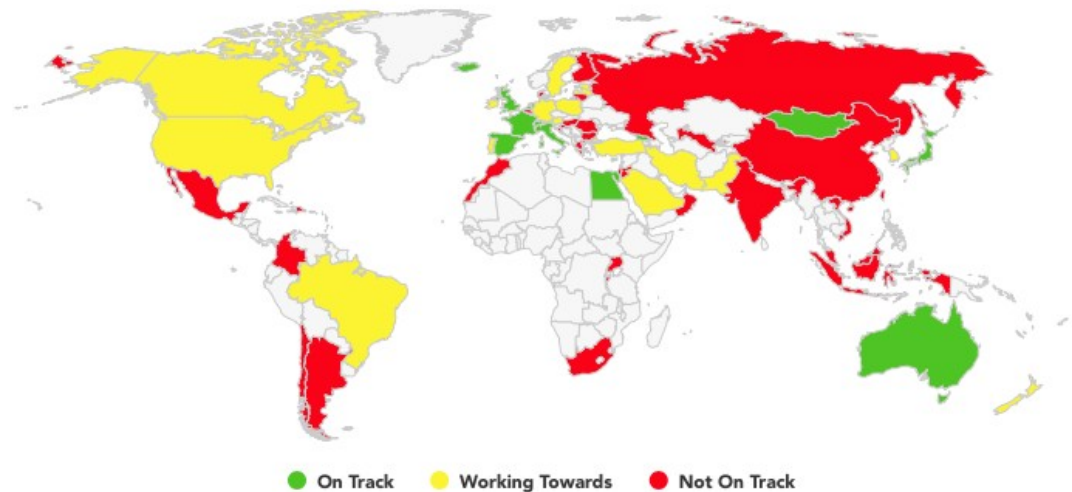


Hepatitis C elimination – Macro Elimination

HCV Elimination Targets

2017



Ola Weiland
Senior professor
Karolinska Institutet
Stockholm, Sweden

Weiland - disclosures

- Speakers' bureau: AbbVie, Gilead, MSD/Merck, BMS
- Consultant: AbbVie, Gilead, MSD/Merck, BMS
- PI : AbbVie, Gilead, MSD/Merck

HCV macro-elimination- key points

- **WHO elimination goals to be reached 2030**
- HCV diagnosis 90%, treatment coverage 80%, reduction of deaths 65%
- By 2017 only 12 countries on track to reach these goals
- Barriers for elimination still remain, awareness of the infection, economy for testing and treatment, linkage to care
- Reducing global burden depends on success of prevention, outreach screening and treatment and progress in key high-burden countries

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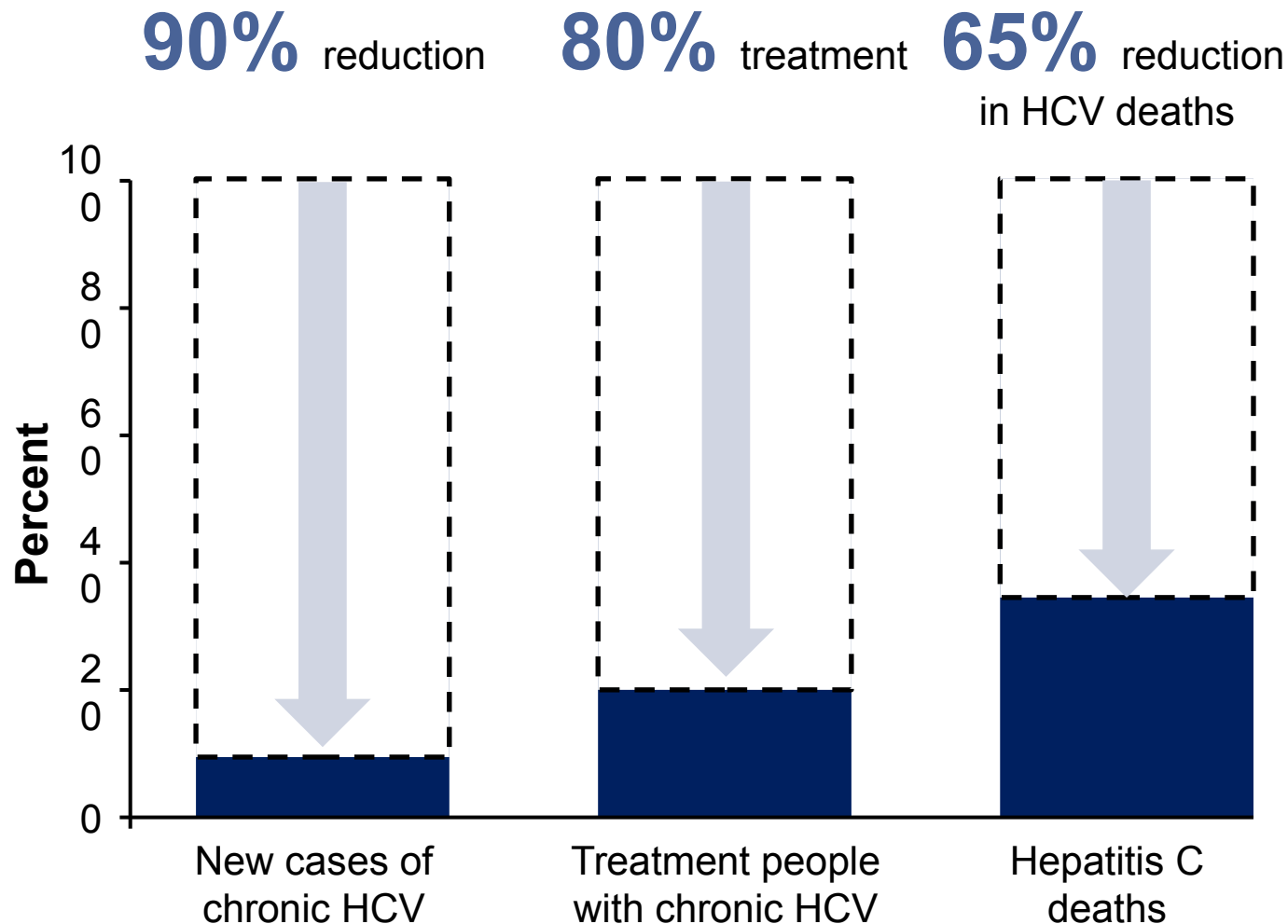
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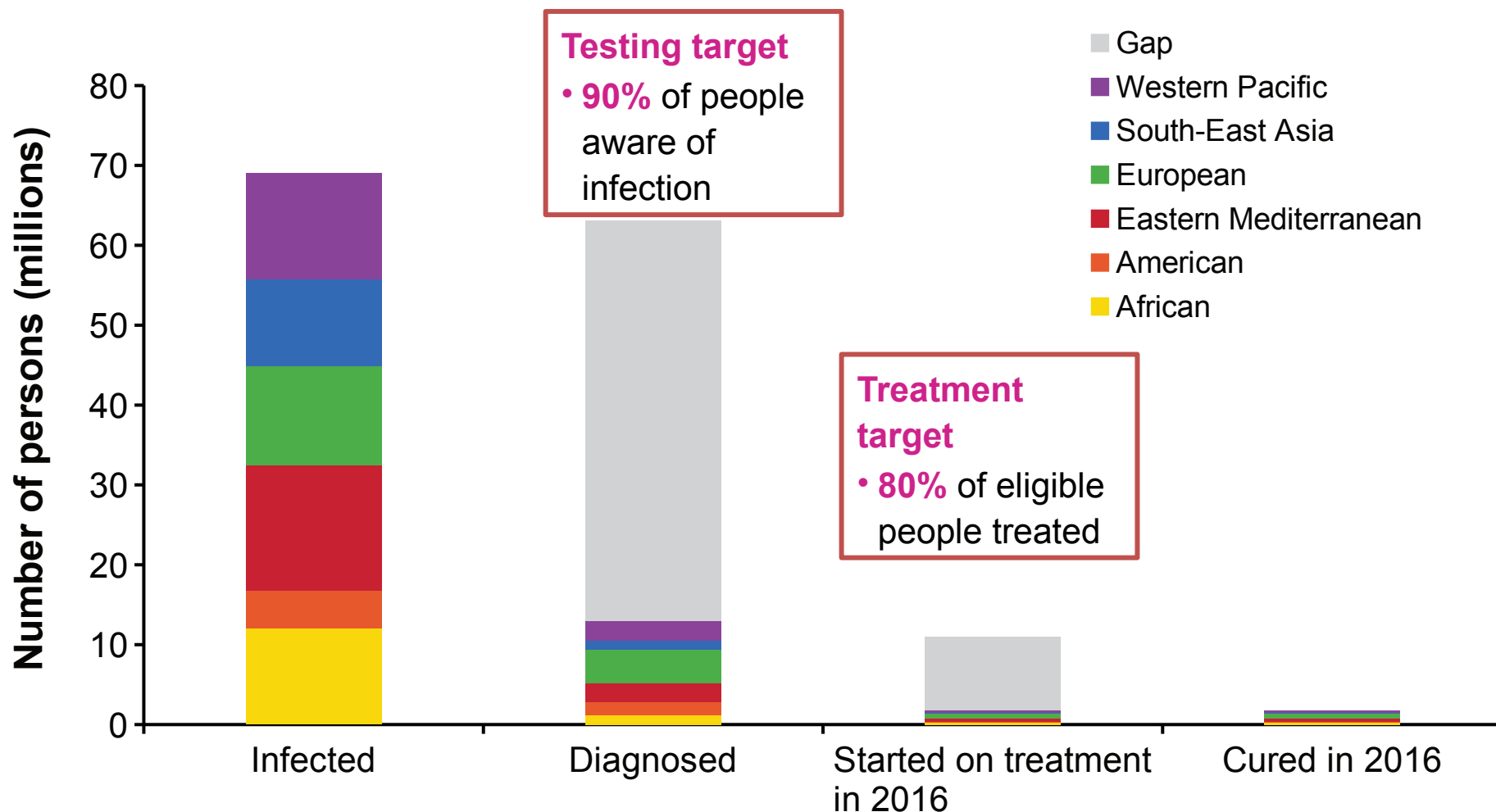
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Global targets achieved if viral hepatitis is controlled by 2030



We still have a long way to go to achieve the WHO HCV elimination targets





Status of HCV

Incidence

- 1.75 million new infections per year

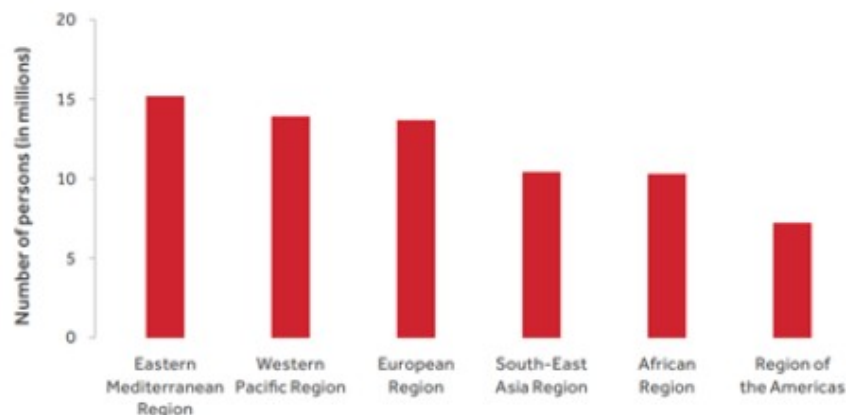
Prevalence

- 71 million infected, all regions

Incidence of HCV infection in the general population, by WHO region, 2015



Prevalence of HCV infection by region



What is needed for HCV elimination and where are the patients?



We just need to simplify HCV management



Test



Treat



Confirm cure?

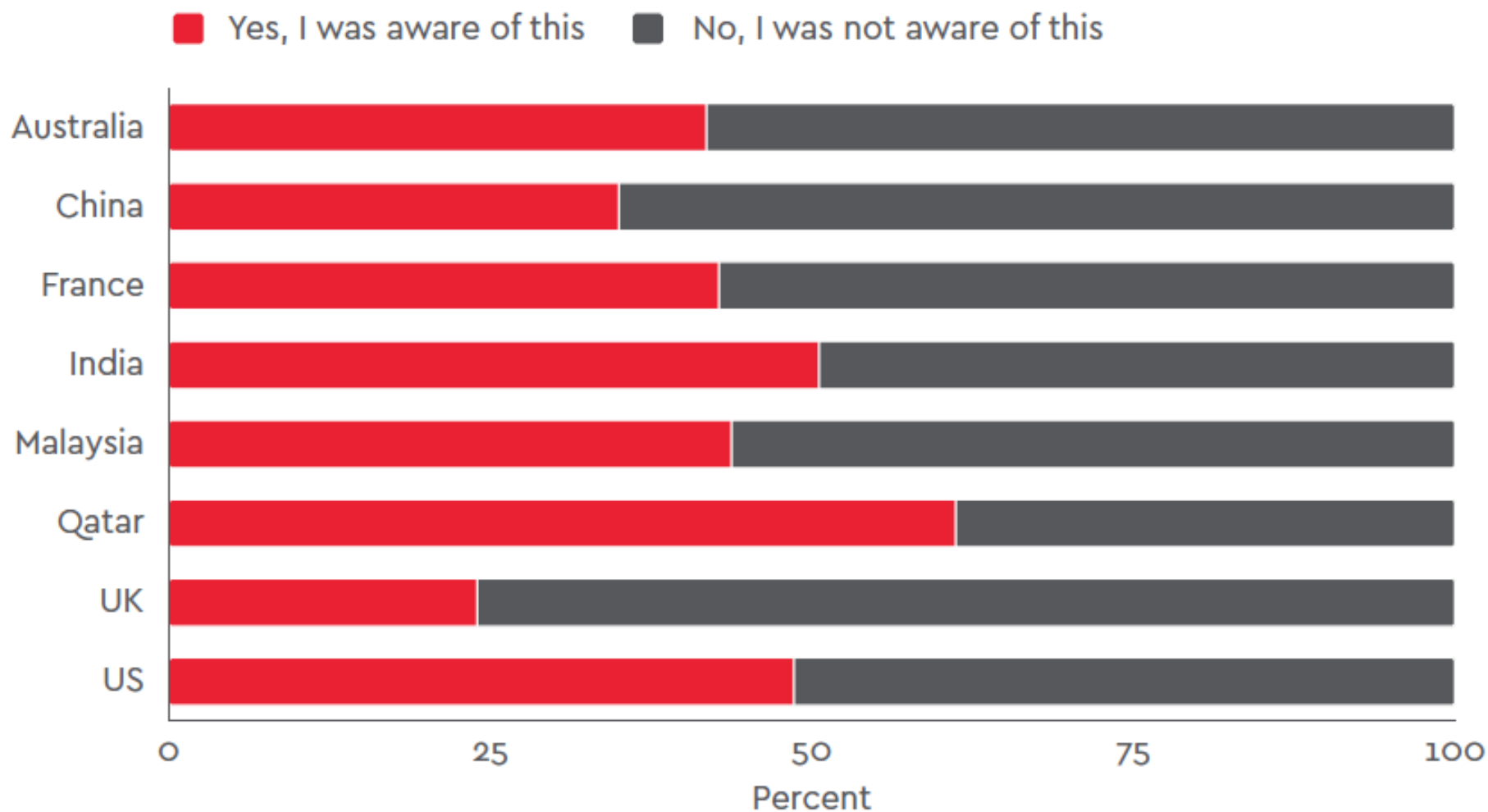
HCV elimination strategy

- **HCV treatment without restrictions such as fibrosis stage**
- **Treatment of PWIDs and MSM**
- **Re-treatment for failures**
- **Wide-scale prevention programs NEP, OST, safe medical procedures - no nosocomial infections**

What is needed for HCV elimination and where are the patients ?



Figure 7. Community awareness of hepatitis C cure



Source: YouGov

<https://www.wish.org.qa/wp-content/uploads/2018/11/IMPJ6078-WISH-2018-Viral-Hepatitis-181026.pdf>

HCV screening strategy

- High risk groups PWID and MSM
- Baby boomers (born 1945-1965)

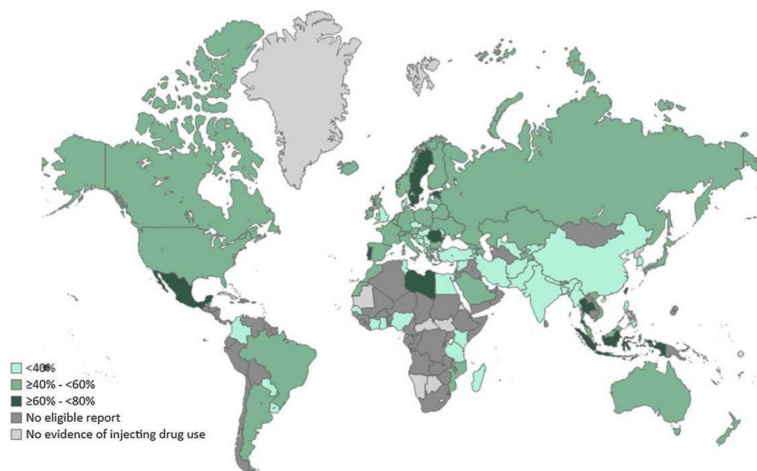
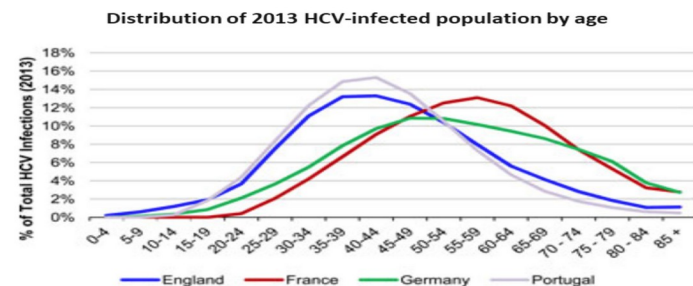


Figure 1 Estimated prevalence of hepatitis C virus (HCV) viraemic infection among people with recent injecting drug use, by country [Colour figure can be viewed at wileyonlinelibrary.com]

HCV Prevalence in Selected European Countries by Age Group



The epidemiology of those infected with HCV will vary from country to country

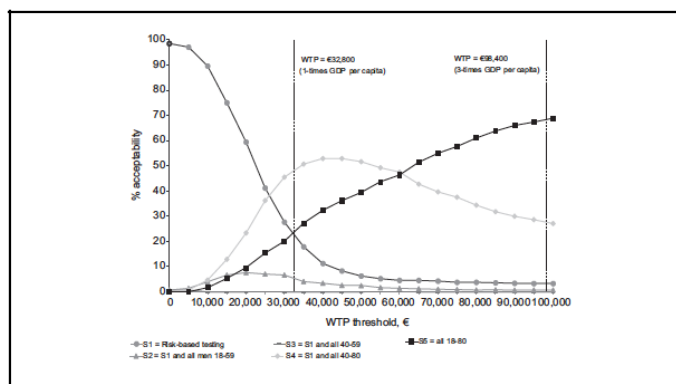
Razavi H, et al. *J Viral Hepat.* 2014;21(suppl 1):34-59.

Grebely, et al, Global, regional, and country-level estimates of hepatitis C infection among people who have recently injected drugs. *Addiction*, 2018 Jul 23.

Population based HCV screening

Assessing the cost-effectiveness of hepatitis C screening strategies in France

Graphical abstract



Highlights

- In France, universal screening is the most effective strategy for HCV.
- Universal screening is cost-effective at the threshold of 1–3 times GDP per capita.
- Cost-effectiveness mainly depends on utility values and time to treatment initiation.

Authors

Sylvie Deuffic-Burban, Alexandre Huneau, Adeline Verleene, ..., Philippe Mathurin, Daniel Dhumeaux, Yazdan Yazdanpanah

Correspondence

sylvie.burban@inserm.fr
(S. Deuffic-Burban)

Lay summary

In the context of highly effective and well tolerated therapies for hepatitis C virus that are now recommended for all patients, a reassessment of hepatitis C screening strategies is needed. An effectiveness and cost-effectiveness study of different strategies targeting either the at-risk population, specific ages or all individuals was performed. In France, universal screening is the most effective strategy and is cost-effective when treatment is initiated regardless of fibrosis stage. From an individual and especially from a societal perspective of hepatitis C virus eradication, this strategy should be implemented.

Hepatitis C virus prevalence and level of intervention required to achieve the WHO targets for elimination in the European Union by 2030: a modelling study



The European Union HCV Collaborators*

Summary

Background Hepatitis C virus (HCV) is a leading cause of liver-related morbidity and mortality worldwide. In the European Union (EU), treatment and cure of HCV with direct-acting antiviral therapies began in 2014. WHO targets are to achieve a 65% reduction in liver-related deaths, a 90% reduction of new viral hepatitis infections, and 90% of patients with viral hepatitis infections being diagnosed by 2030. This study assessed the prevalence of HCV in the EU and the level of intervention required to achieve WHO targets for HCV elimination.

Methods We populated country Markov models for the 28 EU countries through a literature search of PubMed and Embase between Jan 1, 2000, and March 31, 2016, and a Delphi process to gain expert consensus and validate inputs. We aggregated country models to create a regional EU model. We used the EU model to forecast HCV disease progression (considering the effect of immigration) and developed a strategy to achieve WHO targets. We used weighted average sustained viral response rates and fibrosis restrictions to model the effect of current therapeutic guidelines. We used the EU model to forecast HCV disease progression (considering the effect of immigration) under current screening and therapeutic guidelines. Additionally, we back-calculated the total number of patients needing to be screened and treated to achieve WHO targets.

Findings We estimated the number of viraemic HCV infections in 2015 to be 3 238 000 (95% uncertainty interval [UI] 2 106 000–3 795 000) of a total population of 509 868 000 in the EU, equating to a prevalence of viraemic HCV of 0.64% (95% UI 0.41–0.74). We estimated that 1 180 000 (95% UI 1 003 000–1 357 000) people were diagnosed with viraemia (36.4%), 150 000 (120 000–180 000) were treated (4.6% of the total infected population or 12.7% of the diagnosed population), 133 000 (106 000–160 000) were cured (4.1%), and 57 900 (43 900–67 300) were newly infected (1.8%) in 2015. Additionally, 30 400 (26 600–42 500) HCV-positive immigrants entered the EU. To achieve WHO targets, unrestricted treatment needs to increase from 150 000 patients in 2015 to 187 000 patients in 2025 and diagnosis needs to increase from 88 800 new cases annually in 2015 to 180 000 in 2025.

Interpretation Given its advanced health-care infrastructure, the EU is uniquely poised to eliminate HCV; however, expansion of screening programmes is essential to increase treatment to achieve the WHO targets. A united effort, grounded in sound epidemiological evidence, will also be necessary.

Lancet Gastroenterol Hepatol
2017; 2: 325–36

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See [Comment](#) page 314

*Members listed at the end of the Article

Correspondence to:
Dr Homie Razavi, Center for Disease Analysis, Lafayette, CO 80026, USA
homie.razavi@centerforda.com

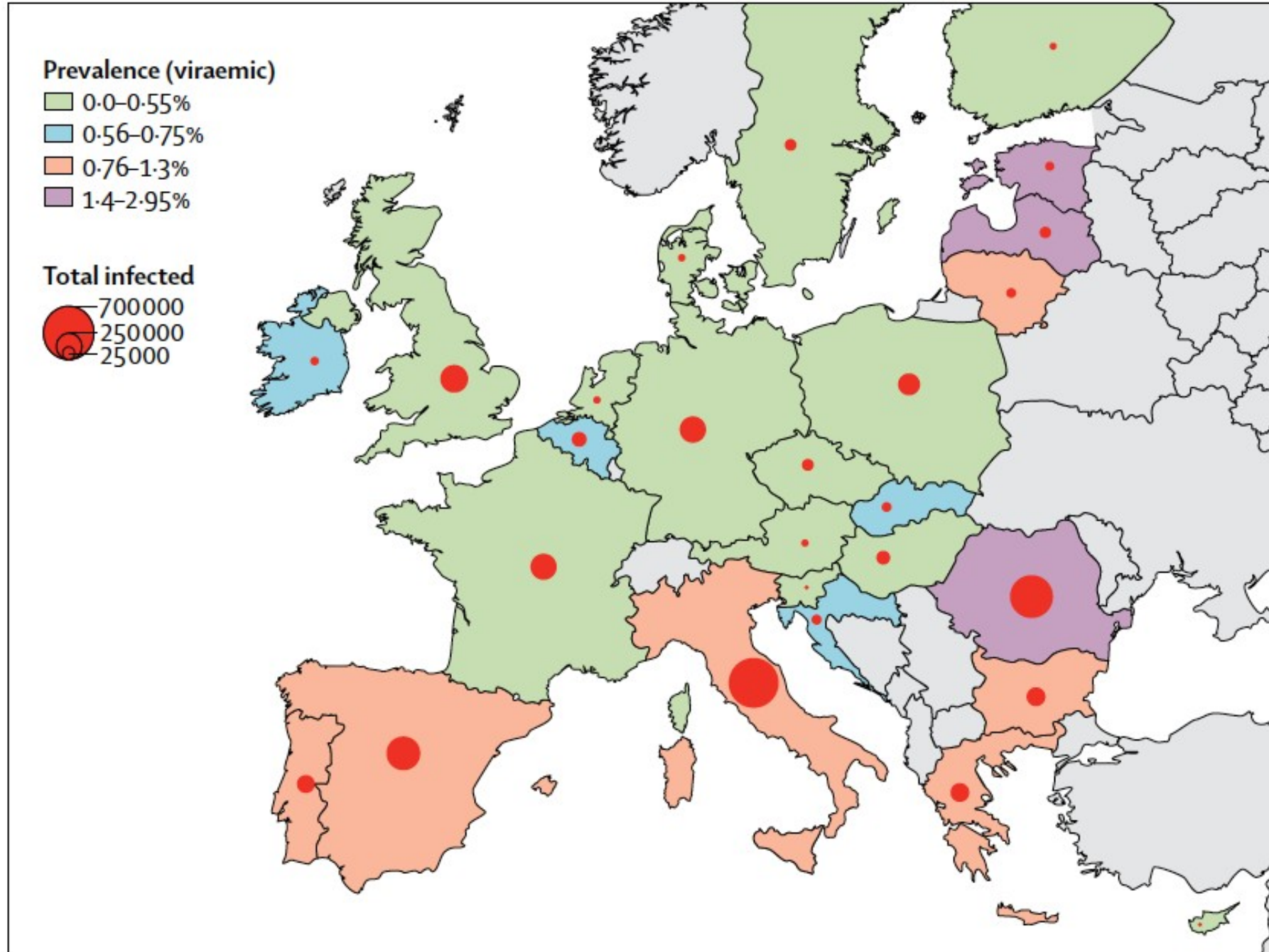


Figure 1: Hepatitis C virus viraemic prevalence and total infected in the European Union

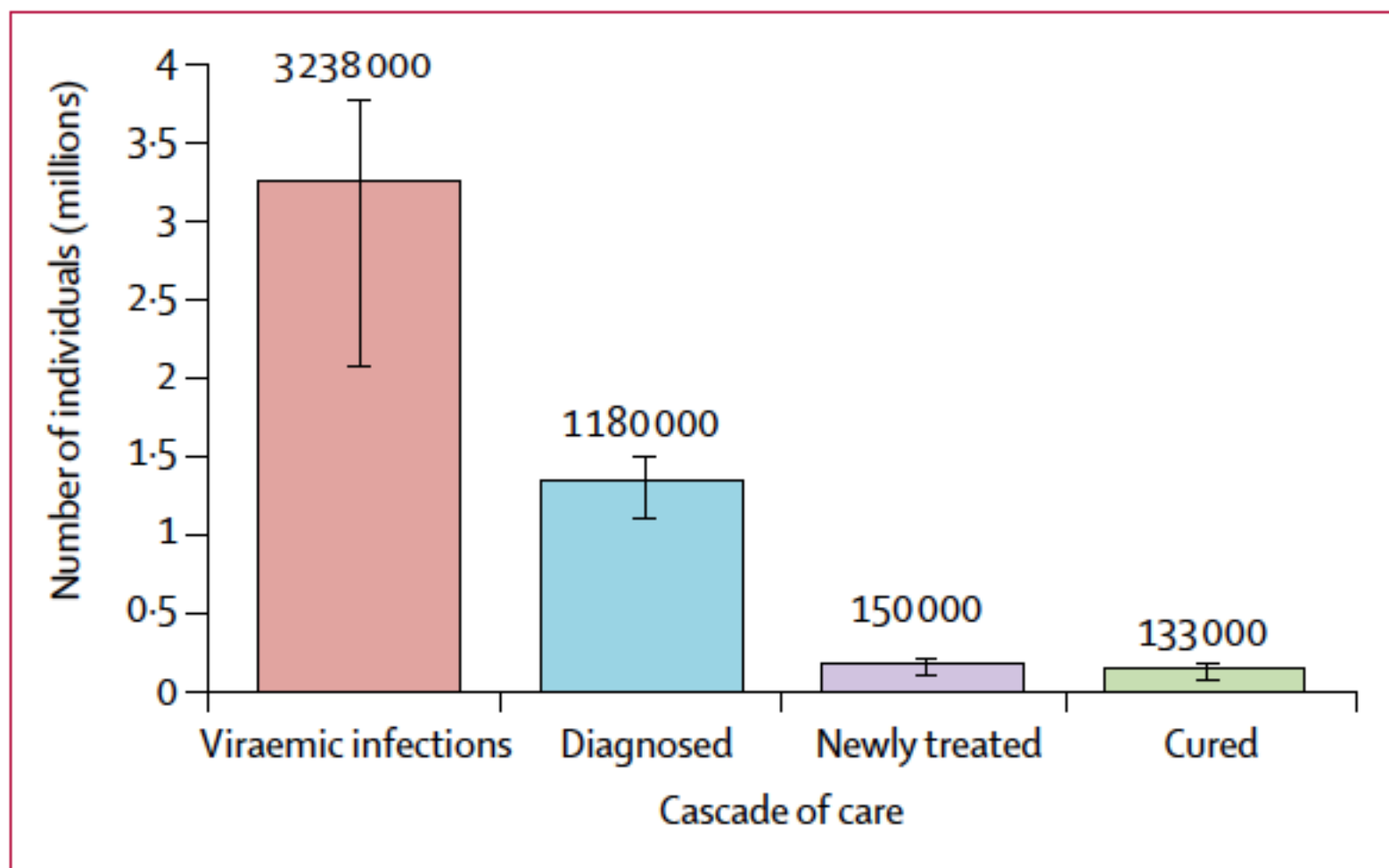


Figure 2: Cascade of care in the European Union, 2015

The error bars represent 95% uncertainty intervals.

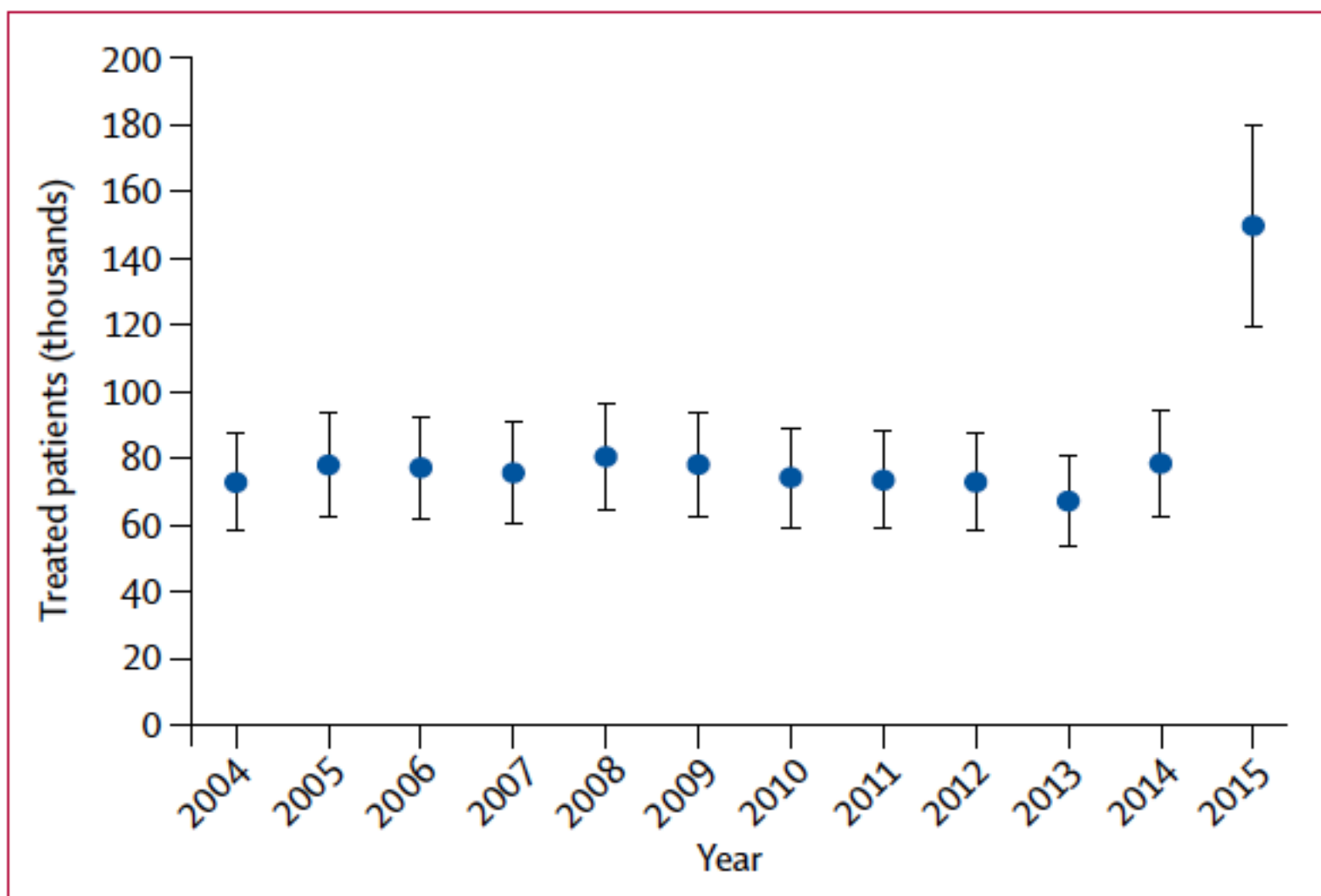


Figure 3: Annual number of patients treated in the European Union, 2004-15
The error bars represent 95% uncertainty intervals.

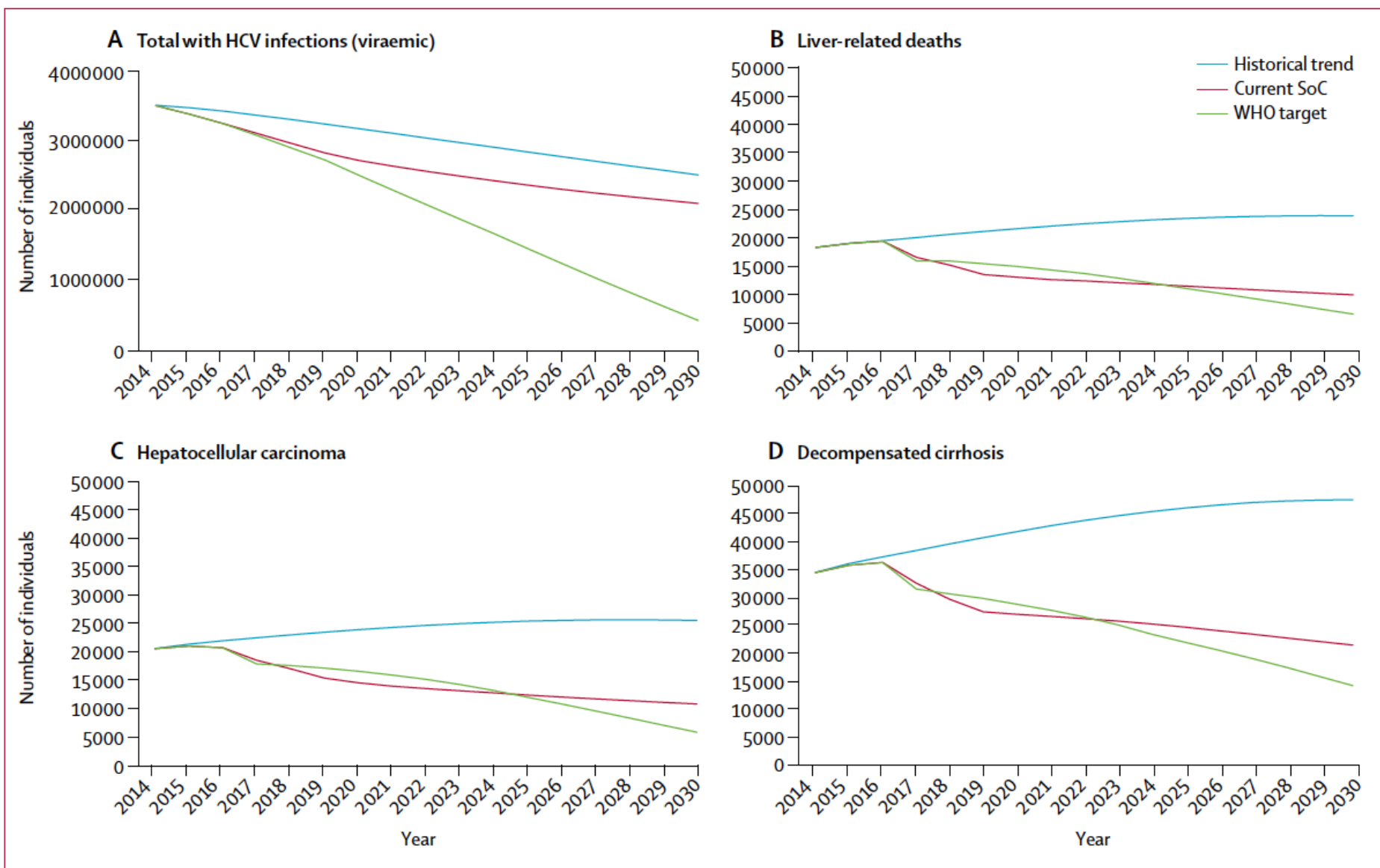


Figure 5: Projection of HCV morbidity and mortality, by diagnosis and treatment strategy, 2014–30
HCV=hepatitis C virus. SoC=standard of care.

The road to elimination of hepatitis C: analysis of cures versus new infections in 91 countries

Andrew M Hill^{1*}, Sanjay Nath² and Bryony Simmons²

¹ Department of Translational Medicine, University of Liverpool, UK

² Faculty of Medicine, Imperial College London, UK

Abstract

Background: Hepatitis C (HCV) can only be eradicated if annual rates of cure (SVR) are consistently and significantly higher than new HCV infections, across many countries. In 2016, the WHO called for a 90% reduction in new HCV infection by 2030. Direct-acting antivirals (DAA) can cure the majority of those treated, at around 90% in most populations, at potentially very low prices. We compared the net annual change in epidemic size across 91 countries using data on SVR, new HCV infections, and deaths. In a further 109 countries, we projected this figure using regional averages of epidemic size.

Methods: Epidemiological data for 2016 were extracted from national reports, publications and the Polaris Observatory. There were 91/210 countries with data on SVR, HCV-related deaths and new infections available for analysis; 109 countries had net change in epidemic size projected from the regional prevalence of HCV, extrapolated to their population size. 'Net cure' was defined as the number of people with SVR, minus new HCV infections, plus HCV-related deaths in 2016.

Results: For the 91 countries analysed, there were 57.3 million people with chronic HCV infection in 2016. In the remaining 109 countries, the projected epidemic size was 12.2 million, giving a global epidemic size of 69.6 million. Across the 91 countries, there was a fall from 57.3 to 56.9 million people in 2017, a 0.7% reduction. The projected global net change was from 69.6 to 69.3 million, a 0.4% reduction. Ten countries had at least five times more people reaching SVR than new HCV infections, including Egypt and USA. In 47/91 countries, there were more HCV infections than SVR in 2016.

Conclusion: Very few countries are on target to achieve elimination of HCV as a public health problem by 2030. While the North American, North African/Middle East and Western European regions have shown small declines in prevalence, the epidemic is growing in sub-Saharan Africa and Eastern Europe. Far higher rates of DAA treatment are required for worldwide elimination of HCV.

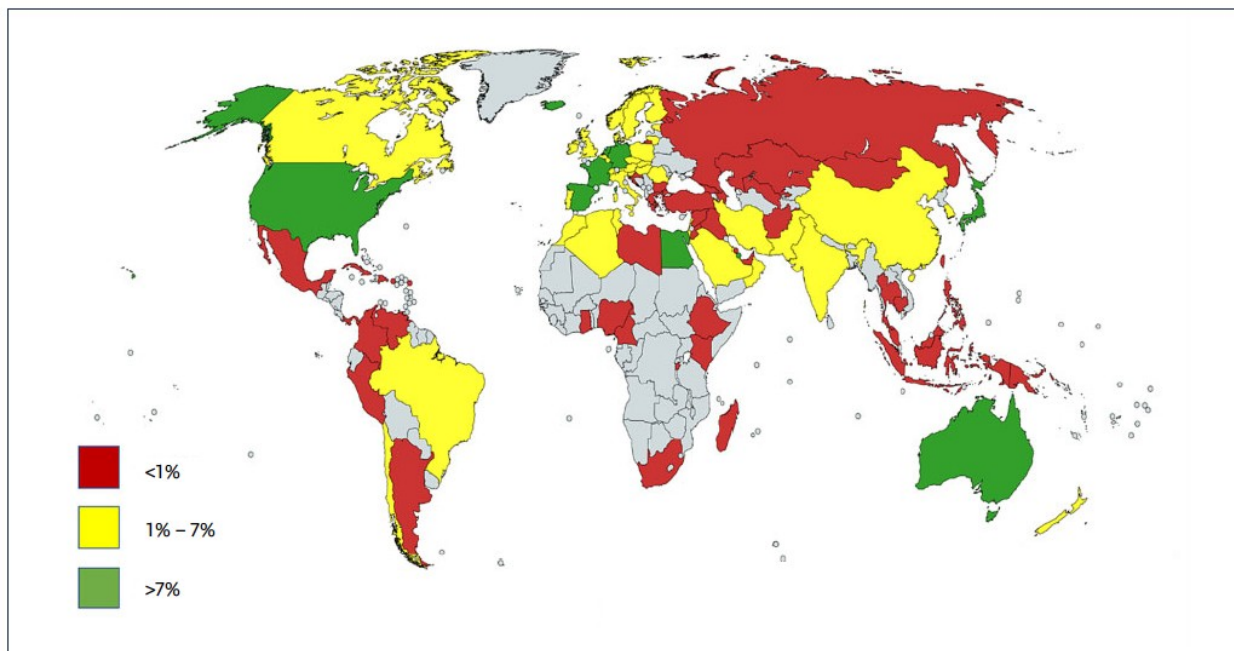


Figure 3. Map showing the percentage treatment rate by country for HCV. Countries shaded in grey were excluded from analysis due to a lack of reliable data

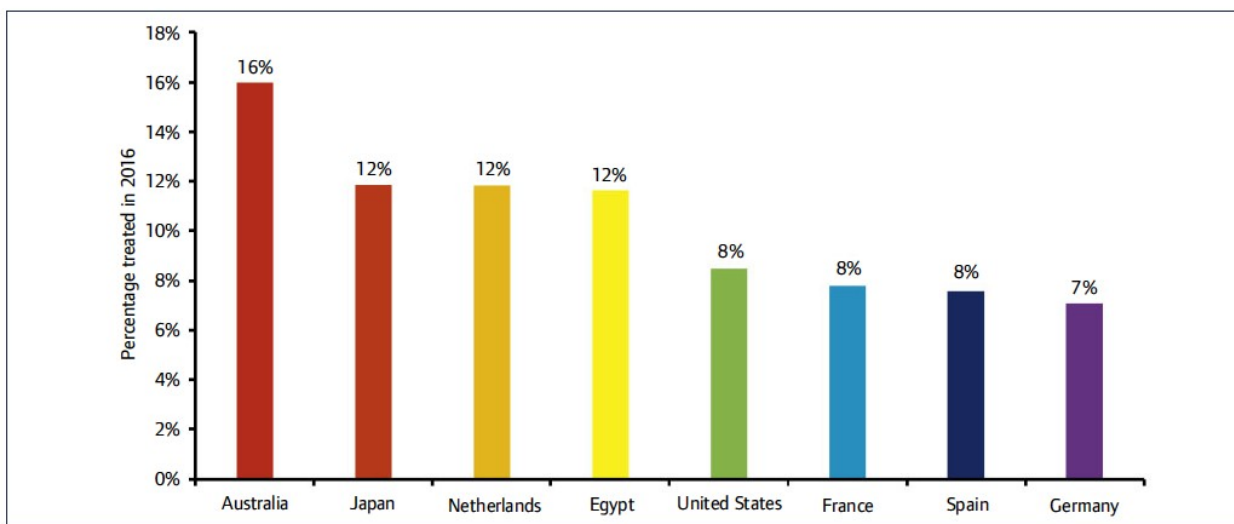
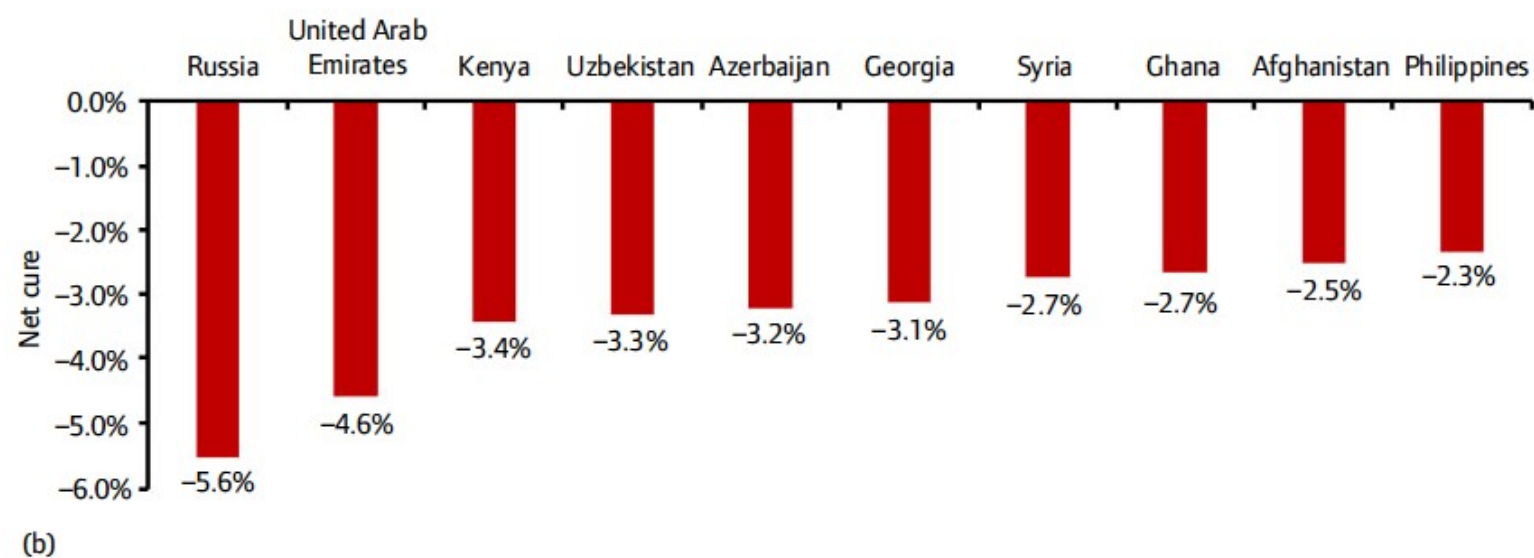


Figure 4. Graph showing the eight countries treating the most people by percentage in 2016. Countries with a viraemic population <1000 (Iceland and Qatar) were excluded from this analysis



The Burden of Chronic Hepatitis C in China From 2004 to 2050: An Individual-Based Modeling Study

Jie Wu,¹ Yuqing Zhou,¹ Xiaofang Fu,¹ Min Deng,¹ Yang Zheng,¹ Guo Tian,¹ Yiping Li,² Chencheng Wang,¹ Cheng Ding,¹
Bing Ruan,¹ Shigui Yang,¹ and Lanjuan Li¹

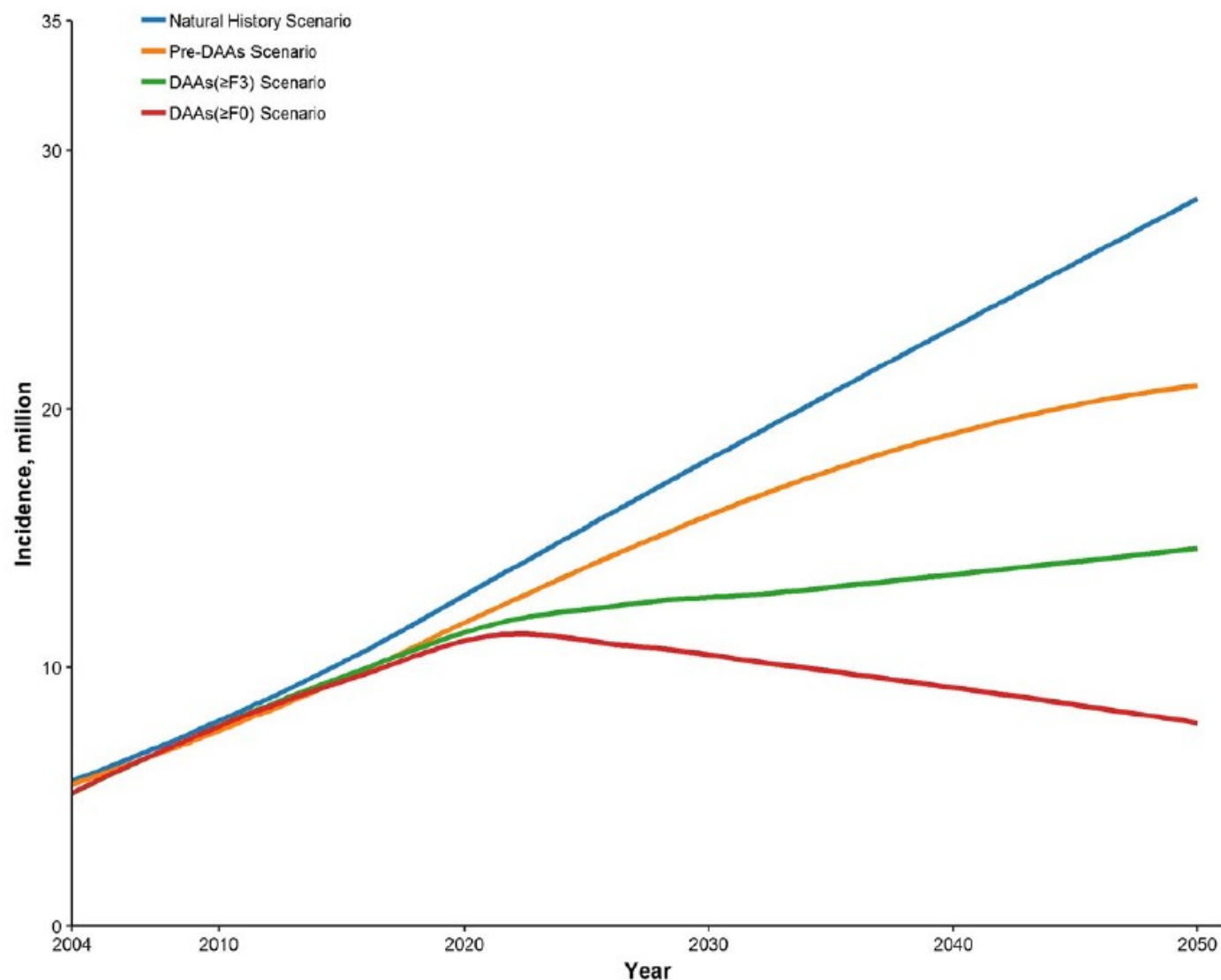


FIG. 1. The changing trend of chronic HCV prevalence by different simulated scenarios in China from 2004 to 2050. F0 = METAVIR stage for no fibrosis; F3 = METAVIR stage for numerous septa without cirrhosis.

China modeling – DAA treat all ($F \geq 0$) scenario

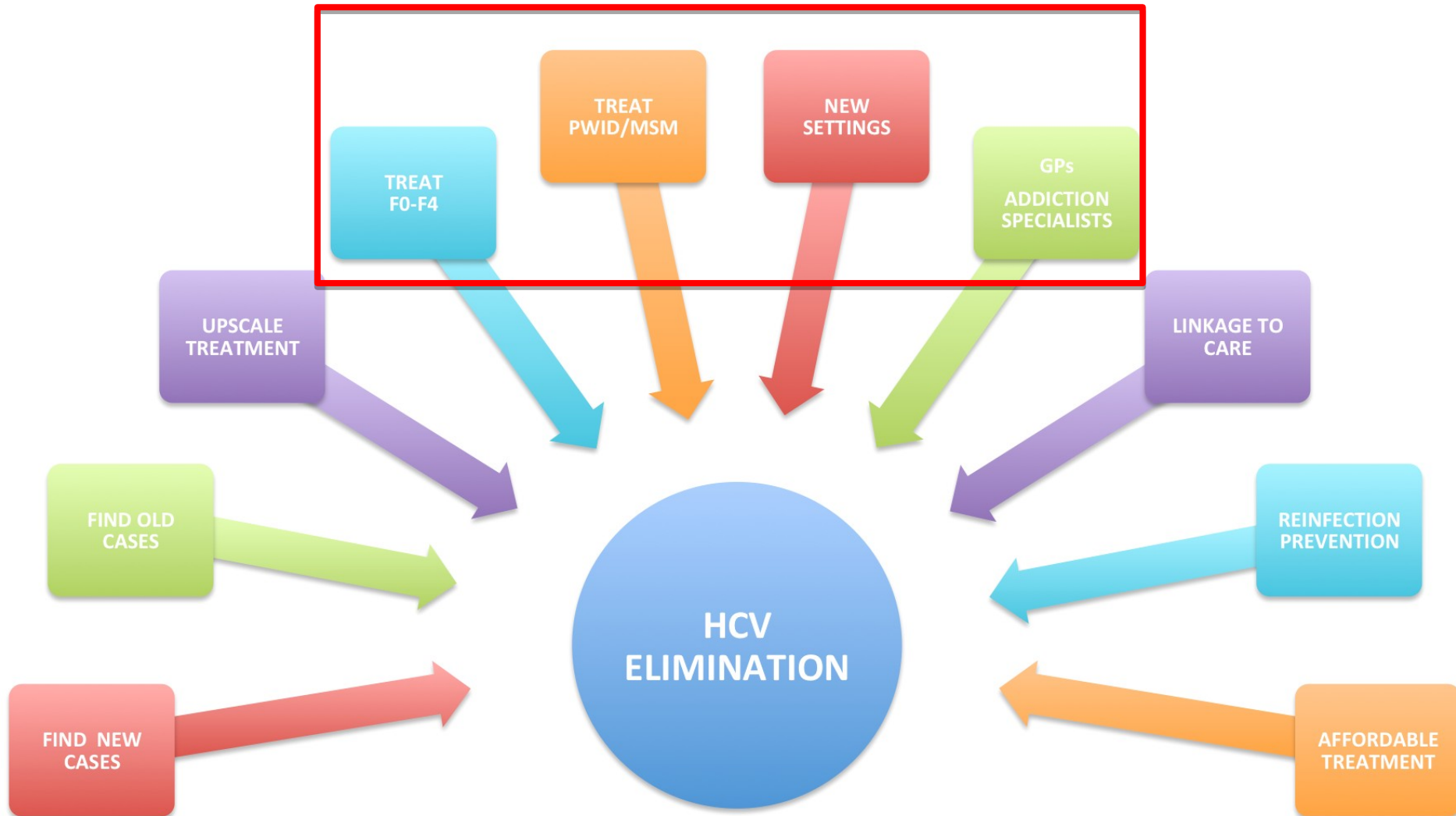
- **HCV treatment to all by 2021**
- **HCV will peak 2020 at 10.75 million**
- **Decrease to 7.92 million by 2050**

China need to

- **Expand screening**
- **Launch DAA use & rapidly expand number treated**

To avert this

What is needed for HCV elimination and where are the patients ?



We have been driving the elimination of viral hepatitis since inception

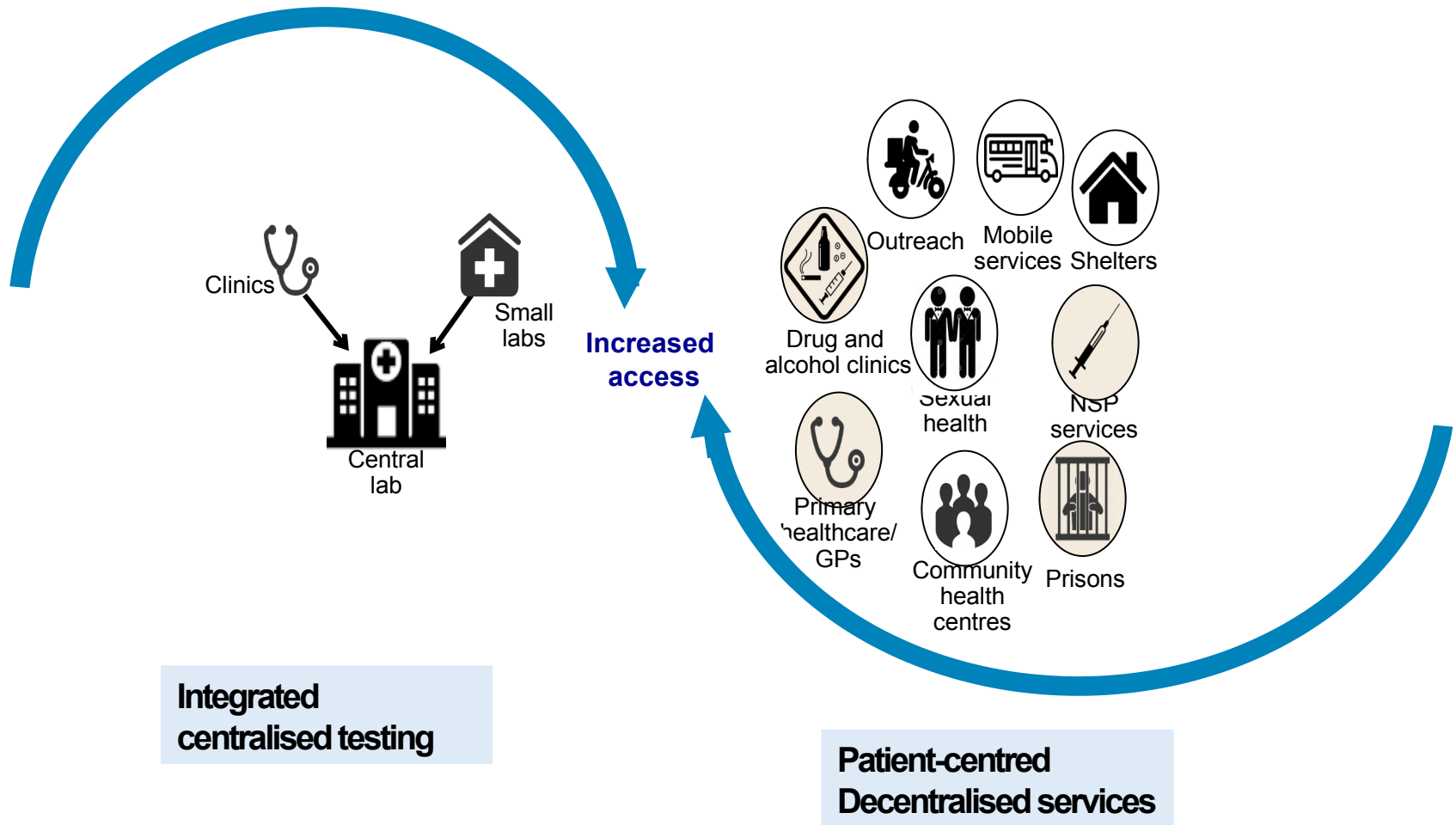
<http://cdafound.org>

Impact

Activity

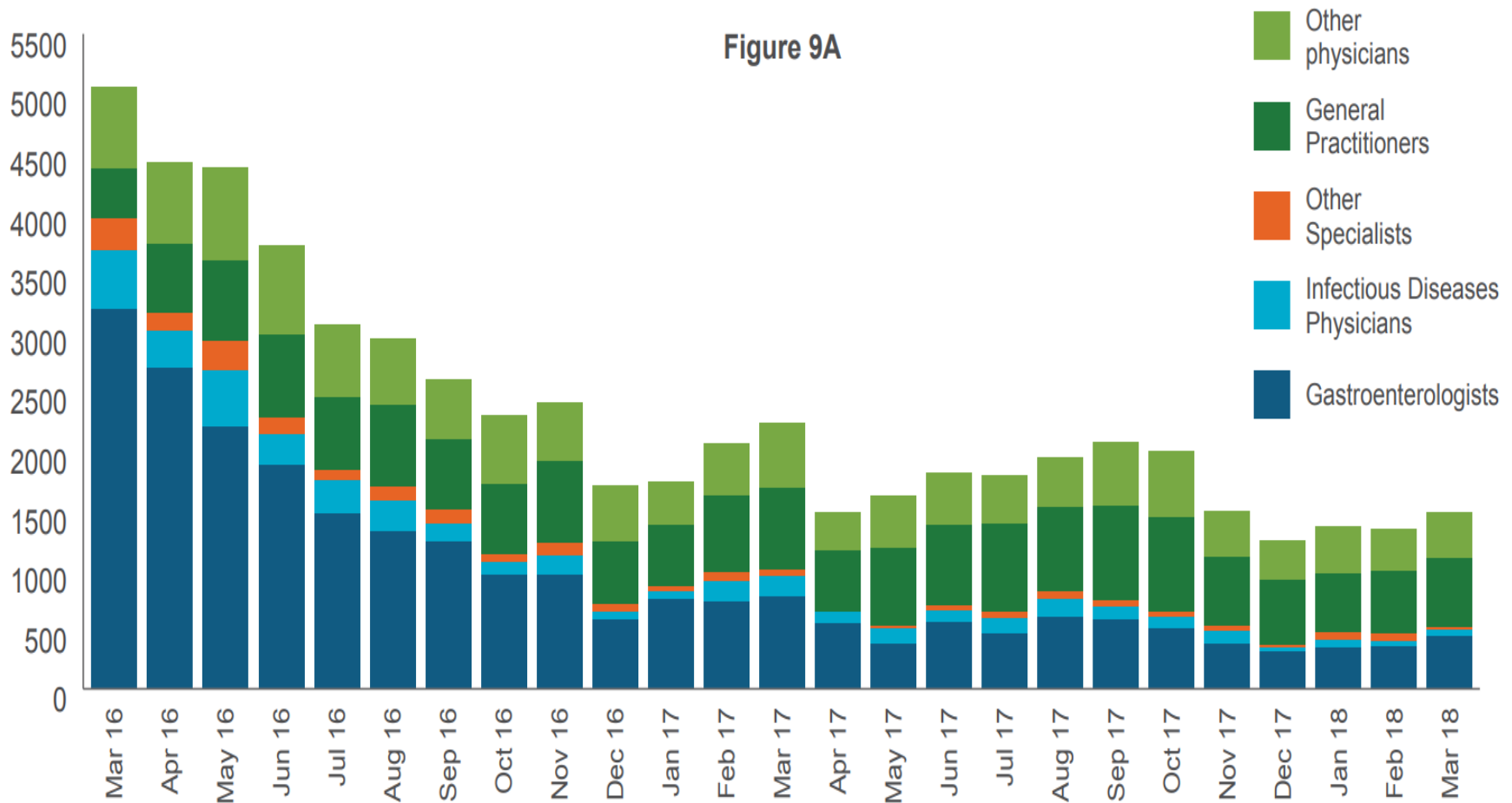
		World Health Assembly endorses hepatitis elimination		WHO adopts Polaris HCV & HBV data for its hepatitis report		Gavi board approves funding HBV birth dose vaccination
	UNITAID board approves to fund HIV/HCV programs	Egypt launches its national HCV elimination plan	MPP expands mandate to include HCV	WHO adopts 71 million as the global HCV prevalence	All EU countries remove restrictions for HCV treatment	Taiwan removes all restrictions & funds the national plan
	Generated HCV Medicines & Diagnostics Report for UNITAID	Published the impact of HCV elimination in 16 countries	Published the impact of HCV elimination in 31 countries	Launched the annual list of countries on path to elimination	Launched the Global Procurement Fund (GPRO)	Assess the impact of HBV BD vaccination for VIMC/ Gavi
	Launched UHEP catalytic financing of hepatitis elimination					
	Showed HCV elimination w/ increased treatment & high SVR	Lowered global HCV prevalence from 185 million to 80 million	Assessed impact of expanding MPP's mandate into HCV	Worked with Taiwan MoH to show the impact of national elimination	Published study on the impact of HCV elimination in EU	Updated global HBV prevalence to 292 million
	Showed HBV test & treat is more effective than SoC					
	Recommended testing & treatment of HCV using oral therapies	Assessed the impact of HCV elimination in Egypt	Launched Polaris Observatory covering >100 countries	Updated global HCV prevalence to 71 million	Assessed HCV elimination strategies for US National Academies	Started shipments of quality hepatitis medicine & diagnostics
	Center for Disease Analysis (CDA)					CDA Foundation (CDAF)
	2013	2014	2015	2016	2017	2018
						2019

Increase the settings that can provide HCV screening interventions



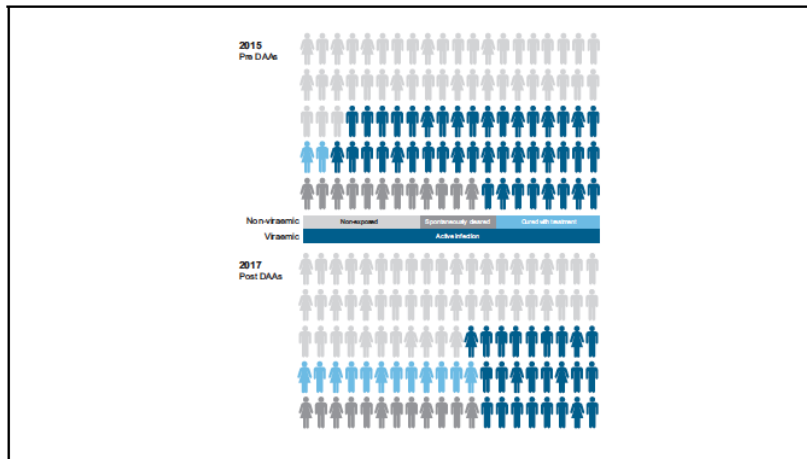
Australia-Number of prescriptions per month

Figure 9: Absolute frequency (A) and relative frequency (B) of prescriber types in each month for individuals initiating DAA treatment during March 2016 to March 2018 in Australia



Association between rapid utilisation of direct hepatitis C antivirals and decline in the prevalence of viremia among people who inject drugs in Australia

Graphical abstract



Highlights

- Evidence to support feasibility of elimination of hepatitis C as a public health threat.
- High uptake of hepatitis C treatment reflected in reduction in viraemic prevalence.
- Surveillance and monitoring are required to track progress toward elimination goals.

Authors

Jenny Iversen, Gregory J. Dore, Beth Catlett, Philip Cunningham, Jason Grebely, Lisa Maher


Correspondence

jiversen@kirby.unsw.edu.au
(J. Iversen)

Lay summary

The World Health Organization's goal to reduce hepatitis C virus incidence by 80% will be difficult to achieve without widespread scale up and a corresponding reduction in viraemic prevalence among those most at risk of onward transmission. Our results indicate that a population-level reduction in viraemic prevalence is achievable through high levels of treatment and cure among people who inject drugs.

Treatment as Prevention for Hepatitis C (TraP Hep C) – a nationwide elimination programme in Iceland using direct-acting antiviral agents

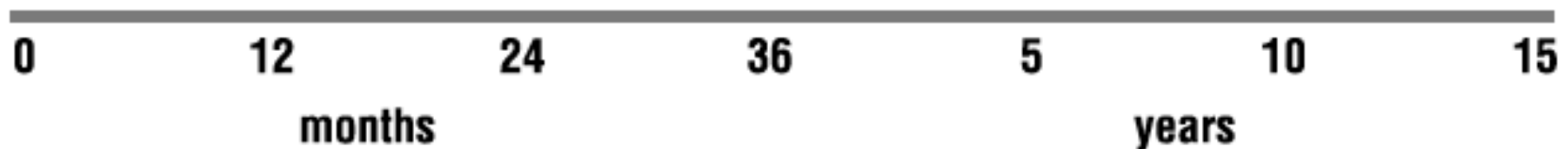
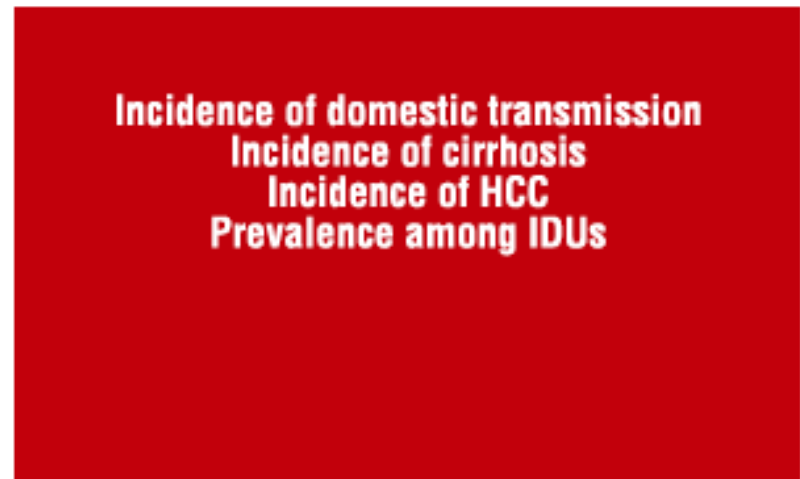
■ S. Olafsson^{1,2}, T. Tyrfinngsson³, V. Runarsdottir³, O. M. Bergmann¹, I. Hansdottir^{3,4}, E. S. Björnsson^{1,2}, B. Johannsson⁵, B. Sigurdardottir⁵, R. H. Fridriksdottir¹, A. Löve^{2,6}, M. Hellard^{7,8,9}, T. J. Löve^{2,10}, T. Gudnason¹¹, M. Heimisdottir^{2,12} & M. Gottfredsson^{2,5,10} 

From the ¹Division of Gastroenterology and Hepatology, Landspítali University Hospital; ²Faculty of Medicine, School of Health Sciences, University of Iceland; ³SAA – National Center of Addiction Medicine; ⁴Faculty of Psychology, School of Health Sciences, University of Iceland; ⁵Division of Infectious Diseases; ⁶Division of Virology, Landspítali University Hospital, Reykjavik, Iceland; ⁷Centre for Population Health, Burnet Institute, Melbourne; ⁸Department of Epidemiology and Preventive Medicine, Monash University, Clayton; ⁹Department of Infectious Diseases, Alfred Hospital, Melbourne, VIC, Australia; ¹⁰Department of Science, Landspítali University Hospital; ¹¹Chief Epidemiologist, Directorate of Health; and ¹²Division of Finance, Landspítali University Hospital, Reykjavik, Iceland

TraP – active treatment*

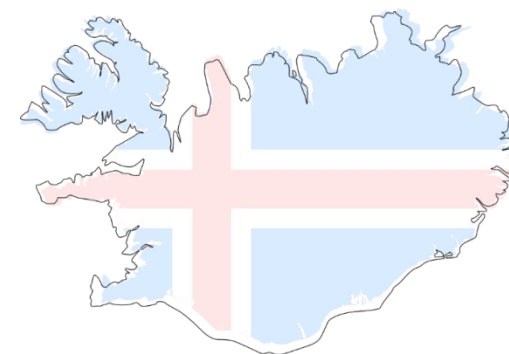


TraP – monitoring of long-term effects



* Endpoints SVR, domestic incidence, Study monitored by CRO

- Iceland has a total population of ~330,000
- Estimated 880–1300 patients are infected with HCV (0.3% population)
- HCV elimination programme (3 year programme)
 - Gilead is providing DAAs free of charge
 - Aiming to treat all patients by the end of 2018

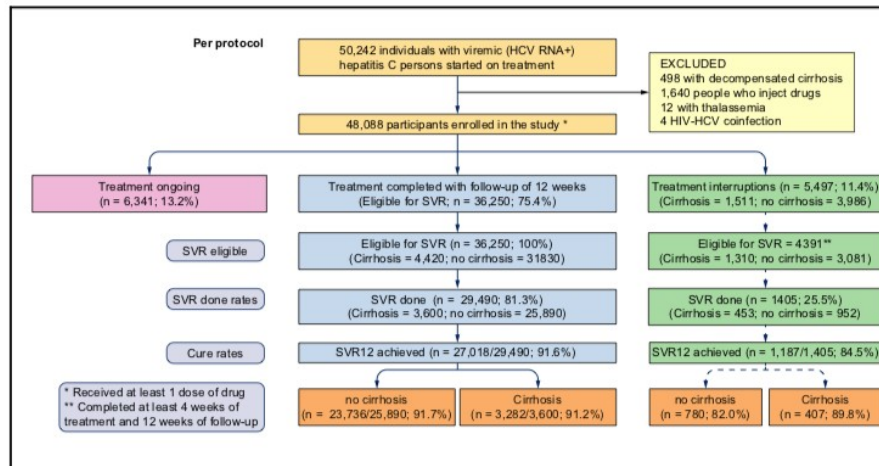


From 12 month evaluation	N=322
Previous treatment for HCV	46 (14)
Encounter site	
University Hospital	208 (65)
Addiction treatment centre	100 (31)
Penitentiary	14 (4)
IV drug use	
Ever	292 (91)
Within 6 months	97 (33)
Within 30 days	49 (15)
Current OST	44 (15)

Iceland treated almost one-half of the diagnosed HCV population in the first year, showing that elimination in a defined region is feasible

Decentralized care with generic direct-acting antivirals in the management of chronic hepatitis C in a public health care setting

Graphical abstract



Highlights

- The goal of the 'Punjab Model' is HCV Elimination by 2030, using primary care providers and remote treatment monitoring.
- We enrolled 48,088 people (14.8% with compensated cirrhosis; 69.9% with genotype 3).
- SVR12 was achieved in 91.6%, 67.6% and 91.2%, per protocol, intention-to-treat (ITT) and a modified ITT, respectively.
- Decentralized care of hepatitis C with direct-acting antiviral - regimens is safe and effective, regardless of genotype or presence of cirrhosis.

Authors

Radha K. Dhiman, Gagandeep S. Grover, Madhumita Premkumar, ..., Sahaj Rathi, Sandeep Satsangi, Akash Roy

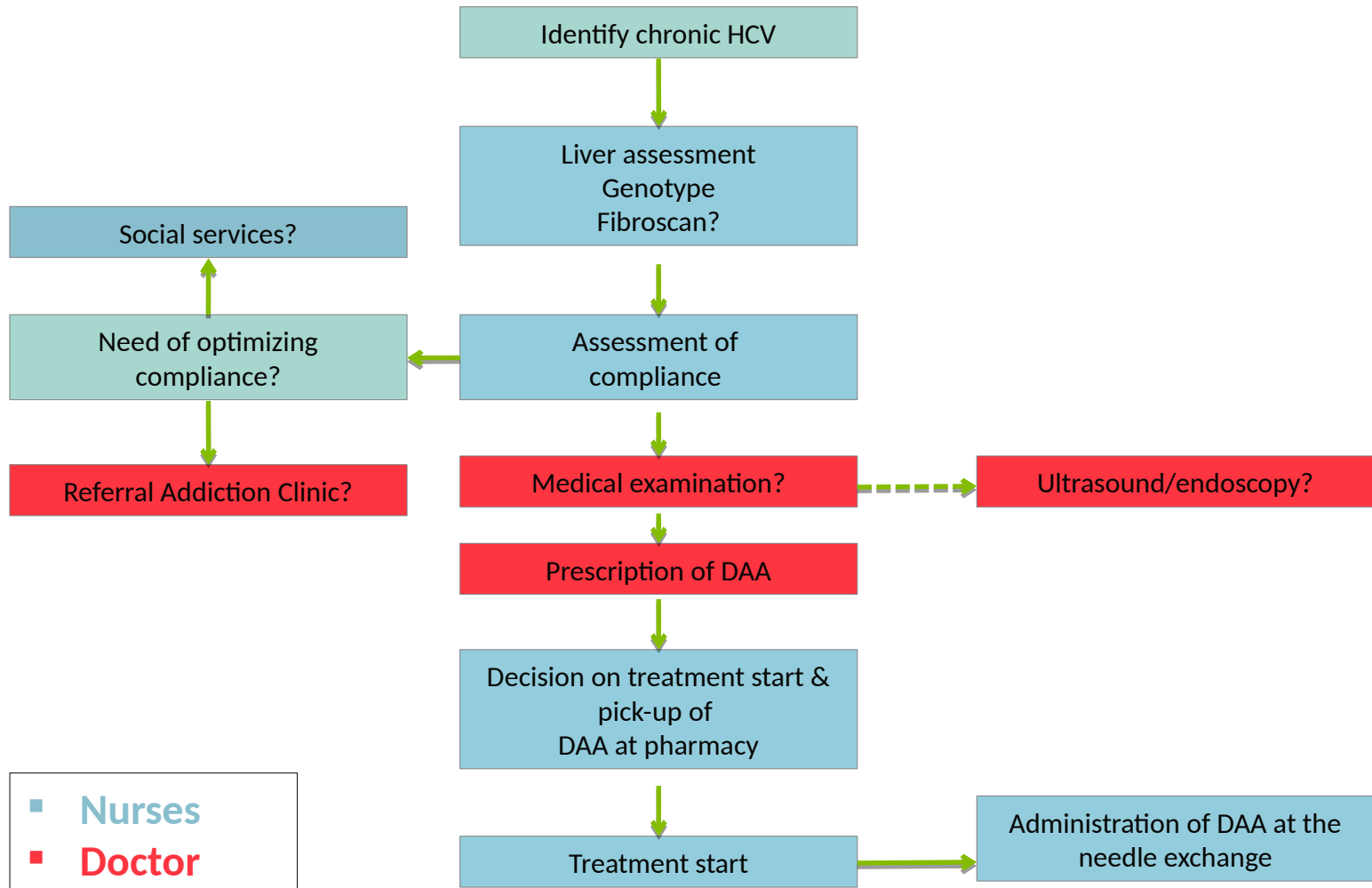
Correspondence

rkpsdhiman@hotmail.com
(R.K. Dhiman)

Lay summary

We assessed the safety and efficacy of public health care using no-cost all-oral generic direct-acting antiviral drugs against hepatitis C in the state of Punjab, India. The goal is elimination of chronic hepatitis C (CHC) by 2030 and involves primary care providers at 25 sites in the state. We enrolled 48,088 individuals (63.8% male; mean age 42.1 years; 80.5% rural; 14.8% compensated cirrhotic; 69.9% genotype 3) between 18th June 2016 to 31st July 2018. Cure was achieved in 91.6% of patients, demonstrating that decentralized care of CHC with generic all-oral regimens is safe and effective.

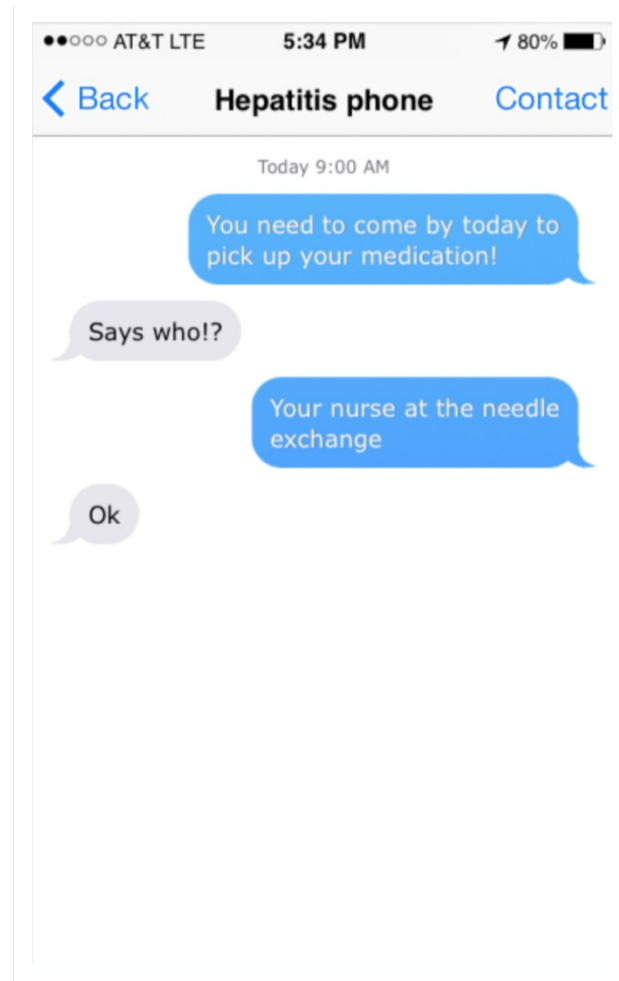
HCV treatment at the Stockholm NEP



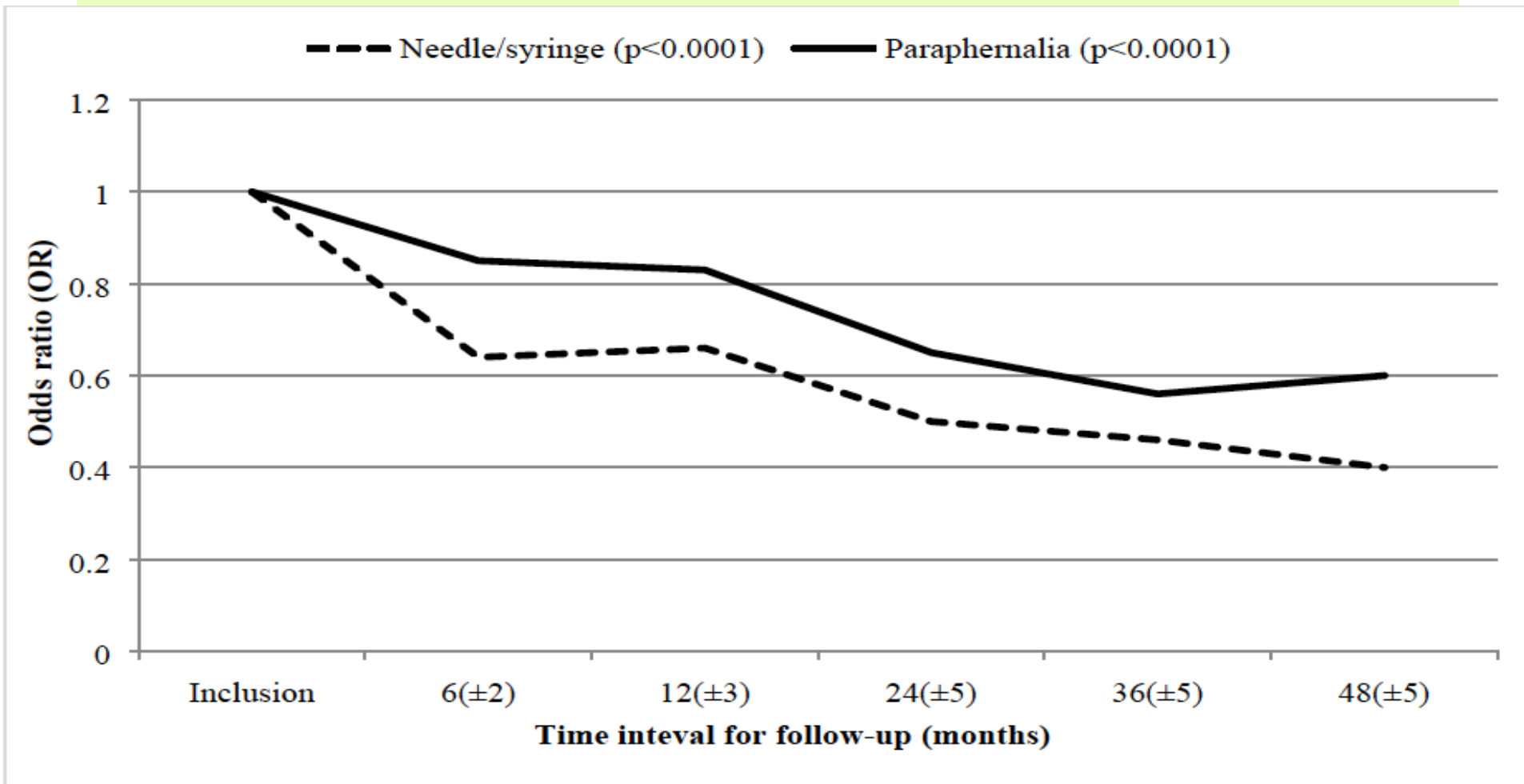
"Housing first?"



Hepatitis phone



Changes in injection risk behaviors following inclusion in the Stockholm NEP program. Odd ratio at inclusion set as 1 as reference value. N = 2860 at inclusion



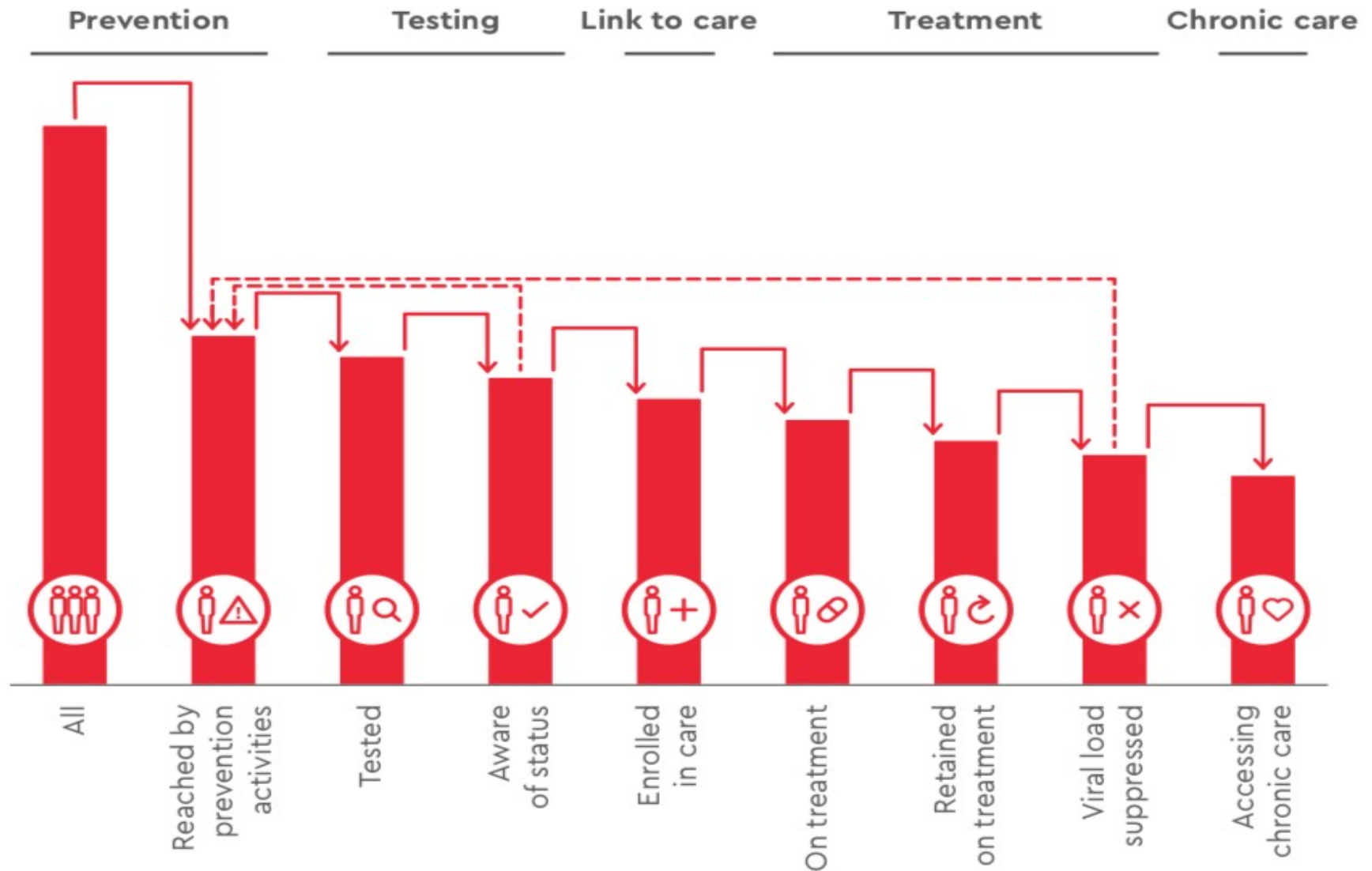
Donut pillbox



What is needed for HCV elimination and where are the patients ?



WHO's continuum of viral hepatitis services and the cascade of care



ORIGINAL ARTICLE

Outcomes of Treatment for Hepatitis C Virus Infection by Primary Care Providers

Sanjeev Arora, M.D., Karla Thornton, M.D., Glen Murata, M.D.,
Paulina Deming, Pharm.D., Summers Kalishman, Ph.D., Denise Dion, Ph.D.,
Brooke Parish, M.D., Thomas Burke, B.S., Wesley Pak, M.B.A.,
Jeffrey Dunkelberg, M.D., Martin Kistin, M.D., John Brown, M.A.,
Steven Jenkusky, M.D., Miriam Komaromy, M.D., and Clifford Qualls, Ph.D.

ABSTRACT

BACKGROUND

The Extension for Community Healthcare Outcomes (ECHO) model was developed to improve access to care for underserved populations with complex health problems such as hepatitis C virus (HCV) infection. With the use of video-conferencing technology, the ECHO program trains primary care providers to treat complex diseases.

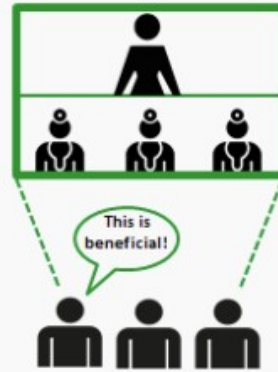
The "Project ECHO" model



People need easier access to specialty care.



There aren't enough specialists to treat everyone, especially in rural areas.



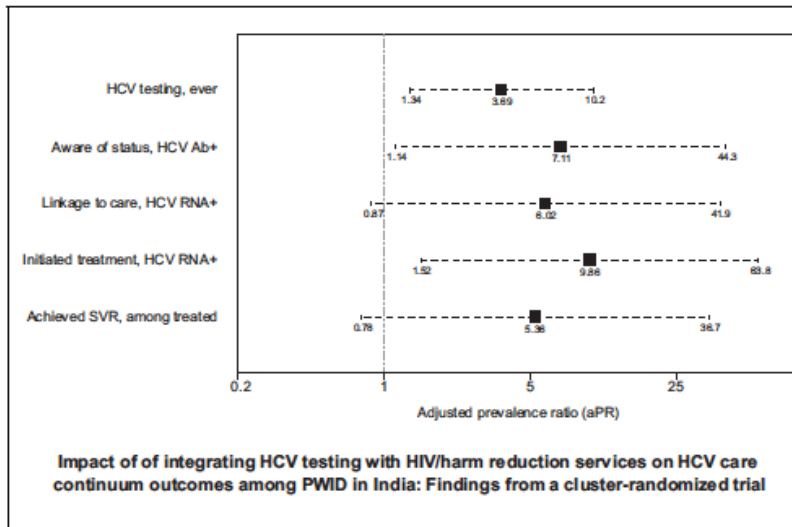
Project ECHO uses specialists to train primary care clinicians remotely.



Now more doctors and nurses can provide specialty care to their patients.

Integrating HCV testing with HIV programs improves hepatitis C outcomes in people who inject drugs: A cluster-randomized trial

Graphical abstract



Authors

Sunil Suhas Solomon, Thomas C. Quinn, Suniti Solomon, ..., Kuldeep Singh Sachdeva, Gregory M. Lucas, Shruti H. Mehta

Correspondence

sss@jhmi.edu
(S.S. Solomon)

Lay summary

Delivering hepatitis C virus (HCV) testing to people who inject drugs (PWID) in places where they also have access to HIV prevention and treatment services is an effective way to improve uptake of HCV testing among communities of PWID. To achieve the World Health Organization's ambitious elimination targets, integrated programs will need to be scaled up to deliver comprehensive HCV services.

Highlights

- Integration of HCV testing with HIV/harm reduction services increased uptake of HCV among PWID.
- PWID in intervention vs. usual care sites were more likely to have been tested for HCV.
- PWID in intervention vs. usual care sites were more likely to be aware of their HCV status.
- Despite relative increases, absolute numbers aware of HCV status remained low.
- Integration of services is an important early step towards HCV elimination.

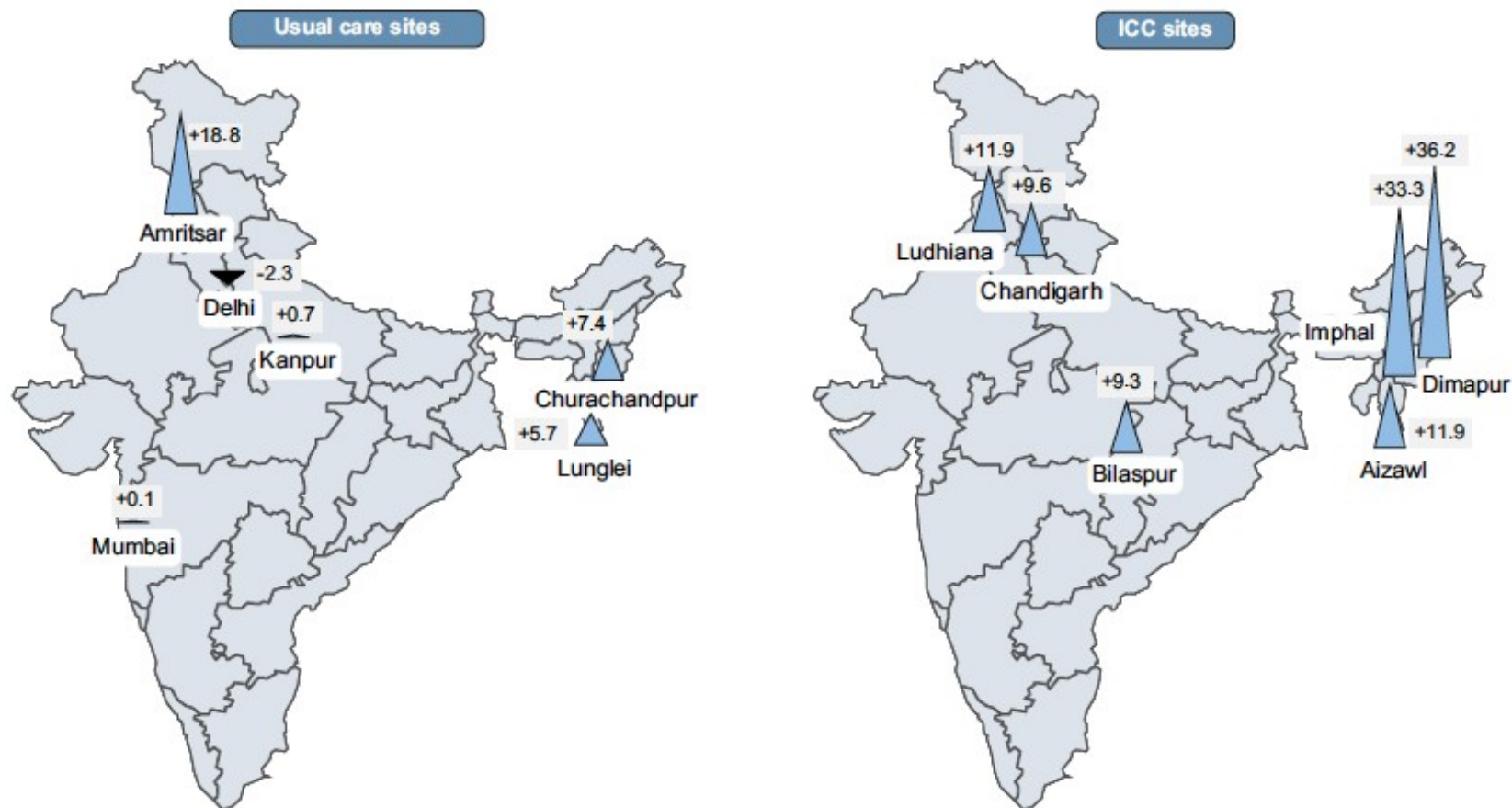
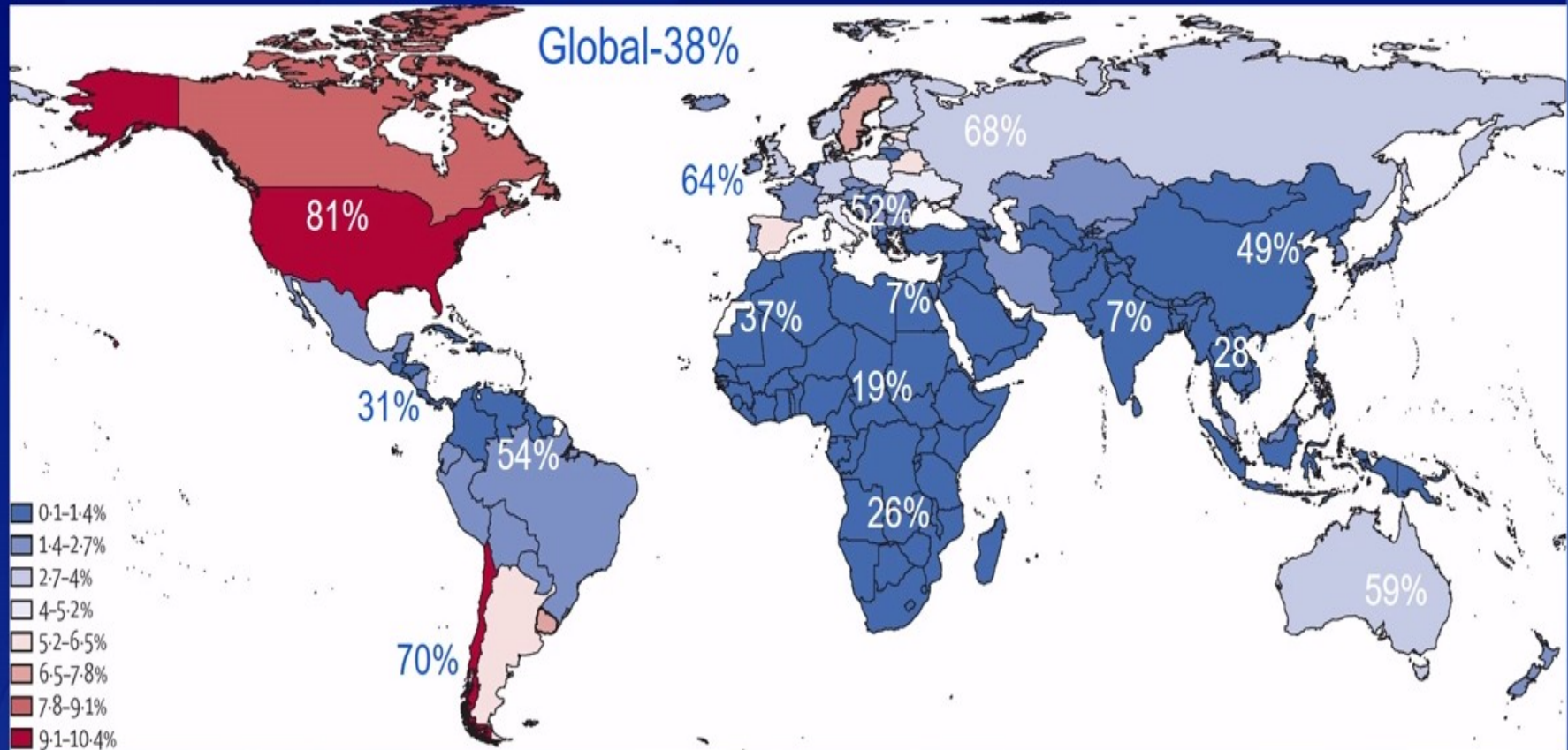
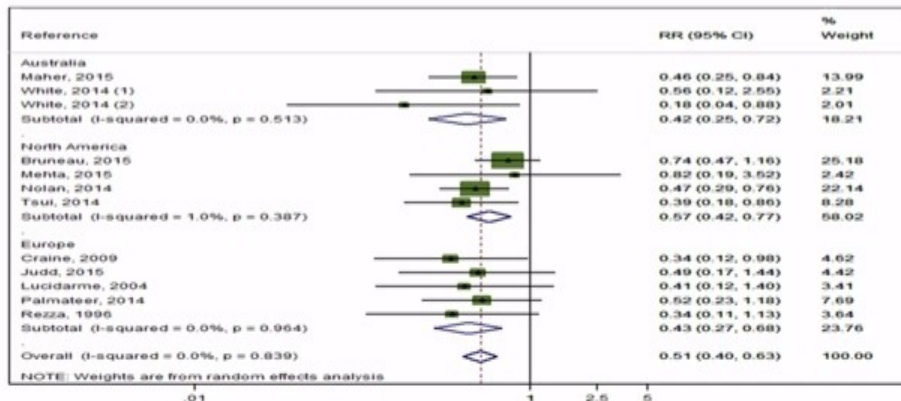


Fig. 2. Indian map depicting the absolute percentage point change in ever being tested for HCV between evaluation and baseline assessment by study arm. Height of triangle is proportionate to the absolute percentage point change at each location. Blue triangle pointing upwards represents a positive change and black triangle pointing downwards represents a negative change.

Proportion of Total Burden of Hepatitis C Virus Infection Attributable to Injecting Drug Use by Region, 2013



Impact of Needle Syringe Programs and Opioid Substitution Therapy on HCV Transmission



Current OST

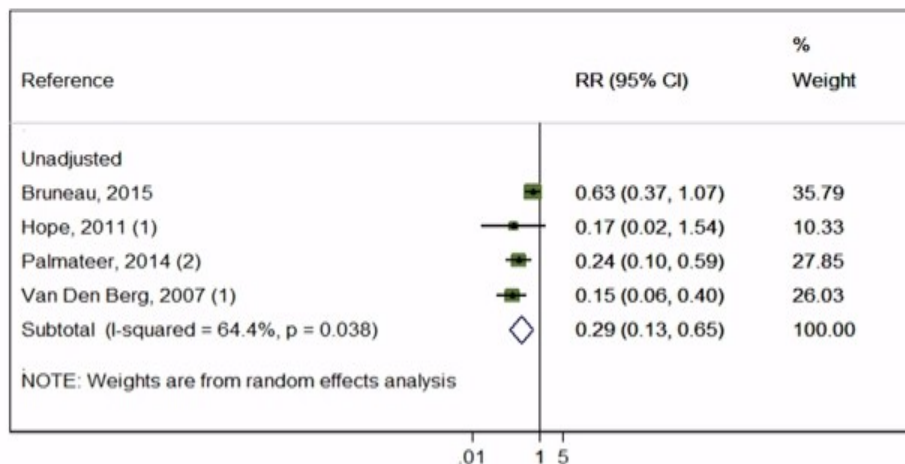
12 studies:

6361 participants

1030 HCV cases

50% reduction in HCV

Little heterogeneity



High NSP with OST

4 studies

3356 participants

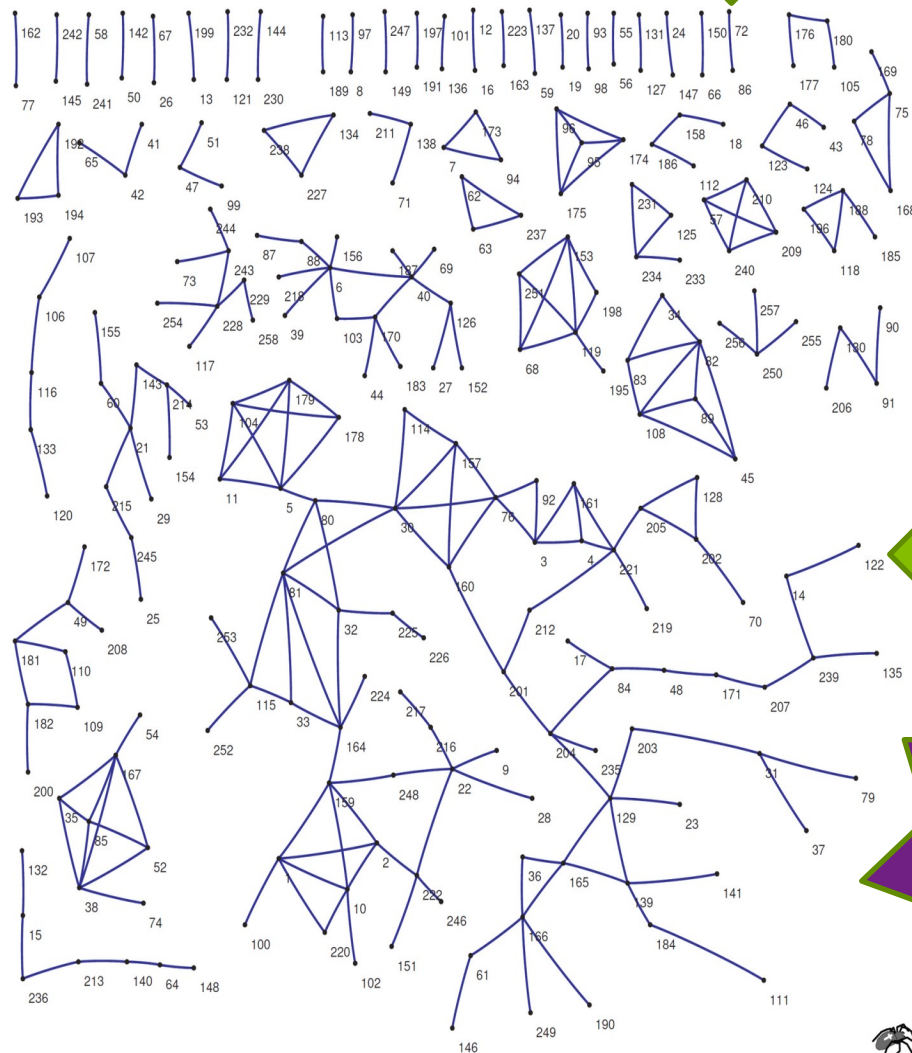
518 HCV cases

71% reduction in HCV

moderate heterogeneity

Empirical social network of

200%
SVR



8,100%
SVR



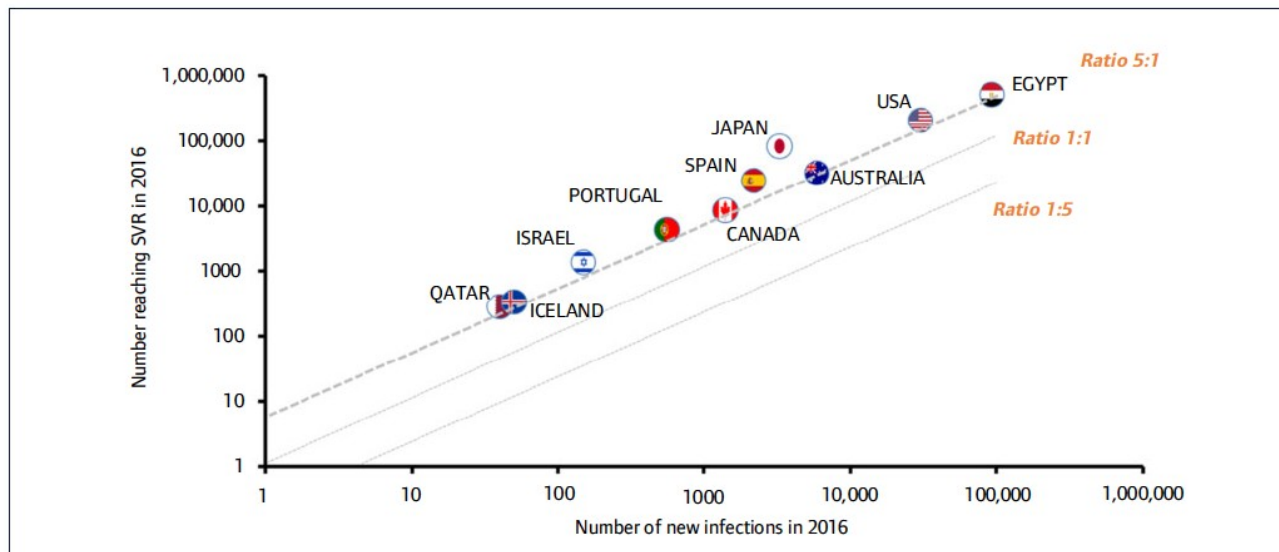


Figure 7. Scatter plot showing the 10/91 countries where there were >5 times more people reaching SVR than there were new infections in 2016. The guideline represents the mark of five people reaching SVR for every single new HCV infection

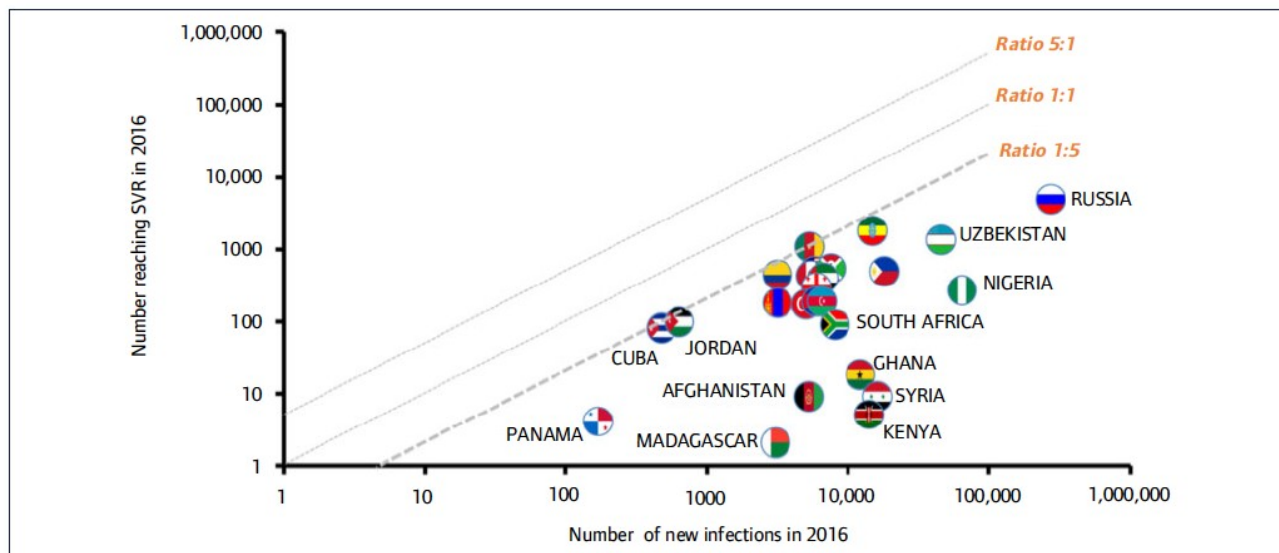
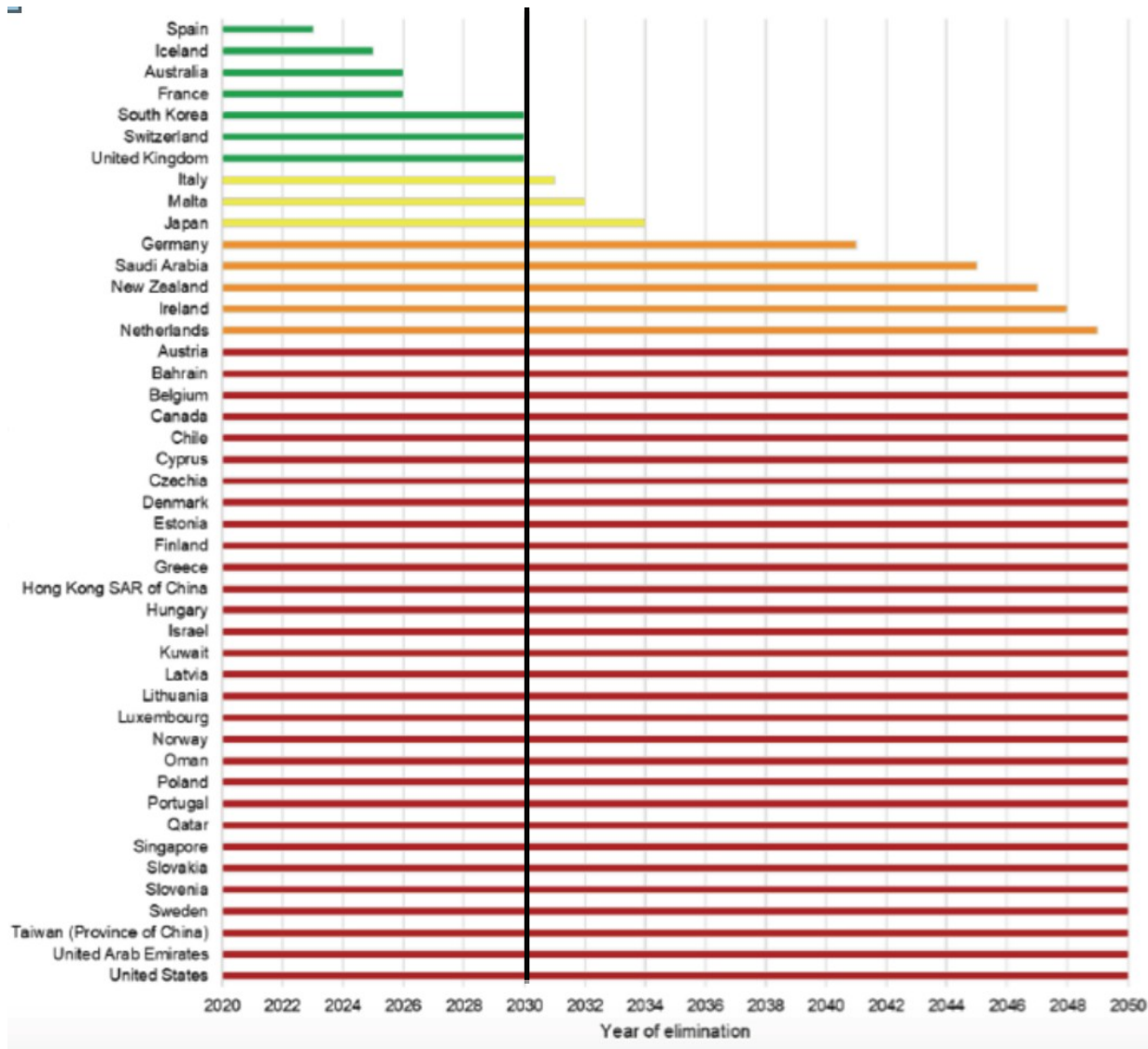


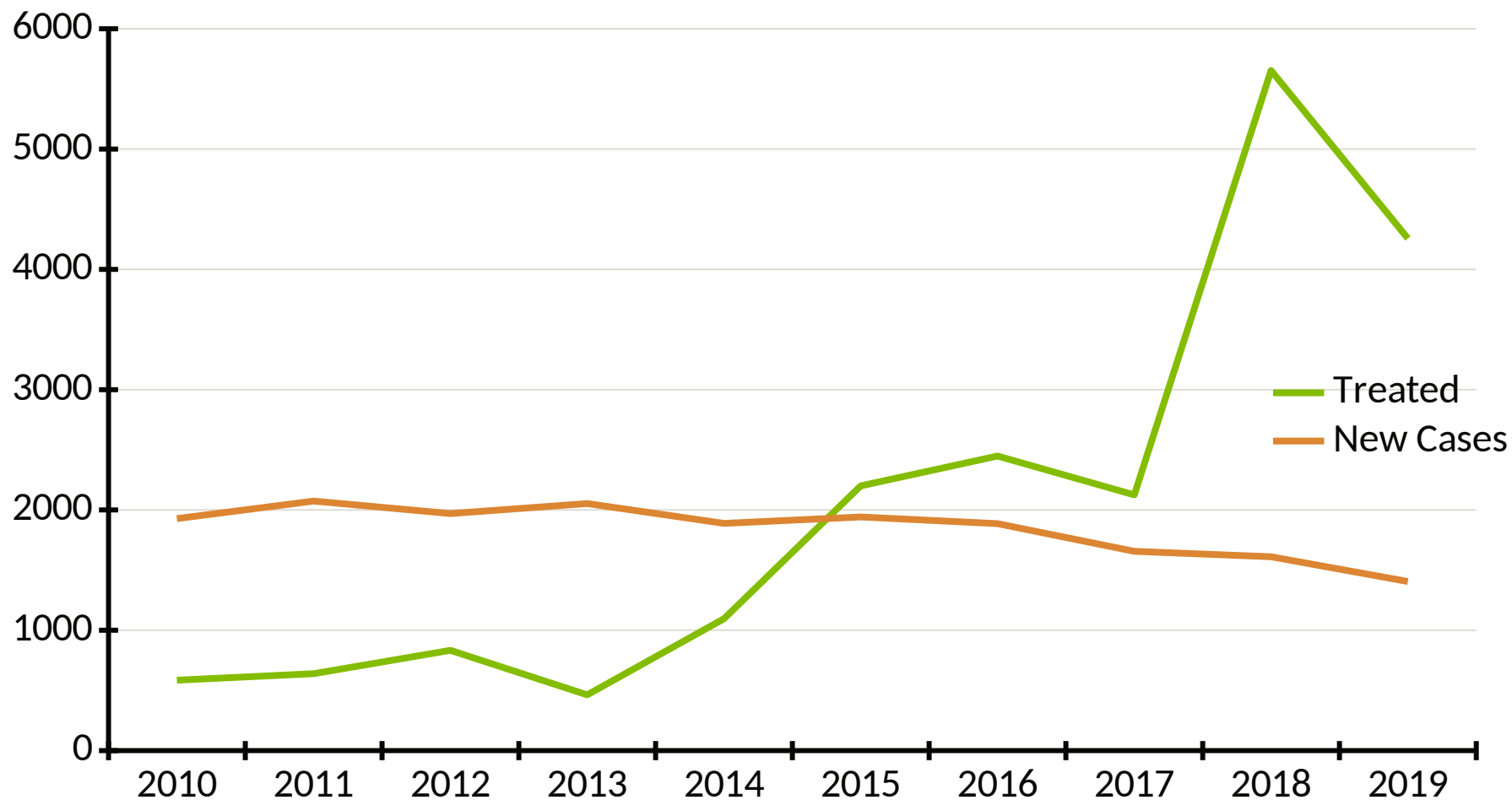
Figure 8. Scatter plot showing the 23/91 countries where there were 5 times fewer people reaching SVR than there were new infections in 2016. The guideline represents the mark of one person reaching SVR for every five new HCV infections in 2016

HCV elimination off track WHO targets/countries estimate

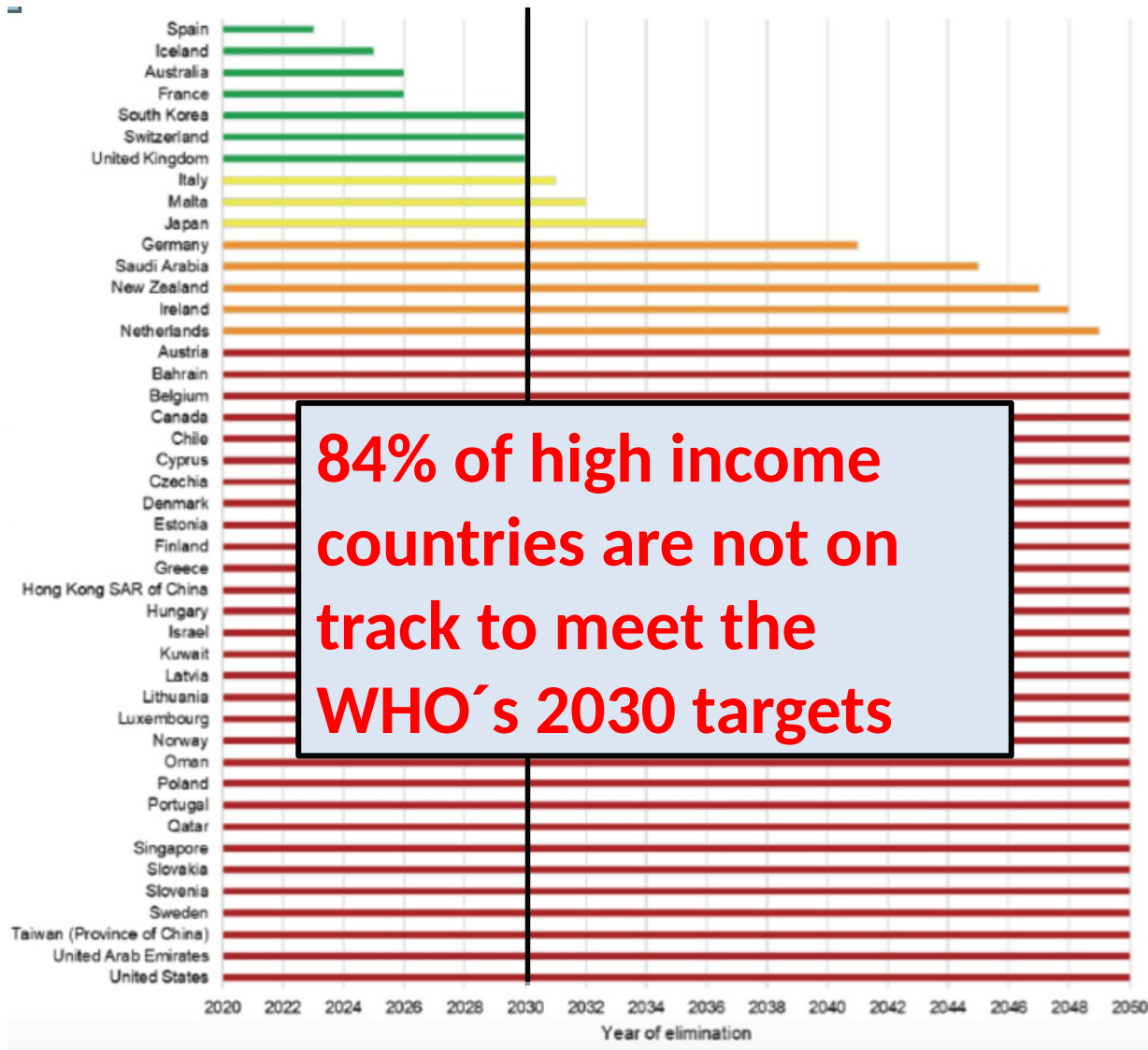


http://www.natap.org/2019/EASL/EASL_24htm

Treated and new HCV cases in Sweden 2010-2019



HCV elimination off track WHO targets/countries estimate



Key elements in Macro Elimination of chronic HCV as a public health threat

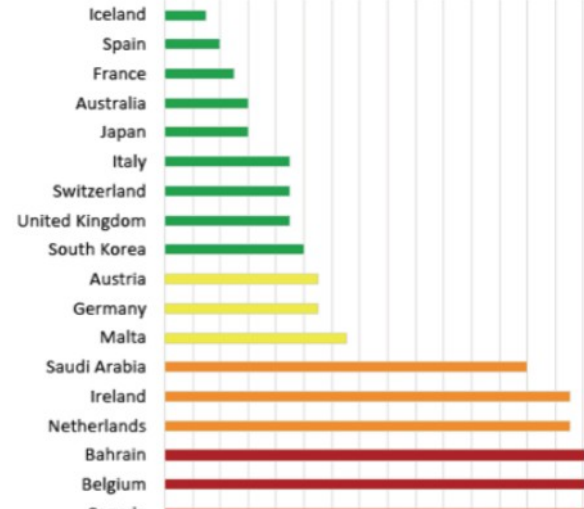
- 1. Awareness of HCV status and prevention from new infections**
- 2. Access to HCV testing and diagnosis**
- 3. Linkage to care**
- 4. Access to DAA treatment decentralized**
- 5. Development of national plans**

Adopted and modified from: BCG. Road to elimination: barriers and best practices in hepatitis C management.

http://image-src.bcg.com/image/BCG-Road-to-Elimination_tcm-166034.pdf (assessed Sep 2018)

HCV elimination off-track WHO targets

Year of elimination by country



84% of
count
track
WHO

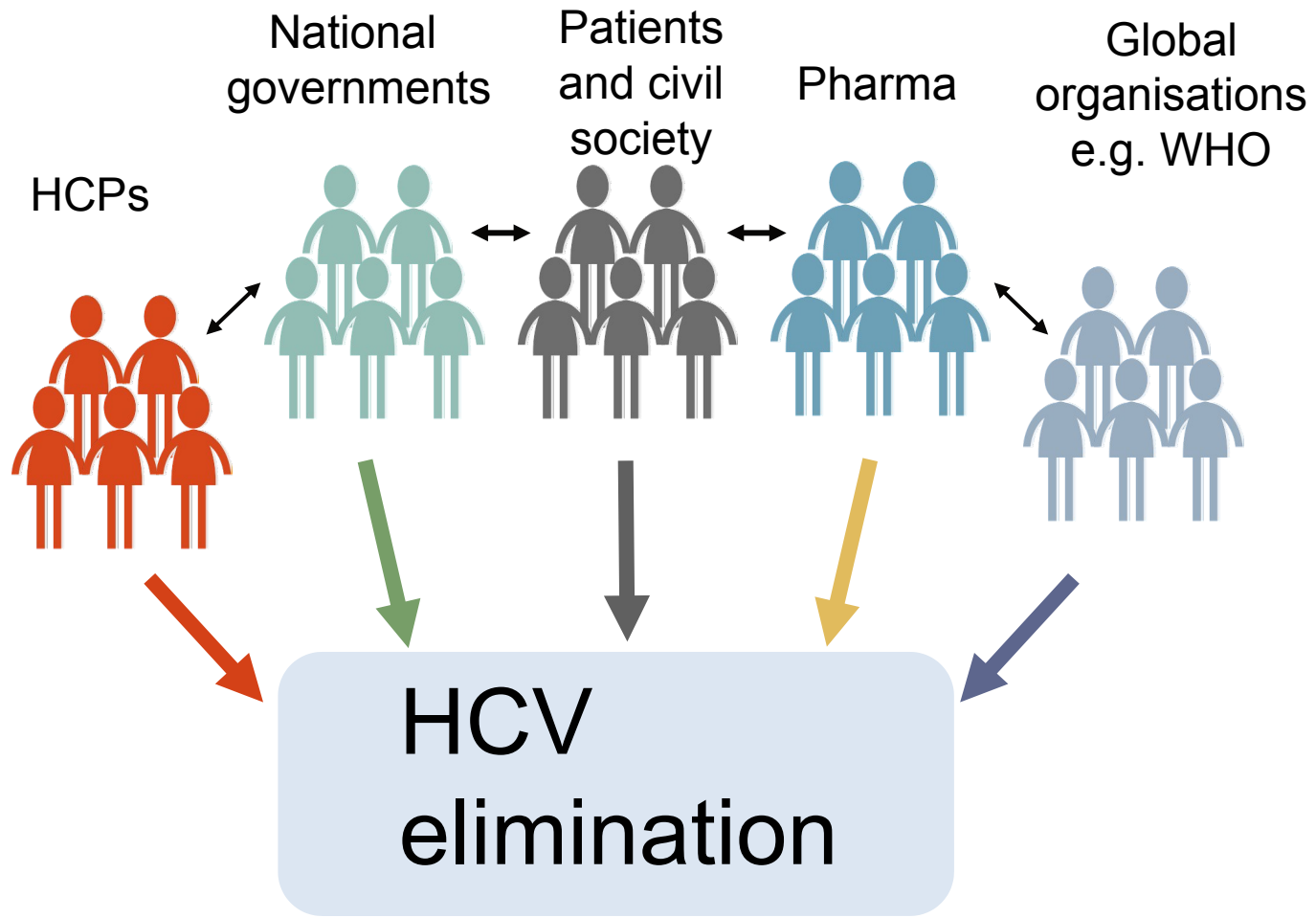
To improve this
We need





FIGURE 3 Key success factors for HCV elimination, a conceptual framework. HCV, hepatitis C virus

Collaboration between stakeholders is essential to achieve HCV elimination



Thanks

