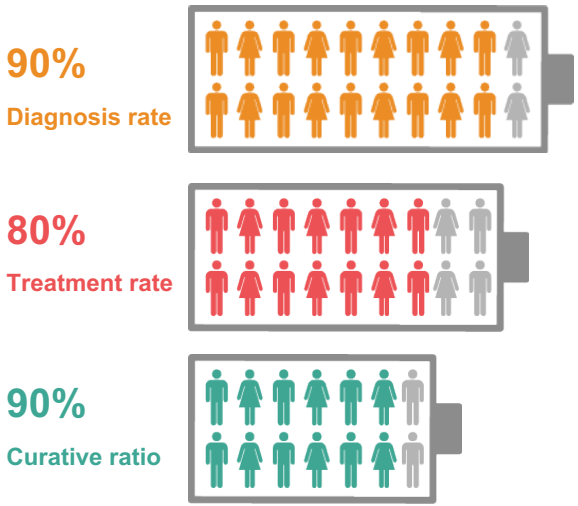


Data on deaths from 1990 to 2017 are from the Institute for Health Metrics and Evaluation as of November 14, 2018.

Thomas D. *N Engl J Med*. 2019

WHO Global Strategy for Eliminating Hepatitis C by 2030

WHO Target: Serious public health threats from elimination of viral hepatitis in 2030



New chronic infections drop by 90%

↓

Death reduced by 65%

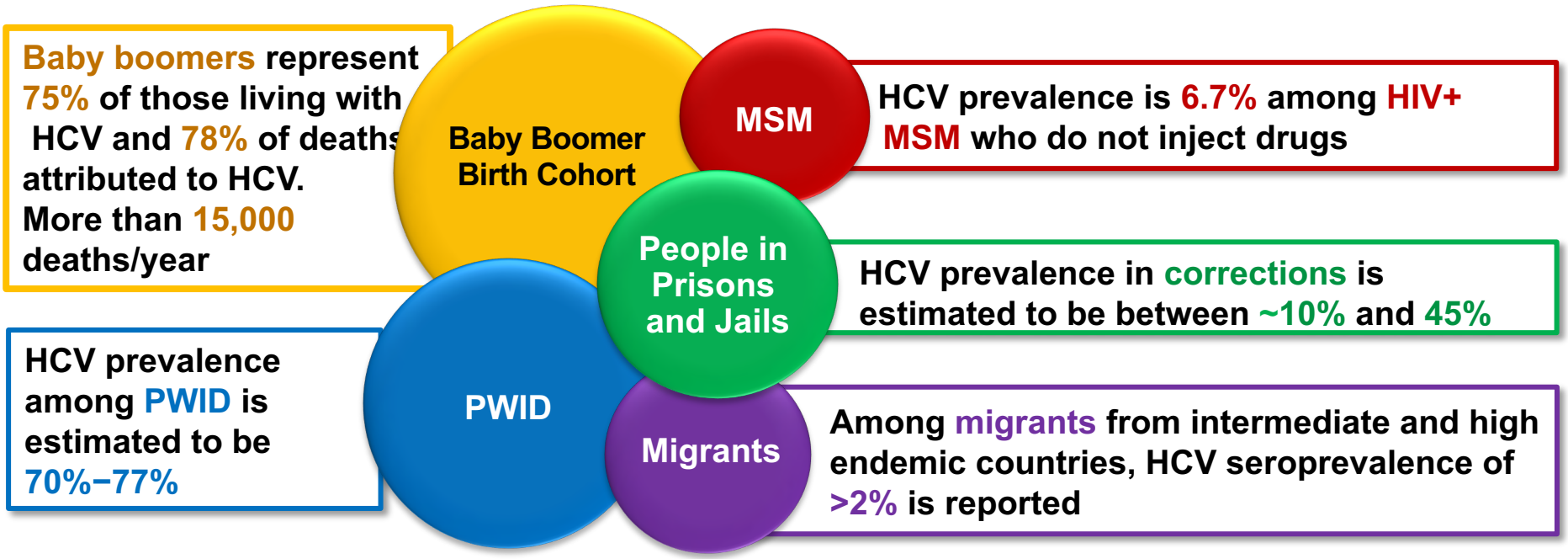
↓

Reducing the burden of disease globally

WHO: World Health Organization

69th World Health Assembly. Draft Global Health Sector Strategies. April 2016. Available at: http://apps.who.int/gb/ebwha/pdf_files/WHA69/A69_32-en.pdf?ua=1 (accessed February 2017)

High Seroprevalence of HCV in Certain Subpopulations



Individual and Societal Benefits of Hepatitis C Cure

Individual benefits of Hepatitis C cure

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- Prevents progression to cirrhosis and hepatocellular carcinoma[1,2]
- Reduces morbidity and mortality[1]
- Improves quality of life[1]

Societal benefits of Hepatitis C cure

The image part with relationship ID rId5 was not found in the file.

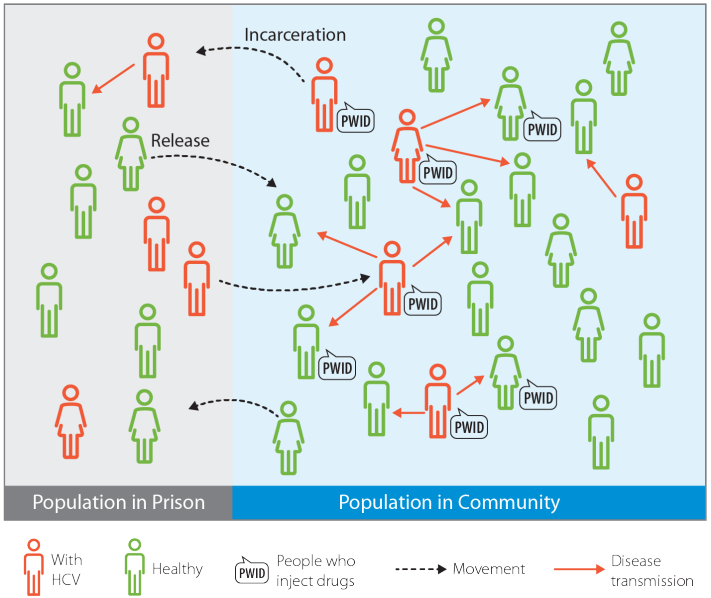
- Prevents onward transmission[1]
- Reduces health service usage and costs[1,3,4]

1. AASLD/IDSA Guidance. Available at: www.hcvguidelines.org (accessed August 2017). 2. Backus LI, et al. Clin Gastroenterol Hepatol 2011. 3. Leidner AJ, et al. Hepatology 2015. 4. Gordon SC, et al. Hepatology 2012;56:1651–60

People With HCV Released From Prison May Spread Infection in the Community

- Incarcerated people with HCV who are released and resume risk behaviors
  (ie, injecting drugs and sharing needles) can potentially spread infection to others in their communities[1]
  - Sharing of drug use equipment can be common among PWID[2]

Model of HCV Disease Transmission Among Incarcerated Individuals and the General Population[1,a]



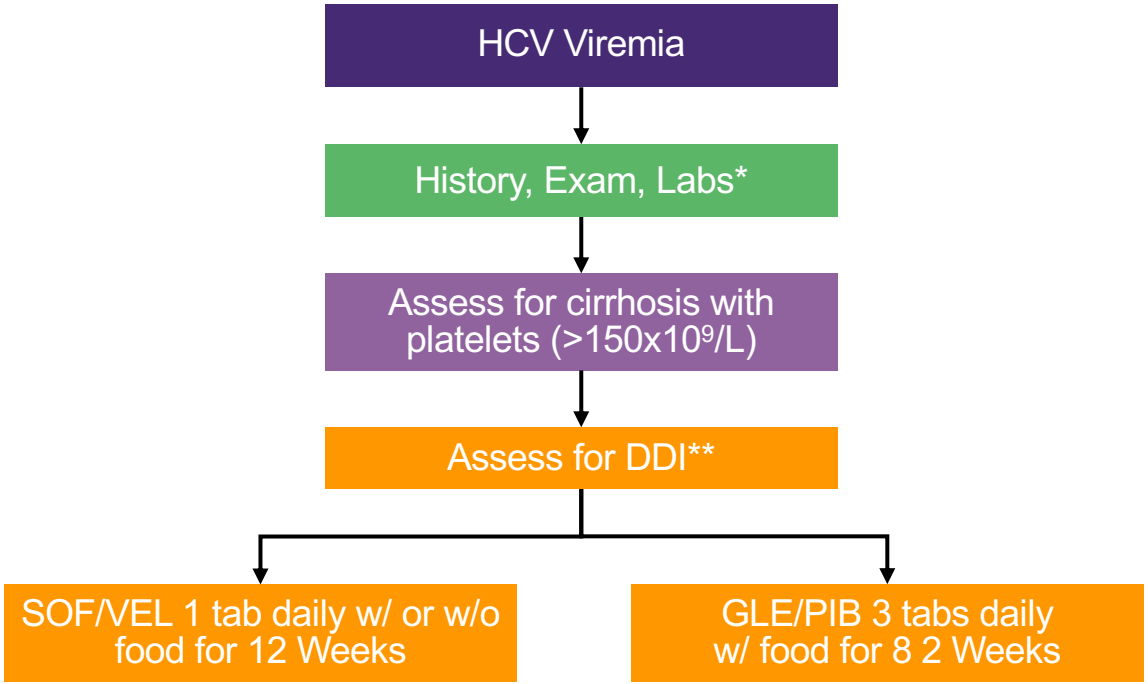
1. He T, et al. *Ann Intern Med*. 2016. **2.** Suryaprasad AG, et al. *Clin Infect Dis.* 2014. **3.** *Hepatitis C in Corrections Trends Report With Parallels and Perspectives on HIV.* 1st ed. Foster City, CA: Gilead Sciences, Inc.; 2017.

The Approach to Testing, Diagnosis and Treatment of Hepatitis C Must Evolve to a Decentralized Model of Care

	Testing	Linkage to care	Treatment uptake	Treatment adherence
Barriers	**Asymptomatic disease** **Poor awareness/education** **Lack of medical coverage** **MD failure to screen/test**	**Non-adherence** **MD failure to refer** **Logistical concerns** **Limited specialist availability**	**Patient fears/misunderstandings** **Stigmatization** **Substance abuse** **Psychiatric comorbidity** **Financial concerns** **Transportation/logistical concerns** **Communication difficulties**	
Corrective	Improved access to HCV testing Improved education about testing Prompts for testing	Access to HCV care providers Improved access to care (universal access) Co-localized testing and treatment facilities	Education about Importance of treatment Psychological and harm reduction services for comorbid conditions Resources for primary care to treat HCV	Treatment of opioid addiction Psychological and harm reduction services for comorbid conditions Directly observed therapy

McGowan CE, et al. *Liver Int.* 2012. Millman A, et al. *Top Antivir Med*. 2017.

How Simple Can Treatment Become for Most Patients?



*Assessment labs: CBC, AST, ALT, bilirubin, albumin, creatinine, HBV, HIV, HAV; eGFR
**HCPs should consult prescribing information, their local pharmacist and/or online tools (eg, HEP Drug Interactions; http://www.hep-druginteractions.org) to confirm interaction or lack of interaction for specific drugs within a class, as exceptions may exist.

Modified from Dieterich et al, *Gastroenterol Hepatol* 2019

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- Clarify milestones needed for hepatitis C elimination

Declining HCV incidence following rapid HCV treatment scale-up in a prison network in Australia: Evidence of treatment as prevention from the SToP-C study

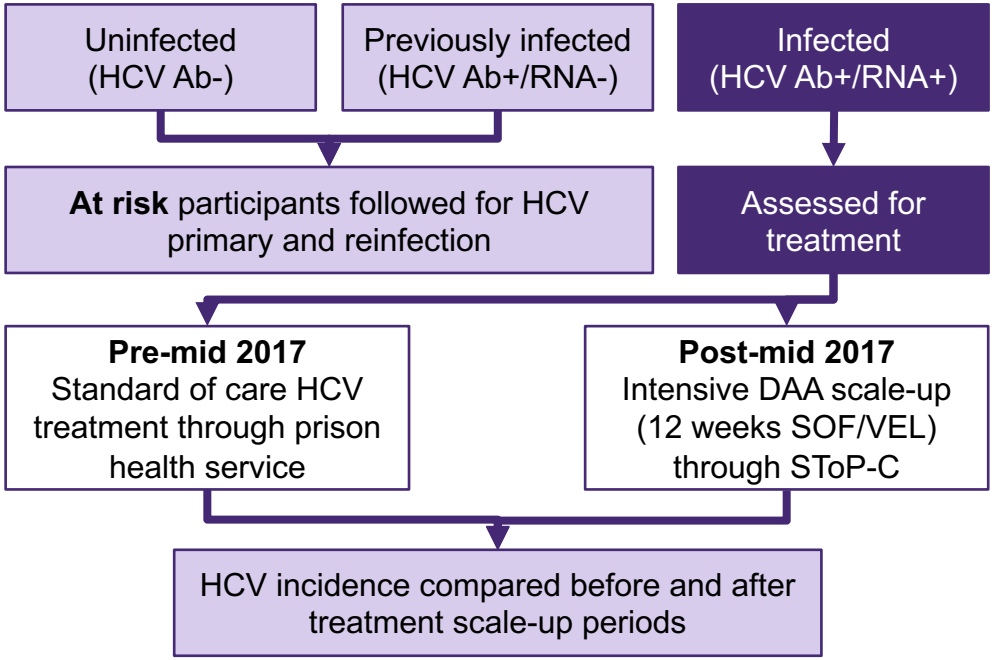
BACKGROUND AND AIMS

- There are no large-scale interventional trials supporting HCV treatment as prevention
- **AIM**: the Surveillance and Treatment of Prisoners with hepatitis C (SToP-C) study aimed to assess HCV treatment as prevention in 4 Australian prisons

METHODS

- SToP-C enrolled people incarcerated in 4 prisons*
  - 2 maximum security: both male
  - 2 medium security: 1 male, 1 female
- OAT but no NSP was available

- 3 populations of participants were monitored every 6 months for risk factors and HCV†



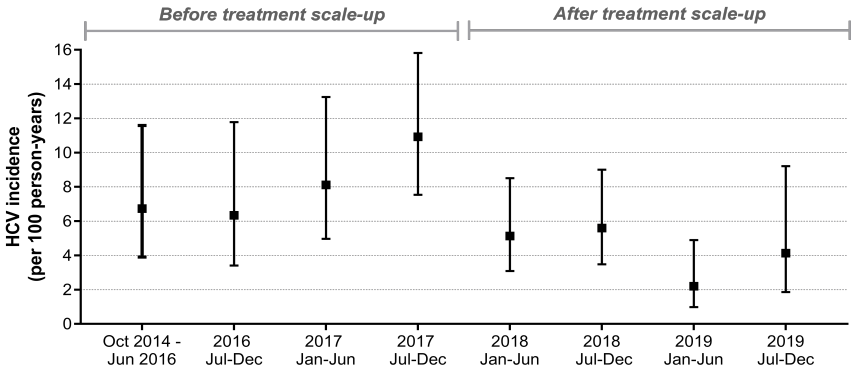
*Enrolment commenced in October 2014 with final follow-up in November 2019;
†Following HCV antibody and RNA screening

Dore G, et al. DILC 2020; LBP07

Declining HCV incidence following rapid HCV treatment scale-up in a prison network in Australia: Evidence of treatment as prevention from the SToP-C study

RESULTS

- 3,691 participants enrolled*
  - At risk of primary infection (Ab-): 2,240 (61%)
  - At risk of reinfection (Ab+/RNA-): 725 (20%)
  - HCV RNA+: 719 (19%)
- DAA treatment initiated in 352/484 (73%) HCV RNA+ participants during scale-up period
- At-risk population with longitudinal follow-up (n=1,643)
  - Median age 33 years; 82% male
  - 31% reported injecting drug use in prison
- HCV incidence (1,818 person-years [py] follow-up)
  - Overall: 6.1/100 py (95% CI: 5.1, 7.4)
  - Primary infection: 4.6/100 py (95% CI: 3.6, 5.9)
  - Reinfection: 9.3/100 py (95% CI: 7.2, 12.2)



- Overall HCV incidence: ↓48% from 8.3/100 py (95% CI: 6.5, 10.6) to 4.4/100 py (95% CI: 3.2, 5.6; p<0.001)
- Primary infection: ↓67% from 6.6 to 2.9/100 py (p=0.02)
- Reinfection: ↓41% from 12.4 to 7.3/100 py (p=0.05)

CONCLUSION Rapid scale-up of DAA therapy associated with HCV incidence reduction in prison, indicative of HCV treatment as prevention. Findings support broad DAA scale-up and enhanced harm reduction in prison, particularly for prevention of reinfection

*Enrolment coverage was 53−89% across prisons

Dore G, et al. DILC 2020; LBP07

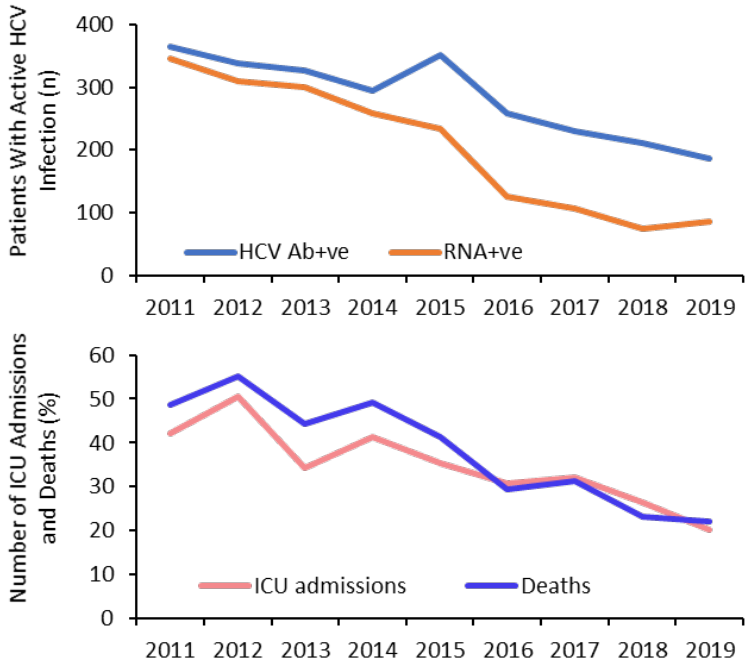
DAAs Have Substantially Modified the Profile of Patients With Cirrhosis Who Require Hospitalization in Spain

A review of electronic health records to evaluate the impact of DAAs on patients with liver cirrhosis admitted to a referral liver unit of a Spanish university hospital

Between 2011 and 2019, 6272 patients were identified:

- **HCV-related hospital admissions** remained stable during 2011–2014 (525/year, 48.8% of total), and decreased after 2015 (P<0.001)
- **HCV liver cirrhosis** accounted for **3885 inpatient days/years** (44.9%) during 2011–2014 and decreased steadily after (P>0.001)
- A significant increase in hospital admissions due to **metabolic fatty liver disease** (5-fold) and **autoimmune hepatitis** (4-fold) was observed during 2011–2019

Using a binomial regression model analysis, **hospital admissions due to HCV liver cirrhosis will be residual by 2025** (2.3%, 95% CI: 0–10.9%)



Data from a Spanish database showed that use of DAAs has resulted in a marked decrease in hospital morbidity and mortality attributable to patients with HCV-related liver cirrhosis

Rodríguez-Tajes, EASL 2020 Poster 384

Recent decline in hepatocellular carcinoma rates in the United States

BACKGROUND & AIMS

- Rates of HCC in the US have increased over several decades
- Rates were projected to increase ~3% per year through 2030
- **AIM**: to assess HCC rates through 2016

METHODS

- HCC incidence data were obtained from SEER-21, a group of population-based cancer registries covering 37% of the US population
- HCC cases identified using ICD-O, 3rd edition codes
  - Site: C22.0,
  - Histology: 8170−8175
- Estimated incidence rates were age-standardized to the 2000 US population
  - Estimated overall and by sex, age and ethnicity
- Annual percent changes (APCs) estimated using joinpoint regression*
- Rate ratios (RRs) comparing 2016 to 2015 were estimated

*Identifies statistically significant inflection points in rate trajectories

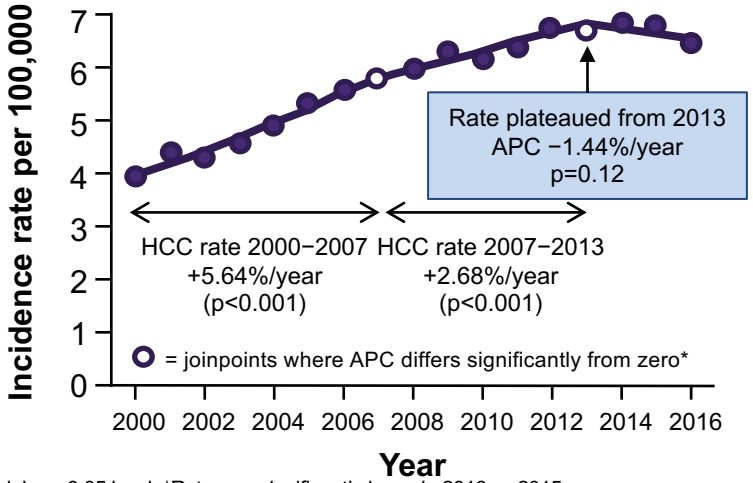
Shiels M, O'Brien T. DILC 2020; SAT331

Recent decline in hepatocellular carcinoma rates in the United States

RESULTS

- HCC rates increased between 2000 and 2013
  - Rates started to plateau in 2013
  - HCC incidence significantly lower in 2016 vs 2015 (RR=0.96; p=0.007)

HCC incidence rates in 21 US cancer registries



*At the alpha = 0.05 level; †Rate was significantly lower in 2016 vs 2015

Trends in HCC change by age and ethnicity

	From year	APC (%/yr)	p-value
Age			
35−49 years	2006	↓ 4.93	<0.001
50−64 years	2014	↓ 6.64	0.04
≥65 years	Throughout	↑ 2.69	<0.001
Ethnicity			
Caucasian	2013	↓ 0.91	0.45
Black	2009	↑ 0.27	0.65
Hispanic†	2014	↓ 6.55	0.08
Asian	2007	↓ 2.72	<0.001
Native American	Throughout	↑ 4.60	<0.001

CONCLUSION

- Decades-long increasing HCC incidence was projected to continue in the US through 2030
- However, HCC rates flattened in 2013, declining in 2016
- Tide has begun to turn for HCC incidence in the US

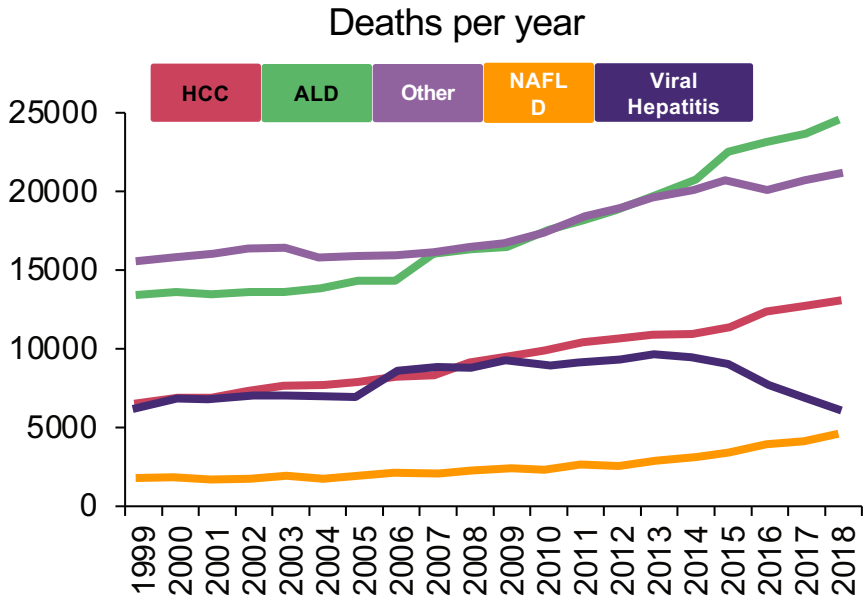
Shiels M, O'Brien T. DILC 2020; SAT331

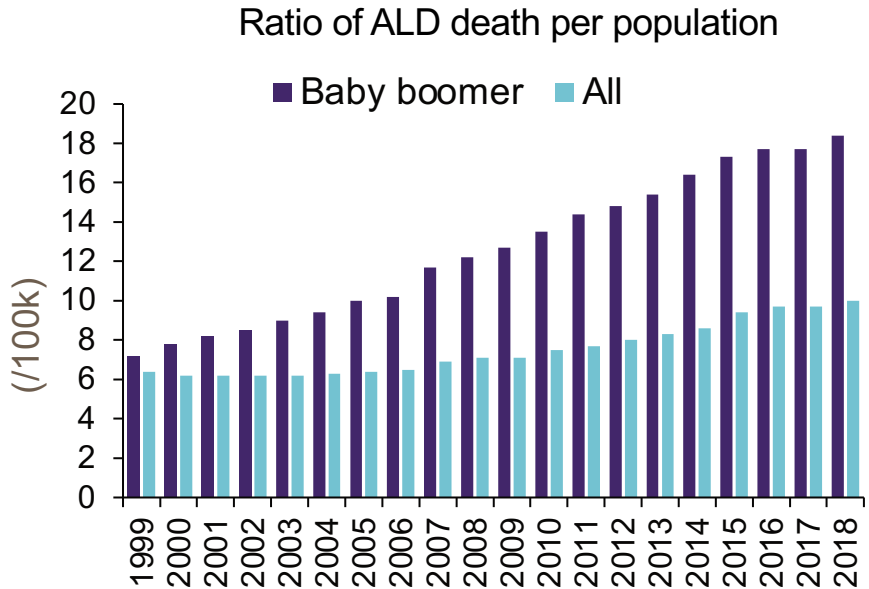
The 22-year trend of liver diseases in the US

Data were extracted between 1999 - 2018 from the annual National Vital Statistics Reports (deaths: Final Data) from the CDC

ICD 10 codes defined as:

- Alcohol liver diseases: K 70
- Others: K73–74
- Viral hepatitis: B15–19
- Non alcoholic fatty liver disease: K 76.0





HCC, hepatocellular carcinoma; ALD, alcoholic liver disease; NAFLD, non-alcoholic fatty liver disease.

Okumura K, AASLD 2020 Poster Presentation #715

The 22-year trend of liver diseases in the US

	Mortality rate (per 100k)		Trend segment 1		Trend segment 2	
	1999	2018	Year	APC	Year	APC
HCC	1.8	3.6	1999–2018	**3.7***		
ALD	4.3	7.1	1999–2005	0.07	2005–2018	**4.0***
Others	5.1	6.0	2005–2014	**3.0***	2014–2018	0.3
NAFLD	0.1	0.9	1999–2006	**5.8***	2006–2018	**14.4***
Viral hepatitis	1.7	1.5	2007–2014	0.6	2014–2018	**-12.6***

*P<0.05.
HCC, hepatocellular carcinoma; ALD, alcoholic liver disease; NAFLD, non-alcoholic fatty liver disease; APC, annual percent change.

- Deaths from liver disease in the US have increased, and in 2018 they were the highest ever reported by the CDC
- While the deaths from viral hepatitis showed dramatic improvement due to therapy drugs, deaths from ALD, NAFLD, and HCC continued to increase
- The burden of alcoholic liver disease has increased, especially in baby boomers

Okumura K, AASLD 2020 Poster Presentation #715

Incidence Of Liver-related Events In 647 DAA-cured HCV Cirrhotic Patients: A 5-year Single-center Study

AIMS

Study long-term impact of an SVR on liver-related events (LRE) incidence and mortality in a large cohort of HCV cirrhotics

METHODS

Consecutive HCV cirrhotics treated with DAA (December 2014-June 2019) from single center.

Exclusion criteria were treatment on liver transplant waiting list and LRE before SVR.

LRE included hepatocellular carcinoma (HCC), ascites, variceal bleeding and encephalopathy (PSE).

Cohorts: A ~ CPT-A without previous LRE
B ~ previous non-HCC LRE
C ~ previous HCC

Characteristics at Baseline	Cohort A (n=486)	Cohort B (n=91)	Cohort C (n=70)
Age, years	64 (24-92)	63 (42-92)	73 (51-86)
Males	286 (59%)	50 (55%)	42 (60%)
BMI, Kg/m^2	25 (16-42)	25 (18-35)	25 (18-36)
Diabetes	94 (19%)	26 (29%)	11 (15%)
LSM, kPa	17.0 (4.9-75.0)	22.5 (6.9-75.0)	18.0 (3.5-36.3)
HCV-1b	234 (48%)	43 (47%)	48 (53%)
HBsAg Anti-HBc positive	6 (1%) 196 (40%)	2 (2%) 45 (49%)	3 (4%) 35 (50%)
ALT, U/L	81 (9-770)	49 (8-233)	58 (16-268)
GGT, U/L	72 (10-890)	60 (11-400)	67 (16-643)
Platelets, 10^3/mm^3	129 (27-753)	79 (26-393)	128 (32-471)
Bilirubin, mg/dL	0.8 (0.2-5.4)	1.5 (0.3-6.3)	0.9 (0.3-2.7)
INR	1.0 (0.8-1.9)	1.2 (0.9-2.0)	1.1 (0.9-1.6)
Albumin, g/dL	4.2 (2.1-5.5)	3.4 (2.3-5.1)	4.0 (2.7-4.9)
AFP, µg/L	9 (1-468)	9 (1-537)	10 (2-192)
Varices	118 (33%)	65 (75%)	29 (47%)
Child-Pugh Score A	486 (100%)	29 (32%)	62 (89%)

Values expressed as n (%) or median (range)

Roberta D'Ambrosio et al. AASLD 2020

Incidence Of Liver-related Events In 647 DAA-cured HCV Cirrhotic Patients: A 5-year Single-center Study

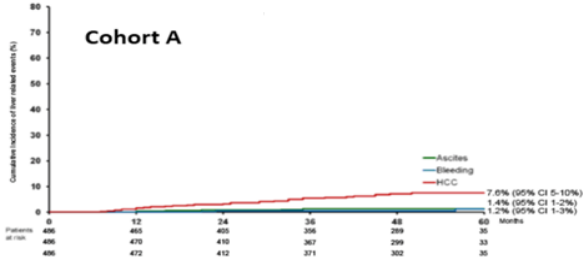
RESULTS ~ Multivariable analysis

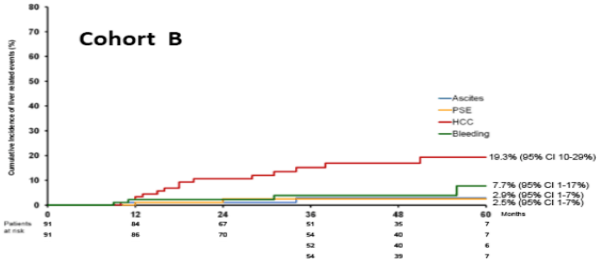
- **Cohort A ~** male gender (HR 2.93, p=0.03), diabetes (HR 2.49, p=0.02), anti-HBc positivity (HR 2.20, p=0.04) and liver stiffness at DAA start (HR 1.05, p=0.01) were independently associated with post- SVR Lre

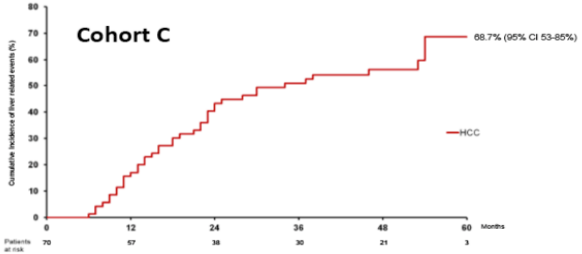
- **Cohorts B and C** ~ diabetes (HR 2.50, p=0.001), anti-HBc positivity (HR 2.13, p=0.007), yGT (HR 1.00, p=0.009) and albumin values at DAA start (HR0.54, p=0.01) independently predicted HCC (Cohorts A+B).

~ Mortality

- 21 patients died because of LRE (57% HCC, 43% ESLD).
- 5-year cumulative mortality
  - Cohort A 0.5% (95% CI 0.2-1%); Cohort B 16.5% (95% CI 0.2-1%); Cohort C, 16.5% (95% CI 6-27% (respectively (p<0.0001).







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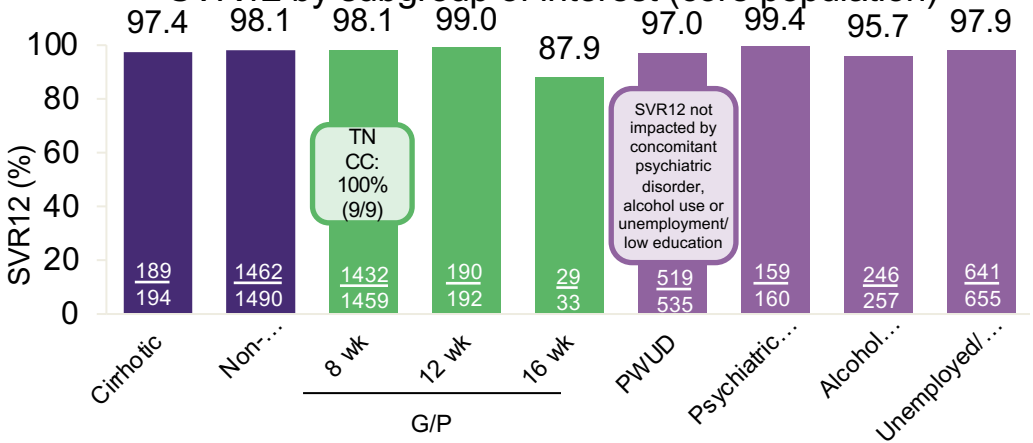
Real-world clinical outcomes in HCV-infected patients with psychiatric and substance use disorders treated with G/P for 8 or 12 weeks: Pooled analysis across 9 countries

- PMOSs across 9 countries to evaluate outcomes of G/P in 2036 marginalized patients

Baseline characteristics, n (%)		Total population (N=2036)
GT1/2/3/4–6		1048 (52) / 191 (9) / 581 (29) / 192 (9)
Non-cirrhotic		1782 (88)
HCV Tx-naïve		1760 (87)
HCV Tx-experienced		271 (13)
G/P	8 weeks	1701 (84)
	12 weeks	295 (14)
	16 weeks	40 (2)
PWUD		697 (35)
Psychiatric disorder		200 (10)
History of alcohol use		322 (18)
Unemployed/no–low education		835 (45)

SVR12 in the core population with sufficient F/U: 98% (1651/1684)
6 VF, 15 relapse, 4 d/c, 2 missing data, 6 other

SVR12 by subgroup of interest (core population)



- SVR12 not impacted by the number of concomitant medications
- Clinically meaningful improvement in MCS and PCS scores (≥2.5) were experienced by 49.5% and 43.8% of patients, respectively
- G/P was well tolerated with low rates of AEs leading to d/c and no DILI

- Patients with substance use and psychiatric disorders managed with multiple medications to achieve high rates of SVR with G/P similar to the general population

Lampertico P, et al. EASL dILC2020. #THU440

Opportunities to enhance linkage to HCV care among people hospitalised for injection drug use-related complications: population-based study

BACKGROUND AND AIMS

- To achieve HCV elimination by 2030, testing and treatment among high-risk populations need to be enhanced
- **AIMS**:
  - To characterise subpopulations of people with HCV based on indicators of recent and distant drug dependence during the DAA era*
  - To assess DAA treatment initiation by recent (2016−2018) hospitalization history
  - To evaluate the potential for hospital admissions to improve linkage to HCV care among people with evidence of recent drug dependence

METHODS

- HCV notifications in NSW, Australia between 1995 and 2017 were linked to:
  - OAT (1985–2018)
  - Hospital admissions (2001–June 2018)
  - Deaths (1993–2018)
  - HCV treatment (2010–2018)
- Drug dependence was defined as:
  - Injecting drug use-related hospitalization† OR
  - Receipt of OAT
- Drug dependence between 2016–2018 was ‘recent’, while pre-2016 was ‘distant’
- HCV treatment-eligible population estimated
  - Records weighted to account for potential spontaneous clearance
- Primary diagnosis for each hospital episode was categorized using ICD
  - Re-categorized into cause-specific outcomes including mental health, drug, alcohol, and liver-related admissions (2015–2018)

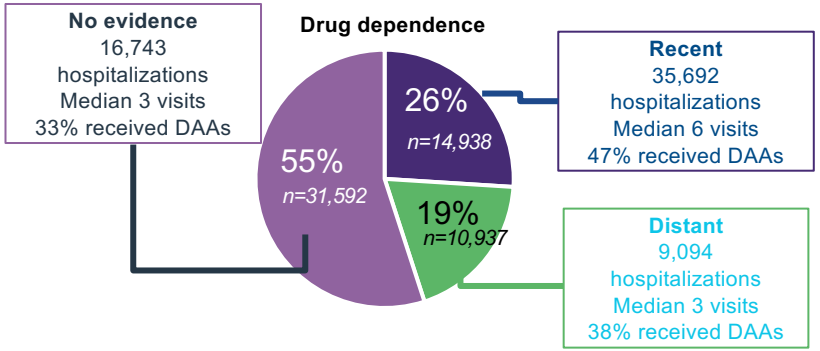
*2015−2018; †Admissions occurring due to injectable drugs and/or injection-related infections

Valerio H, et al. DILC 2020; SAT309

Opportunities to enhance linkage to HCV care among people hospitalised for injection drug use-related complications: population-based study

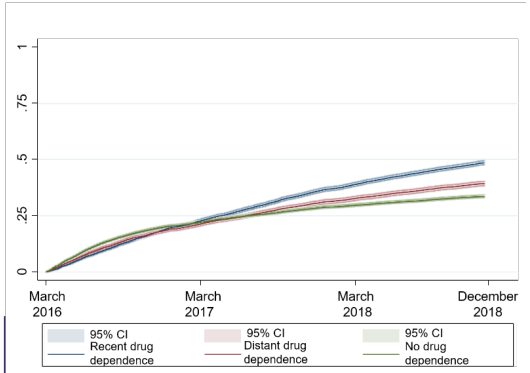
RESULTS

- 57,467 people with HCV notification were alive and treatment eligible (2016–2018)

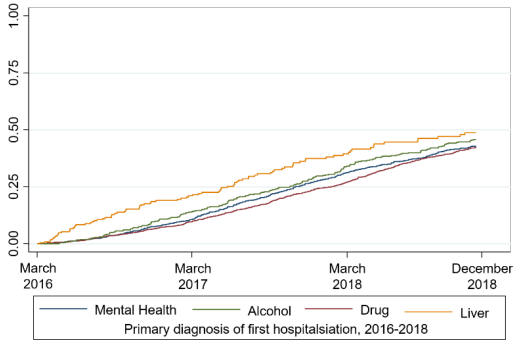


- 2016–2018: mental health, drug, alcohol and liver-related hospitalization incidence highest in people with recent drug dependence
- People with recent drug dependence 28% (n=4,222) contributed to a total of 14,938 long-stay (≥7 days) hospital admissions
  - Majority due to mental and behavioural disorders, particularly those relating to schizophrenia

KM curve: estimated time to initiation onto DAA therapy by drug dependence



KM curve: estimated time to initiation onto DAA therapy by primary diagnosis of first hospitalization, among those with recent drug dependence



CONCLUSION

- In people with HCV notification and evidence of recent drug dependence frequent hospitalization, particularly mental health, drug, and alcohol admissions, is an opportunity for HCV testing and linkage to care

Valerio H, et al. DILC 2020; SAT309

Externalized HCV linkage-to-care cascade in the biggest harm reduction center in Barcelona: Approaching a high-risk PWID population

- Recruitment and treatment of PWID in an externalized outpatient clinic

845 PWID offered screening

386 (46%) accepted

459 (54%) declined

212 (55%) HCV-RNA +ve

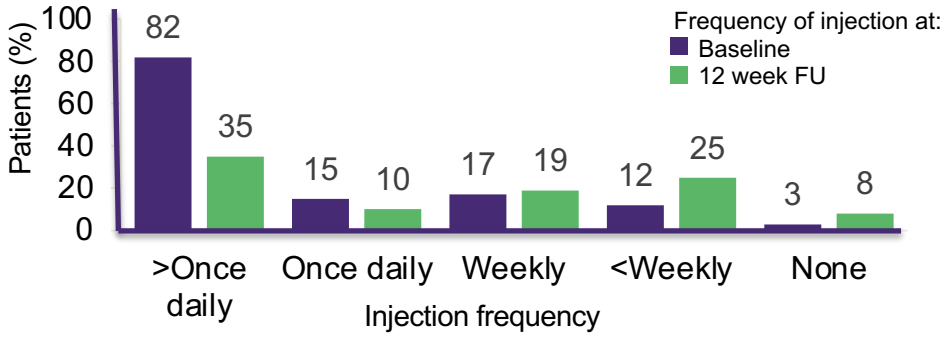
63 (30%) did not initiate therapy

149 (70%) initiated DAA

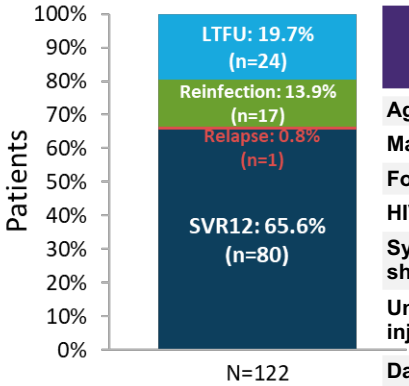
98 (66%) SVR assessment

- 85% completed ≥80% of therapy (43% within expected 8/12 wks)
- Daily drug use associated with lower rates of tx completion within 8/12 wks

Treatment was associated with a significant decrease in injection frequency, regardless of outcome (P<0.001)



Outcomes at 12 week follow-up

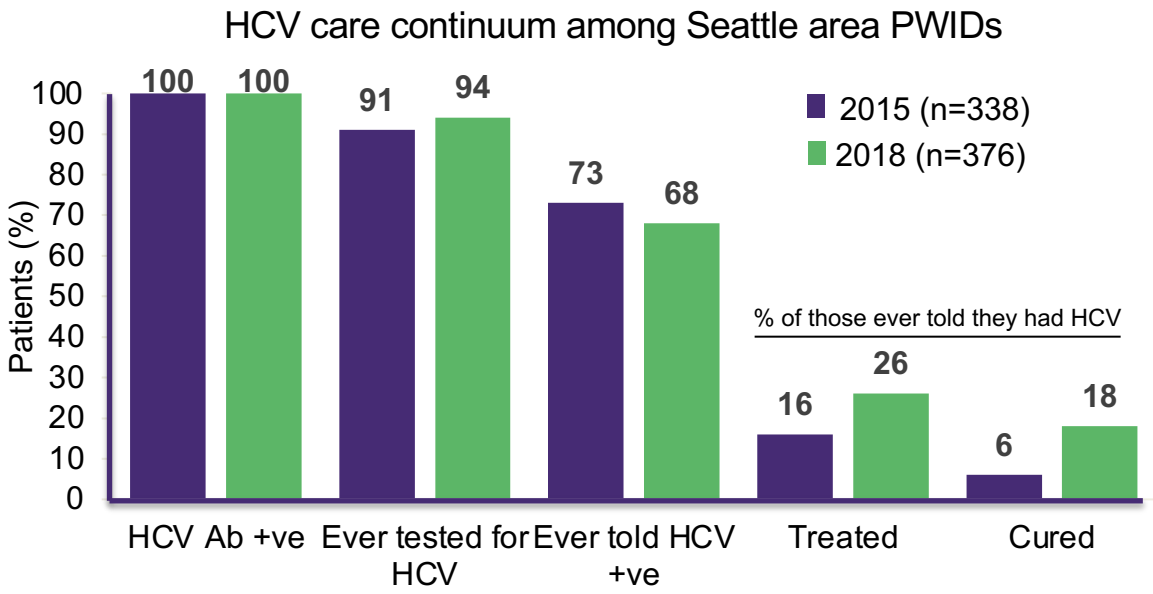


	Reinfection n=17	No reinfection n=80	P
Age (years)	42 (35–47)	44 (34–49)	0.62
Male	100%	85%	0.23
Foreign	53%	30%	0.002
HIV +ve	41%	15%	0.039
Syringe sharing	30%	10%	0.03
Unsafe injection	80% (12/15)	38% (27/70)	<0.001
Daily drug use at FU12	65%	56%	0.45

- Despite the use of onsite POC testing, screening in this setting remained low (46%)
- Initiation of HCV therapy resulted in reduced rates of injection use
- Reinfection rates were high in patients with ongoing risk behavior

Lens S, et al. EASL dILC2020. #THU444

HCV continuum of care and predictors of DAA treatment among PWIDs in Seattle, Washington, USA



- Of 533 PWID identified in 2018, 376 (71%) were HCV Ab +ve:
  - Mean age 41.6 years, 60% male, 73% white, 59% homeless
  - HCV Ab prevalence increased with age
  - 48 (13%) reported prior DAA treatment

- In 2018, disparity was evident between genders among PWIDs who had ever been told they had HCV (male n=160; female n=92):
  - Treated: males 31% vs females 16%
  - Cured: males 22% vs females 12%

Predictors of having received DAA therapy, 2018

		Adjusted OR (95% CI)
Age	+ve predictor	1.04 per year (1.01, 1.07)
Homelessness	–ve predictor	0.43 (0.21, 0.86)
Female gender	–ve predictor	0.33 (0.15, 0.70)

- Despite high rates of screening among PWID, linkage to care and treatment initiation remains low
- Women are less likely to initiate treatment with DAA regimens compared to men

Corcorran M, et al. EASL dILC2020. #SAT291

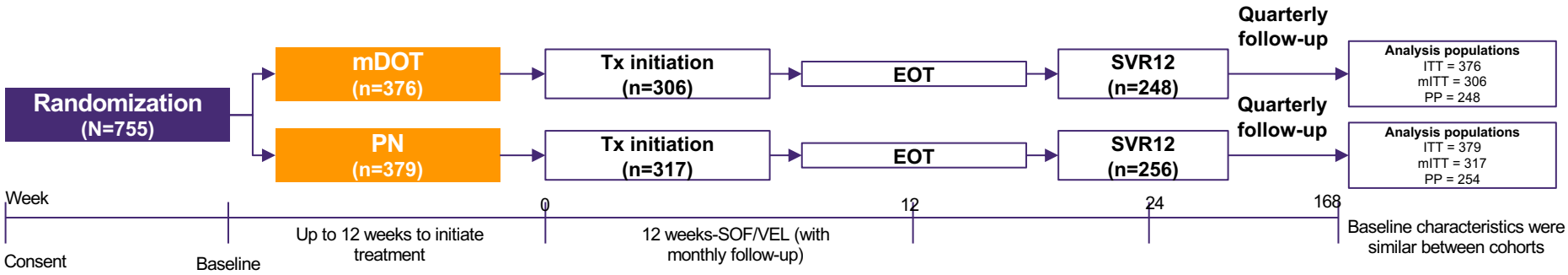
HERO Study: Patient-centered PWID Model
Methods

Objective

- To compare real-world SVR12 rates in active PWID among those who initiated treatment using modified Directly Observed Therapy (mDOT) compared with Patient Navigation (PN)

Study design

- The Hepatitis C Real Options (HERO) Study:
  - TN active PWID (use within the last 3 months) with HCV GT1–6 with and without HIV
  - Patients enrolled at community-based clinics / opioid treatment programs across 25 sites in 8 US states



mDOT, modified Directly Observed Therapy; PN, patient navigation; Tx, treatment; EOT, end of treatment; ITT, intent to treat; mITT, modified intent to treat; PP, per protocol.

Litwin A, AASLD 2020 Late Breaking Oral Presentation LO10

HERO Study: Patient-centered PWID Model
Baseline characteristics

Baseline characteristics, n (%)*	mDOT n=376	PN n=379	Total n=755
Male	262 (70)	266 (70)	528 (70)
Race			
White	226 (62)	250 (68)	476 (65)
Black	66 (18)	37 (10)	103 (14)
Other	70 (19)	81 (22)	151 (21)
Age <40 years	165 (44)	169 (45)	334 (44)
GT1	185 (74)	183 (69)	368 (72)
GT2	22 (9)	23 (9)	45 (9)
GT3	39 (16)	55 (21)	94 (18)
Unstable living situation	192 (52)	207 (56)	399 (54)
Employed with regular job or informal work	135 (37)	122 (33)	257 (35)
Opioid treatment program	153 (41)	159 (42)	312 (41)
Community-based clinic	223 (59)	220 (58)	443 (59)
Buprenorphine in past 3 months	59 (16)	48 (13)	107 (15)
Methadone in past 3 months	194 (54)	205 (57)	399 (56)
HIV coinfection	52 (20)	50 (19)	102 (20)
Urine drug screen results at baseline			
Any drug	326 (96)	329 (96)	655 (96)
Benzodiazepine	175 (52)	183 (53)	358 (53)
Opiate	180 (53)	170 (49)	350 (51)
Cocaine	148 (44)	139 (41)	287 (42)
Amphetamine	97 (29)	96 (28)	193 (28)
Methamphetamine	106 (31)	112 (33)	218 (32)
Oxycodone	94 (28)	88 (26)	182 (27)

*N (%) as reported in the presentation. %'s not aligning with n's may be due to missing data.

- 76% had injected within the past month prior to baseline
- 48% injected >2 times/day
- Urine toxicology conducted every 4 weeks showed no change in drug use during treatment

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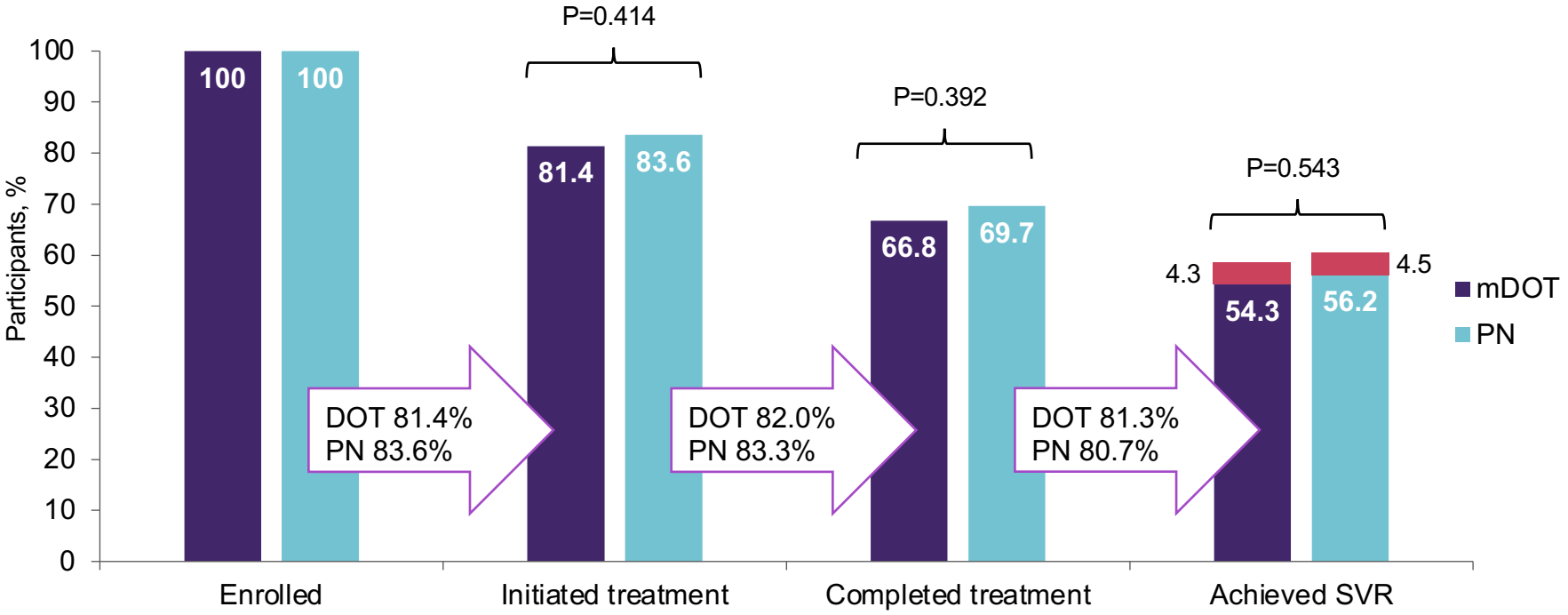
HERO Study: Patient-centered PWID Model
Cascade of care



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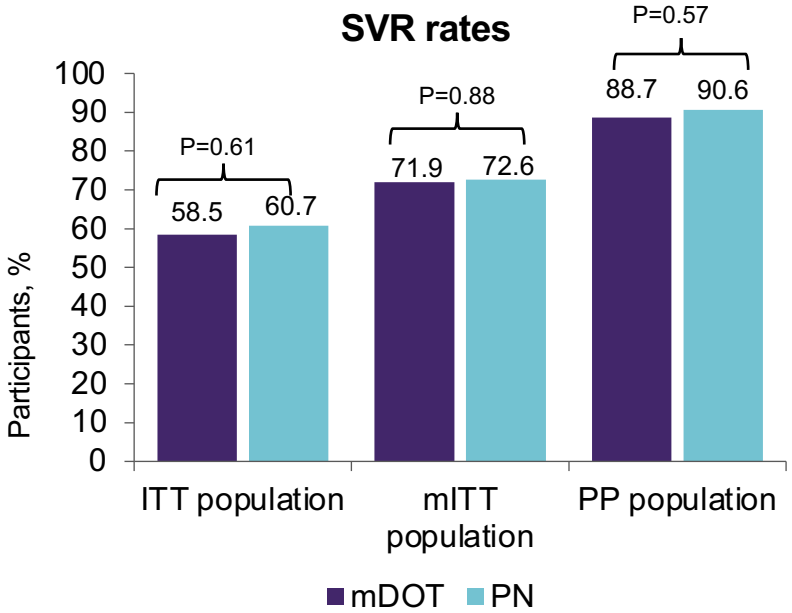
HERO Study: Patient-centered PWID Model
Results



19% of patients were LTFU in the mITT analysis

Predictors of SVR

	mITT population		PP population	
	OR (95% CI)	P	OR (95% CI)	P
10% increase in adherence	1.5 (1.3–1.7)	<0.0001	1.5 (1.3–1.9)	<0.0001
100% treatment completion	9.5 (5.8–15.6)	<0.0001	9.0 (4.3–18.8)	<0.0001
10-day increase in treatment duration	1.3 (1.2–1.4)	<0.0001	1.7 (1.4–2.1)	<0.0001

70% increased odds of achieving SVR with every 10 days of adherence to a 12-week treatment

mDOT, modified Directly Observed Therapy; PN, patient navigation; ITT, intent to treat; mITT, modified intent to treat; PP, per protocol; OR, odds ratio; LTFU, lost to follow-up.

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HERO Study: Patient-centered PWID Model Predictors of SVR

		mITT population	
		SVR	Adjusted OR (95% CI; p-value)
Age	≥40 <40	272/348 (78.2) 178/75 (64.7)	1.77 (1.2-2.62; p=.004)
Hispanic/Latino	Yes No	112/136 (82.4) 338/487 (69.4)	2.14 (1.12-4.07; p=.021)
Housing	Stable Unstable	241/299 (80.6) 208/323 (64.4)	2.56 (1.72-3.81; p<.001)
OUD Tx 3 mo. Prior	Methadone Buprenorphine	280/358 (78.2) 45/85 (52.9)	2.24 (1.3-3.85; p=.004)
Injecting/day	>2 ≤2	175/274 (63.9) 249/316 (78.8)	0.53 (0.36-0.78; p=.001)
Last drug injection	5-12 weeks 0-4 weeks	122/152 (80.3) 328/471 (69.6)	2.17 (1.35-3.49; p=.001)

Estimates are adjusted for study arm and site.
OR, odds ratio; OUD, opioid use disorder; Tx, treatment;

Litwin A, AASLD 2020 Late Breaking Oral Presentation LO10

HCV elimination in homeless patients is possible: a pooled real-world analysis of homeless with HCV treated with SOF/VEL for 12 weeks

BACKGROUND AND AIMS

- This real-world analysis evaluates the effectiveness of SOF/VEL as a simple strategy to treat HCV-infected patients who are homeless, and the feasibility of a test-and-treat strategy in this vulnerable population

Patient characteristics	Overall population (n=153)	Effectiveness population (n=122)
Age, years, mean (standard error)	45* (0.9)	46.3 (11)
Sex, male, n (%)	136 (88.9)	109 (89.3)
Fibrosis stage, n (%)		
F0–F2	108 (70.6)	82 (67.2)
F3	21 (13.7)	18 (14.8)
F4	19 (12.4)	18 (14.8)
Unknown	5 (3.3)	4 (3.3)
Treatment history, n (%)		
Treatment-naïve	140 (91.5)	111 (91.0)
Treatment-experienced (DAA-naïve)	13 (8.5)	11 (9.0)
Treatment history unknown	0 (0)	0 (0)
HCV GT, n (%)		
GT1	56 (36.6)	43 (35.2)
GT2	2 (1.3)	2 (1.6)
GT3	65 (42.5)	54 (44.3)
GT4–6	7 (4.6)	6 (4.9)
GT mixed/unknown	23 (15.0)	17 (13.9)
Time from RNA diagnosis to SOF/VEL treatment start, n (%)		
<1 day	17 (12.7†)	14 (13.1†)
≤1 week	27 (20.1†)	22 (20.6†)
≤1 month	78 (58.2†)	64 (59.8†)
≤3 month	112 (83.6†)	89 (83.2†)
≤6 months	117 (87.3†)	93 (86.9†)
>6 months	17 (12.7†)	14 (13.1†)
Unknown	19 (12.4)	15 (12.3)

*Data available for 149 patients
†Percentages calculated with the number of patients with time to treatment start available as denominator.

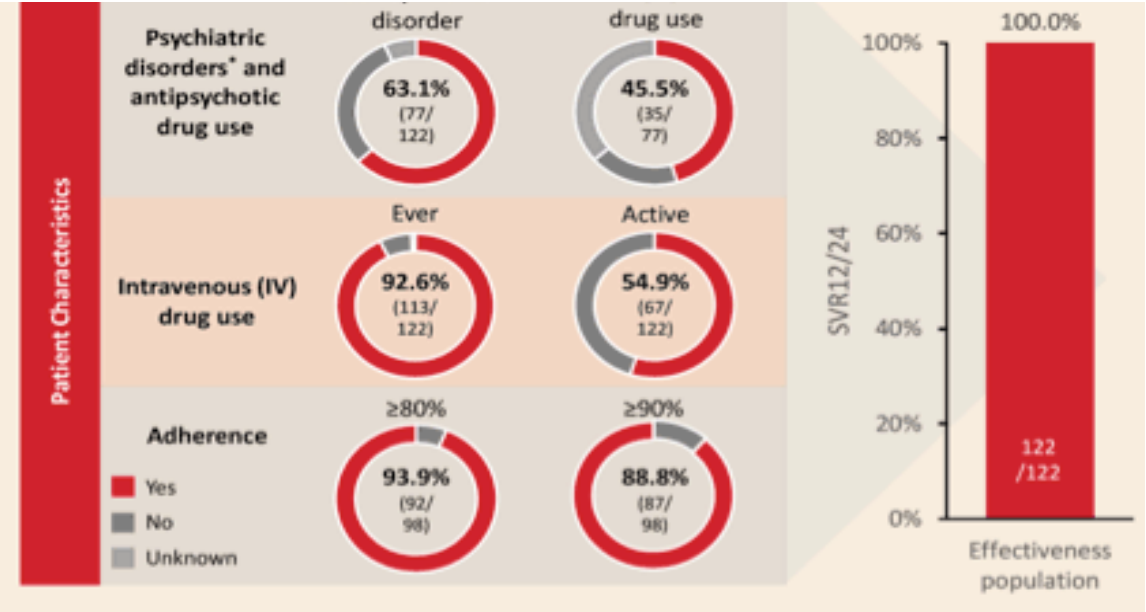
Rodriguez-Tajes et al. AASLD 2020

HCV elimination in homeless patients is possible: a pooled real-world analysis of homeless with HCV treated with SOF/VEL for 12 weeks

RESULTS

- Psychiatric disorders included anxiety (24.7%). Depression (29.9%). Mania/bipolar (6.5%), and cognitive/psychiatric disorder (71.4%): Advanced fibrosis is defined as F3 and F4, according to the treating physician.
- **SVR12/24** was **100%** across different **genotype (GT)** and **fibrosis (F)** stages, regardless of complicating factors such as **GT3 and advanced fibrosis** (20/122)

Patient characteristics and SVR12/24



Rodriguez-Tajes et al. AASLD 2020

Real World Expericence 8-week G/P in Substance Use Disorder Patients

- Data from 9 countries pooled for TN patients with HCV without cirrhosis or with compensated cirrhosis who had been prescribed 8-week G/P between 11/13/2017 & 3/5/2020*
- Eligible patients: ≥18 years, chronic HCV GT1–6, receiving G/P*
- Subgroups of interest: Patients who used illicit or non-prescribed drugs, had a psychiatric disorder, consumed ≥2 alcoholic drinks/day, were unemployed, or who had low/no education†

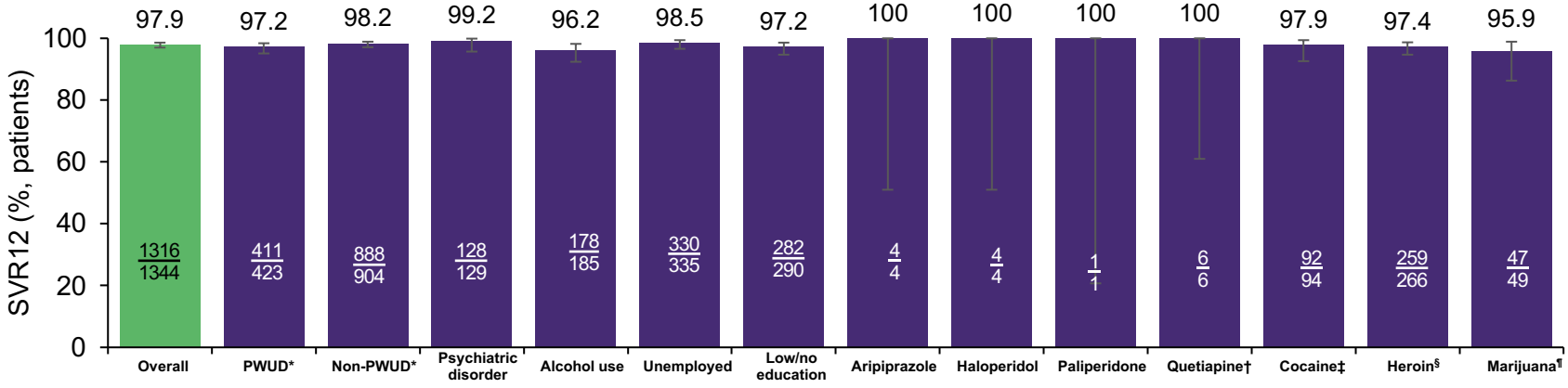
Characteristic, n (%)	Total population N=1522	CPSFU n=1344
Psychiatric disorders	128 (9.7)	129 (9.6)
History of alcohol use (≥2 drinks/day)	208 (13.7)	185 (13.8)
Unemployed	412 (27.1)	335 (24.9)
Low-to-no education	342 (22.5)	290 (21.6)
Prescribed psychotropic drug use		
Quetiapine	NR	6 (0.4)
Haloperidol	NR	4 (0.3)
Aripiprazole	NR	4 (0.3)
Paliperidone	NR	1 (<0.1)
PWUD total	500 (32.9)	423 (31.4)

Drugs* taken by >1% of the PWUD (safety population), n (%)	Total PWUD n=500
Heroin	318 (63.6)
Cocaine	110 (22.0)
Marijuana	55 (11.0)
Hashish	38 (7.6)
Opioids	19 (3.8)
Amphetamine	9 (1.8)
LSD	7 (1.4)
Opium	7 (1.4)
MDMA	7 (1.4)
Benzodiazepine	6 (1.2)

*Subgroups are nonmutually exclusive.
CPSFU, core population with sufficient follow-up; PWUD, person who uses drugs; LSD, Lysergic acid diethylamide; MDMA, 3,4-Methylenedioxymethamphetamine

Rizzardini G, AASLD 2020, Poster 929

Real World Experience 8-week G/P in Substance Use Disorder Patients: SVR12 of 8-weeks of G/P across patient subgroups, CPSFU (n=1344)



	Overall	PWUD*	Non-PWUD*	Psychiatric disorder	Alcohol use	Unemployed	Low/no education	Aripiprazole	Haloperidol	Paliperidone	Quetiapine†	Cocaine‡	Heroin§	Marijuana¶
On-treatment failure	6	1	5	1	2	2	2	0	0	0	0	1	0	0
Relapse	11	4	7	0	1	1	1	0	0	0	0	0	2	0
Treatment discontinuation	4	2	2	0	1	1	2	0	0	0	0	1	1	1
Missing SVR12 data	2	2	0	0	1	1	2	0	0	0	0	0	2	1
Other	5	3	2	0	2	0	1	0	0	0	0	0	1	0

*PWUD and non-PWUD subgroups (n=1,327) do not equal the Overall subgroup (n=1,344) because some patients did not have data related to PWUD status; †An additional 4 treatment-naïve/experienced patients taking quetiapine received G/P for 12 weeks, with a SVR12 of 100%; ‡An additional 22 treatment-naïve/experienced patients taking cocaine received G/P for 12 weeks, with a SVR12 of 100%; §An additional 44 treatment-naïve/experienced patients taking heroin received G/P for 12 weeks, with a SVR12 of 100%; ¶An additional 10 treatment-naïve/experienced patients taking marijuana received G/P for 12 weeks, with a SVR12 of 100%.

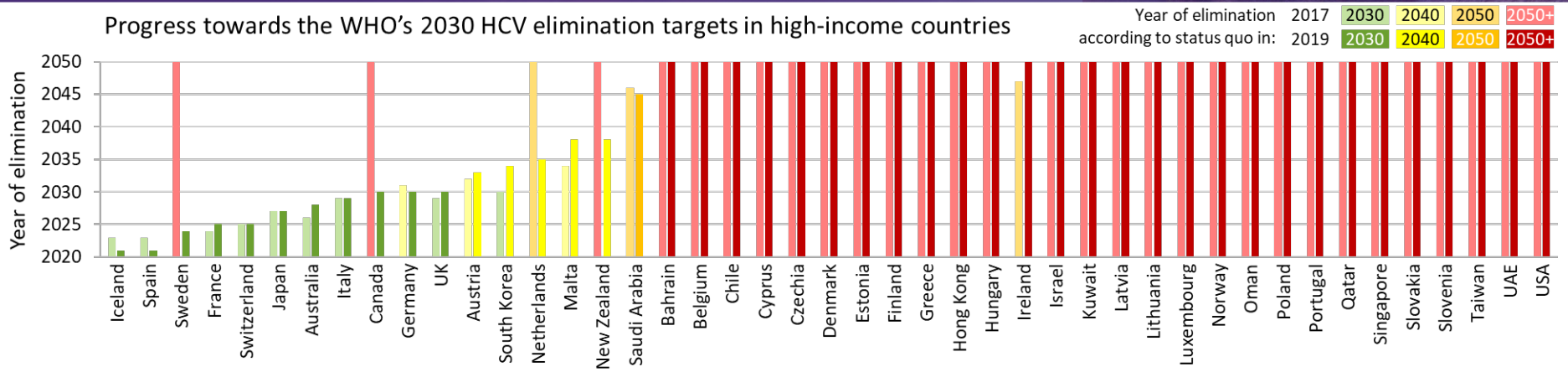
- Across a variety of real-world clinical settings, 8-week G/P treatment was effective in HCV-infected PWUD and other historically underserved patients
  - SVR12 rates were high despite complex patterns of drug use

Rizzardini G, AASLD 2020, Poster 929

Aims

- Demonstrate how the natural history and relative contribution to liver diseases have been altered by hepatitis C treatment
- Describe novel techniques to improve linkage of care and extend therapy to vulnerable populations infected with hepatitis C
- Clarify milestones needed for hepatitis C elimination

Global timing of HCV elimination in high-income countries: An updated analysis



- 11/45 high-income countries are on track to meet the 2030 HCV elimination target, 5 by 2040 and 1 by 2050
  - None of these has restrictions on treatment by fibrosis
- 28/45 high-income countries are off track by ≥20 years
  - 11 still have treatment restrictions by fibrosis score

3 countries off track in 2017 are now on track for 2030:

- **Canada**: via elimination efforts in two populous provinces
- **Germany**: via improved diagnosis
- **Sweden**: removed restrictions on treatment by fibrosis score

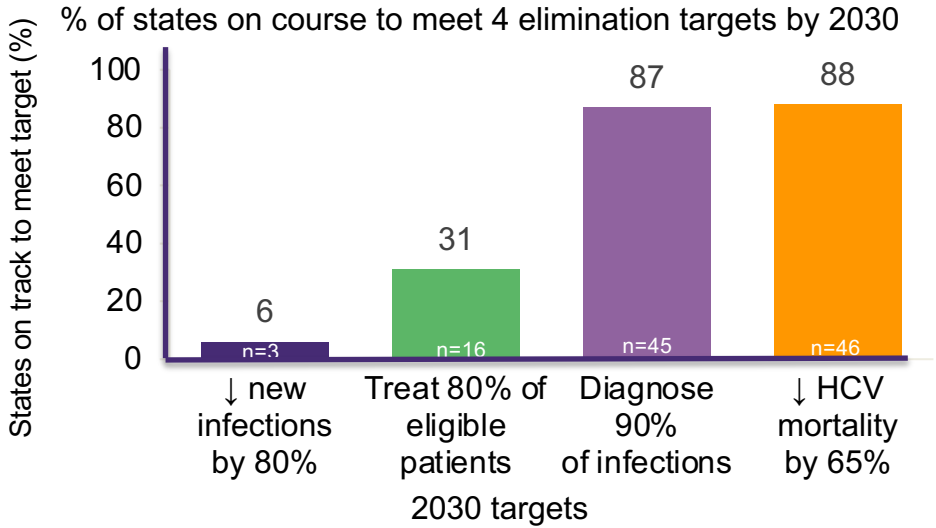
- A limited number of high-income countries are on track to meet the WHO HCV elimination target
- Improvements in the cascade of care are mandatory, including wide HCV screening (reflex testing after national recommendations), access to DAA without restrictions on liver fibrosis, preventive policies (OST, syringe exchanges…)

Razavi H, et al. EASL dILC2020. #THU365

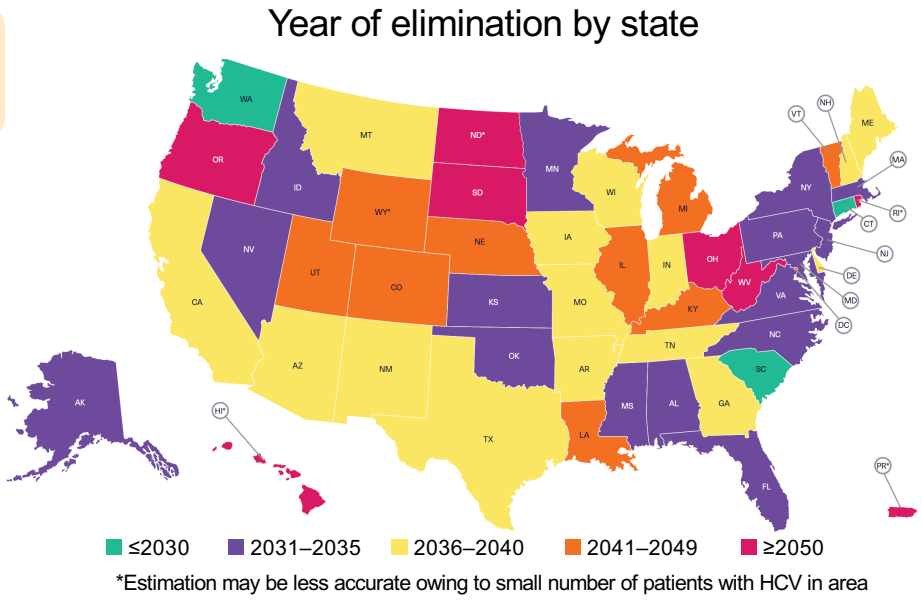
Timing of HCV elimination in the United States: Estimating the year each state will meet the WHO's elimination targets

The US is predicted to achieve elimination by 2037

- Diagnosis: 2027
- Incidence: 2037
- Treatment: 2033
- HCV mortality: 2020



- Of 9 states with treatment restrictions by liver fibrosis in 2017, none are on track to achieve elimination by 2030



*Estimation may be less accurate owing to small number of patients with HCV in area

- Significant progress in the US despite lingering barriers
- HCV elimination requires:
  - Unfettered access to HCV treatment
  - Prevention of acute HCV with harm reduction and treatment

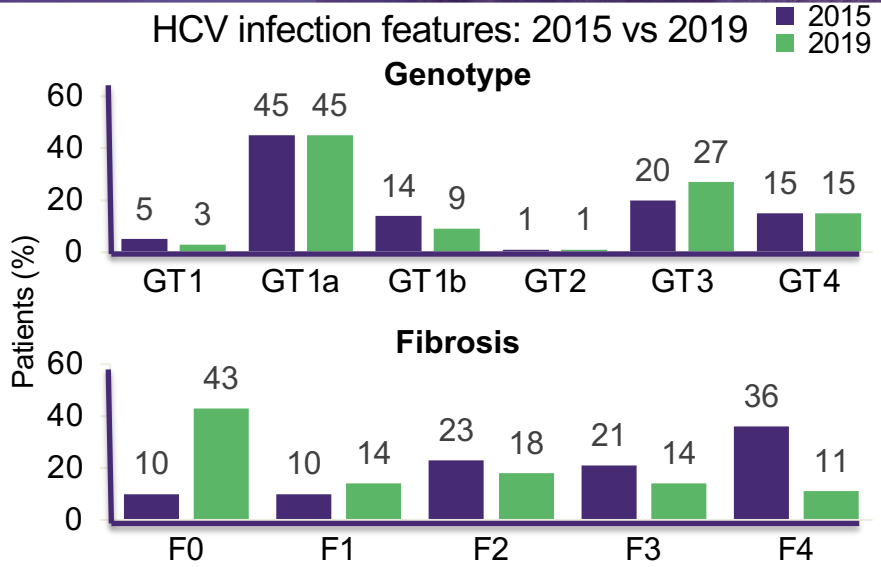
Sulkowski M, et al. EASL dILC2020. #THU375

Hepatitis C infection in the Spanish Prison System. Elimination is a dream at our fingertips

- HCV status in 71 prisons across Spain (excluding Catalonia) following initiation of a program to tackle HCV in 2015
  - Universal test-and-treat strategy

Prison population	2015	2016	2017	2018	2019
# inmates	49,976	49,224	47,803	47,901	47,499
HCV screening rate	**79%**	**80%**	**75%**	**79%**	**79%**
HCV Ab +ve	19.5%	18.7%	16.7%	10.6%	10.2%
HCV RNA +ve	**-**	**11%**	**9%**	**3%**	**1.9%**
HCV incidence	0.2	0.4	0.4	0.29	-
HCV treatment rate	-	24%	52%	~100%	~100%

- Decrease in HCV prevalence was independent of region, type of prison, number of inmates and rotation rate
- SVR rates: 95–98% in the modified ITT population
- HCV-related mortality decreased from 0.018% in 2015 to 0.002% in 2018



- Systematic test-and-treat strategy in Spanish prisons led to a significant decrease in prevalence of HCV infection
- Prison systems providing high screening and treatment rates can expect to achieve earlier HCV elimination in this special population

Cabezas J, et al. EASL dILC2020. #AS040

Monitoring SOF/VEL in Treatment Naïve, HCV Participants With Active Infection (MINMON)

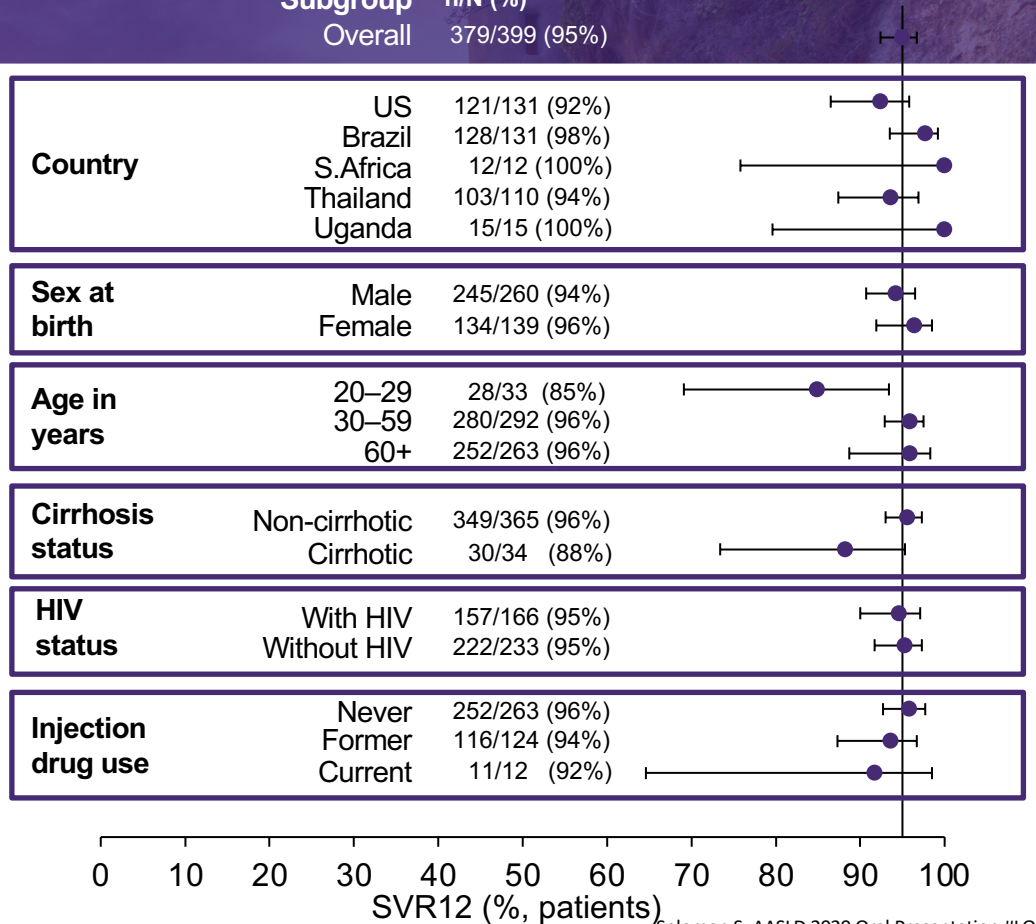
Single arm, open-label study to evaluate the minimal monitoring approach to HCV therapy in TN HCV with no evidence of decompensated cirrhosis treated with SOF/VEL for 12 weeks:

- No genotyping
- All tablets dispensed at entry
- No on-treatment visits/labs
- 2 remote contacts at Wks 4 (adherence assessment) & 22 (scheduling SVR visit)

SVR rate was 95% (379/399)
(95% CI: 92.4, 96.7)

Reasons for non-SVR

- 17 HCV RNA ≥LLOQ
- 2 LTFU
- 1 Sample collected before SVR visit



Solomon S, AASLD 2020 Oral Presentation #LO7

Positive Predictive Value of SVR4 for SVR12 in Pts Treated with G/P

Objective

- Determine the PPV of SVR4 for achievement of SVR12 in patients receiving G/P in clinical trials

Study Design & Methods

- Two separate integrated datasets from 20 Phase 2 and 3 clinical trials of G/P:
  - **Label-consistent group:** Patients treated with G/P (8, 12, or 16 weeks) consistent with current USPI
  - **Overall group:** All patients, regardless of consistency of the treatment duration with the current USPI
- The PPV, NPV, sensitivity, and specificity of SVR4 were calculated for achieving SVR12 in both groups, as well as by treatment duration in the label-consistent group

	Achieved SVR12	Didi not achieve SVR12	
Achieved SVR4	True positive	False positive	**PPV** = True positives / total with SVR4
Did not achieve SVR4	False negative	True negative	**NPV** = True negatives / total without SVR4
	Sensitivity = True positives / total with SVR12	**Specificity** = True negatives / total without SVR12	

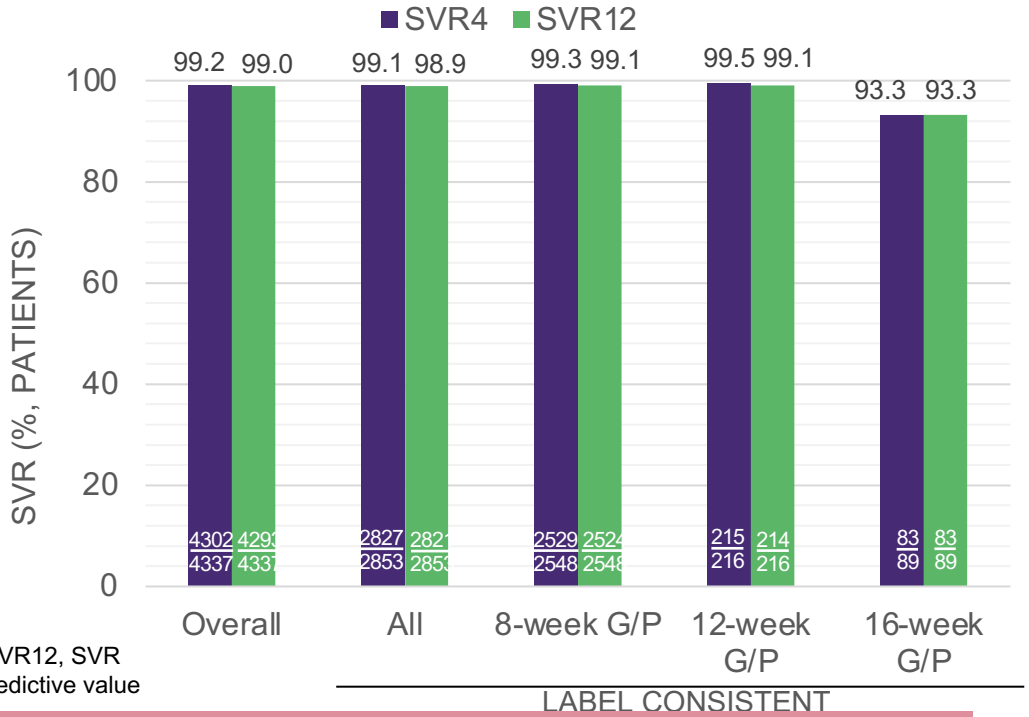
NPV, negative predictive value; PPV, positive predictive value

Gane E, AASLD 2020, Poster 884

Positive Predictive Value of SVR4 for SVR12 in Pts Treated with G/P

- Patients receiving G/P in clinical trials
- >99% of patients that achieved SVR4 achieved SVR12
- All patients that did not achieve SVR4 did not achieve SVR12 (NPV=100%; sensitivity=100%)
- Specificity was 79.5%, indicating the majority of patients relapsing do so by post-treatment week 4
- Similar results were seen when missing data were treated as failures

	Overall	All	8-wk G/P	12-wk G/P	16-wk G/P
PPV	99.8	99.8	99.8	99.5	100.0
NPV	100.0	100.0	100.0	100.0	100.0
Sensitivity	100.0	100.0	100.0	100.0	100.0
Specificity	79.5	81.3	79.2	50.0	100.0



SVR, sustained virologic response; SVR4, SVR at post-treatment Week 4; SVR12, SVR at post-treatment Week 12; PPV, positive predictive value; NPV, negative predictive value

- Achieving SVR4 was highly predictive of long-term SVR for patients treated with G/P, regardless of treatment duration
- All measures of concordance were similar between the overall group and the 8-week treatment duration group, demonstrating the high effectiveness of the shortest treatment regimen

Gane E, AASLD 2020, Poster 884

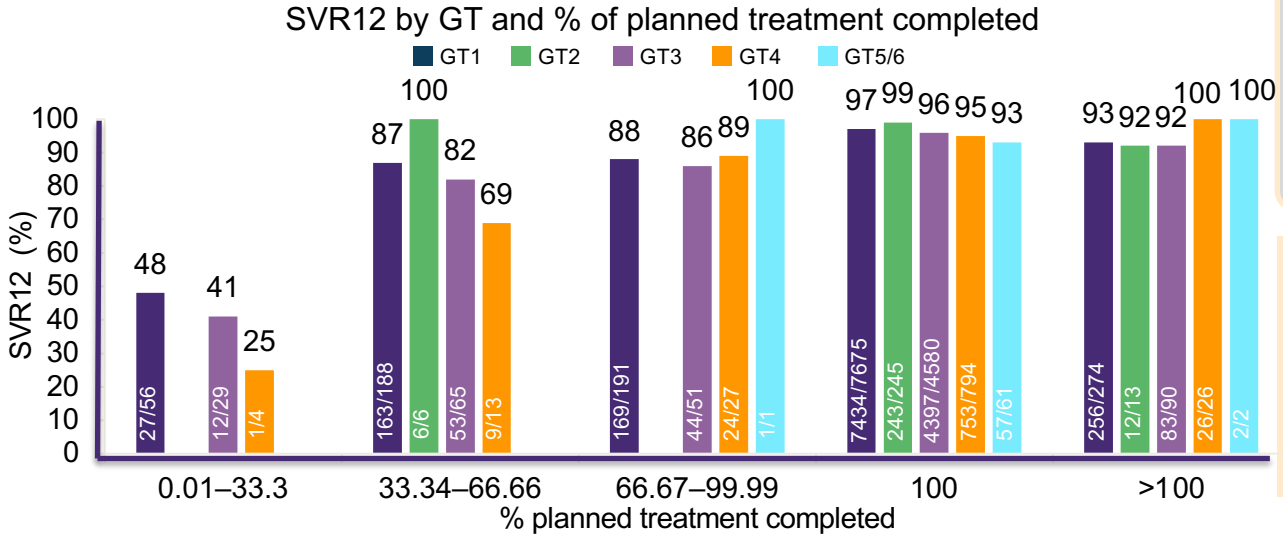
English HCV registry shows only a modest effect from non-completion of DAAs for HCV: SVR rates >80% in GT1, 2 or 3 HCV if >one third of planned treatment is completed

- Aim: to quantify the effect of DAA non-completion in 14,603 patients from the English HCV registry
- Actual/planned treatment duration was recorded for 98.5% (14,391) of patients with an outcome 12 weeks post-treatment
  - 4.4% (631) did not complete treatment

Overall SVR:
- **80.7%** treatment non-completion
- **96.5%** treatment completion

In patients with GT1, 17.7% did not complete 16 weeks EBR/GZR + RBV vs 1.9%–4.9% for other regimens (P<0.001)

OR for non-completion vs completion:
- **GT1: 0.149** (95% CI 0.107, 0.209)
- **GT3: 0.102** (95% CI 0.062, 0.168)



Higher SVR rates associated with:

- **GT1:** younger age, female gender, GT1b, HCC –ve, treatment completion
- **GT3:** female gender, milder liver disease, HCC –ve, treatment completion

- Most patients take full course of therapy
- With even 1/3–2/3 of treatment course, SVR >80% & >2/3 → >85% – quite forgiving…we are overtreating most people
- Adherence concerns should NOT be a major deterrent to treatment initiation

Drysdale K, et al. EASL dILC2020. #THU422

The best strategy for retrieval of hepatitis C patients lost to follow up: randomized clinical trial

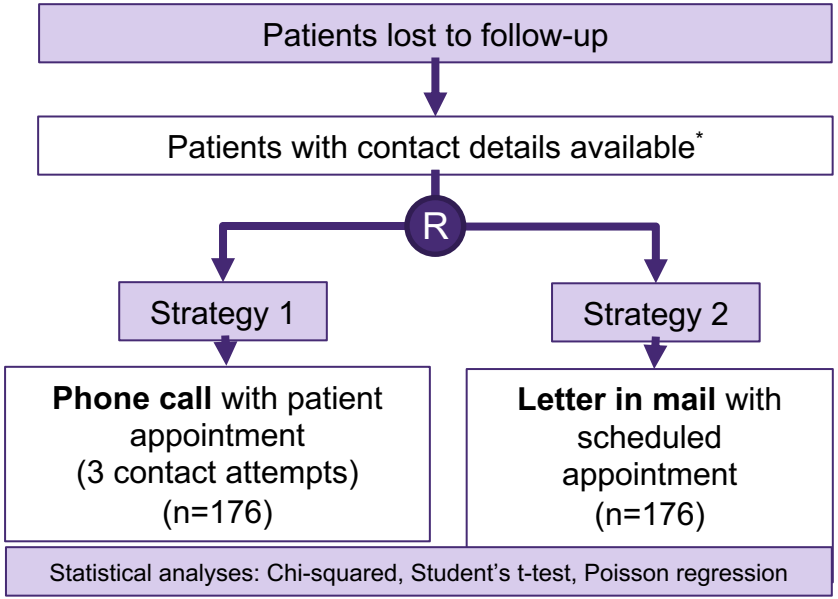
BACKGROUND AND AIM

- To achieve HCV WHO 2030 elimination goals:
  - Need to increase the rate of new diagnoses
  - Need to link to care those lost to follow-up
- Strategies exist to increase diagnosis
- Studies are lacking on how best to retrieve patients lost to follow-up
- **AIM**: to evaluate 2 strategies for retrieval of HCV patients lost to follow-up

METHODS

- Efficacy and efficiency of 2 strategies assessed through review of laboratory and microbiology charts since 2005
  - **Efficacy:** rate of patients keeping appointment
  - **Efficiency:** use of resources

- Patients identified as **lost to follow-up**:
  - Anti-HCV-positive without HCV RNA request
  - HCV RNA-positive without subsequent negative test



*NCT04153708; approved by the local Hospital Ethics Committee

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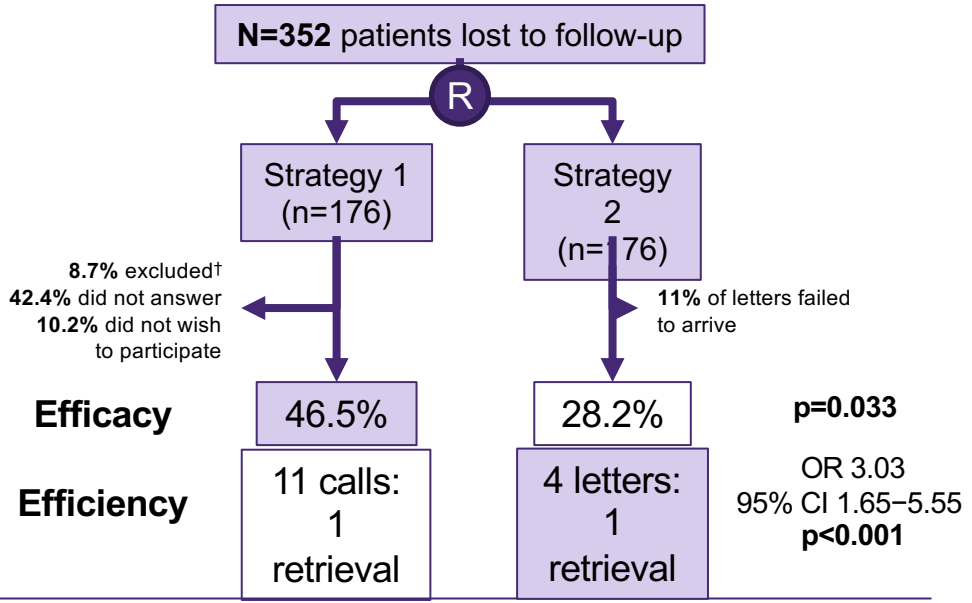
The best strategy for retrieval of hepatitis C patients lost to follow up: randomized clinical trial

RESULTS

- No differences between groups
  - 74.6% men; mean age 51.3 ±13.3 years
- **Efficacy**:
  - More patients kept scheduled appointment with strategy 1 vs strategy 2
    - Median interval from appointment made (by phone or letter) and appointment date: 9 days (1–17) vs 12 days (11–13)
    - 46.5% vs 28.2% (p=0.033)
- **Efficiency**:
  - Strategy 1: 11 phone calls needed for 1 retrieval
  - Strategy 2: 4 letters* needed for 1 retrieval



CONCLUSION

- Retrieval of patients with HCV diagnosis lost to follow-up is feasible through both strategies
- Phone calls seemed to be more effective, while invitation via mail was more efficient

*Reaching correct address; †Change in holder of phone line

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Conclusion

- Hepatitis C has emerged as public health concern among homeless, incarcerated and PWIDs
- High Sustained Viral Rates may be achieved in these vulnerable populations
- Survival improved after HCV cure, including those with cirrhosis but risk of hepatocellular carcinoma persists.
- Hepatitis C elimination can be achieved in our lifetime