

LA SFIDA DELLA TERAPIA DIFFUSA AI PWID

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DIPARTIMENTO MALATTIE INFETTIVE E TROPICALI



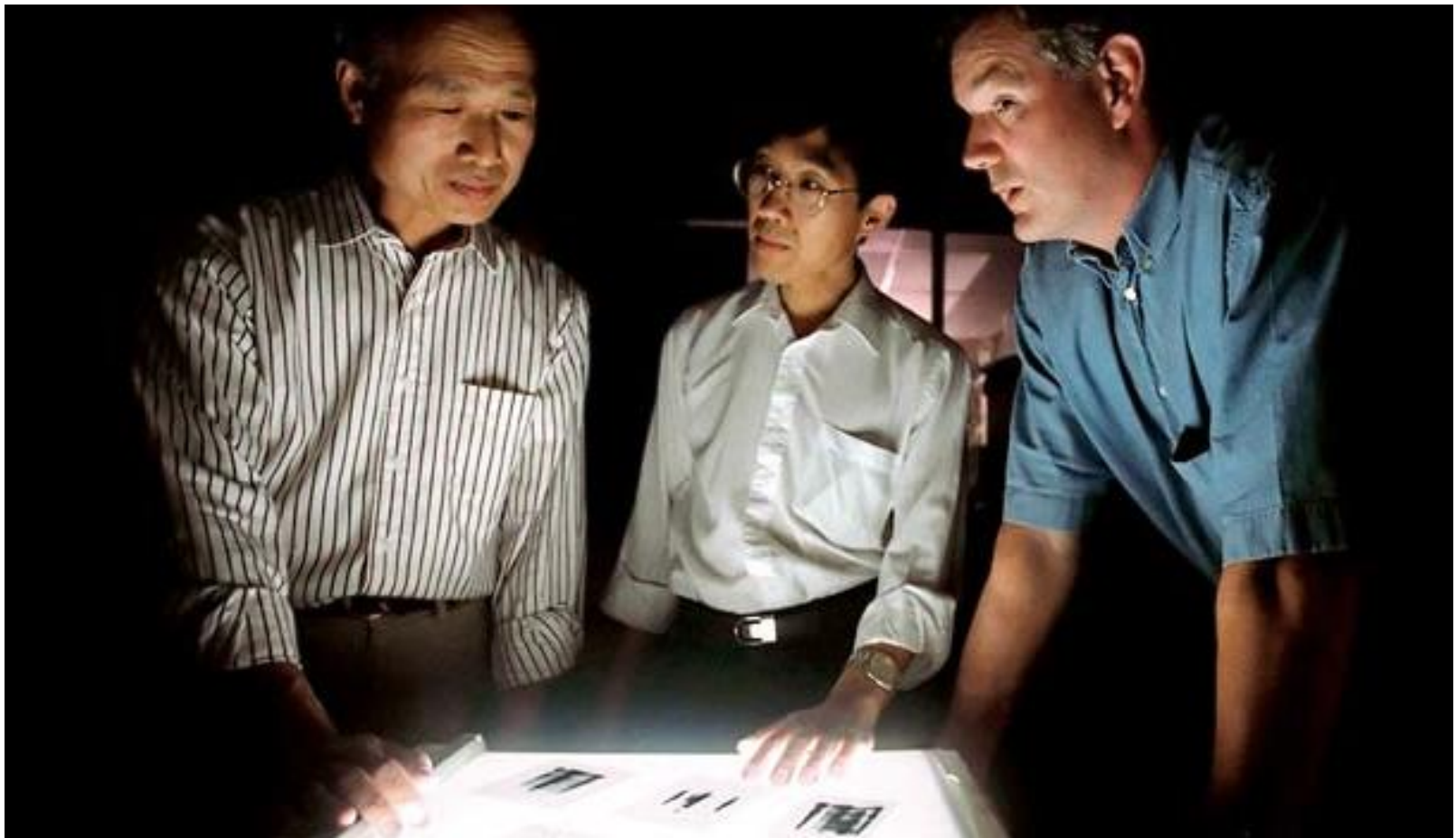
**IRCCS
Policlinico
S. Matteo
di Pavia**



Isolation of a cDNA Clone Derived from a Blood-Borne Non-A, Non-B Viral Hepatitis Genome

QUI-LIM CHOO, GEORGE KUO, AMY J. WEINER, LACY R. OVERBY,
DANIEL W. BRADLEY, MICHAEL HOUGHTON

April 21, 1989



Lifecycle of the Hepatitis C Virus

Release

Differently from HIV and HBV:

- HCV replication occurs only in cytoplasm
- Viral genome is not archived into the genome of infected cells

This makes HCV curable!!!!

- Structural and nonstructural proteins contribute to different processes in the viral life cycle

Global Call for HCV Elimination

Vision: “A world where viral hepatitis transmission is stopped and everyone has access to safe, affordable, and effective treatment and care”

2020 target: 3 million HCV infections treated

Feasible by scaling up **6 key interventions** to high coverage:

Hepatitis B vaccination (including birth dose)

Safe injection practices and safe blood

Harm reduction for injecting drug users

Safer sex (including condom promotion)

Hepatitis B treatment

Hepatitis C cure

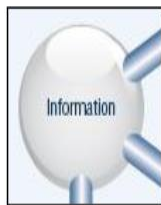
2030 Targets

90% Diagnosed

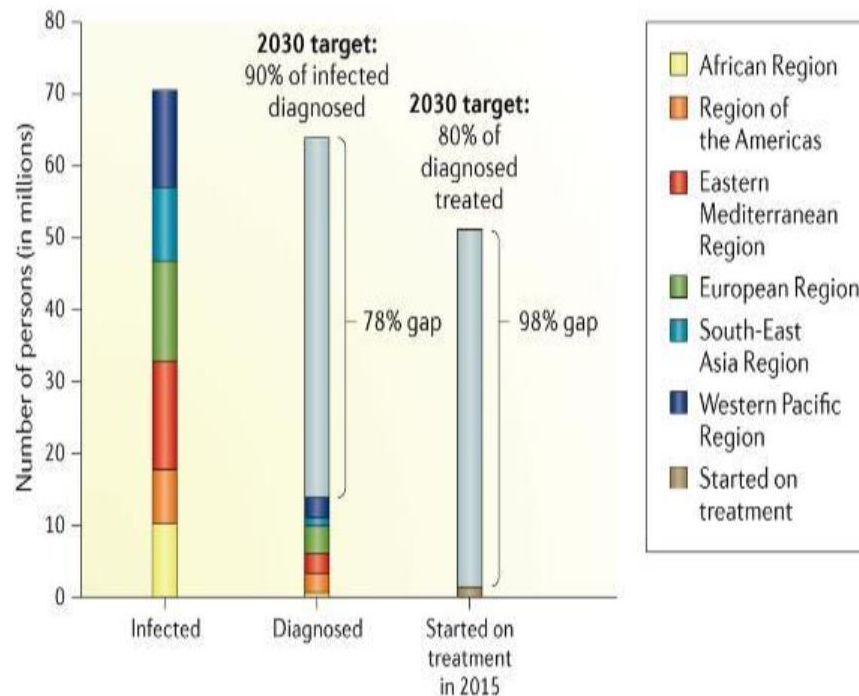
80% Treated

65% Reduced Mortality

WHO. Towards the elimination of hepatitis B and C by 2030.
Draft WHO Global Hepatitis Strategy, 2016-2021.



The global cascade of care for chronic HCV infection in 2015



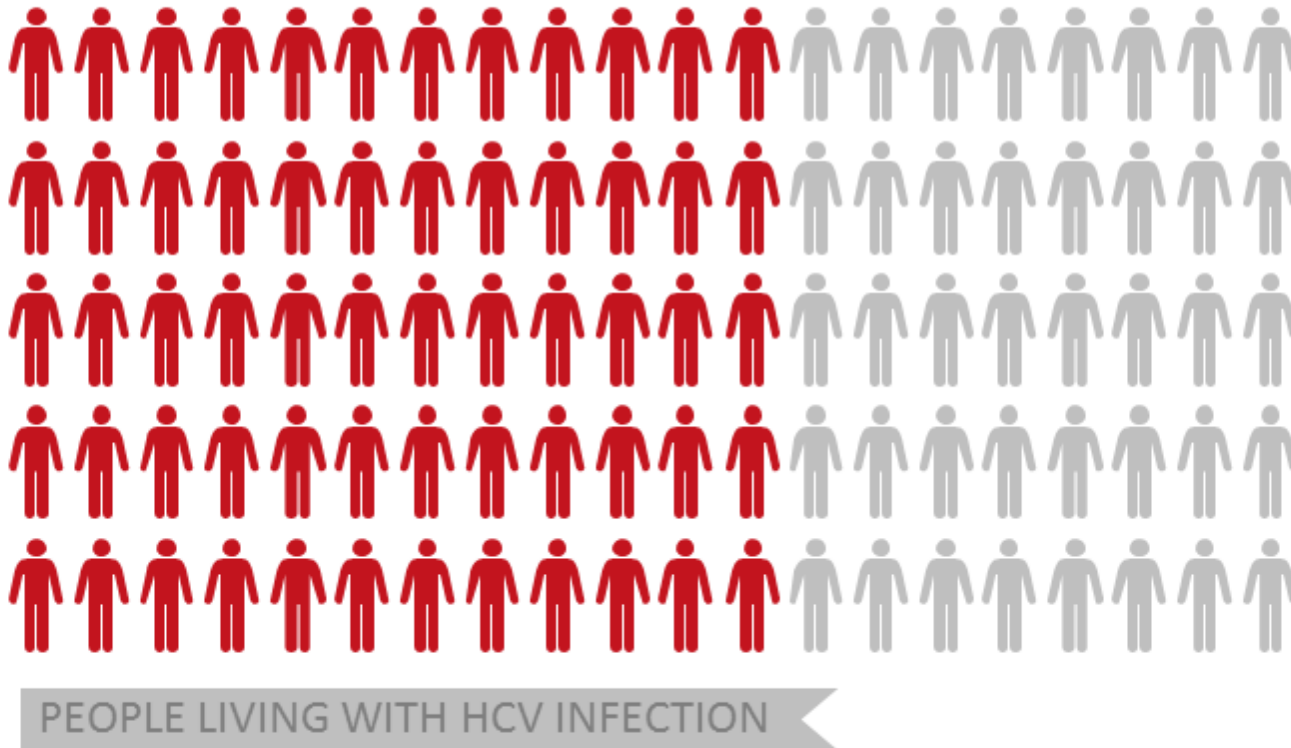
Nature Reviews | Gastroenterology & Hepatology

Adapted by Macmillan Publishers Ltd, part of Springer Nature with permission, from *Global Hepatitis Report, 2017*, World Health Organization, page 30, figure 8, 2017.

Source: Lazarus JV. *et al.* Many European countries 'flying blind' in their efforts to eliminate viral hepatitis. *Nat. Rev. Gastroenterol. Hepatol*, 2017

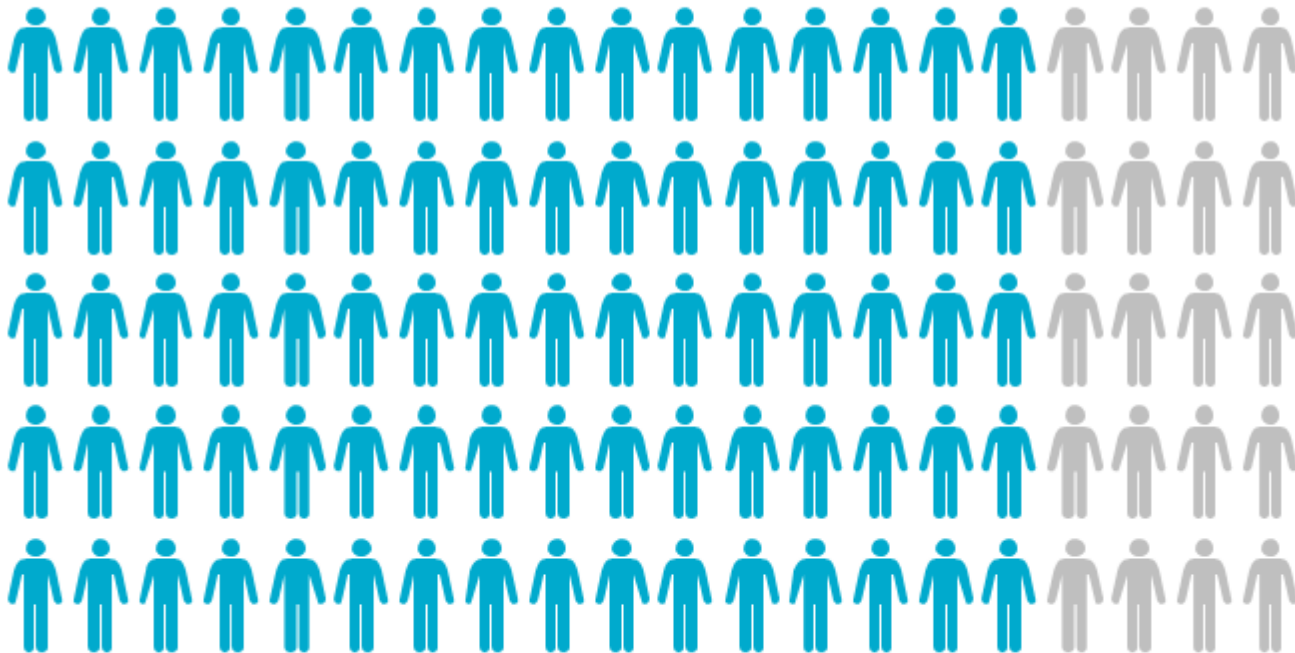
The majority of existing HCV cases occur in PWID

60% OF EXISTING INFECTIONS ARE
AMONG CURRENT & FORMER PWID



The majority of new HCV cases occur in PWID

80% OF NEW INFECTIONS OCCUR
AMONG CURRENT PWID



PEOPLE LIVING WITH HCV INFECTION

The Lancet Global Health – 23 October, 2017

- Global prevalence of injecting drug use and sociodemographic characteristics and prevalence of HIV, HBV, and HCV in people who inject drugs: a multistage systematic review. *Louisa Degenhardt et al.*
- 179 of 206 countries or territories report IDU (31 new compared to 2008)
- **15.6 million PWID worldwide**
 - **17.8% HIV+ (2.77 million people)**
 - **52.3% HCV+ (8.2 million people)**
 - **9% Hepatitis B surface antigen (HBsAg)+**
 - **83% mainly opioids**
 - **33% mainly stimulants**
 - **58% history of incarceration**

Global Health Sector Strategy

HCV targets at a glance



Incidence targets

- **30%** reduction in new HCV infections by 2020
- **80%** reduction in new HCV infections by 2030



Mortality targets

- **10%** reduction in mortality by 2020
- **65%** reduction in mortality by 2030



Harm reduction

- Increase in sterile needle and syringes provided per PWID/year from **20** in 2015 to:
 - **200** by 2020
 - **300** by 2030



Testing targets

- **90%** of people aware of HCV infection by 2030

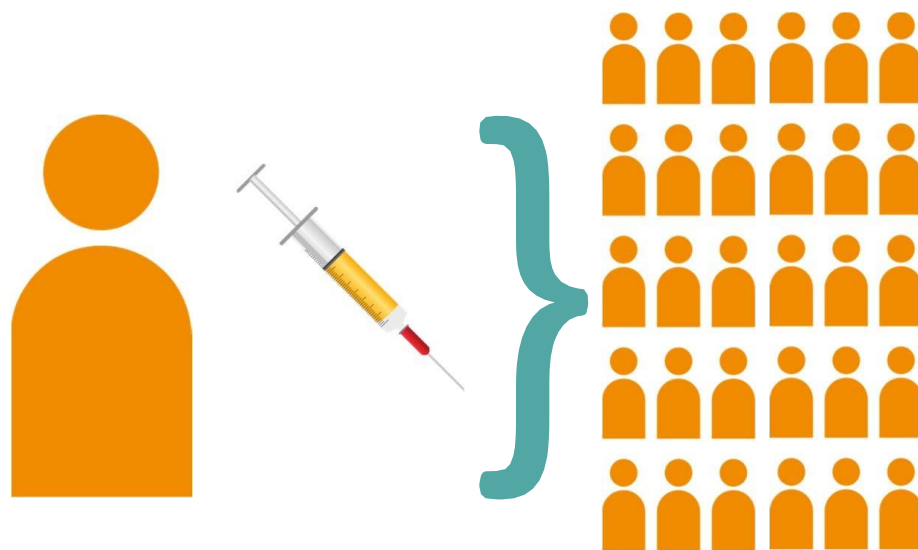


Treatment targets

- **80%** of people treated by 2030

Source: http://apps.who.int/gb/ebwha/pdf_files/WHA69/A69_32-en.pdf?ua=1 (Accessed August 2016)

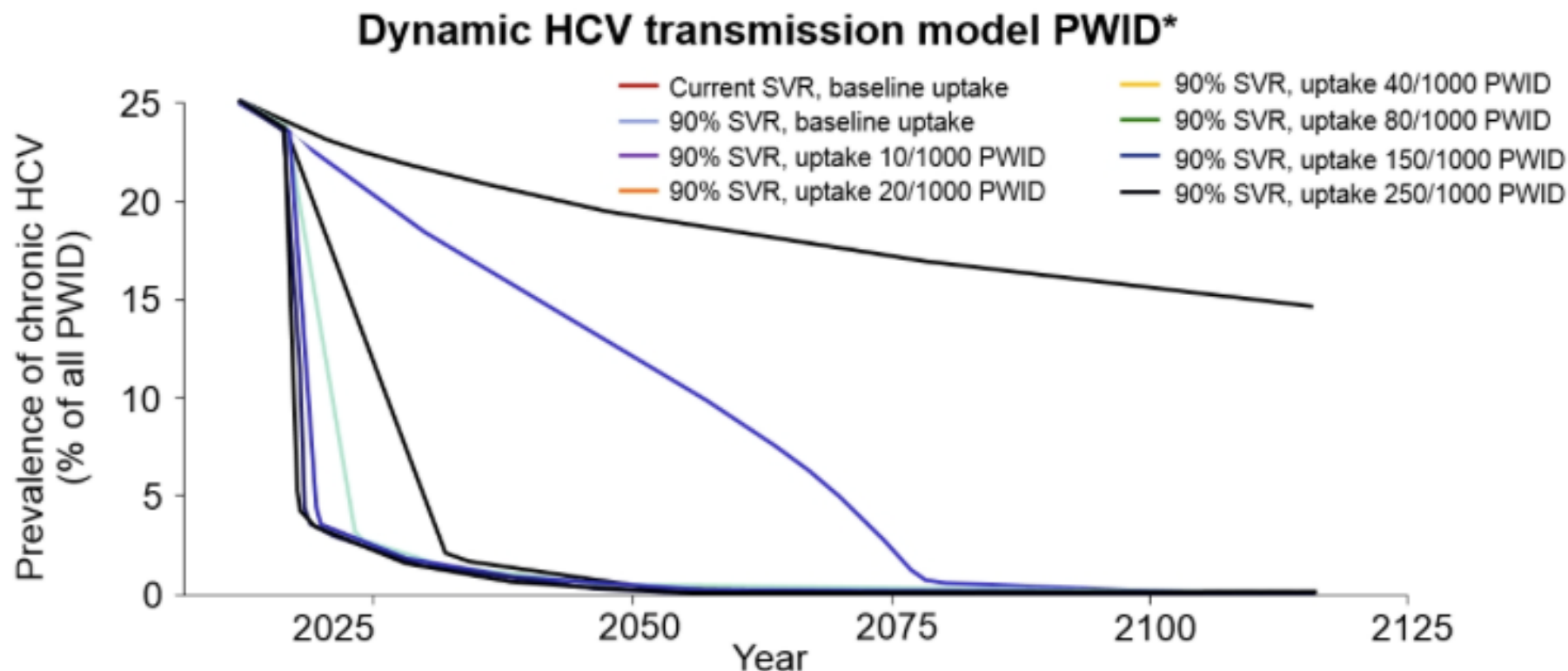
Urgently needed: treat all PWID !!



Ogni PWID con infezione da HCV è capace di infettare almeno 20 altri consumatori entro i primi 3 anni dall'inizio del contagio !!

Magiorkinis G et al. Plos Comput Biol, 2013. 9(1): p. e1002879

To gain population benefits, all PWID should be treated

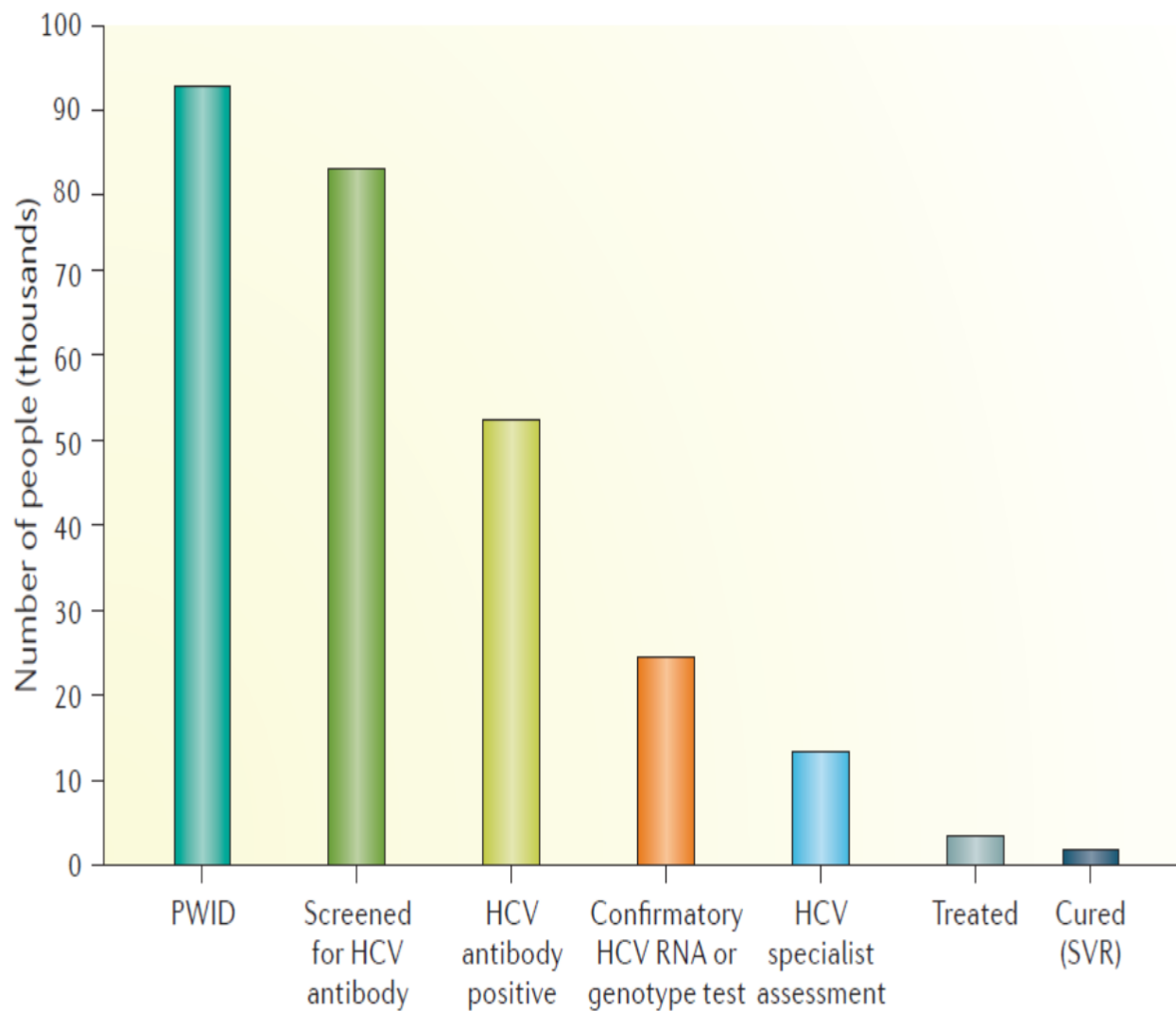


- ◆ With treatments now achieving 90% SVR, increased treatment uptake would have a dramatic impact on chronic HCV prevalence
- ◆ If all chronically infected PWID could be treated from 2015–2017 onwards, a prevalence of less than 1% could be achieved within 20 years

*Values for all parameters included in the model are derived from the data published by Martin NK, et al. Hepatology 2013;58:1598–609 and are based on PWID population of Edinburgh. Current treatment = PEG-IFN + RBV up to 2012 and addition of telaprevir or boceprevir since 2012.

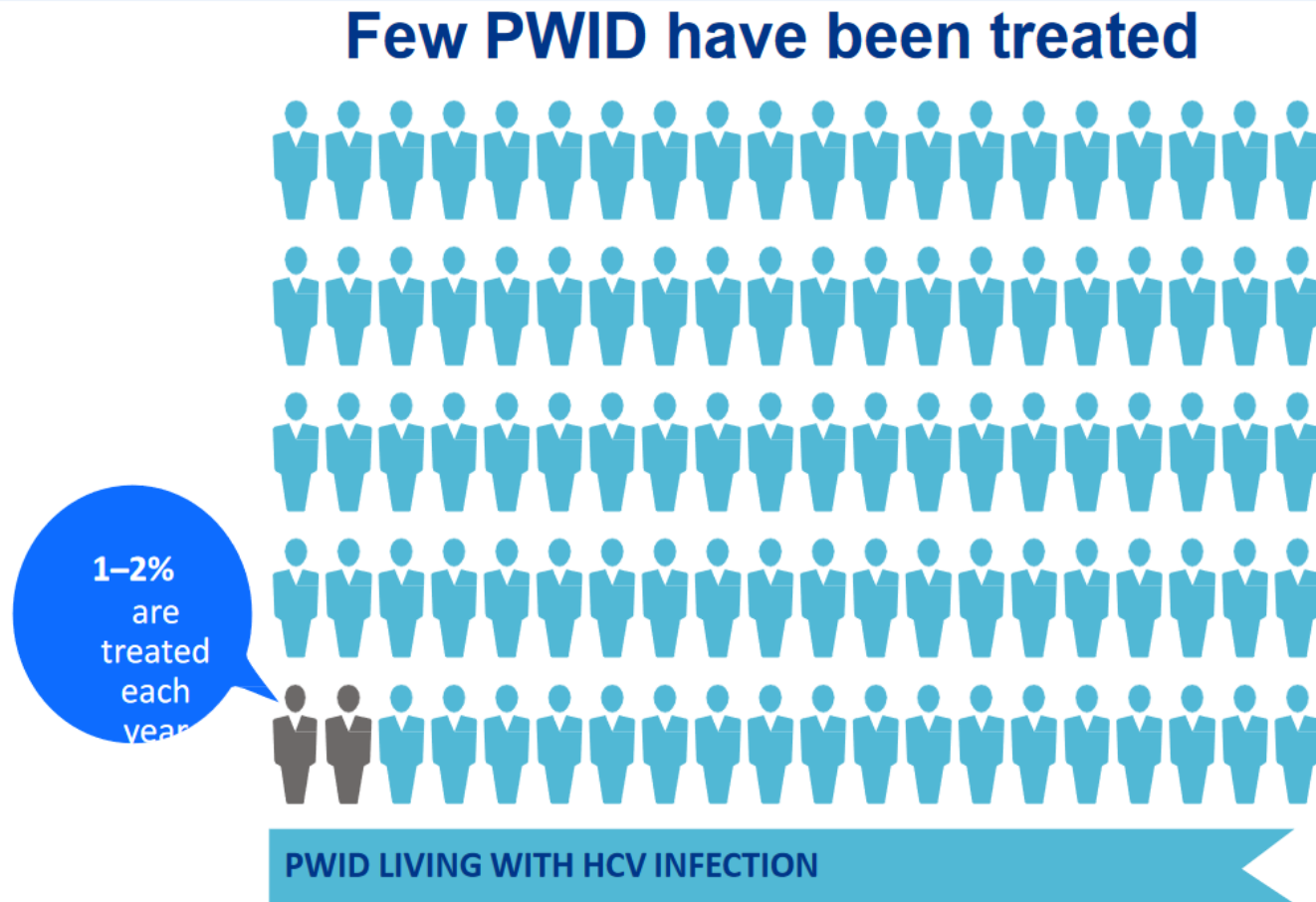
PEG-IFN: pegylated interferon; PWID: people who inject drugs; RBV: ribavirin; SVR: sustained virological response

HCV care cascade among PWID



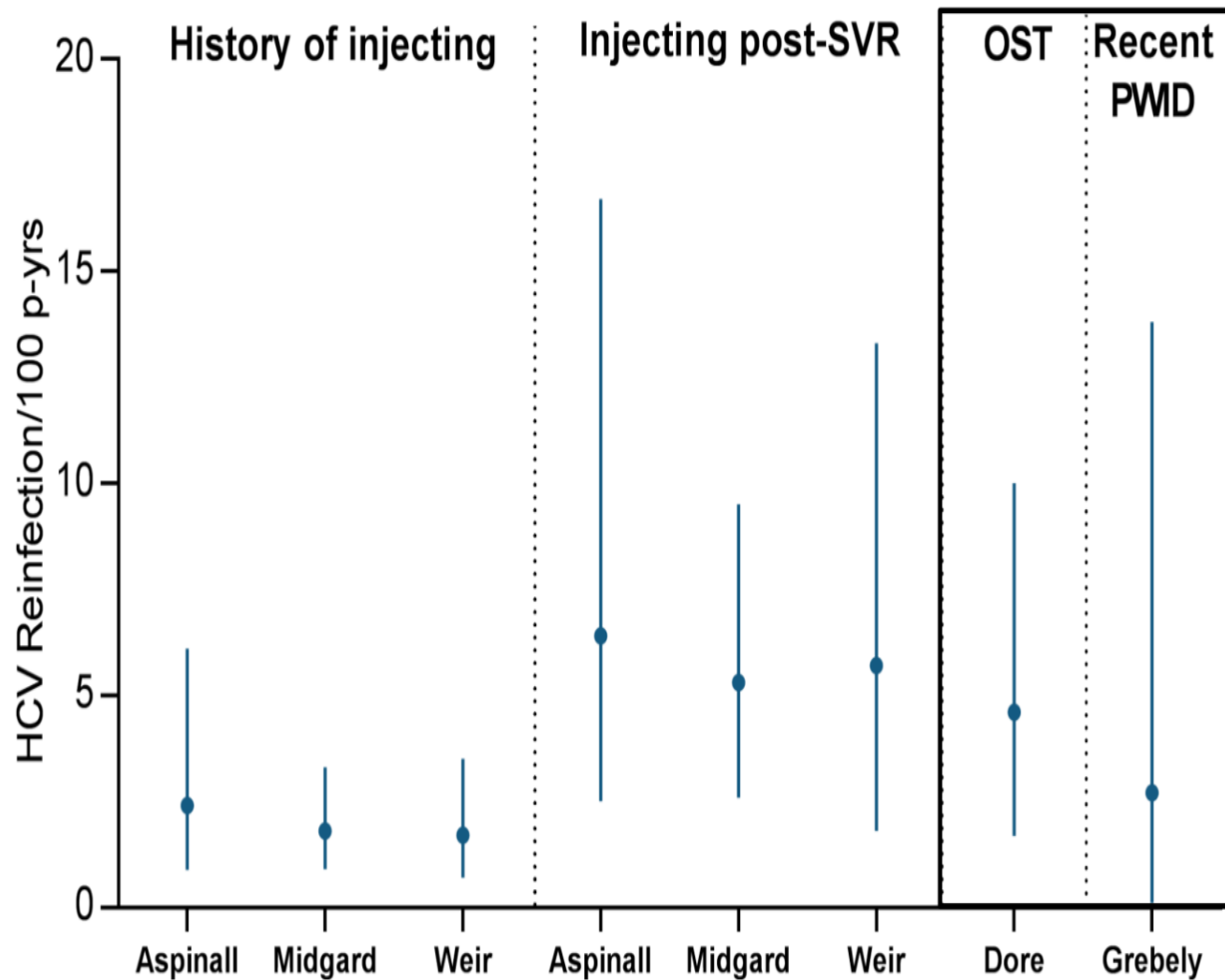
Strategies for harm reduction among PWID:

Linkage-to-care with HCV DAAs



1. Aspinall EJ, et al. *Clin Infect Dis* 2013; **57**(s2):S80–S89;
2. Dimova RB, et al. *Clin Infect Dis* 2013; **56**:806–816;
3. Hellard M, et al. *Clin Infect Dis* 2009; **49**:561–573;
4. Dalgard O. *Clin Infect Dis* 2005; **40**(s5):S336–S338;
5. Grebely J, et al. *J Gastroenterol Hep* 2010; **25**:1281–1284;
6. Grebely J & Dore GJ. *Antiviral Res* 2014; **104**:62–72.

What is the risk of HCV reinfection following therapy?



Not calculated
among people
with recent
injecting post-
therapy

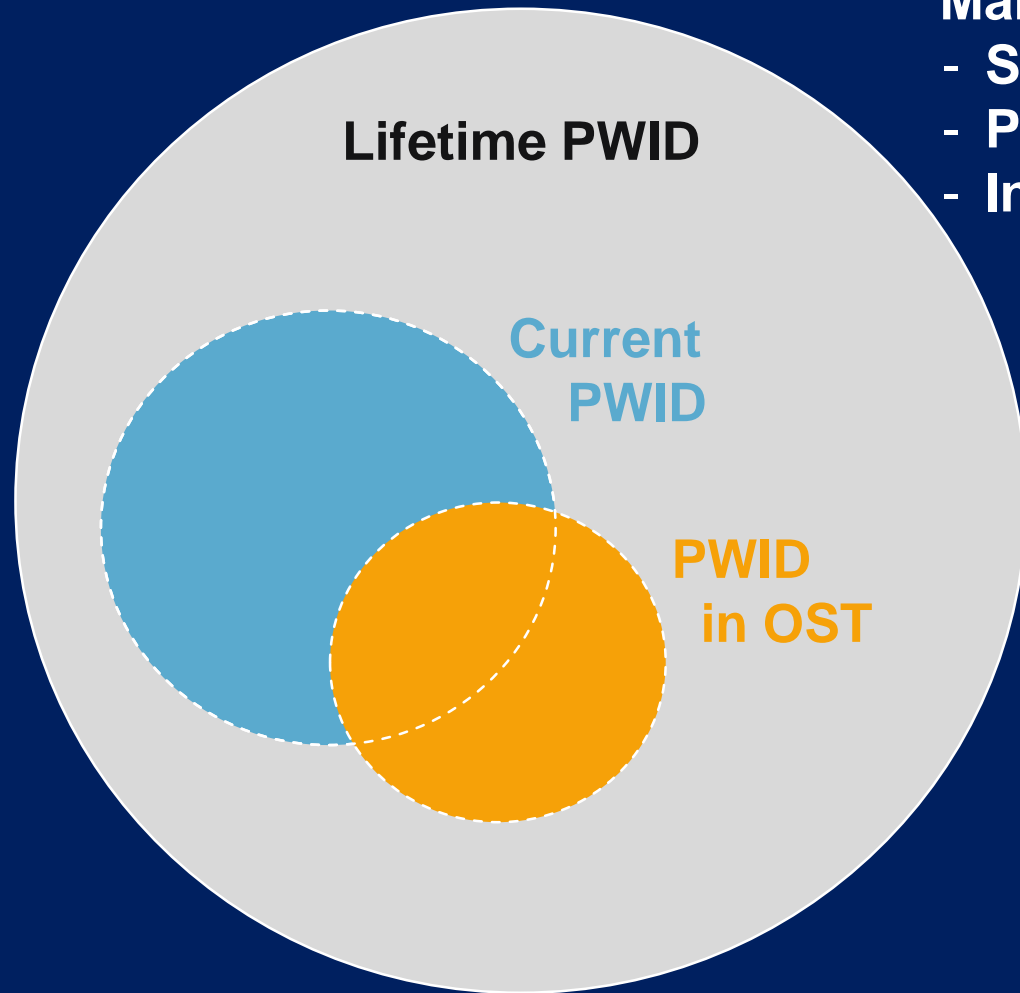
Prevention of reinfection in at risk populations

EASL recommendations ■ Grade of evidence ■ Grade of recommendation		
Harm reduction, education and counselling should be provided to PWID undergoing HCV treatment to prevent reinfection following successful treatment	B	1
Following SVR, PWID with ongoing risk behaviour should be monitored for HCV reinfection (ideally biannually, at least annually)	A	1
If reinfection is identified post-SVR, retreatment should be made available	A	1

Enhancing testing, linkage to care, and treatment in PWID

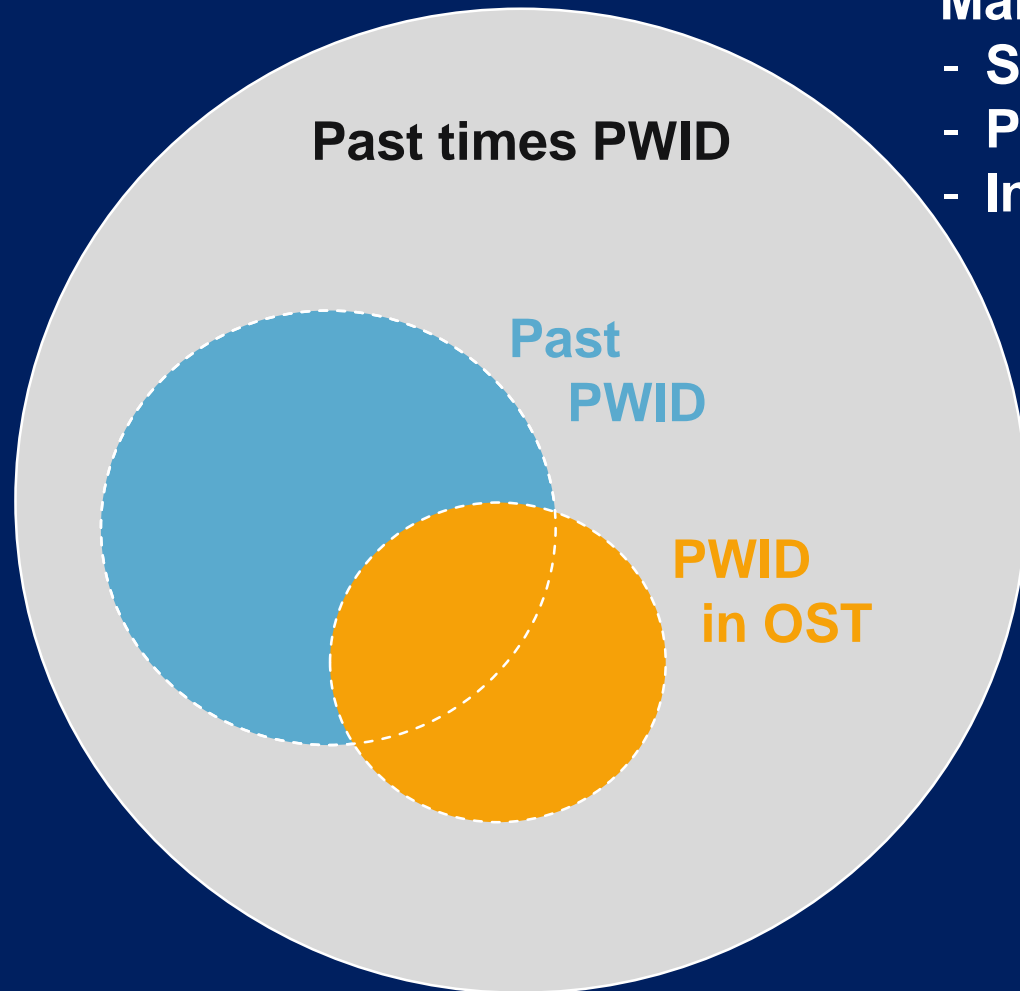
- Systematic review of interventions to enhance HCV testing, linkage to care or treatment among PWID
- 10,116 records – 14 studies with comparative interventions included
- Interventions to enhance HCV testing
 - On-site testing with pre-test counselling and education
 - Dried-blood spot testing
- Interventions to enhance linkage to care
 - Facilitated referral for HCV
- Interventions to enhance HCV treatment
 - Integrated care for HCV and drug use delivered by a multidisciplinary team (with or without non-invasive liver disease assessment)

PWID Population Definitions



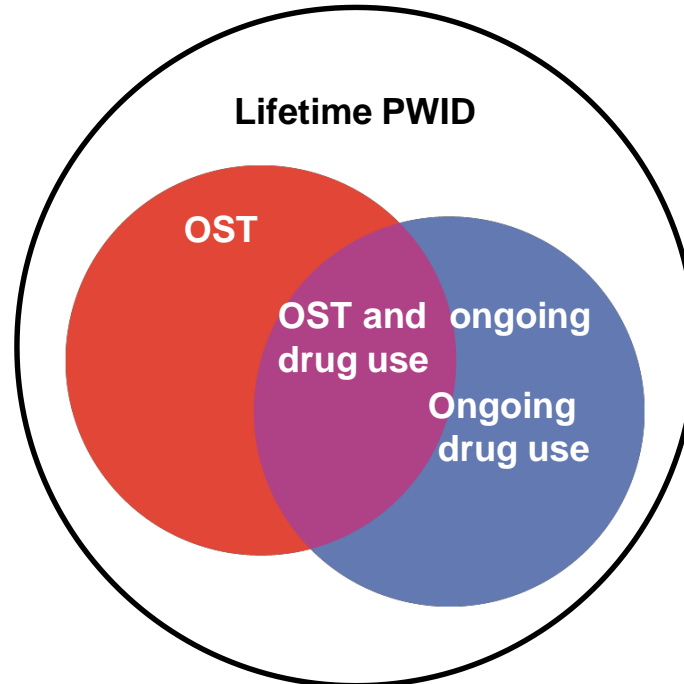
- Marginalized:**
- Socioeconomic
 - Prisoners
 - Indigenous

PWID Population Definitions



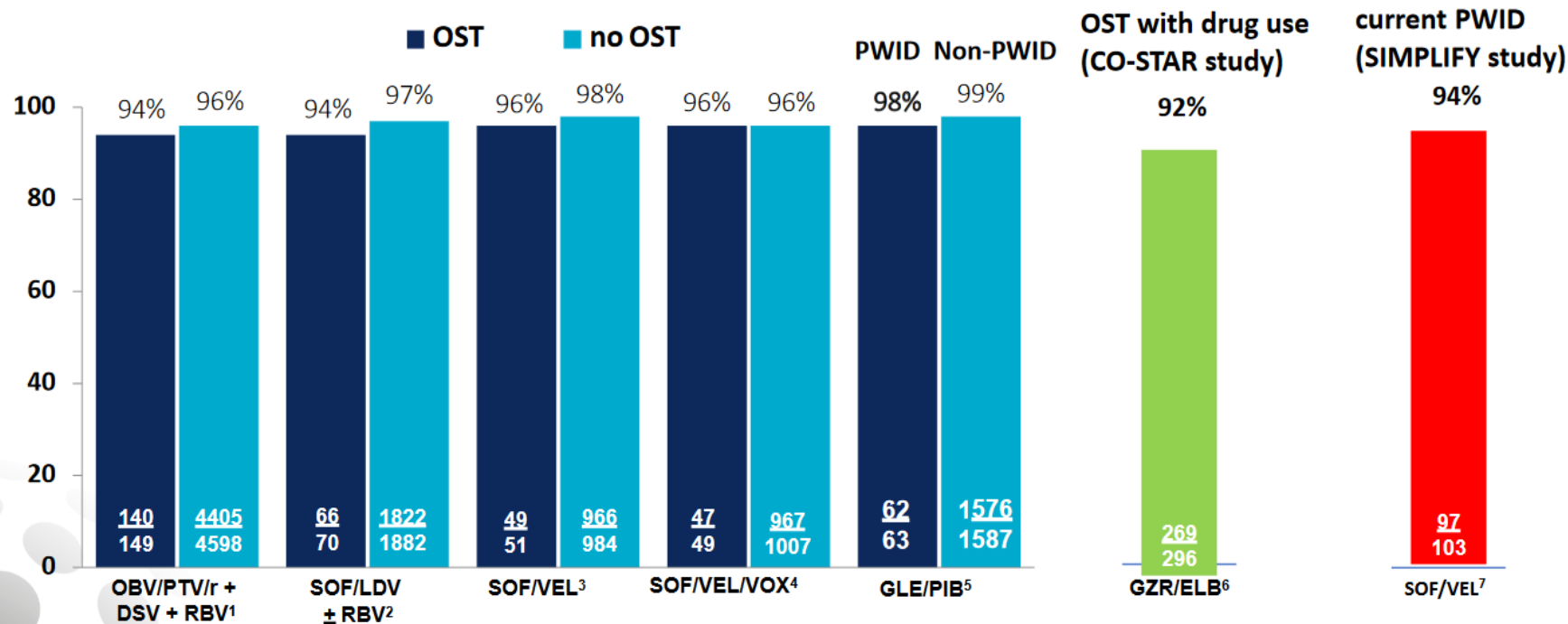
- Marginalized:**
- Socioeconomic
 - Prisoners
 - Indigenous

PWID populations included in clinical trials with DAAs



- PWID populations included in clinical trials with DAAs
 - Patients on OST (Phase 2 AbbVie trial; ION-1, 2 and 3, ASTRAL-1, 2 and 3)
 - Patients on stable OST, ongoing injection use permitted (C-EDGE CO-STAR)
 - Patients on and not on OST with ongoing injection use (SIMPLIFY)

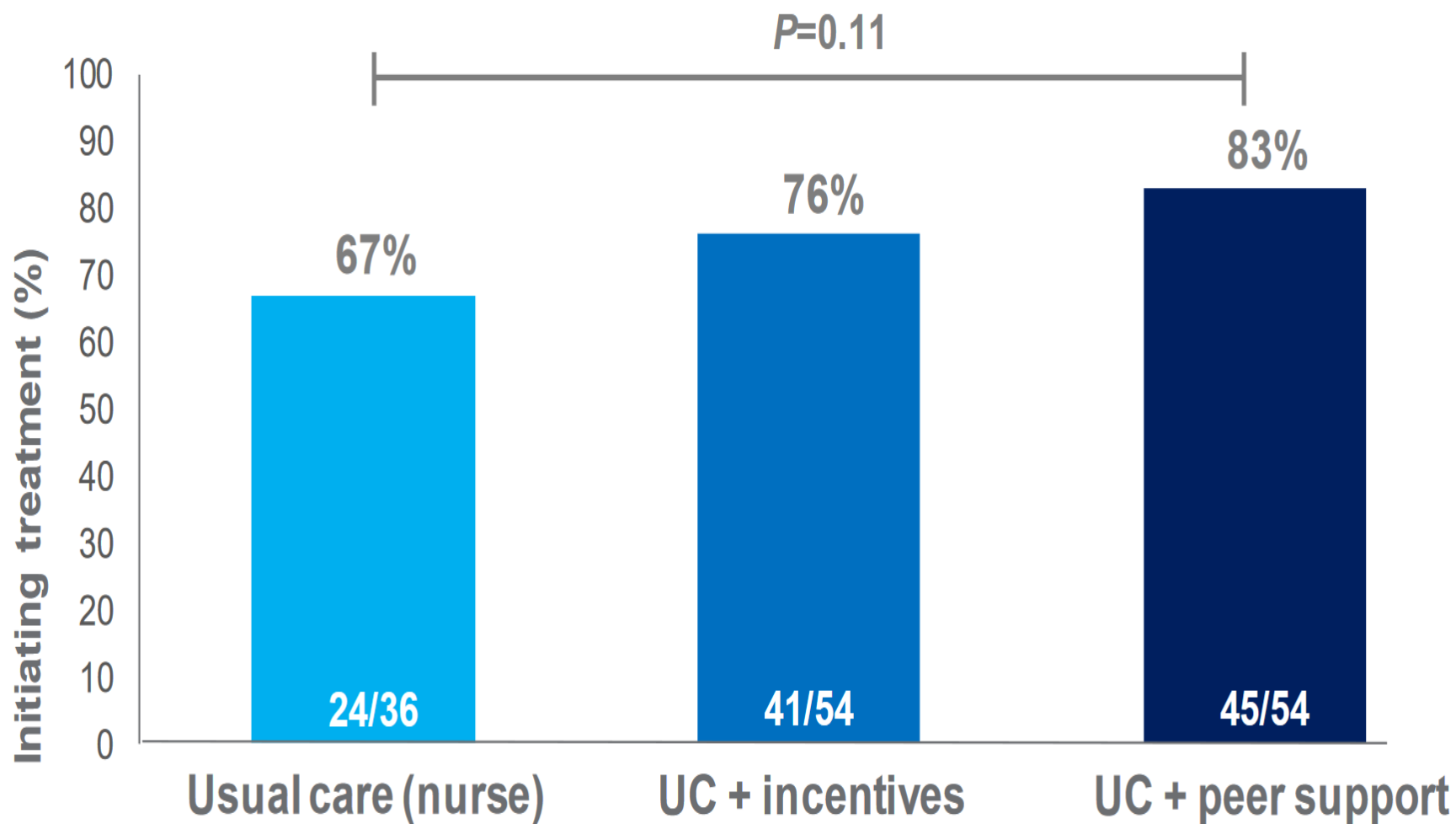
PWID have favourable DAA outcomes



1) Grebely J, ILC 2017. 2) Grebely J, *CID* 2016. 3) Grebely J, *CID* 2016. 4) Grebely J, ILC 2017. 5) Foster GR, AASLD 2017 #1182, Dore GJ, *Ann Intern Med* 2016. 7) Grebely J, *Lancet Gastroenterol Hepatol* 2018.

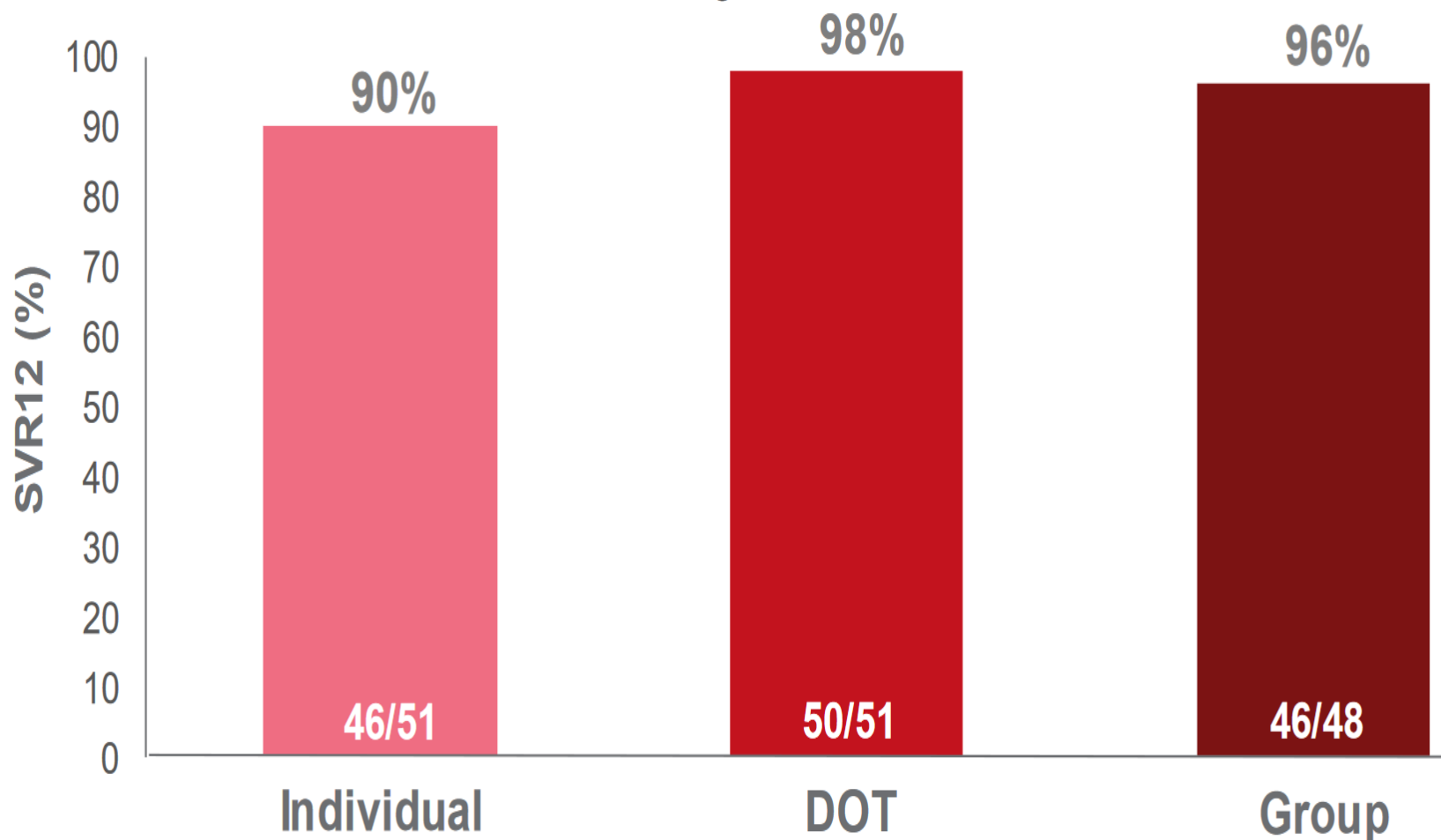
CHAMPS: HCV treatment uptake

- HCV genotype 1, 12% cirrhosis, 25% recent cocaine/heroin use



PREVAIL: Individual vs. DOT vs. group

- 85% genotype 1a, 27% cirrhosis, 11% treatment-experienced, 14% HIV
- 98% methadone, 65% with recent drug use in last 6 months



Reinfection following successful HCV DAA therapy among people with recent injecting drug use: the SIMPLIFY and D3FEAT studies

7th International Symposium on Hepatitis Care in Substance Users
Cascais, Portugal 19 - 21 September 2018

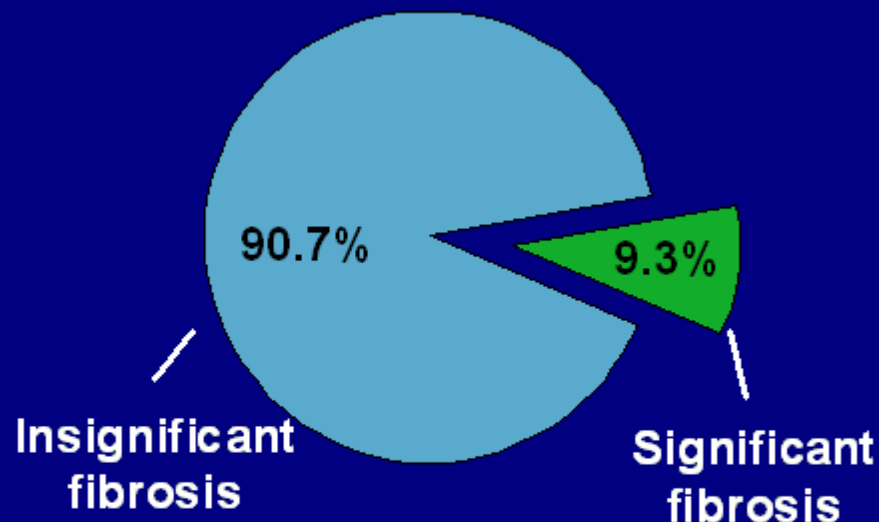
Evan Cunningham, Grebely J, Dalgard O, Hajarizadeh B, Conway B, Powis J, Bruneau J, Feld JJ, Read P, Cooper C, Amin J, Bruggmann P, Lacombe K, Stedman C, Hellard ME, Marks P, Dunlop A, Quiene S, Moriggia A, Applegate TL, Litwin AH, Matthews GV, and Dore GJ
on behalf of the SIMPLIFY and D3FEAT Study Groups

“Reinfections are simply an indicator that we are treating the right population. People who become reinfected are not only at risk of HCV infection but likely HCV transmission as well and so treatment among this population is crucial in order to reduce the incidence of new HCV cases. It’s important that reinfection cases are seen in this framework and patients are given access to timely retreatment without any stigma or discrimination.”

A. H . Litwin

Progression of Liver Fibrosis Among IDUs With Chronic HCV

- 119 prospectively followed IDUs
- Significant fibrosis at first biopsy
- After median follow-up of 4.2 years, 21% had progression of fibrosis
 - Progression significantly associated with serum level of HCV RNA and ALT



Significant fibrosis defined as a modified Ishak score of 3 or greater, and progression of fibrosis defined as an increase of 2 or more units or clinical evidence of end-stage liver disease.

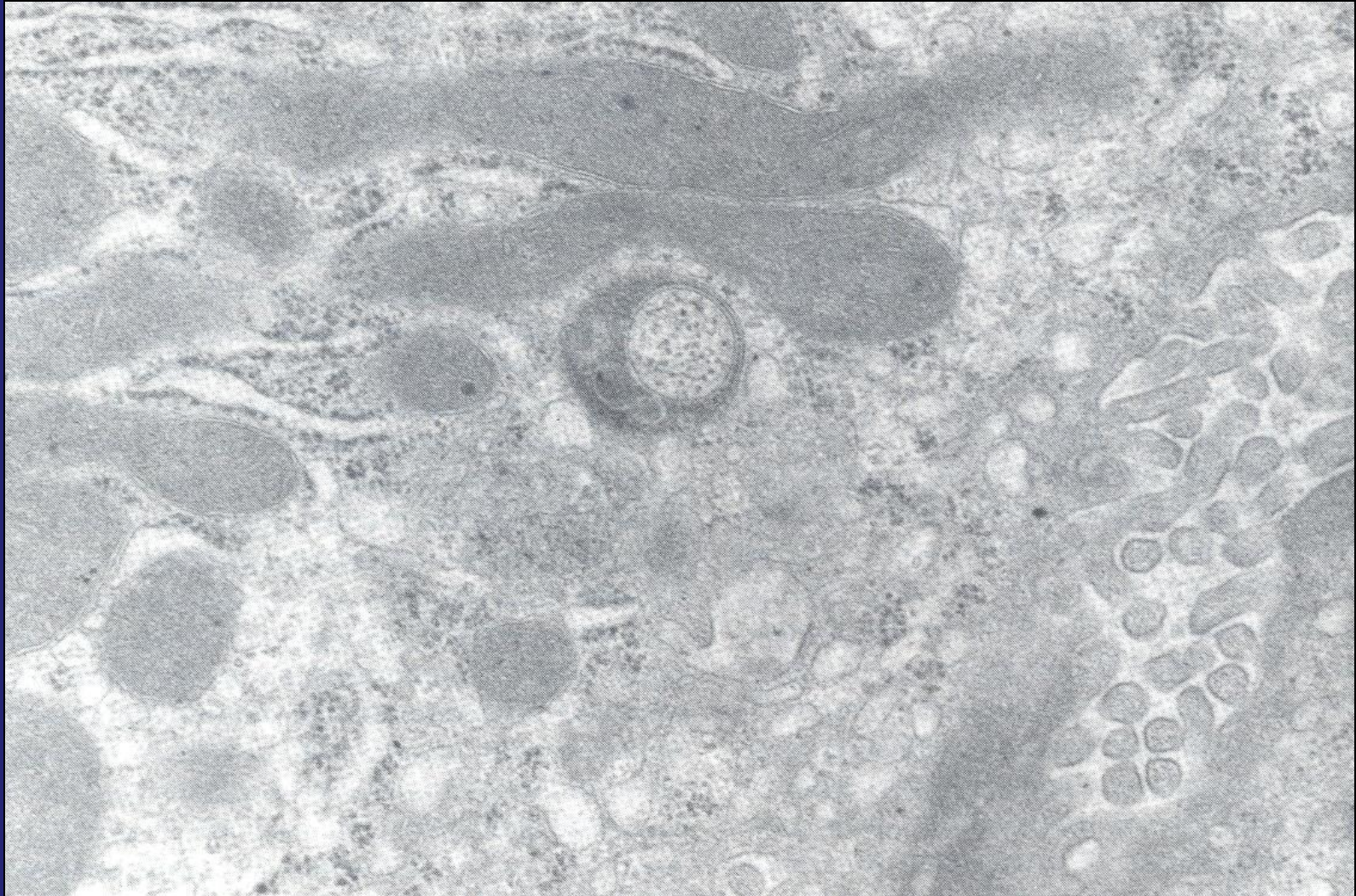
Giorgio Barbarini and Alessandro Perretti

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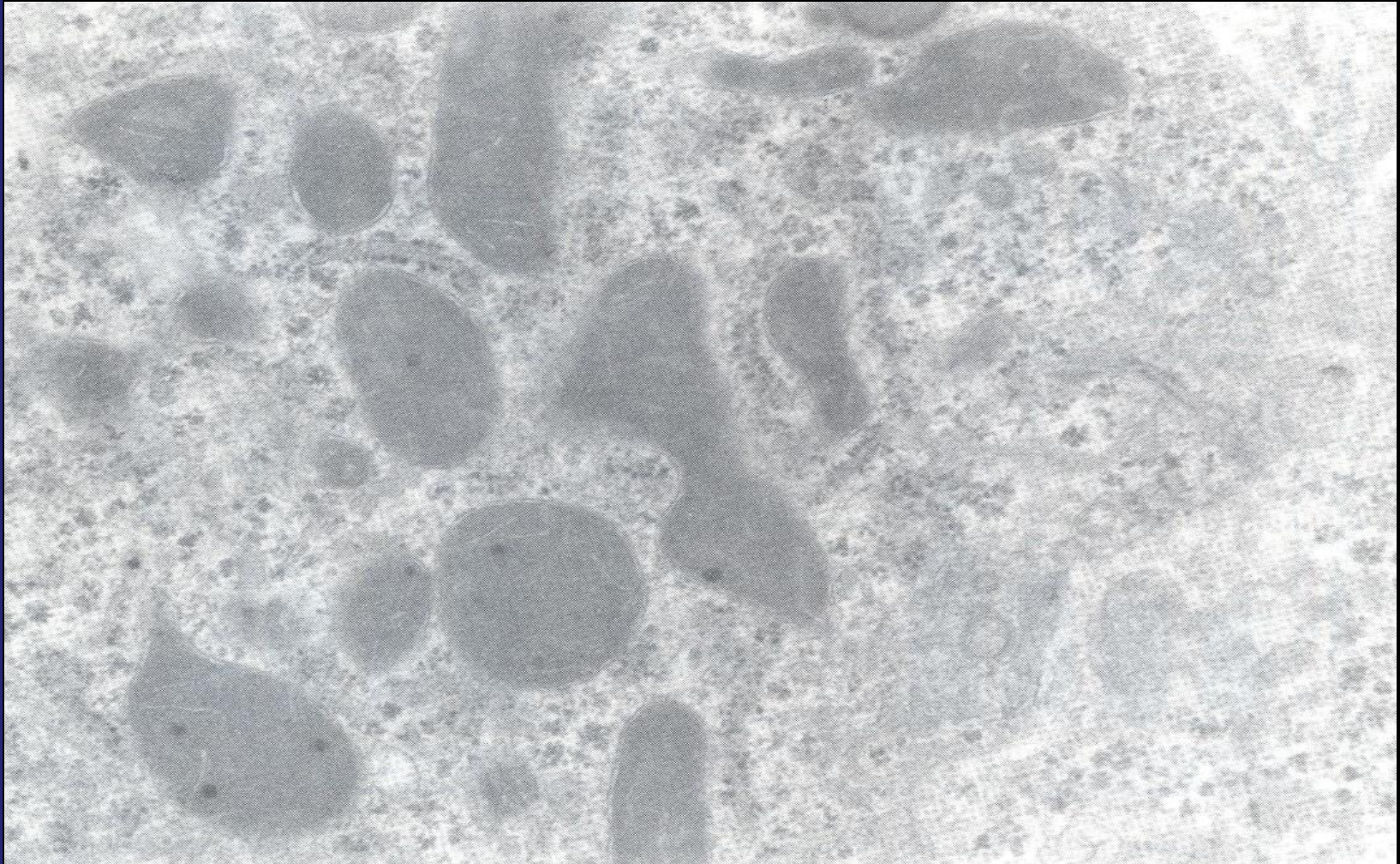
Abstract

In the human body, the liver is the most susceptible organ to injury by foreign molecules, as a consequence of its primary role in their metabolism and of its position as the first organ encountered by ingested substances after absorption. When any drug or toxin is abused heavily, the liver can be overwhelmed with the task of processing it out of the body, resulting in liver damage and liver failure. Because in any urban area worldwide (but in many countries also in



Ultrastructural finding in a chronic hepatitis C patient IVDA with genotype 1a. Note the irregular shapes of the mitochondria, which appear oblong with thin cristae, with electron-dense grains into mitochondrial matrix (x20,000).

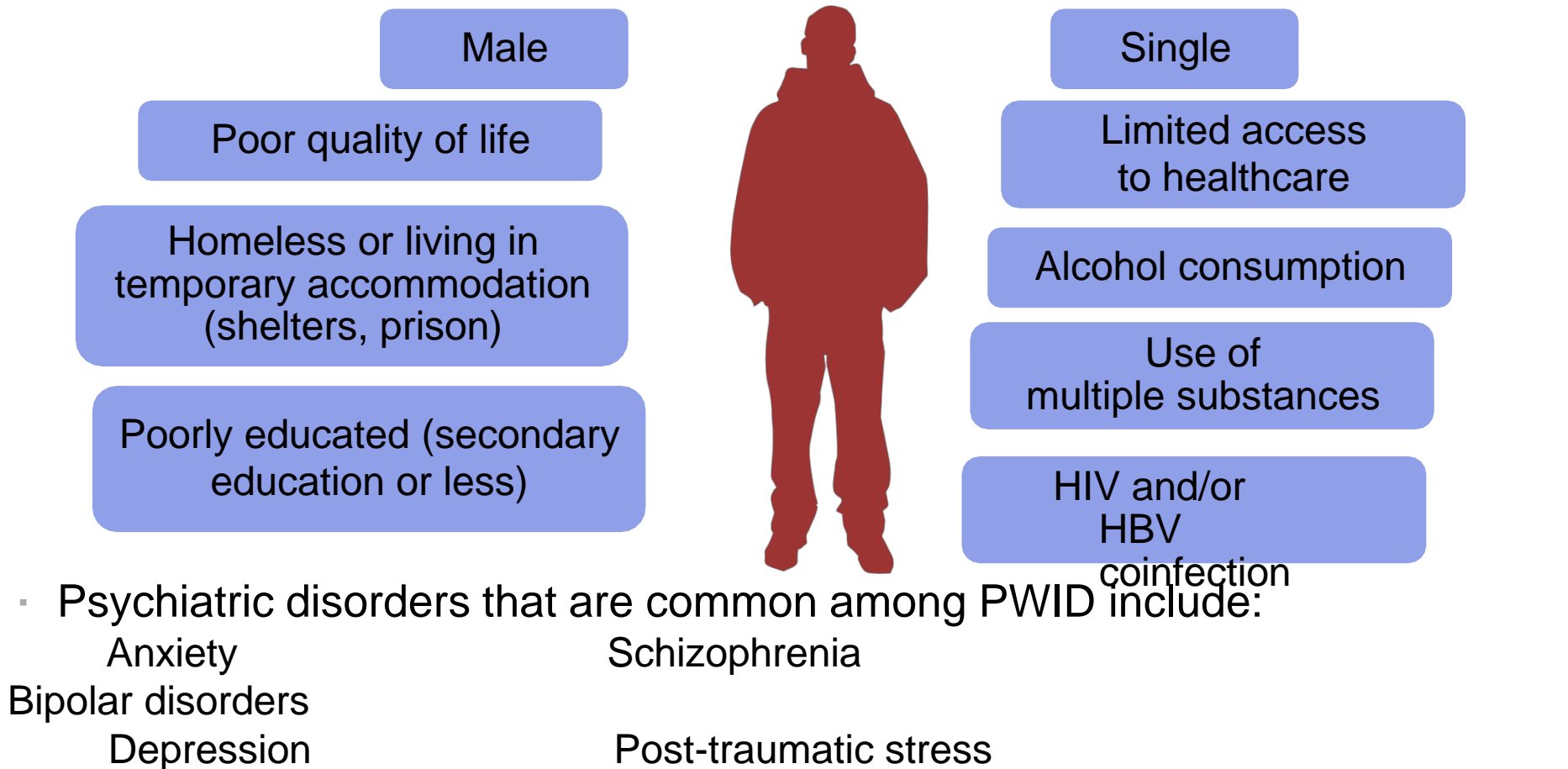
G.Barbaro,G.DiLorenzo,A.Asti,M.Ribersani,G.Belloni,B.Grisorio,G.Filice and G.Barbarini Am J Gastreter 1999



Ultrastructural finding in a chronic hepatitis C IVDA patient with genotype 1a. Note the presence of dumpy mitochondria with thin and fragmented cristae. Note also the presence of electron-dense grains into mitochondrial matrix (x20,000).

G.Barbaro,G.DiLorenzo,A.Asti,M.Ribersani,G.Belloni,B.Grisorio,G.Filice and G.Barbarini Am J Gastroenter 1999

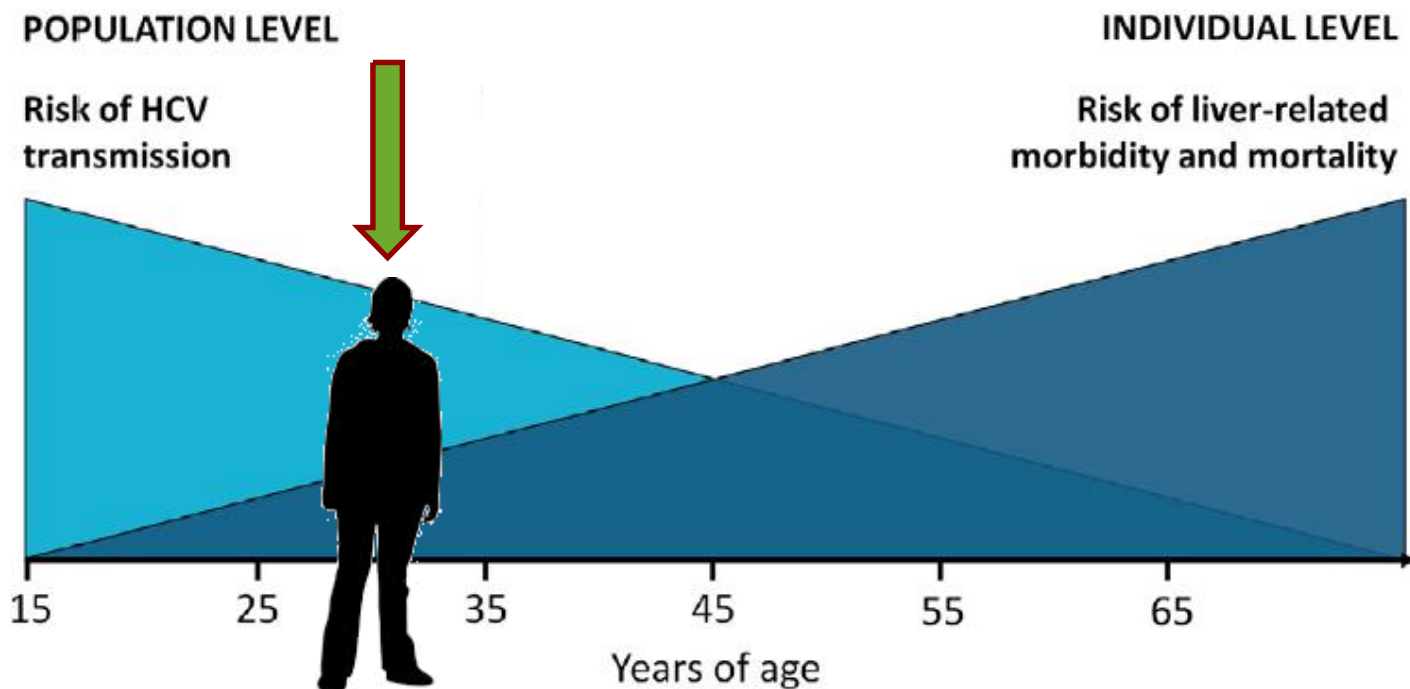
Snapshot of PWID

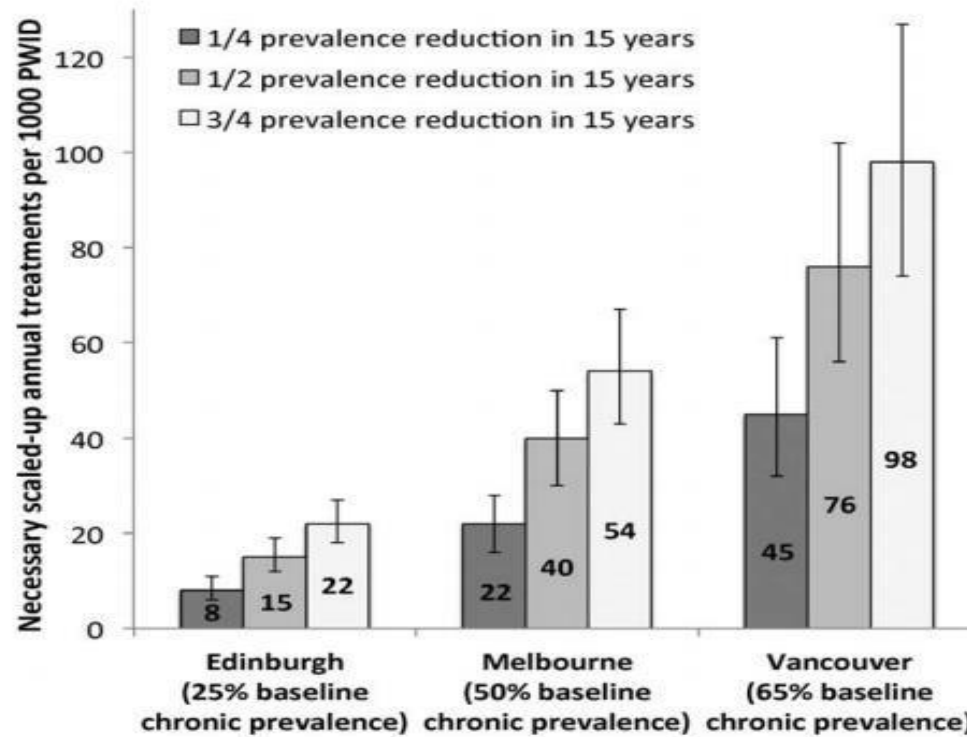


Potential benefits of treatment in PWID :

Societal benefits and Individual benefits

- Target therapy to those at greatest risk of transmitting infection (younger injectors or newer initiates to injecting)





Modest rates of HCV treatment among active injecting drug users could effectively reduce transmission in 25% prevalence group

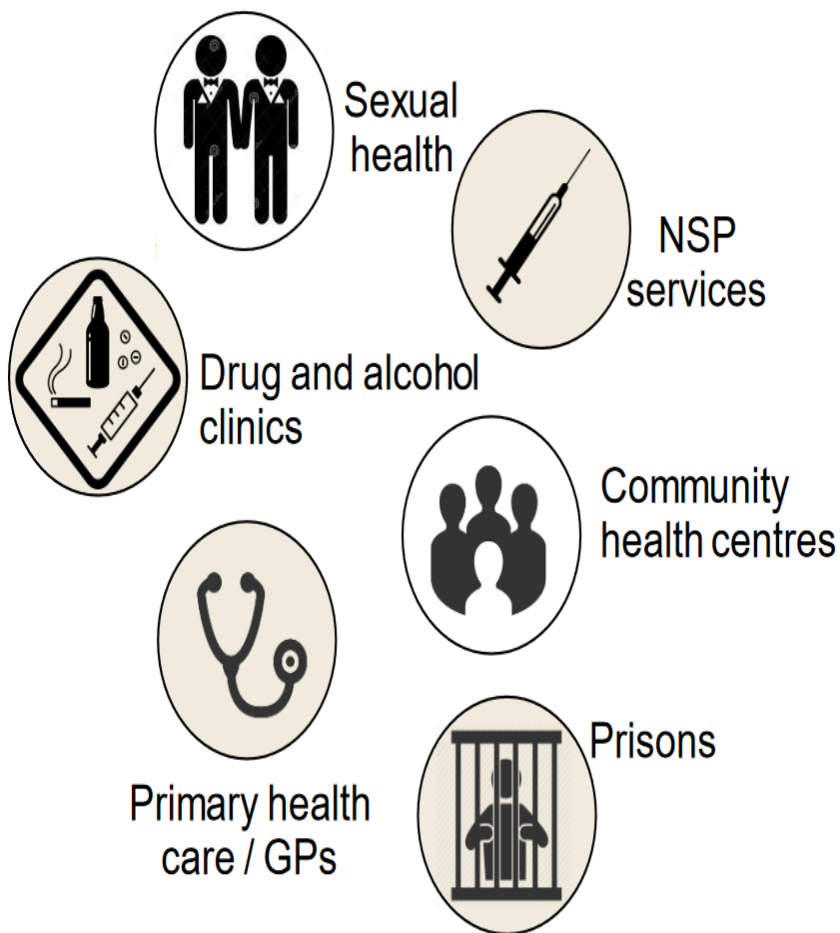
TraP HepC: 2-Yr Results From HCV Treatment as Prevention in PWID in Iceland

- Dramatic reduction in community viral load and HCV incidence between 2015-2017 at National Addiction Hospital
 - **53% reduction in new HCV infections**
 - **72% reduction in HCV PCR positivity among PWID from 43% to 12%**

SVR12, %	Treated Pts (N = 518)	<i>P</i>
Current IVD use (last 6 mos)	87	.0033
Not currently using IVD	95	
Homeless	74	.0005
Not homeless	94	

Settings, services, and providers

Settings



Services



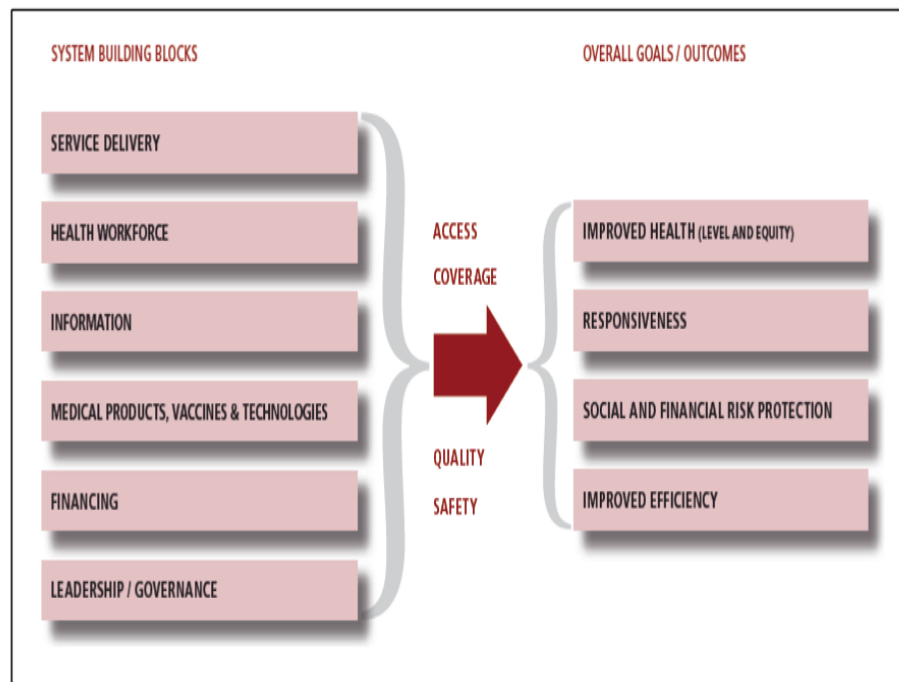
Providers



- Specialists
- Primary care providers
- Drug and alcohol providers
- Nurses
- Peer support workers
- Others

A health systems approach to HCV elimination

"A health system consists of all organisations, people and actions whose primary intent is to promote, restore or maintain health." – World Health Organization, 2007



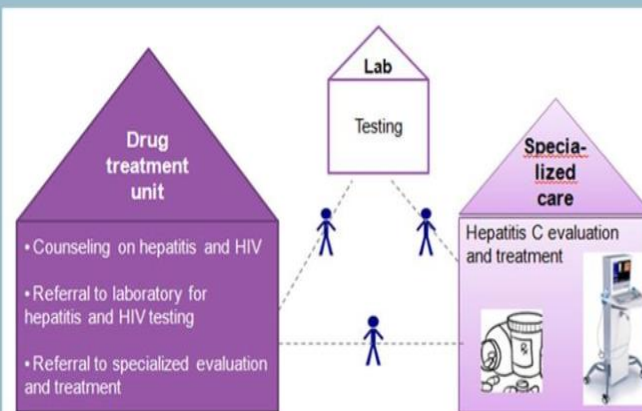
Source: WHO 2017



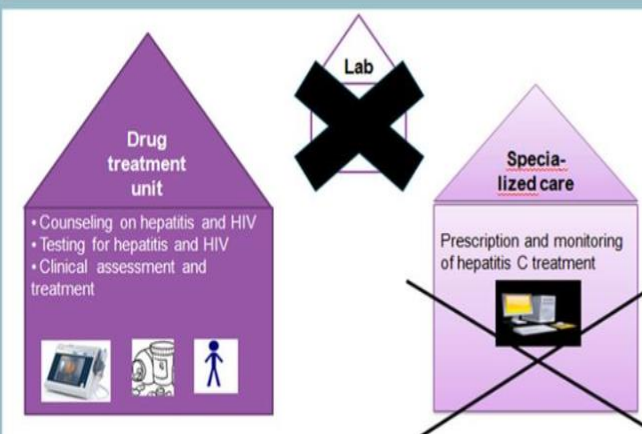
SACC: “Borgernær” shared care

Figure 1

Former organization



Future organization





Venezia Mestre, 12 ottobre 2017
Hotel NH Laguna Palace

CONVEGNO NAZIONALE

La gestione dell'infezione da HCV nel consumatore di sostanze: **mind the gaps**

Chair **Felice Alfonso Nava**

Con il Patrocinio di



programma scientifico

Faculty

Alfredo Alberti, Università degli Studi di Padova

Massimo Andreoni, Università degli Studi "Tor Vergata", Roma

Sergio Babudieri, Presidente Onorario SIMSPE, Università degli Studi di Sassari

Roberta Balestra, Azienda Sanitaria Universitaria Integrata di Trieste

Giorgio Barbarini, Fondazione IRCCS Policlinico San Matteo, Pavia

Pietro Fausto D'Egidio, Presidente FeDerSerD, Pescara

Ivan Gardini, Associazione EpaC Onlus, Vimercate (Mi)

Claudio Leonardi, Presidente S.I.Pa.D., U.O.C. Prevenzione e Cura Tossicodipendenze ed Alcolismo SERT. D/11 ASL, Roma

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CONVEGNO NAZIONALE
La gestione dell'infezione da HCV
nel consumatore di sostanze: **mind the gaps**

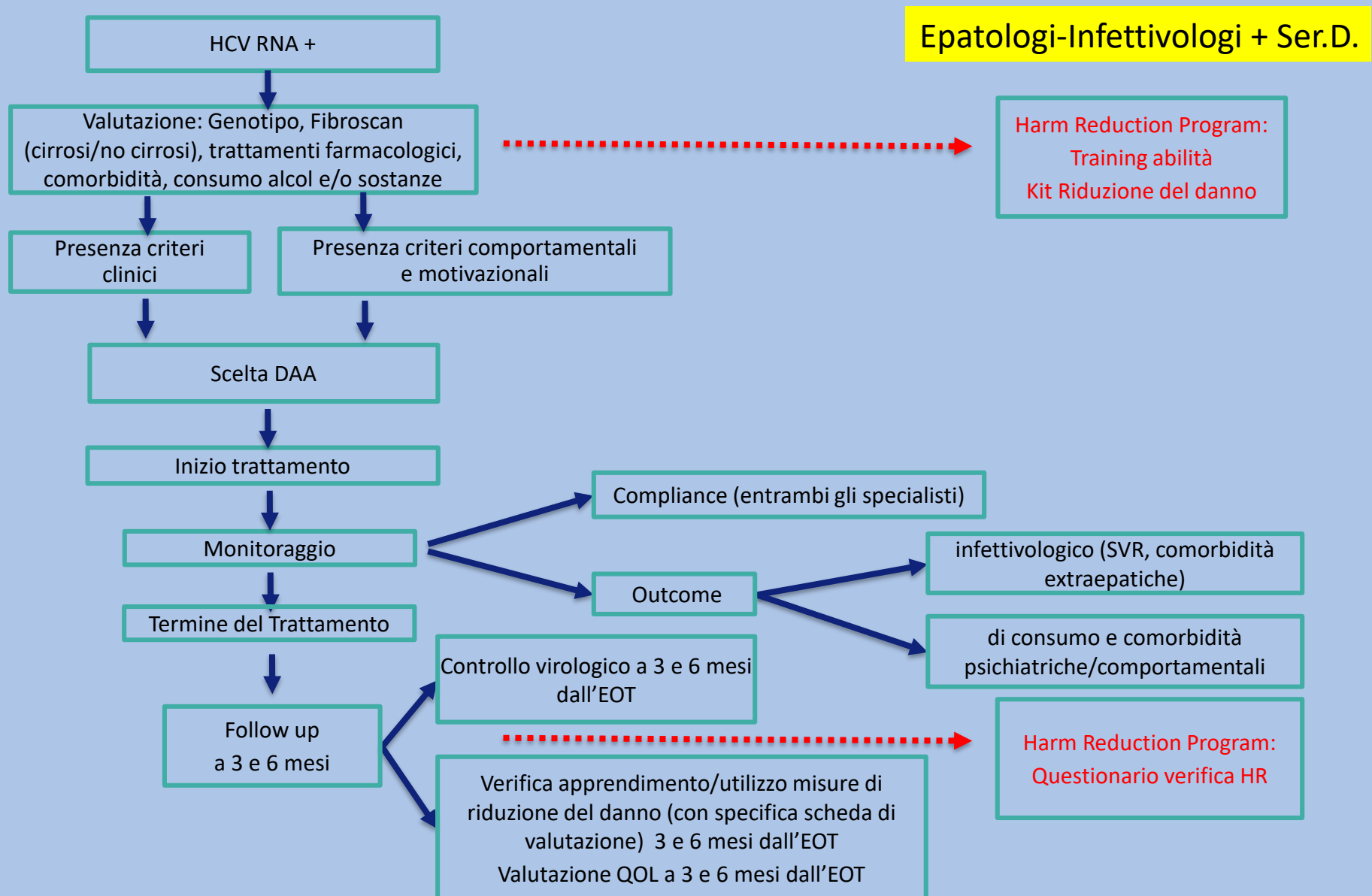
POSITION PAPER

PER UN PROGRAMMA DI ELIMINAZIONE DELLA EPATITE C NELLA POPOLAZIONE A RISCHIO DEI CONSUMATORI DI SOSTANZE E DEI DETENUTI

**Felice A. Nava¹, Alfredo Alberti², Massimo Andreoni³, Sergio Babudieri⁴, Giorgio Barbarini⁵, Pietro Fausto D'Egidio⁶,
Claudio Leonardi⁷, Alfio Lucchini⁸**

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Presidente Onorario SIMSPE, ⁵Clinica Malattie Infettive e Tropicali Fondazione IRCCS San Matteo, Pavia, Ufficio di
Presidenza CLEO, ⁶Internista, Presidente Nazionale FeDerSerD, ⁷Direttore U.O.C. Patologie da Dipendenze ASL Roma 2,
Presidente S.I.Pa.D., ⁸Dipartimento di Salute Mentale e delle Dipendenze, ASST Melegnano e della Martesana (Città
Metropolitana di Milano), Past President FeDerSerD*

Trattamento



GESTIONE MULTIDISCIPLINARE INTEGRATA

LA DECISIONE DI EFFETTUARE IL TRATTAMENTO
VIENE ASSUNTA CONGIUNTAMENTE DAL
CENTRO SPECIALISTICO E DAL SERD.

IL PAZIENTE VIENE TRATTATO NEL SERD, DAGLI
OPERTORI DEL SERD O NELLA STRUTTURA
CARCERARIA DAL CONSULENTE
INFETTIVOLOGO DI CONCERTO CON IL
CONSULENTE SERD (DOT)

Medications don't work
in patients who don't
take them

- C. Everett Koop, MD

The good physician treats the disease ;
the best physician treats the patients
with the disease

William Osler



ORA.....

LAVORIAMO

INSIEME !!!!!



The Rollercoaster, Jim Clark