EPATOLOGI OSPEDALIERI CLUB

OSPEDALI DEI COLLI
MONALDI - COTUGNO - C.T.O.

Azienda Ospedaliero di Rilievo Nazionale (A.O.R.N.) " Dei Colli"
"Monaldi-Cotugno-CTO"-

Ceglie Messapica
22-23 Settembre 2023

Eliminazione di HCV :
A che punto siamo ?

Antonio Izzi

Dipartimento Malattie Infettive e Urgenze Infettivologiche

Outline

- **Elimination of HCV in 2030: WHO elimination goals**
- **Elimination of HCV: where we are now ?**
- **Strategies needed for HCV elimination**

Disease Eradication vs Elimination vs Control

- **Eradication: permanent reduction to zero of the worldwide incidence of infection**; intervention measures no longer needed

- **Elimination: reduction to zero of incidence in a defined geographical area as a result of deliberate efforts**; continued intervention measures required

- **Control: reduction in the incidence, prevalence, morbidity, or mortality of an infectious disease to a locally acceptable levels**; continued intervention measures required

Molyneux DH, et al. Trends Parasitol. 2004;20:347-351.

Editorial

JOURNAL OF HEPATOLOGY

Viral hepatitis: "E" is for equitable elimination

Jeffrey V. Lazarus[1,2,*], Juan M. Pericàs[1], Massimo Colombo[3], Michael Ninburg[4], Stefan Wiktor[5], Mark Thursz[6]

[1]*Barcelona Institute for Global Health (ISGlobal), Hospital Clínic, University of Barcelona, Barcelona, Spain;* [2]*CHIP, Rigshospitalet, University of Copenhagen, Copenhagen, Denmark;* [3]*Clinical and Research Center Humanitas, Rozzano, Italy;* [4]*World Hepatitis Alliance, London, United Kingdom;* [5]*Department of Global Health, University of Washington, USA;* [6]*Division of Digestive Diseases, St Mary's Hospital, Imperial College London, London, United Kingdom*

Journal of Hepatology **2018** vol. 69 | 762–764

"**Elimination – a reduction in HCV incidence and HCV- related mortality to a level that are no longer a public health concern"**

!

JOURNAL OF HEPATOLOGY

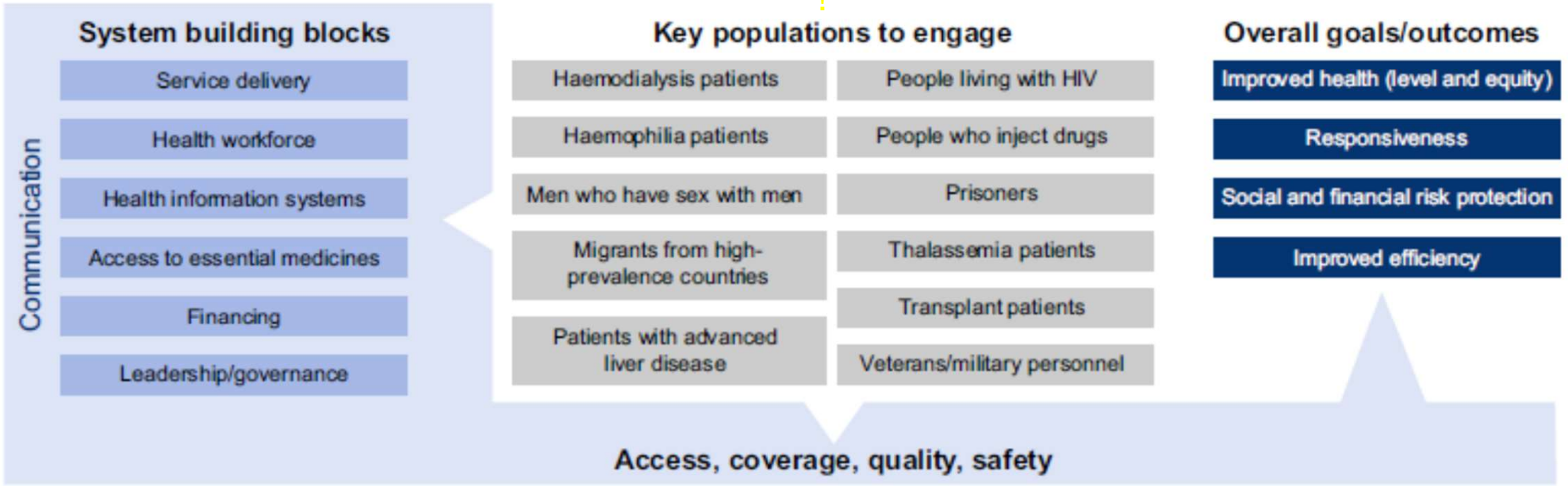


Fig. 1. The WHO health systems framework needs to be at the service of equitable elimination of viral hepatitis.

Why Talk About Elimination?

We Now Have the Tools: They Fall Under 3 Main Pillars

Effective Care and Treatment

- 1-3 pills/day for 2-3 mos
- Cure rates > 95%
- Few or no adverse events

Prevention Strategies

- Harm reduction
- Needle/syringe programs
- Opioid agonist therapy

Simple Testing and Diagnosis

- Available blood tests
- Point-of-care tests
- Reflex testing

Combined, these tools can be used to eliminate hepatitis C as a public health problem

JJ Feld. Blueprint to inform hepatitis C elimination efforts in Canada. Canadian Network on Hepatitis C. March 13 2019.

Approaches to HCV Elimination

Global Elimination
- WHO Elimination Targets

National/Regional Elimination
- National strategies to meet WHO targets

Micro-elimination
- Elimination in a defined population
- HIV/HCV, hemophilia, prison

Global timing of hepatitis C virus elimination: Estimating the year countries will achieve the World Health Organization elimination targets

- Progress made in 45 high-income countries and territories towards meeting the WHO 2030 HCV elimination targets:

80% reduction
in the incidence of chronic HCV infection between 2015 and 2030

65% reduction
in liver-related deaths due to chronic HCV infection between 2015 and 2030

90% diagnosis
coverage of HCV-infected population in 2015

80% treatment
coverage of eligible HCV-infected population in 2015

Markov disease progression model

- Previously published[1]
- Demographic inputs from UN World Population Prospects
- Epidemiological inputs from Polaris Observatory
- Primary modification to published model:
  - Incident cases of HCV were separated into vertically and horizontally acquired infections
  - Future incidence was assumed to change at the same annual rate as prevalence

1. Blach S, et al. Lancet Gastroenterol Hepatol 2017;2:161–176.

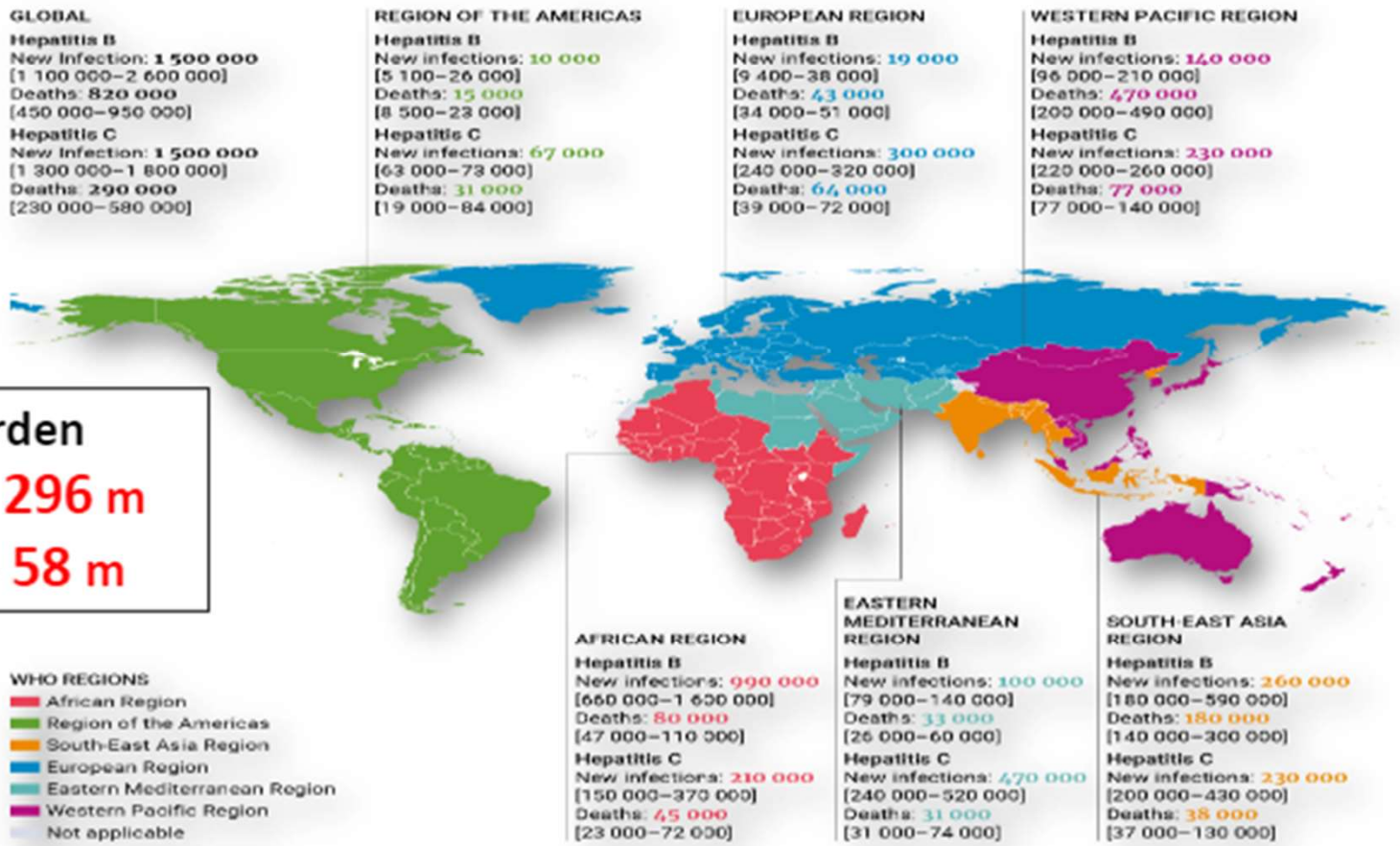
- Maintaining the standard of care in 2017 (new diagnoses, treatment eligibility, treatment rate, and average SVR) was defined as the status quo
- Modeled outcomes were analyzed to determine which year countries were projected to meet 2030 targets
  - Earliest year in which all targets were met was defined as the year of HCV elimination

Razavi H, et al. EASL 2019, Vienna, Austria. #SAT-260

Outline

- Elimination of HCV in 2030: WHO elimination goals
- Elimination of HCV: where we are now ?
- Strategies needed for HCV elimination

New data on Hepatitis B and C burden, incidence and mortality by WHO region (2021 WHO Global progress report)



Global Burden

Hepatitis B - 296 m

Hepatitis C - 58 m

World Health Organization

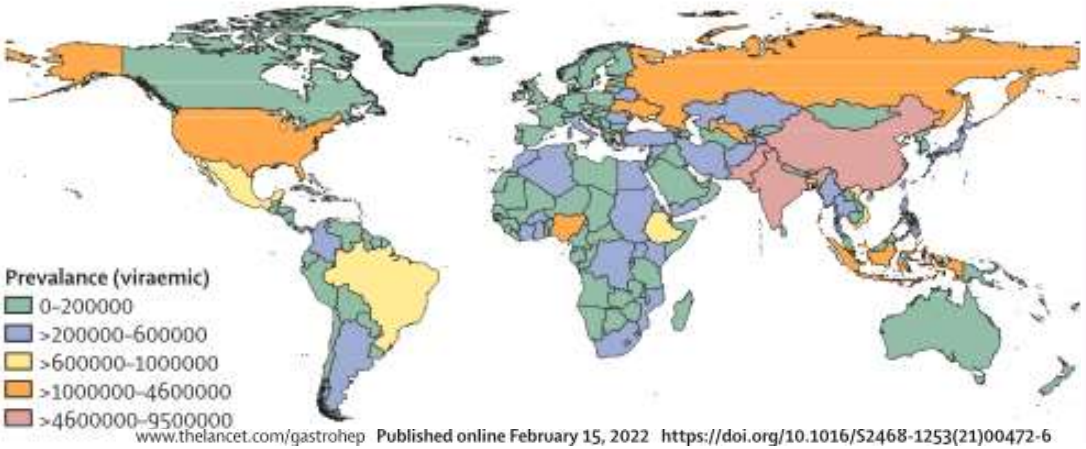
Global change in hepatitis C virus prevalence and cascade of care between 2015 and 2020: a modelling study

*The Polaris Observatory HCV Collaborators**

Lancet Gastroenterol Hepatol 2022

Published Online February 15, 2022

C



	Viraemic prevalence in 2015*†	Viraemic population (1000s) in 2015*†	Viraemic prevalence in 2020*†	Viraemic population (1000s) in 2020*†
(Continued from previous page)				
Europe, western				
Austria	0·3% (0·1–0·4)	25 (5–39)	0·2% (0·0–0·3)	15 (3–23)
Belgium	0·3% (0·2–0·6)	31 (22–77)	0·2% (0·1–0·5)	24 (17–59)
Denmark	0·2% (0·2–0·3)	11 (10–16)	0·1% (0·1–0·2)	7 (6–10)
Finland	0·4% (0·3–0·5)	22 (17–28)	0·3% (0·3–0·4)	19 (15–25)
France	0·3% (0·2–0·3)	183 (143–234)	0·2% (0·1–0·2)	112 (88–143)
Germany	0·3% (0·2–0·5)	254 (152–457)	0·2% (0·1–0·4)	189 (113–340)
Greece	1·0% (0·7–1·3)	106 (75–136)	0·9% (0·7–1·2)	96 (68–123)
Iceland	0·2% (0·2–0·3)	0·7 (0·6–0·9)	0·1% (0·1–0·1)	0·3 (0·2–0·3)
Ireland	0·6% (0·4–1·1)	30 (20–51)	0·6% (0·4–0·9)	27 (18–46)
Israel	0·9% (0·6–1·3)	73 (47–111)	0·7% (0·5–1·1)	61 (39–91)
Italy	1·4% (0·6–2·0)	888 (388–1298)	1·0% (0·4–1·4)	577 (252–843)
Luxembourg	0·9% (0·5–1·1)	5 (3–6)	0·8% (0·4–0·9)	5 (3–6)
Malta	0·3% (0·2–0·6)	1·2 (1·1–2·6)	0·2% (0·2–0·4)	0·9 (0·8–1·9)
Netherlands	0·1% (0·0–0·2)	20 (8–34)	0·1% (0·0–0·1)	14 (5–24)
Norway	0·3% (0·2–0·5)	14 (9–29)	0·1% (0·1–0·3)	7 (4–14)
Portugal	0·5% (0·5–0·8)	61 (55–92)	0·4% (0·4–0·6)	42 (38–64)
Spain	0·3% (0·2–1·3)	201 (112–742)	0·1% (0·1–0·4)	56 (31–205)
Sweden	0·4% (0·3–0·5)	41 (34–50)	0·3% (0·2–0·3)	26 (22–31)
Switzerland	0·5% (0·5–0·5)	44 (40–47)	0·4% (0·3–0·4)	32 (29–35)
UK	0·3% (0·2–0·4)	177 (132–247)	0·2% (0·1–0·3)	127 (95–177)

Hepatitis C: The first ever curable chronic viral infection in medical history

Actual Burden of HCV Infection Worldwide: WHO

58 million
Infected

21%
Diagnosed

13%
Treated

152,000
New liver cancers

300,000
Annual Deaths

One death every
1.5 minutes

Clinical Gastroenterology and Hepatology 2023;21:1978–1991

2. WHO. *Hepatitis C* (2021) Available online at: https://www.who.int/news-room/fact-sheets/detail/hepatitis-c

REVIEW ARTICLES

The Global Burden of Liver Disease

Zobair M. Younossi,[1,2,3] Grace Wong,[4] Quentin M. Anstee,[5,6] and Linda Henry[1,3,7]

Clinical Gastroenterology and Hepatology 2023;21:1978–1991

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Table 1. Chronic Liver Disease Prevalence Rates by Global Organization (2019)

Chronic liver disease	WHO	GBD	Polaris Observatory
Hepatitis B virus	296 million infected 820,000 annual deaths 1.5 million new infections 10% diagnosed 2% treated Areas most affected: Western Pacific, Africa, Southeast Asia, Eastern Mediterranean	316 million infected 555,000 annual deaths Areas most affected: Africa and Burma	2.91 million infected (2016) 10% diagnosed 8% treated Areas most affected: Africa, Western Pacific
Hepatitis C virus	58 million infected (3.2 million children) 300,000 annual deaths 1.5 million new infections 21% diagnosed 13% treated Areas most affected: Eastern Mediterranean, Europe, South East Asia, Western Pacific, Africa, regions of the Americas	113 million infected (58.8 million females, 54.4 million males) 500,000 annual deaths 82.5 new cases per 100,000 people 9.4 million people treated from 2015–2019 Areas most affected: Asia and Africa	56.8 million infected 1.42 million new infections until 2030 2.3% diagnosed 5% treated Areas most affected: Eastern Europe, Asia (Central and Southeast)

2. WHO. *Hepatitis C* (2021) Available online at: https://www.who.int/news-room/fact-sheets/detail/hepatitis-c

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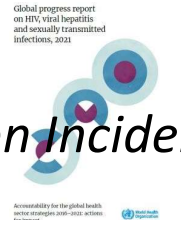
WHO Global Progress Report (Hepatitis B and C)



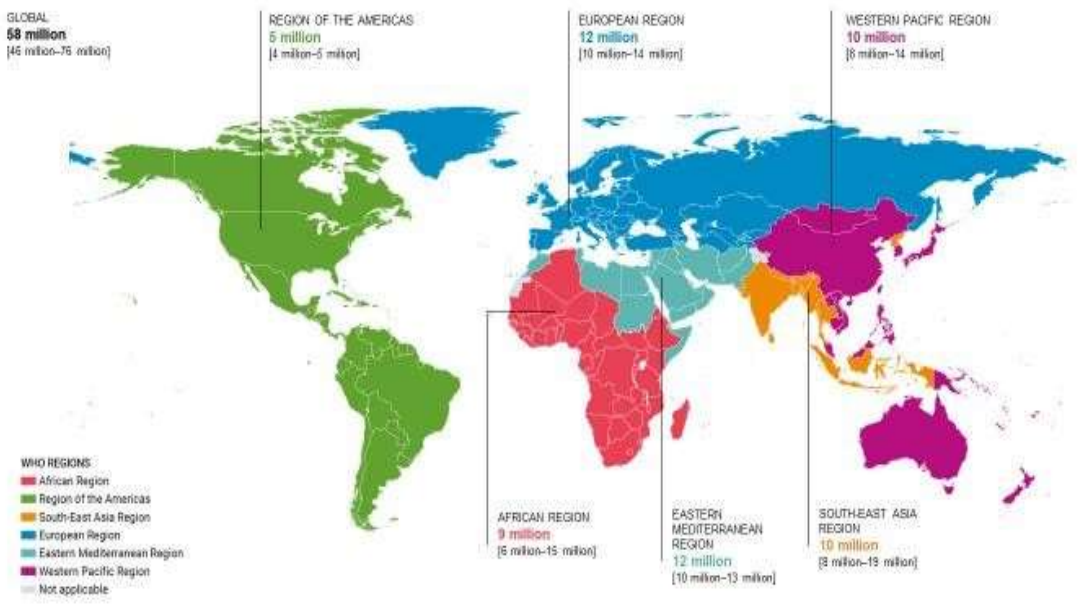
New 2019 data on Incidence, burden, mortality, testing/treatment cascade

HCV GLOBAL
56.8 million
[46 million–76 million]

Highlights

- **1.1 million deaths in 2019 mainly due to HBV, w[illegible] signs of HCV decline (299,000 deaths)**
- **3 million new infections (1.5 m HBV and 1.5 m HCV) largerly due to PWUD**
- **Note decrease in HCV burden**
- **9.4 million people received HCV treatment (9-fold increase from 1 million baseline in 2015)**
- **21% HCV diagnosed (62% of Diagnosed received treatment)**
- **10% HBV diagnosed (22% of diagnosed on treatment)**

Burden [illegible] hepatitis C viraemic infection by WHO Region, 2019



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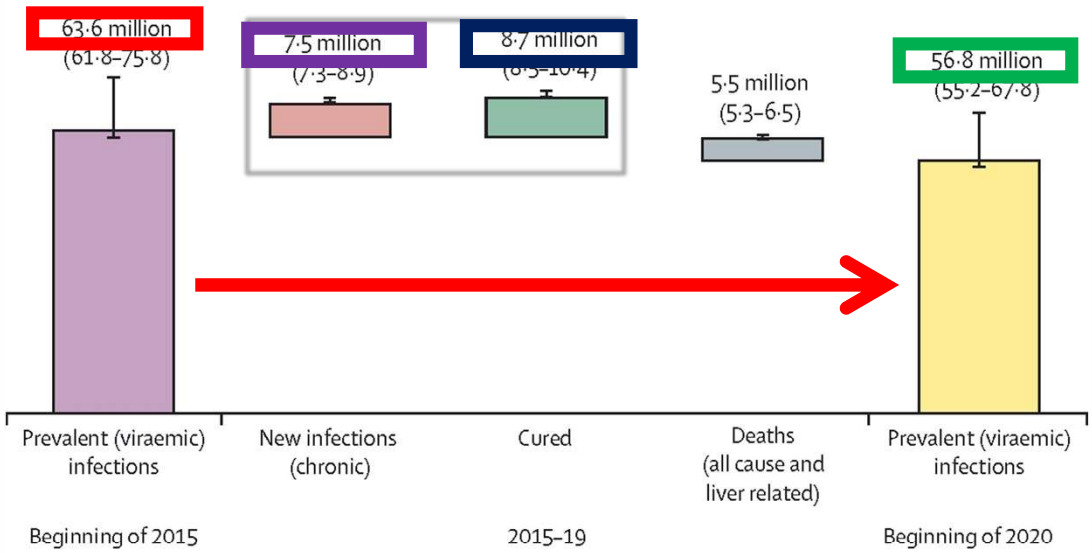
The Global Burden of HCV: Polaris Observatory 2022



The Polaris Observatory 2022

HCV Debrief JJ Feld

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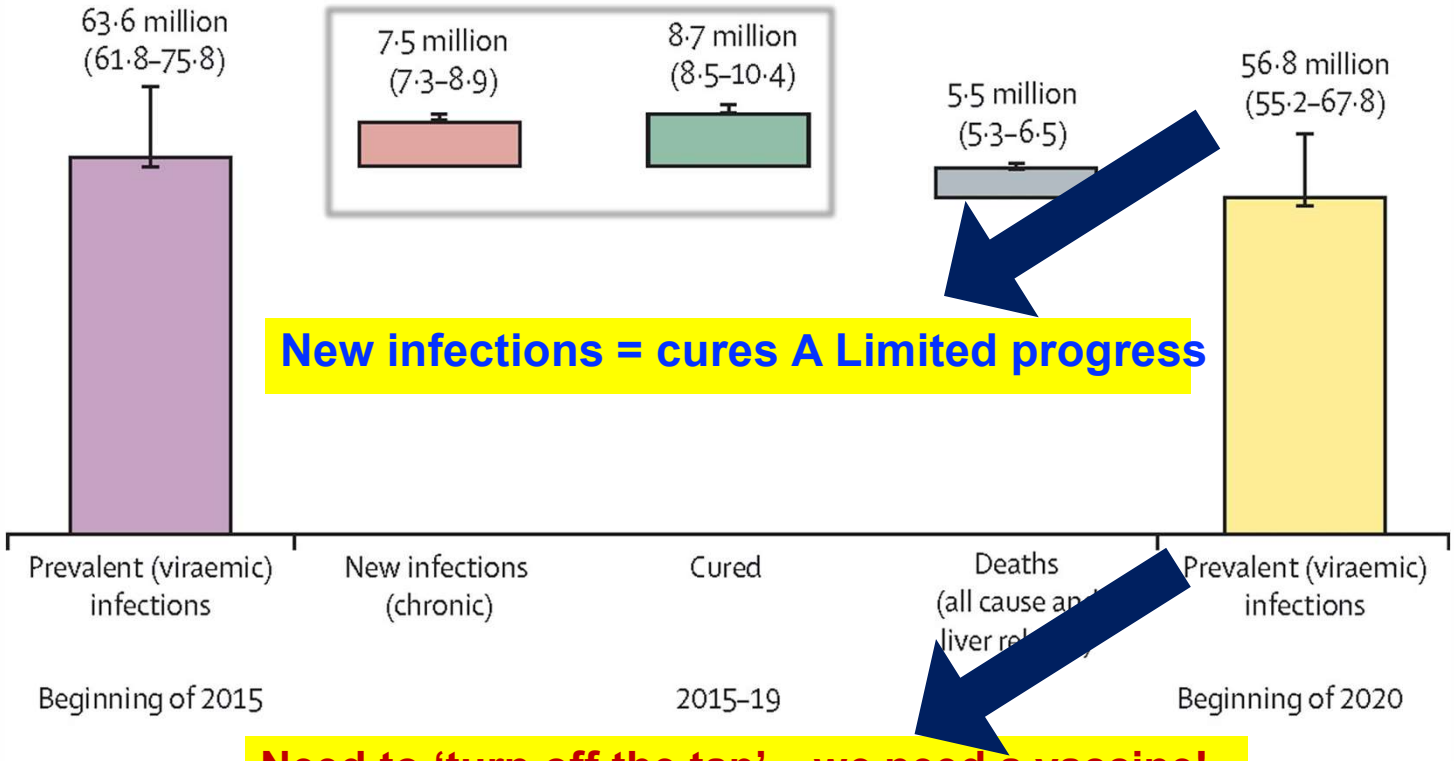
GLOBAL HEPATITIS SUMMIT 2023 PARIS FRANCE April 25 – 28, 2023

The 18th International Symposium on Viral Hepatitis and Liver Disease (ISVHLD)

The Global Burden of HCV: Polaris Observatory 2022



New infections = cures A Limited progress

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

The Polaris Observatory 2022

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Lancet Gastroenterol Hepatol 2022

Published Online February 15, 2022

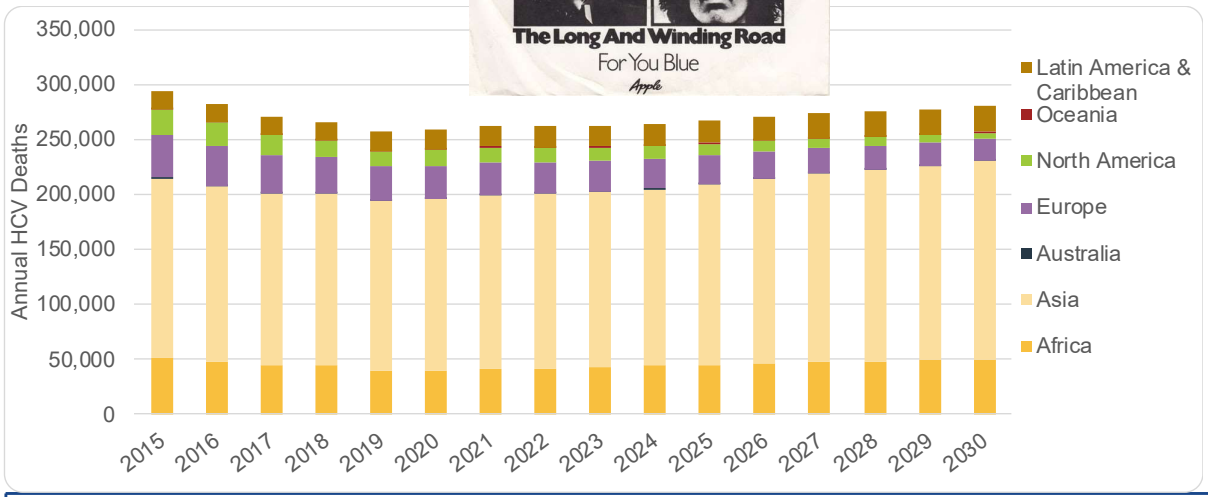
The disease burden of hepatitis B and hepatitis C from 2015 to 2030: the long and winding road

RESULTS (CONT.)

HCV

Between 2015 and 2030:

- **Prevalence is expected to decrease from 65 million in 2015 to 52 million**
  - **20% global decrease**
  - **Cases in Oceania expected to increase**
- **Incidence of chronic HCV expected to decline from 1,510,000 to 1,297,000 new cases/year**
  - **14% decrease**
  - **Cases in North America expected to increase**
- **Global mortality expected to decrease from 295,000 to 281,000**
  - **5% decrease**
  - **Increases expected in Asia, Oceania and Latin America & the Caribbean**
- **Incidence of HCC expected to increase from 210,000 to 215,000 cases/year**
  - **3% increase**
  - **Increases expected in Asia, Oceania and Latin America & the Caribbean**



CONCLUSION

- Progress has been made in regard to prevalence and incidence
- However, **without additional interventions, almost 12 million individuals will die from preventable deaths !!!**
- Early gains made by Egypt, high-income countries and other early adopters are offset by increasing disease burden in the rest of the world
- Innovative guidelines and funding mechanisms are needed to help countries meet international commitments to elimination

D Razavi-Shearer, et al. ILC 2022; OS050

EASL™ The Home of Hepatology

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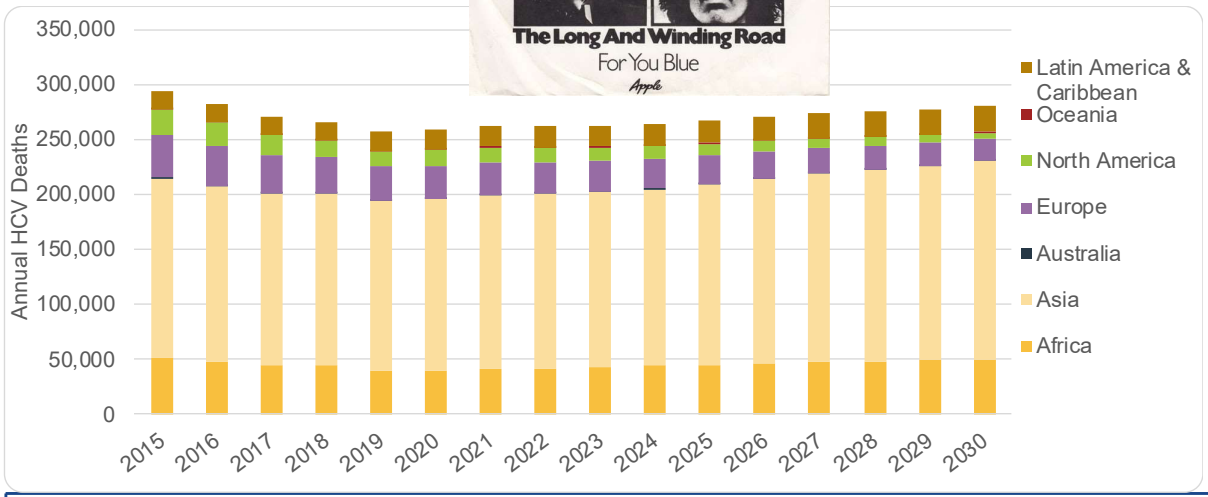

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Micro-elimination
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- HIV/HCV, hemophilia, prison

JOURNAL
OF HEPATOLOGY

Global burden of liver disease: 2023 update

Harshad Devarbhavi[1], Sumeet K. Asrani[2,*], Juan Pablo Arab[3,4], Yvonne Ayerki Nartey[5], Elisa Pose[6], Patrick S. Kamath[7]

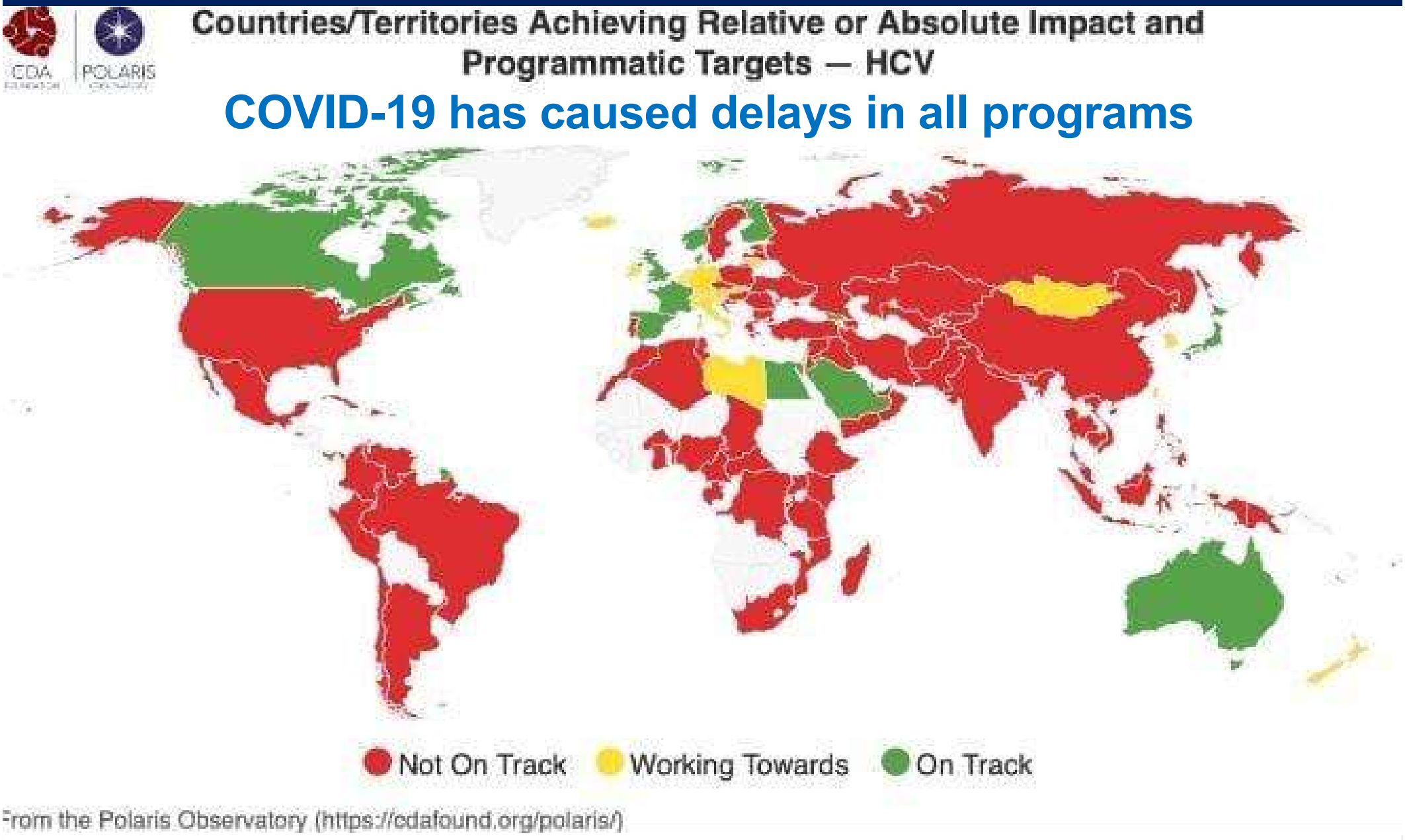
Table 2. Burden of hepatitis B and C across WHO regions.*

WHO region	African Region	Region of Americas	South East Asian Region	European Region	Eastern Mediterranean Region	Western Pacific Region
Prevalence of HBV infection among general population (%) 2019	7.5	0.5	3	1.5	2.5	5.9
Hepatitis B Incidence, number of cases 2019	990,000	10,000	260,000	19,000	100,000	140,000
People living with HBV infection among general population 2019	82.3 million	5.4 million	60.5 million	13.6 million	18.2 million	115.7 million
People dying from HBV infection 2019	80,000	15,000	180,000	43,000	38,000	470,000
Prevalence of Hepatitis B infection among children younger than 5 years (%) 2019	2.5	0.1	0.4	0.3	0.8	0.3
Children younger than 5, living with hepatitis B infection 2019	4.3million	51,000	640,000	150,000	720,000	360,000
Prevalence of HCV infection among general population (%) 2019	0.8	0.5	0.5	1.3	1.6	0.5
People living with HCV infection among general population 2019	9.3 million	4.8 million	10 million	12.5 million	11.8 million	9.5 million
Hepatitis C Incidence, number of cases 2019	210,000	67,000	230,000	300,000	470,000	230,000
People dying from HCV infection 2019	45,000	31,000	38,000	64,000	31,000	77,000

*Data adapted from WHO, 2021 (Global progress report on HIV, viral hepatitis, and sexually transmitted infections, 2021. Accountability for the global health sector strategies 2016–2021: actions for impact).

2. WHO. *Hepatitis C* (2021) Available online at: https://www.who.int/news-room/fact-sheets/detail/hepatitis-c

On May 15 2023, ten countries were on track to eliminate HCV by 2030 and few others working towards



On Track: Australia, Canada, Egypt, Finland, France, Japan, Norway, Saudi Arabia, Spain, United Kingdom

JOURNAL
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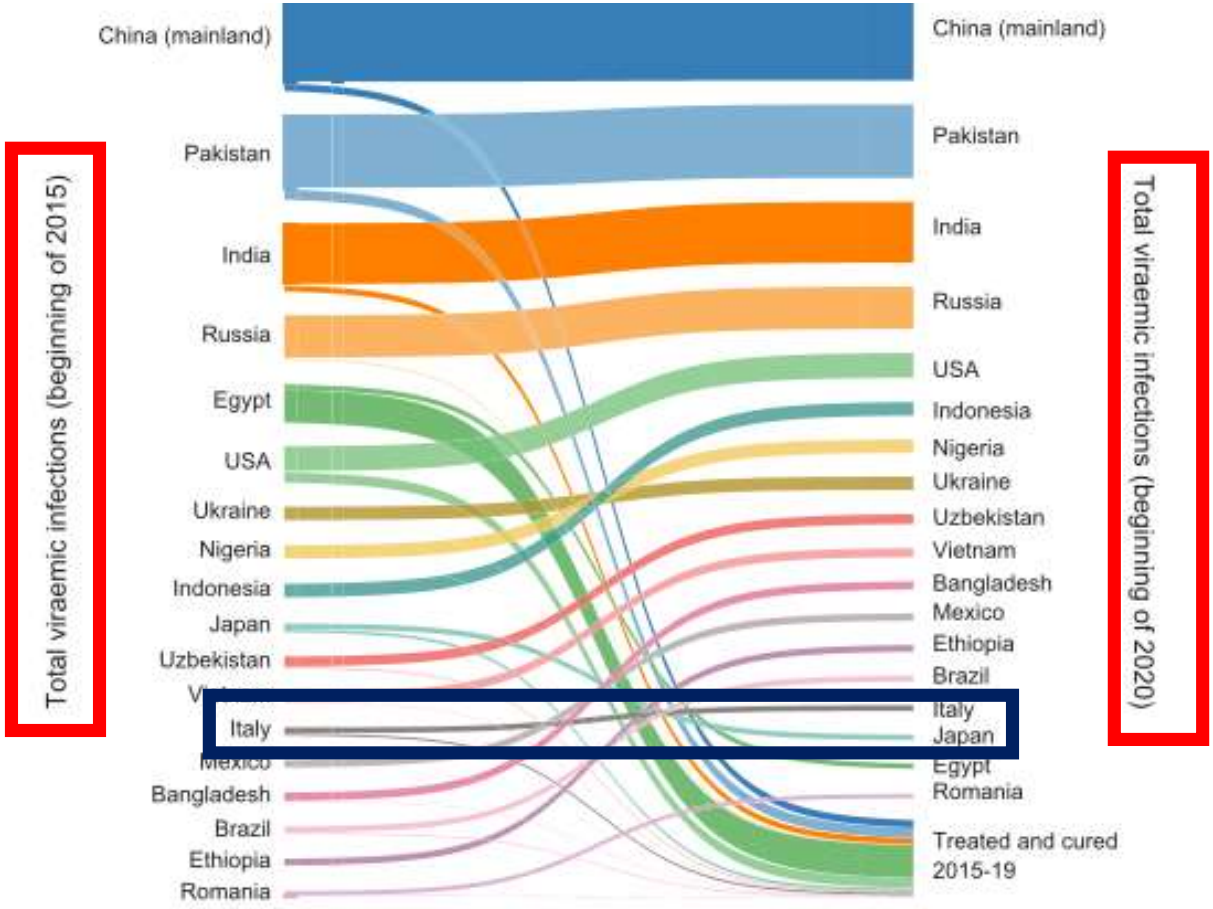


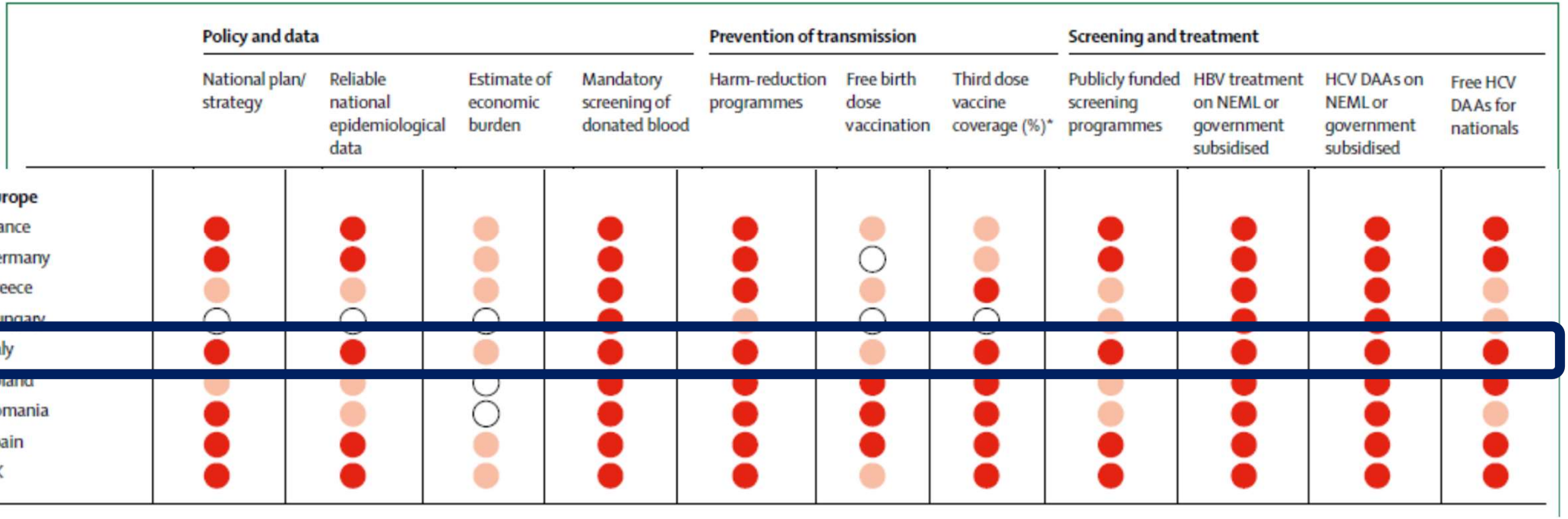
Fig. 3. Global change in viraemic HCV infections, 2015–2020. (A) Waterfall gram of viraemic HCV infections in 2020, compared with viraemic infections at the beginning of 2015, including the fraction attributable to treatment and cure, among countries accounting for more than 70% of viraemic infections in 2015. Bar width is proportional to the size of the viraemic population. Figure reproduced with permission from Polaris Observatory HCV Collaborators 2022 [83].

The Lancet Gastroenterology & Hepatology Commission

Accelerating the elimination of viral hepatitis: a *Lancet Gastroenterology & Hepatology* Commission

Lancet Gastroenterol Hepatol
2019; 4: 135–84

*Graham S Cooke, Isabelle Andrieux-Meyer, Tanya L Applegate, Rifat Atun, Jessica R Burry, Hugo Cheinquer, Geoff Dusheiko, Jordan J Feld, Charles Gore, Max G Griswold, Saeed Hamid, Margaret E Hellard, JinLin Hou, Jess Howell, Jidong Jia, Natalia Kravchenko, Jeffrey V Lazarus, Maud Lemoine, Olufunmilayo A Lesi, Liudmyla Maistat, Brian J McMahon, Homie Razavi, Teri R Roberts, Bryony Simmons, Mark W Sonderup, C Wendy Spearman, Bridie E Taylor, David L Thomas, Imam Waked, John W Ward, Stefan Z Wiktor, on behalf of The Lancet Gastroenterology & Hepatology Commissioners**



Strategie di Eliminazione dell'HCV in Italia ed Evoluzione delle Politiche Sanitarie

2015 **2016** **2017** **2018** **2019** **2020** **2021** **2022**

Accesso Prioritizzato alla Terapia Antivirale

Accesso Universale alla Terapia Antivirale

Fondo Dedicato Farmaci Innovativi

Screening Attivo Approvato

Piano Nazionale per l'eliminazione delle Epatiti Virali

Evidenze Scientifiche

- Accesso universale è costo-efficace versus accesso prioritizzato.
- Lo screening attivo è costo efficace versus il trattamento dei pazienti ad oggi *linked to care*.

		2018	2019
Trattamenti Annuali		56,499	36,348
Anno in cui i Target OMS per l'eliminazione saranno raggiunti	Incidenza	2028	2037
	Mortalità	2023	2025
	Diagnosi	*	2037
	Trattamento	2029	2035
Anno di Eliminazione		**2029**	**>2038**
***On Track* per l'eliminazione**		**SI**	**No**

Investimento Continuo in Screening e Terapia anti-HCV elementi indispensabili ai fini dell'eliminazione HCV

36,348

Evidenze Economiche a supporto per allocazione fondi ad hoc per screening e trattamento

>2037

No

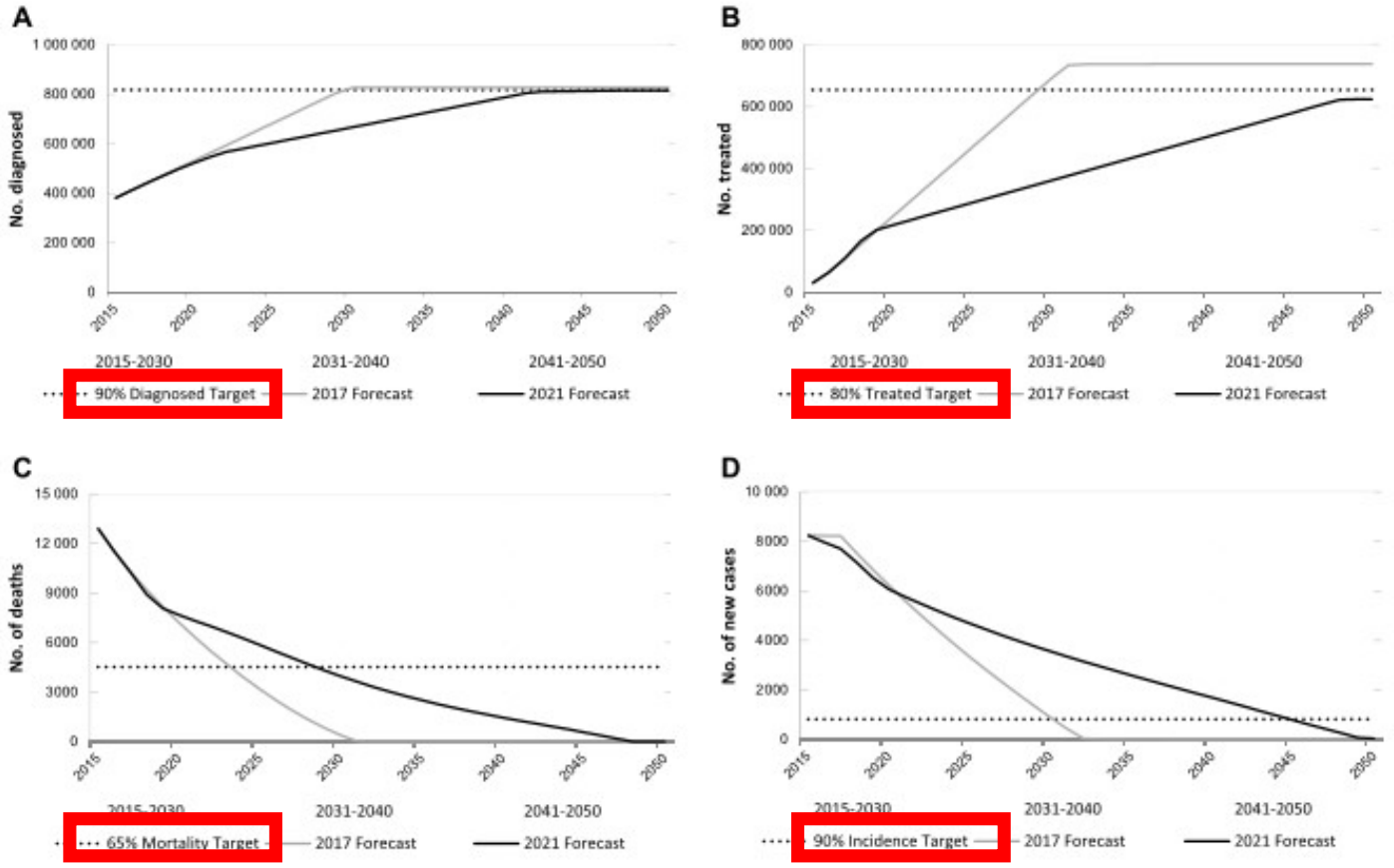
Pubblicazione del PDTA per l'infezione da HCV

Creazione del Gruppo tecnico presso il Ministero della Salute per lo screening HCV

The Journal of Infectious Diseases
SUPPLEMENT ARTICLE

From Prioritization to Universal Treatment: Successes and Challenges of Hepatitis C Virus Elimination in Italy

Loreta A. Kondili,[1,2,a,©] Lucia Craxì,[3,a] Felice Nava,[4,5] Sergio Babudieri,[6,7] Roberta D'Ambrosio,[8] Andrea Marcellusi,[9] Francesco Saverio Mennini,[9,10,11] Sabrina Valle,[12] Pierluigi Russo,[13,14] Pier Paolo Olimpieri,[14] Massimo Andreoni,[15,16] and Alessio Aghemo[17,18,19]



The Journal of Infectious Diseases, Volume 228, Issue Supplement_3, 15 September 2023, Pages S211–S220

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From Prioritization to Universal Treatment: Successes and Challenges of Hepatitis C Virus Elimination in Italy

Loreta A. Kondili,[1,2,a,©] Lucia Craxì,[3,a] Felice Nava,[4,5] Sergio Babudieri,[6,7] Roberta D'Ambrosio,[8] Andrea Marcellusi,[9] Francesco Saverio Mennini,[9,10,11] Sabrina Valle,[12] Pierluigi Russo,[13,14] Pier Paolo Olimpieri,[14] Massimo Andreoni,[15,16] and Alessio Aghemo[17,18,19]

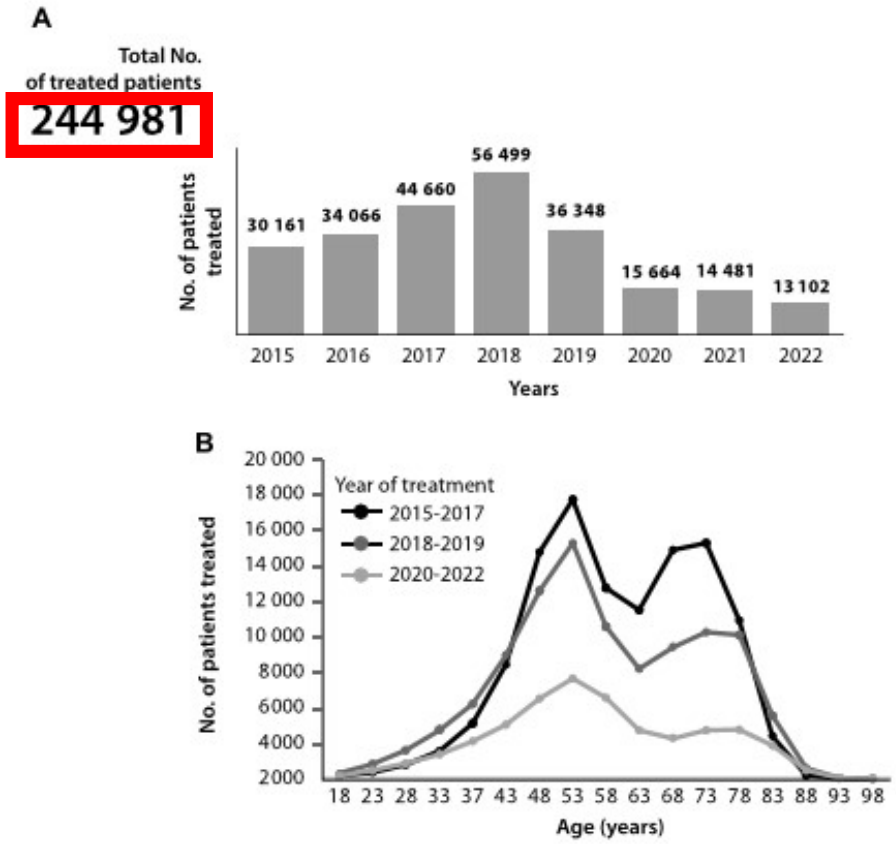


Figure 1. *A*, Number of patients with HCV treated per year; and (*B*) number of patients with HCV treated per year by age group as reported by the Italian Medicines Agency Registry for Direct Acting Antivirals (DAA) Monitoring.

The Journal of Infectious Diseases, Volume 228, Issue Supplement_3, 15 September 2023, Pages S211–S220

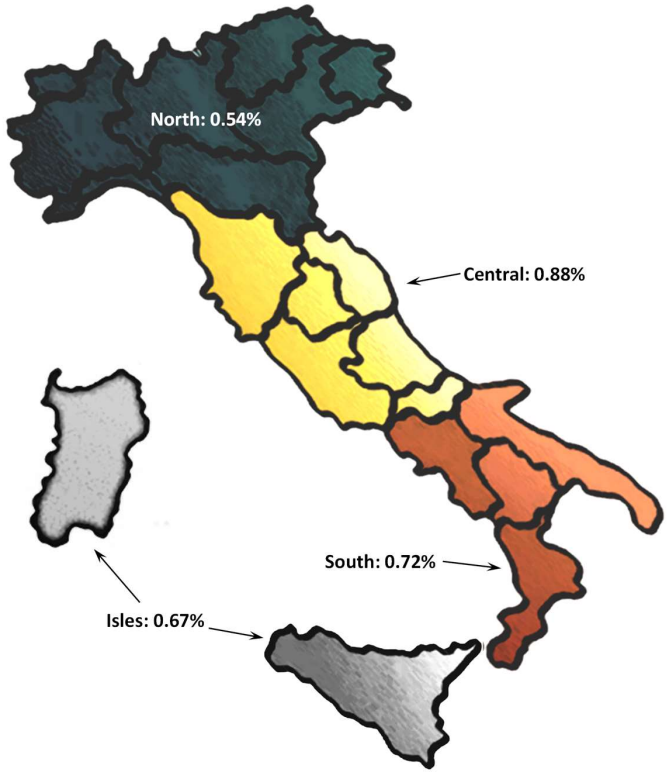
18 Settembre 2023

Ufficio Registri di Monitoraggio AIFA

Prevalence of Undiagnosed HCV Estimated by Regional Mathematical Modeling: the 2021 update

Estimates of the absolute number and percentage of viraemic HCV individuals in Italy according to fibrosis stage and macroarea.

Macroarea/ fibrosis stage	Absolute number and 95% CI	Prevalence (%) and 95% CI (%)	Percentage
F0-F3	287,730 (279,911-295,549)	0.48 (0.46-0.59)	100
F4	110,880 (103,130-118,630)	0.18 (0.17-0.20)	100
Total	398,610 (396,960-400,260)	0.66 (0.66-0.67)	100



Prevalence of hepatitis C virus estimates of undiagnosed individuals in different Italian regions: a mathematical modelling Approach by route of transmission and fibrosis progression with results up to January 2021

Kondili LA, Andreoni M, Aghemo A, Mastroianni CM, Merolla R, GallinaroV, Craxì A.
New Microbiologica 2022, May 25;45(4). Online ahead of print.

Prevalence of hepatitis C virus estimates of undiagnosed individuals in different Italian regions: a mathematical modelling Approach by route of transmission and fibrosis progression with results up to January 2021

Stima dei pazienti ancora non trattati in Italia per lo stadio di Fibrosi e Fattori di Rischio per l'acquisizione dell'infezione (Aggiornamento : Gennaio 2021)

All routes	Prevalence rate
F0-F3	0.48 (0.46-0.59)
F4	0.18 (0.17-0.20)
Total	0.66 (0.66-0.67)

		Numeri Assoluti	
	Referenza	Limiti di Coenfidenza (95%)	
Totale	398610	396.960	400260
Totale Fo-F3	287.730	279.911	295.549
Totale F4	110.880	103.130	118.630
"Popolazioni chiave" Secondo fattori di rischio			
Consumatori di droghe endovena			
Fo-F3	144.307	139.845	148.768
F4	49.404	45.371	53.437
Tattuaggi/ piercing			
Fo-F3	89.491	84161	88.822
F4	13.681	11895	15466
Trasmissione Sessuale			
Fo-F3	42.141	41.117	43.165
F4	3.496	2.915	4.078
Uso di siringhe di vetro e Trasfusioni di sangue e derivati			
Fo-F3	13553	7064	14956
F4	43073	40858	45290
Trasmissione Verticale			
Fo-F3	1237	1034	1440
F4	1227	997	1458

Kondili LA, Andreoni M, Aghemo A, Mastroianni CM, Merolla R, GallinaroV, Craxì A. New Microbiologica 2022, May 25;45(4). Online ahead of print.

- **Il sommerso dell'infezione da HCV**

Rimane un numero cospicuo rappresentato una popolazione con una fibrosi F4 che non ha eliminato il virus per mancata diagnosi o linkage to care di età media 60 anni

…….e un'altra popolazione con una fibrosi F0-F3 potenzialmente asintomatica con una età media di 46 anni.

In Italia bisogna scoprire un cospicuo sommerso di circa 287.000 persone asintomatiche , ignari dello stato dell'infezione da virus dell'epatite C !

Courtesy of L. Kondili

Screening and Linkage to Care

MINISTERO DELLA SALUTE

DECRETO 14 maggio 2021.

Esecuzione dello screening nazionale per l'eliminazione del virus dell'HCV.

IL MINISTRO DELLA SALUTE

DI CONCERTO CON

IL MINISTRO DELL'ECONOMIA
E DELLE FINANZE

Coorte di nascita 1969-1989

CARCERI

SerD

2. Lo *screening* è rivolto, in via sperimentale, *una tantum* per il biennio 2020-2021, per un unico test, a:

tutta la popolazione iscritta all'anagrafe sanitaria, inclusi gli Stranieri temporaneamente presenti, e nata dal 1969 al 1989;

ai soggetti seguiti dai servizi pubblici per le Dipendenze (SerD), indipendentemente dalla coorte di nascita e dalla nazionalità;

ai soggetti detenuti in carcere, indipendentemente dalla coorte di nascita e dalla nazionalità.

a) per la coorte di nascita dal 1969 al 1989 lo *screening* avverrà, con chiamata attiva attraverso i Medici di medicina generale e/o il Servizio di prevenzione territoriale. Ogni occasione di incontro con una struttura sanitaria sarà, per la coorte indicata, un'opportunità per effettuare lo screening per HCV.

b) per i soggetti in carico ai SerD e la popolazione detenuta lo screening avverrà preferenzialmente attraverso test rapido, eseguibile su sangue intero con prelievo capillare, o con l'HCV Ab (POCT - *Point of Care Test*) o direttamente con l'HCV RNA test rapido (POCT - *Point of Care Test*). La scelta della tipologia di esame avverrà sulla base della valutazione del contesto epidemiologico locale.

HCV Elimination

What are the problems in Italy ?

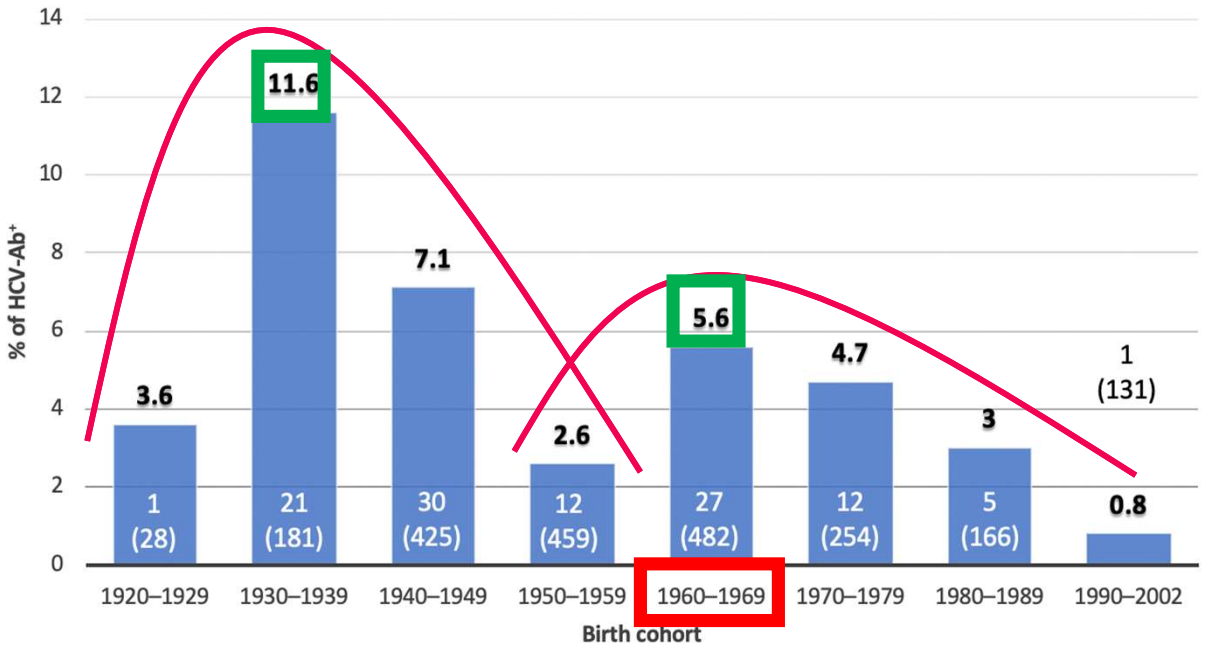
In Italy we have two populations:

Older-Olds

Former or active PWID

Epidemiology of HCV and HBV in a High Endemic Area of Southern Italy: Opportunities from the COVID-19 Pandemic—Standardized National Screening or One Tailored to Local Epidemiology?

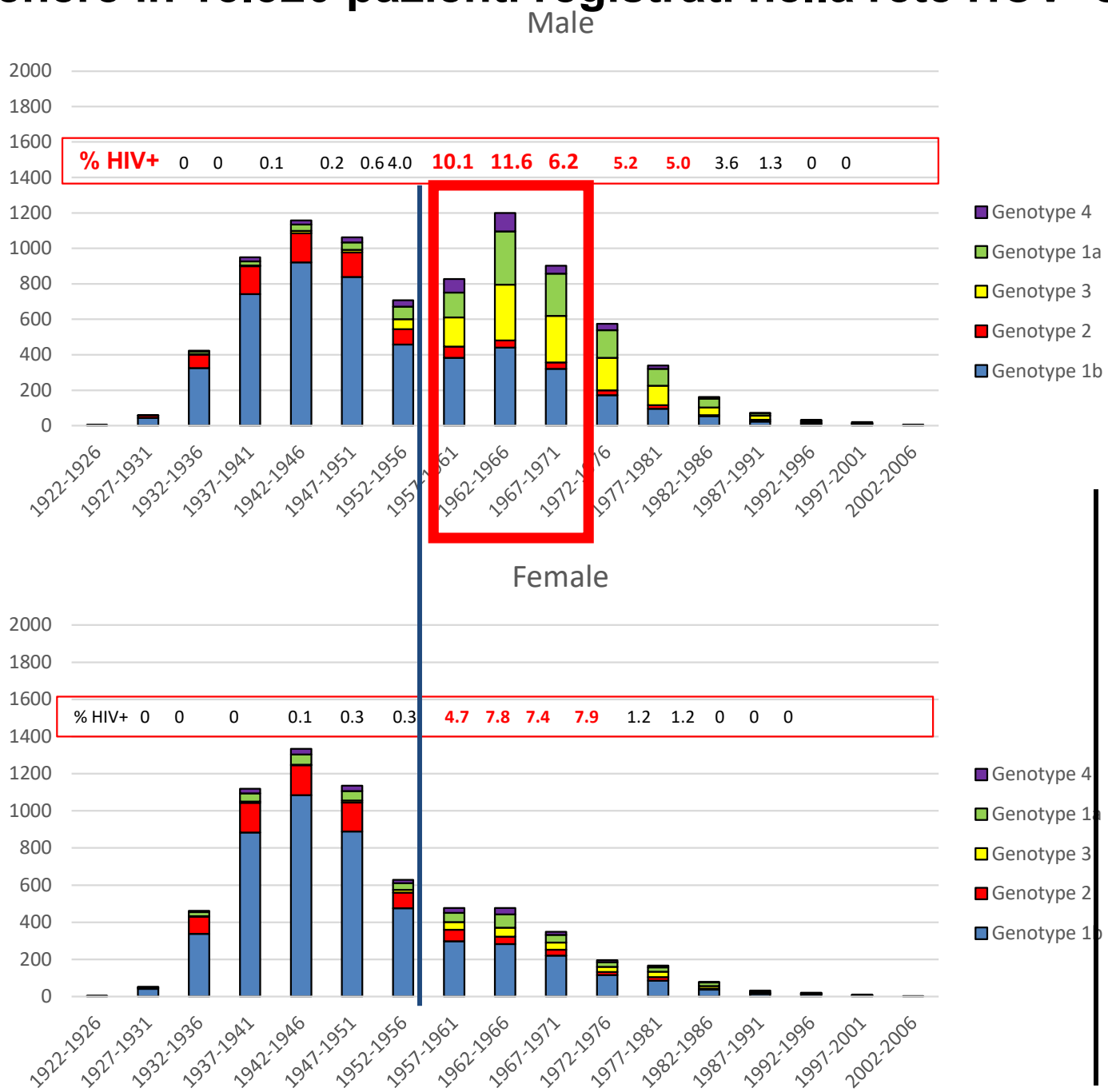
HCV-Ab seroprevalence according to the birth cohort (n = 2126)



Riccardo Nevola [1,2,*], Vincenzo Messina [3], Aldo Marrone [1], Nicola Coppola [4], Carolina Rescigno [5], Vincenzo Esposito [6], Vincenzo Sangiovanni [7], Ernesto Claar [2], Mariantonietta Pisaturo [4], Francesco Maria Fusco [7], Pietro Rosario [6], Antonio Izzi [5], Raffaella Pisapia [5], Valerio Rosato [2], Paolo Maggi [3] and Luigi Elio Adinolfi [1]

Nevola R et al. Biology 2022 Apr

Distribuzione dei singoli genotipi di HCV siciliani per coorte di nascita e per genere in 15.320 pazienti registrati nella rete HCV Sicilia.



The Journal of Infectious Diseases
SUPPLEMENT ARTICLE

From Prioritization to Universal Treatment: Successes and Challenges of Hepatitis C Virus Elimination in Italy

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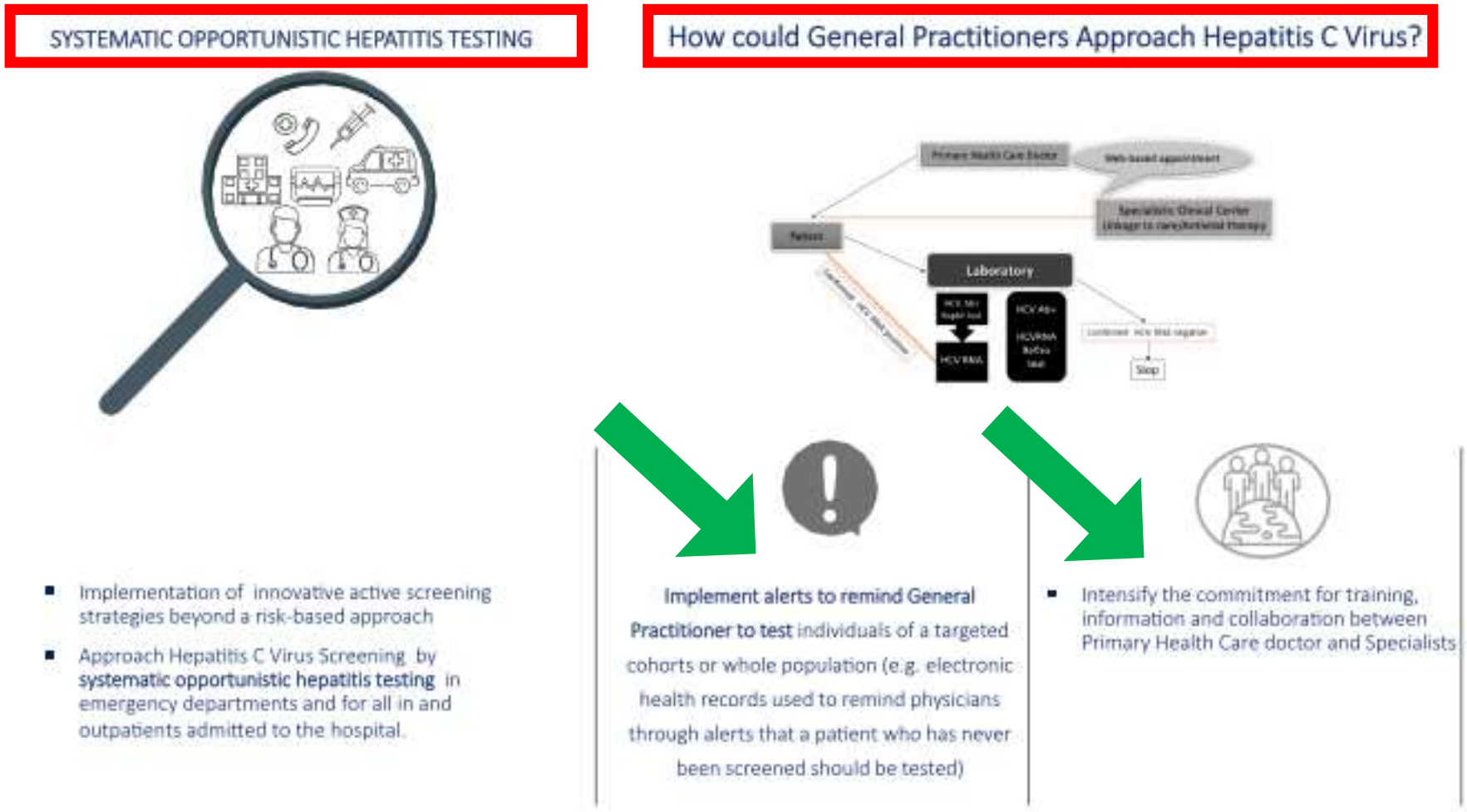


Figure 4. Italian Ministry of Health decree indications regarding HCV screening in the general population. Abbreviations: Ab, antibody; HCV, hepatitis C virus.

Outline

- Elimination of HCV in 2030: WHO elimination goals
- Elimination of HCV: where we are now ?
- Strategies needed for HCV elimination

Barriers to HCV elimination

Patient

- **Comorbidities**
- Competing priorities
- Unstable housing
- Lack of transportation
- **Limited knowledge of HCV**
- **Stigma around HCV**
- Prior negative experiences in healthcare settings

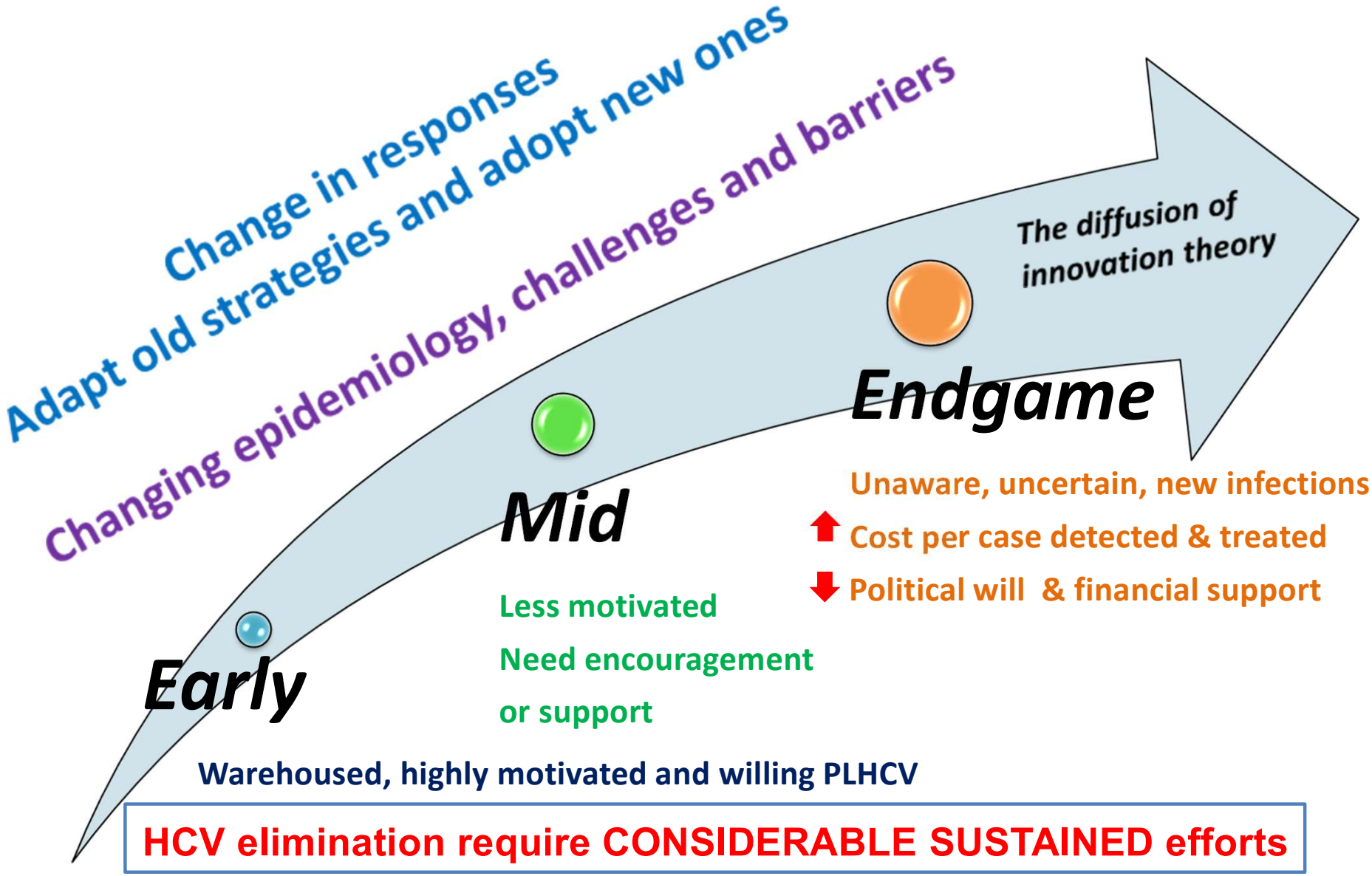
Provider

- **Perceived lack of value in treating some patients**
- **Concerns about adherence**
- **Medical contraindications**
- Competing priorities
- Limited time

System

- Healthcare access
- Availability of HCV providers
- Waiting lists
- COVID-19 related issues

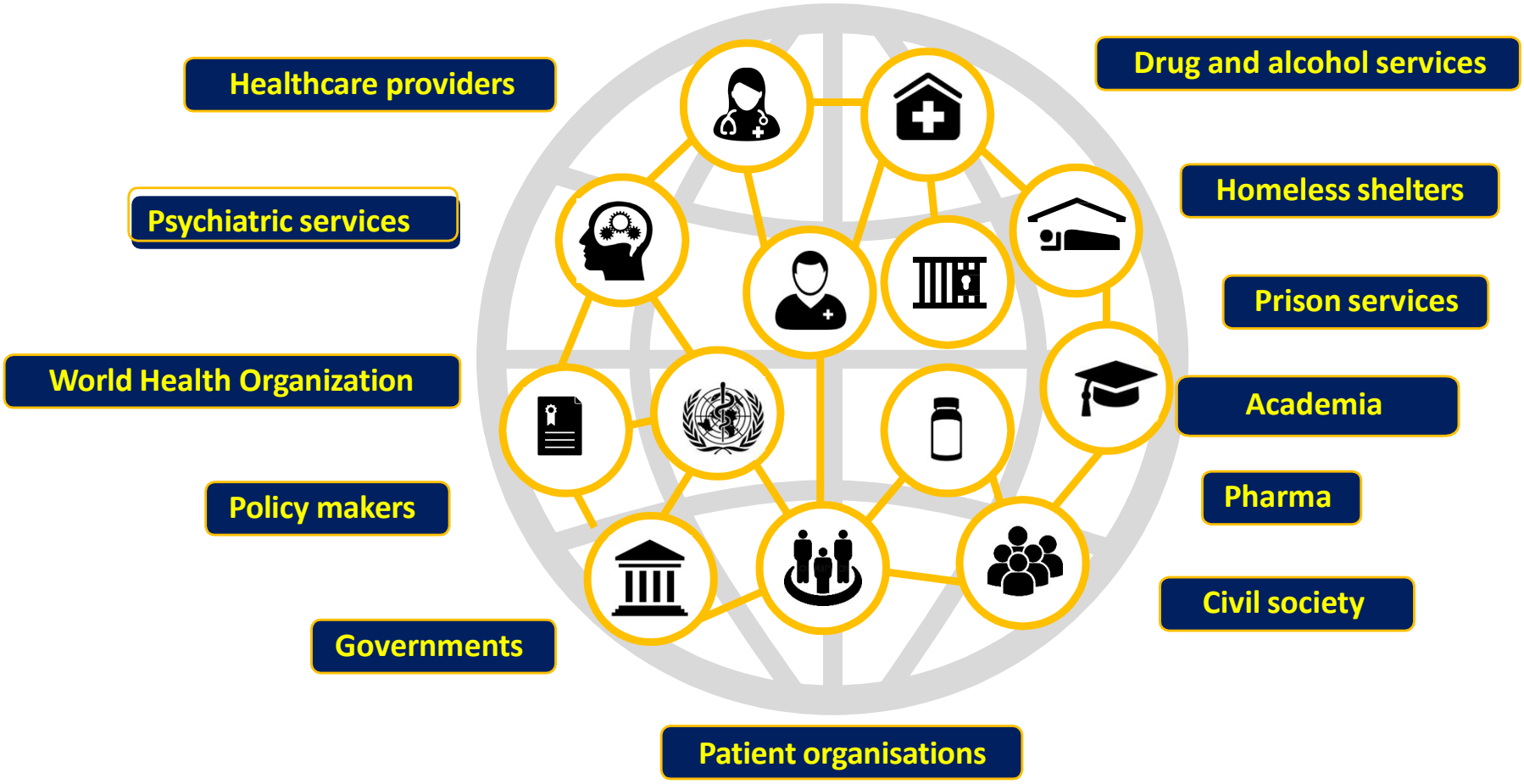
The phases of hepatitis C elimination



A Pedrana et al Lancet GH 2021, Klepac et al. Philos Trans R Soc Land B Biol Sci 2013

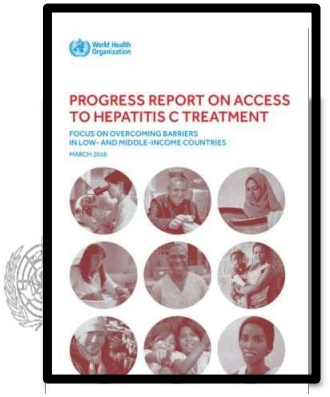
HCV elimination requires broad multi-stakeholder involvement

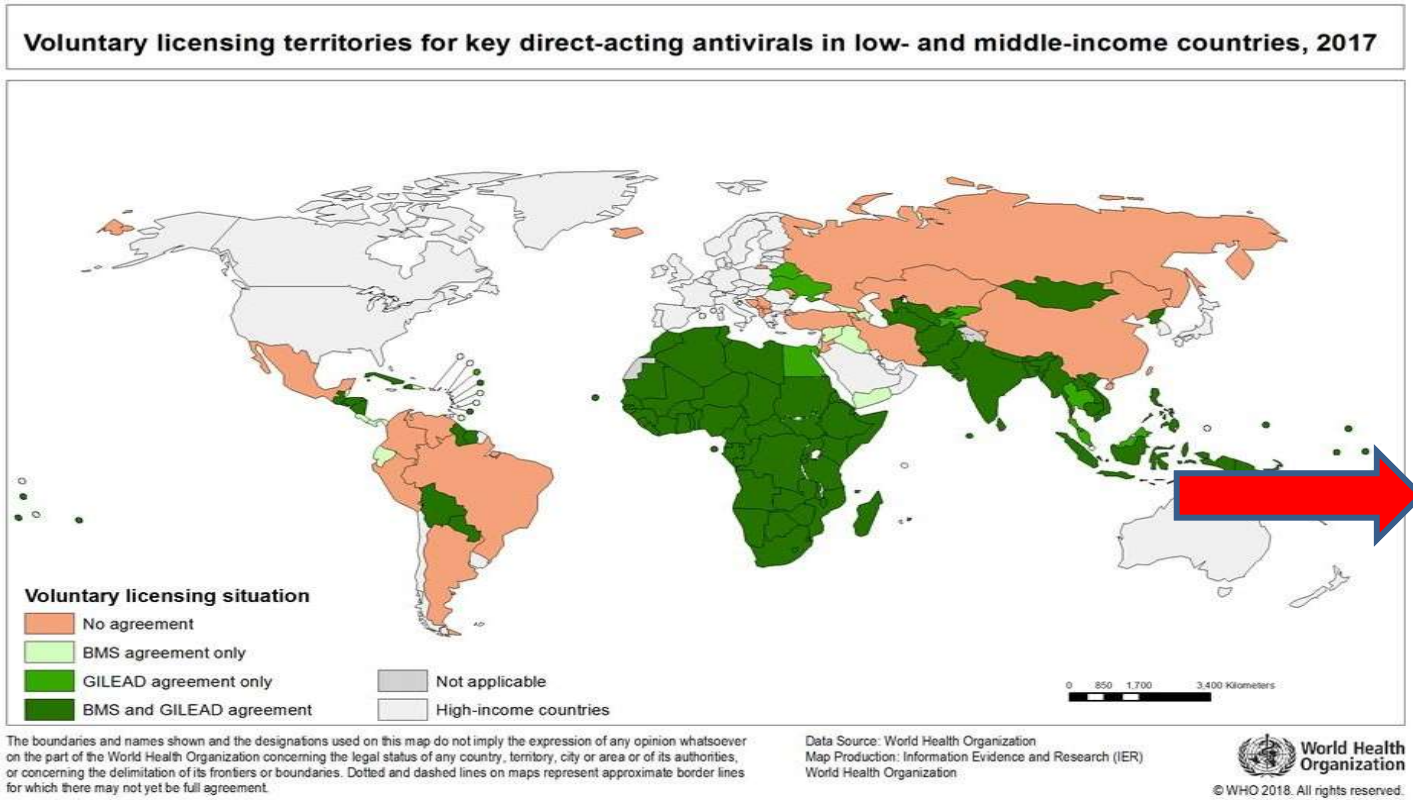
BUT MAINLY AFFORDABLE COST OF THE DRUGS TO ALLOW UNIVERSAL COVERAGE WORLDWIDE !!



1.GS Cooke, TB Hallett. Pricing viral hepatitis as part of universal health coverage. Lancet Glob Health, Sep 1 2019

67% of persons with chronic HCV infection live in countries which could access generic medicines at less than USD 100/cure [1]





High price of DAAs remains a barrier in most upper- middle income countries, despite their deignation as Essential Medicines by WHO.

Source: WHO access report, 2017

1.GS Cooke, TB Hallett. Pricing viral hepatitis as part of universal health coverage. Lancet Glob Health, Sep 1 2019

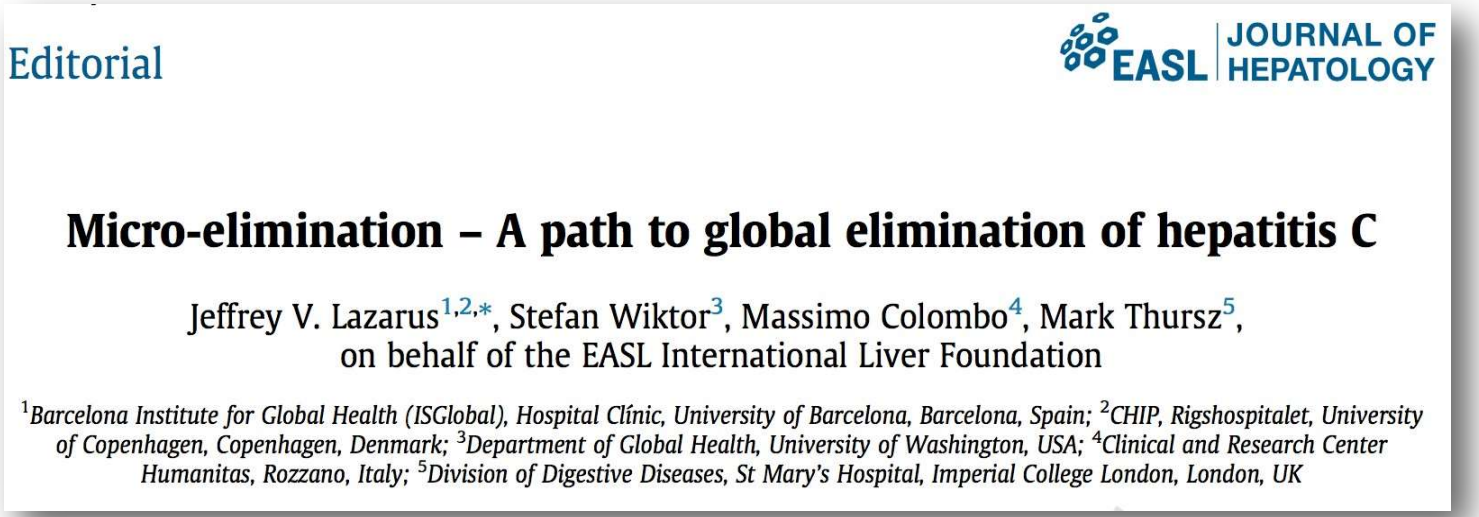
Approaches to HCV Elimination

Global Elimination
- WHO Elimination Targets

National/Regional Elimination
- National strategies to meet WHO targets

Micro-elimination
- Elimination in a defined population
- HIV/HCV, hemophilia, prison

Breaking Down National Goals Into Smaller Goals for Individual Population Segments



Editorial

EASL | JOURNAL OF HEPATOLOGY

Micro-elimination – A path to global elimination of hepatitis C

Jeffrey V. Lazarus[1,2,*], Stefan Wiktor[3], Massimo Colombo[4], Mark Thursz[5], on behalf of the EASL International Liver Foundation

[1]*Barcelona Institute for Global Health (ISGlobal), Hospital Clínic, University of Barcelona, Barcelona, Spain;* [2]*CHIP, Rigshospitalet, University of Copenhagen, Copenhagen, Denmark;* [3]*Department of Global Health, University of Washington, USA;* [4]*Clinical and Research Center Humanitas, Rozzano, Italy;* [5]*Division of Digestive Diseases, St Mary's Hospital, Imperial College London, London, UK*

J Hepatol. 2017 Oct;67(4):665-666.

Differentiation rather than prioritization !

Micro-eliminations: elimination within a defined population

Micro-eliminations can lead to macro or global elimination

TABLE 2. POPULATIONS TARGETED FOR HCV MICRO-ELIMINATION

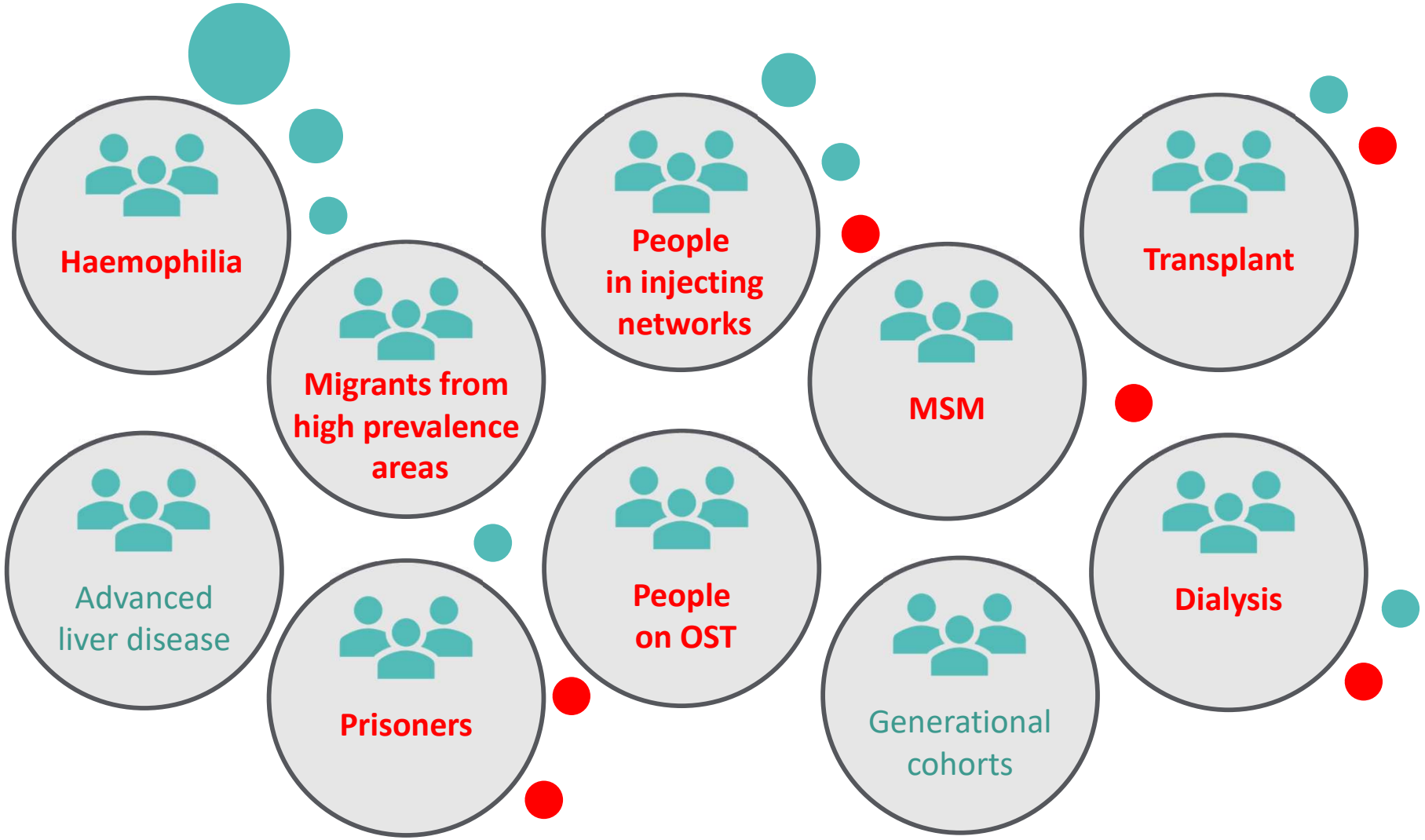
Population	Example	Advantages	Challenges
Outreach setting	• Prison • Homeless population • Needle syringe program	• Clearly defined • Achievable • Measurable • Potential to reduce transmission	• Requires buy-in from setting (e.g., prison) • Unsustainable resources
Clinical population	• Persons living with HIV • Persons with blood disorders • Persons on dialysis/persons in drug treatment	• Well defined • Politically important	• May be difficult to measure/confirm (e.g., HIV underdiagnosis) • May be small scope • May be considered stigmatizing
Health system	• US Veterans Affairs • Health Maintenance Organization	• Access to care • Large potential impact • Achievable targets with good data systems • Model for other chronic disease management	• Need to demonstrate cost benefit • Reimbursement system
Geography	• Village/province, region	• Capitalizes on advocacy of local champions • Politically savvy • Health equity • Feasible costs • Lessons learned build support for a national initiative • Model for other chronic disease management	• Requires sustained buy-in with political and financial support • In absence of national programs, increased need for technical and financial support • Success tempered by migration from neighboring locations without an elimination program

Micro-elimination strategy that succeed have a clear plan, be multidisciplinary, have **clear targets, and monitor outcomes**.

J Feld and JW Ward. Hepatol Comm 2021; JV Lazarus et al .Seminars in Liver Dis 2022

Micro-elimination of HCV

Achieving elimination goals in targeted population groups



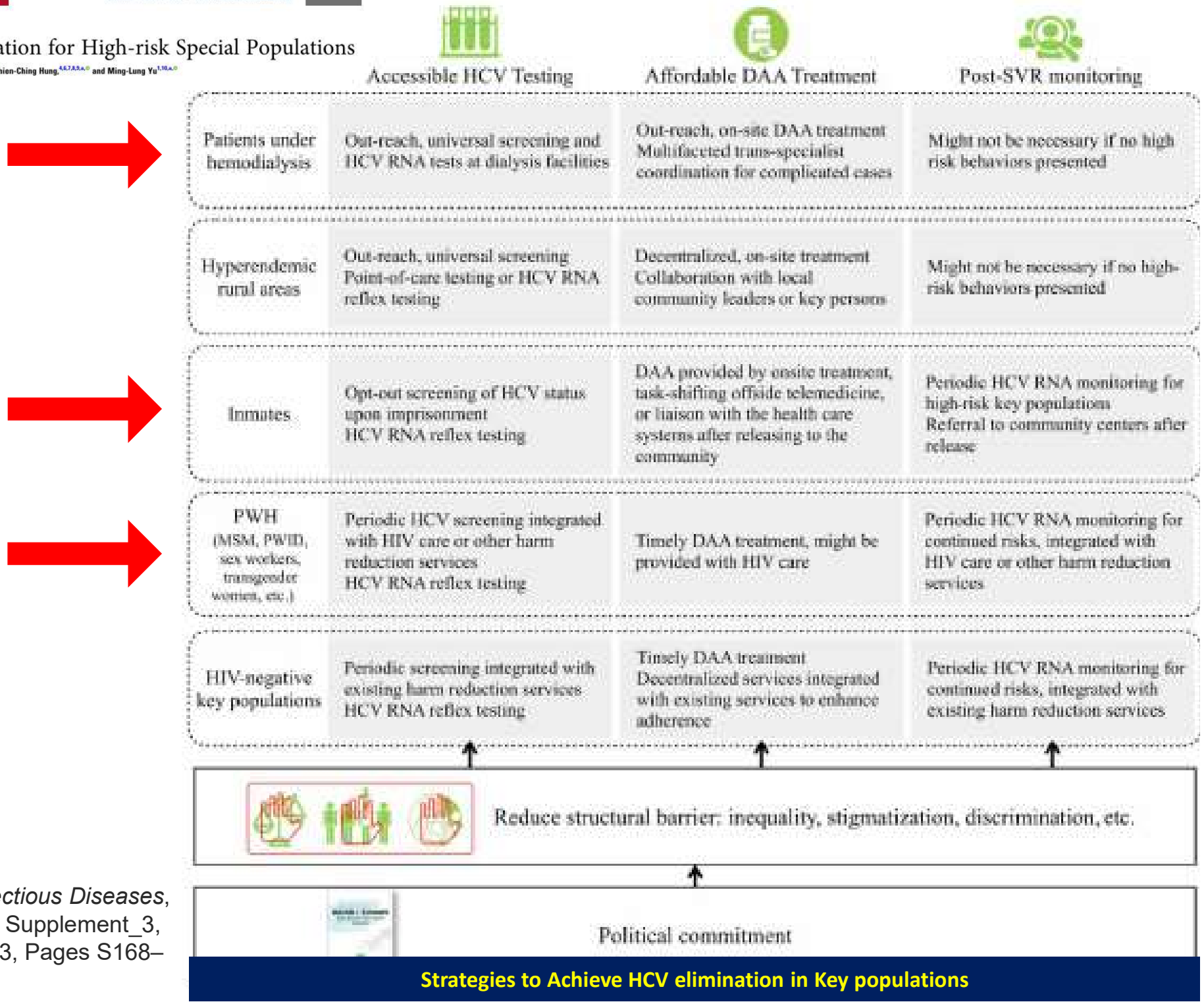
Lazarus J, et al. J Hepatol 2017;67:665–6

MSM: men who have sex with men; OST: opioid substitution therapy

The Journal of Infectious Diseases
SUPPLEMENT ARTICLE

HCV Microelimination for High-risk Special Populations

Chung-Feng Huang,[1,2,3,a] Guan-Jhou Chen,[4,5,a,©] Chien-Ching Hung,[4,6,7,8,9,a,©] and Ming-Lung Yu[1,10,a,©]



Strategies to Achieve HCV elimination in Key populations

The Journal of Infectious Diseases, Volume 228, Issue Supplement_3, 15 September 2023, Pages S168–S179

People with Hepatitis C Who Inject Drugs — Underserved, Not Undeserving

Gregory J. Dore, M.B., B.S., Ph.D., M.P.H., and Stacey

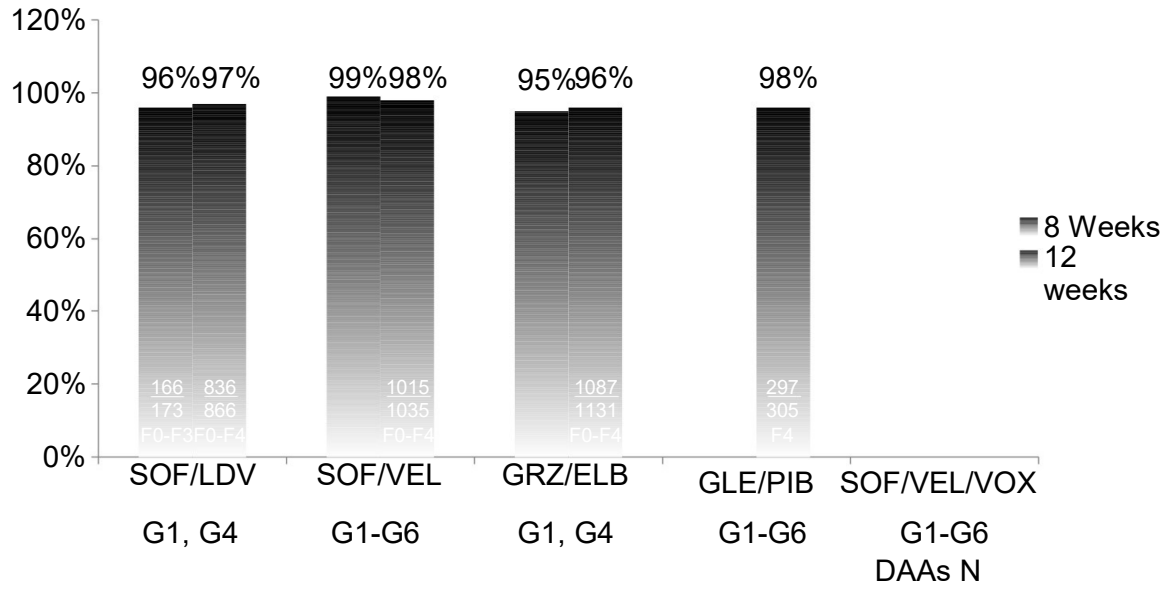
To reduce the burden of HCV, it will be important to expand harm reduction for PWID.

One model comes from Australia, where high treatment uptake has reduced the prevalence of active infection in this population.

Demographics and Statistics Related to Injection Drug Use and Hepatitis C Virus Infection in Australia, Canada, and the United States.*

Factor	Australia	Canada	United States
Overall			
Total population 15–64 yr of age (millions)	16.6	25.3	216.9
Estimated no. of people with HCV infection	129,000	205,000	2,936,000
No. of new HCV diagnoses	11,890	8,378	146,502
Year of DAA availability, by type			
Early access or licensed	2014	2014	2013
Government-subsidized	2016	2014	Limited
National unrestricted access	2016	2019	None
DAA treatment uptake among people with HCV (%)	39	19	37
HCV-related deaths per 1000 population			
2015	3.6	6.1	7.6
2018	2.5	5.3	6.2
People who have recently injected drugs			
No. of people who inject drugs per 1000 people 15–64 yr of age	6	7	10
No. of people who inject drugs (total)	93,000	171,900	2,248,500
No. of people with HCV infection who inject drugs	16,700	65,000	895,000
Proportion of overall HCV infections (%)	14	31	31
HIV prevalence (%)	1.3	11.3	8.7
Needles and syringes distributed per person who injects drugs (per year)	461	148	30
Opioid agonist therapy coverage (%)	52	24	19
DAA treatment uptake (%)	47	NA	NA
HCV RNA prevalence			
2015 (%)	51	53	40
2019 (%)	18	NA	NA

Almost all HCV infected patjents reach SVR and viral cure today….



Lawitz E et al EASL 2017; Abs THU-273. Afdhal N et al. NEJM 2014:370: 1889-98.Afdhal N et al. NEJM 2014; 370: 1483-93, Kowdley KU et al. NEJM 2014; 370: 1979-88. Agarwal K et al EASL 2016;: SAT-295. Feld JJ et al NEJM 2015; 373: 2599-607. Komatsu TE et al. Gastroenterology 2016. Puoti M et al. EASL 2017; SAT-233. Gane EJ et al. AASLD 2017 abs 73. Roberts SK et al EASL 2017; SAT-280,. Jacobson I et al. Gastroenterology 2017; 153: 113-122.

Factors Enhancing Treatment of Hepatitis C Virus–Infected Italian People Who Use Drugs: The CLEO-GRECAS Experience

AJG The American Journal of GASTROENTEROLOGY

Luca Rinaldi, MD, PhD[1], Vincenzo Messina, MD[2], Vito Di Marco, MD[3], Vincenzo Iovinella, MD[4], Ernesto Claar, MD[5], Giuseppe Cariti, MD[6], Rodolfo Sacco, MD[7], Massimo De Luca, MD[8], Gaetano Scifo, MD[9], Pietro Gatti, MD[10], Giorgio Barbarini, MD[11], Valeria Pace Palitti, MD[12], Mariano Quartini, MD[13], Paolo Tundo, MD[14], Gianpiero D'Offizi, MD[15], Giustino Parruti, MD[16], Maria Antonietta di Rosolini, MD[17], Giovanni Garrucciu, MD[18], Lucio Cosco, MD[19], Francesco Benanti, MD[20], Giancarlo Gimignani, MD[21], Umberto Vespasiani Gentilucci, MD[22], Francesco Di Lorenzo, MD[23], Maria D'Antò, MD[24], Riccardo Nevola, MD[1], Tommaso Lupia, MD[6], Valerio Rosato, MD[5], Valeria Morbiducci, MD[13], Ilaria Luzzitelli, MD[15], Federica Sozio, MD[16], Marco Di Stefano, MD[9], Emanuela Ciraci, MD[10], Fabio Bulla, MD[19], Riccardo Guarisco, MD[21], Cecilia Cangiano, MD[1], Michele Imparato, MD[25], Paolo Maggi, MD[2], Antonio Ascione, MD[25], Antonio Craxì, MD[3] and Antonio Izzi, MD[26]

Factors enhancing treatment of HCV infected Italian people who use drugs: the CLEO-GRECAS experience

- 1,786 PWUDs. 85.4% were managed inside the specialized outpatient addiction clinics (SerDs).
- The overall SVR rate was 95.4%.
- The SerDs group achieved an SVR rate of 96.2% compared to 91.6% of the non-SerDs group (p<0.001).

	SVR, n (%)		p-value
	SerD (n=1460)	*Non-SerD (n=249)*	
Third generation DAA (n=1029)	865/884 (97.9)	137/145 (94.5)	0.019
Second-generation DAA (n=576)	539/576 (93.6)	91/104 (87.5)	0.029
Total (n=1709)	1404/1460 (96.2)	228/249 (91.6)	<0.001

SVR sustained virological response; SERD centres for drug addicts

Rinaldi L, Messina V, Di Marco V, et al. Factors Enhancing Treatment of Hepatitis C Virus-Infected Italian People Who Use Drugs: The CLEO-GRECAS Experience. Am J Gastroenterol. 2021 Jun 1;116(6):1248-1255.

Intervento di microeliminazione di HCV nelle Comunità di Recupero per PWUD in Italia

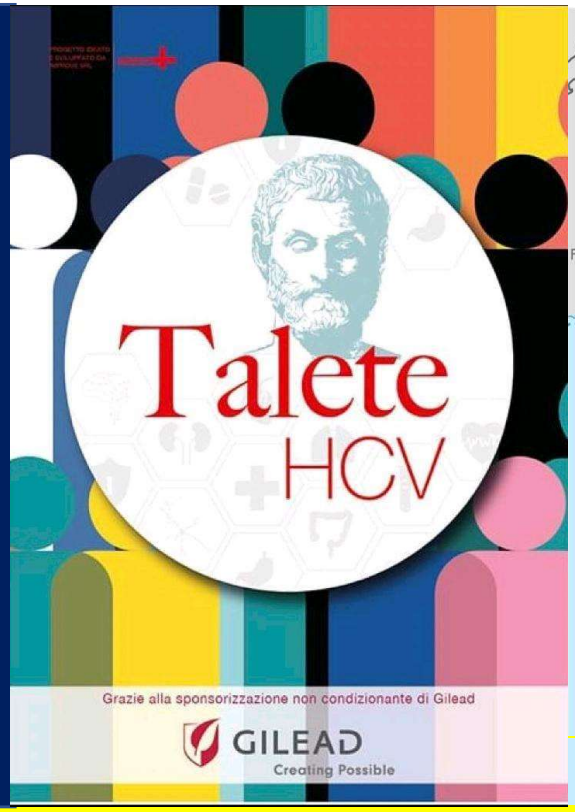
HCV TALETE:

PROGETTO DEDICATO A CLAUDIO PUOTI

- **Estensori del Progetto:**
- **Antonio Izzi- Marco Distefano**
- **Partnership Scientifica: Antonio Craxì**

Coordinatori Regionali:

- **Piemonte: Giuseppe Cariti, Giacomo Stroffolini**
- **Umbria: Chiara Papalini, Giulia Quartini**
- **Lazio: Gianpiero D'Offizi, Chiara Taibi**
- **Campania: Vincenzo Messina, Ernesto Claar**
- **Puglia: Pietro Gatti, Paolo Tundo**
- **Calabria: Lucio Cosco, Jessica Carioti**
- **Sicilia: Vito Di Marco, Antonietta Di Rosolini**



HCV Testing for Addicts Living in Enclaves: Treat to Eradicate

The Journal of Infectious Diseases
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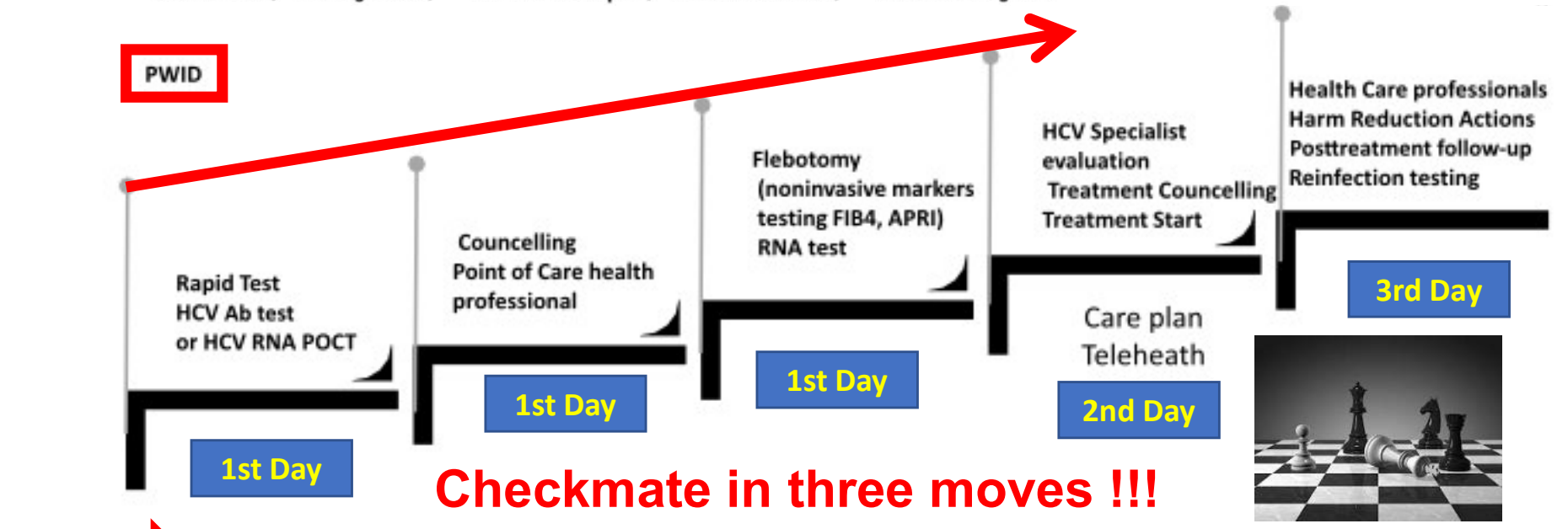

Point-of-care services for screening and linkage to care of PWIDs recommended by the Italian Ministry of Health decree for HCV screening. Abbreviations: Ab, antibody; APRI, aspartate aminotransferase to platelet ratio index; FIB4, Fibrosis 4 score; PWID, people who inject drugs; HCV, hepatitis C virus.

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HCV (micro-) elimination in certain populations is also feasible in the short-to-medium term

Decompensated cirrhotics

Veterans

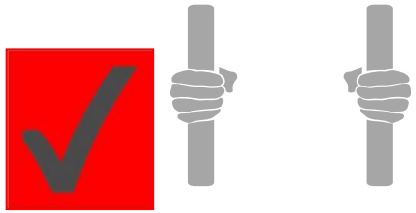
Patients with haemophilia

Patients with chronic kidney disease

Transplant patients

PWID

HIV/HCV co-infected



Incarcerated individuals

Sources: Lazarus JV *et al.* The micro-elimination approach to eliminating hepatitis C: strategic and operational considerations. *Seminars in Liver Disease*, July 2018.

Lazarus JV, Wiktor SZ, Colombo M, Thursz M. Micro-elimination – a path to global elimination of hepatitis C. *Journal of Hepatology*, July 2017.

HCV Elimination: Facts or Fantasy ?

- **Probable Fantasy: Control may be possible and realistic in the short term**
- **Urgent need to implement national screening programs in the aim to enhance case finding and LTC**
- **Access to affordable medicines in all countries will be the key to reach hepatitis C elimination.**

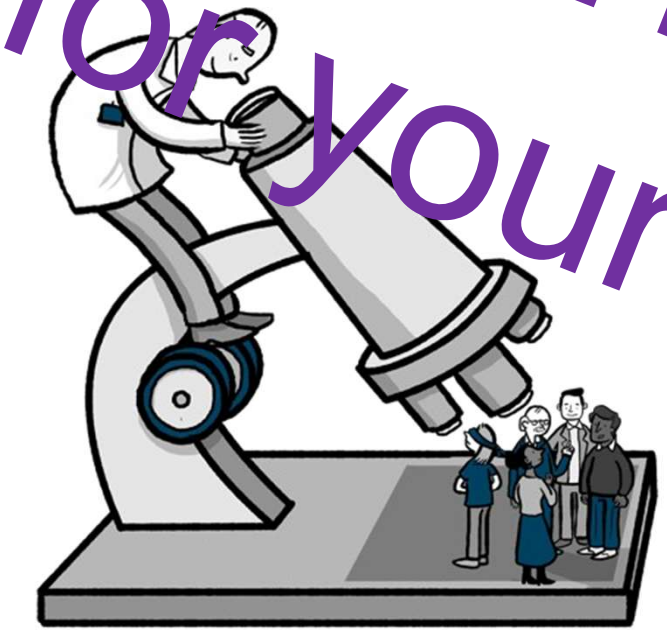
•CURE of HCV in PWID is safe and mandatory because reduces individual mortality and leads to prevention of HCV transmission at population level !

- **HCV (micro-) elimination among PWID is the crucial path for achieving HCV elimination worldwide !!**

A Thousand Mile Journey Begins with a Single Step

Lao Tzu

Goal: Global Elimination of HCV



May begin with
Microelimination

Thanks for your attention!