

Lausanne, January 16, 2020

## Viral hepatitis elimination

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## The global agenda

### Milestones in viral hepatitis global policy

**2010 (resolution WHA63.15) and 2014 (resolution WHA67.6)**

– Viral hepatitis is recognized as a global public health problem

**Sustained Development Goals (September 25, 2015 by the UN General Assembly)**

– Goal 3: Ensure healthy lives and promote well-being for all at all ages [... by 2030, end the epidemics of AIDS, tuberculosis, malaria and neglected tropical diseases and **combat hepatitis**, water-borne diseases and other communicable diseases...]

**Global Health Sector Strategy on Viral Hepatitis (adopted in May 2016 by the WHA)**

– Elimination of viral hepatitis as a public health threat by 2030, i.e. reducing new infections by 90% and mortality by 65%

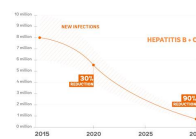
**Towards the Elimination of Hepatitis B and C by 2030**  
The draft WHO Global Hepatitis Strategy, 2016-2021  
and global elimination targets



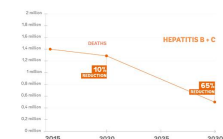
### WHO Global Health Sector Strategy on Viral Hepatitis

Endorsed in May 2016 by 194 countries at the World Health Assembly

**90% reduction of new HBV and HCV infections (from 6-10 million to 900,000)**



**65% reduction of mortality (from 1.4 million to under 500,000)**



### Scaling up 6 interventions to eliminate viral hepatitis by 2030

Interventions	2030 targets
1. Three dose hepatitis B vaccine	90%
2. HBV PMTCT	90%
3. Blood and injection safety	100 % screened donations
	90% reuse-prevention devices
4. Harm reduction	300 injection sets/PWID/year
5. Diagnosis	90% diagnosed
6. Treatment	80% eligible treated

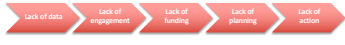
PMTCT: Prevention of mother to child transmission PWID: Person who injects drugs

www.who.org

### Why are a strategy and targets important?

- A powerful tool for mobilizing resources and action
- Promote development of regional and national action plans
- To set common targets for countries – towards joint accountability

### Key challenges/roadblocks confronting countries: The five “lacks” (and the costs)

- 
- **Lack of Data** on disease and economic burden, treatment need, potential impact of treatment scale-up (to build investment case)
  - **Lack of Engagement**, i.e. insufficient advocacy, leadership and commitment for hepatitis response at higher levels
  - **Lack of Funding** at both the global and country funding
  - **Lack of Planning** in terms of national strategies/plans and dedicated hepatitis department/focal persons with insufficient number of resources in MOH in many countries
  - **Lack of Action**, i.e. insufficient testing, whereas the public health sector approach to hepatitis treatment is in its infancy
  - **High cost of diagnostics and antivirals**

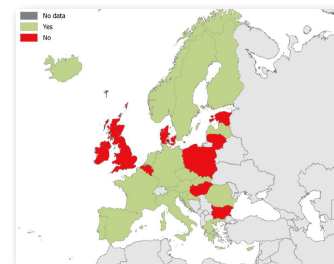
### European regional goals and update

### Viral hepatitis elimination in Europe: baseline and WHO targets

Interventions	Indicator	2015	Target 2020	Target 2030
Hepatitis B vaccination	HEPB3 coverage	81%	90%	90%
Prevention of MoTC transmission	Birth dose coverage	39%	50%	90%
Blood safety	Donations screened with quality assurance	99.9%	95%	100%
Injection safety	% of unsafe injections	4.6%	0%	0%
Harm reduction	Syringes + needles distributed/PWID/year	59	200	300
Testing services	% diagnosed	HBV: 13% HCV: 31%	30%	90%
Treatment	% diagnosed and treated	HBV: N/A HCV: 5%	HBV: 5M HCV: 3M	80% of eligible

WHO Global Hepatitis Report 2017

### National plans or strategies tackling the viral hepatitis elimination in the EU (2019)

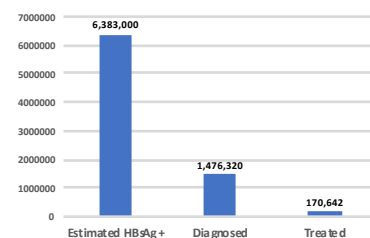


ECDC MS Survey 2019

### Hepatitis B in Europe

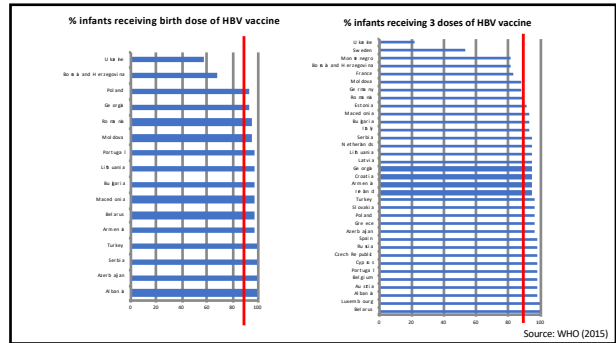
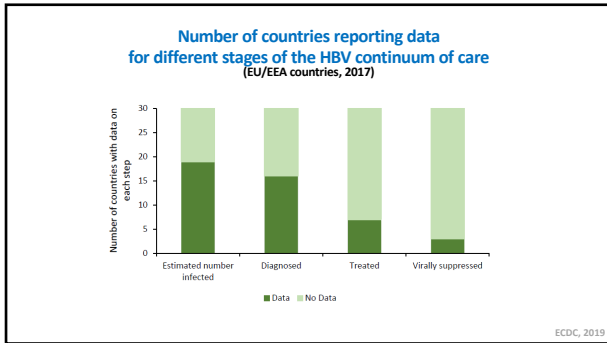
- Vaccination campaigns have been very effective across Europe
- Potent nucleoside/nucleotide analogues available and reimbursed throughout Europe and prescribed according to EASL guidelines, mostly by specialists
- Challenges:
  - ✓ Poor data on continuum of care
  - ✓ Opposition to vaccinations and vaccine hesitancy is growing
  - ✓ Impact of immigrants is significant

### The cascade of care of HBV, Europe\* (2016)



\*Includes Russia, Belarus

Polaris Observatory, Lancet Gastroenterol Hepatol 2018;3:383-403



**The New York Times**

Opinion OF ED CONSTRUCTION

**How the Anti-Vaxxers Are Winning**

By PETER J. HAVES FEB. 3, 2017

HOUSTON — It's looking as if 2017 could become the year when the anti-vaccination movement gains ascendancy in the United States and we begin to see a reversal of several decades in steady public health gains. The first blow will be measles outbreaks in America.

Measles is one of the most contagious and most lethal of all human diseases. A single person infected with the virus can infect more than a dozen unvaccinated people, typically infants too young to have received their first measles shot. Such high levels of transmissibility mean that when the percentage of children in a community who have received the measles vaccine falls below 90 percent to 95 percent, we can start to see major outbreaks, as in the states where four million Americans a year were infected and 450 died. Worldwide, measles will kill around 600,000 children each year.

**VAXXED FROM COVER-UP TO CATASTROPHE**

**MEASLES OUTBREAK WHY PARENTS REFUSE TO VACCINATE**

CNN

**medicina**

Article

**Qualitative Assessment of Vaccine Hesitancy in Romania**

David Mika<sup>1,2</sup>, Carmen Costache<sup>2,3,4</sup>, Horia Alexandru Colosi<sup>2,4</sup>, Vlad Neculicic<sup>2</sup> and Ioana Alina Cofan<sup>2</sup>

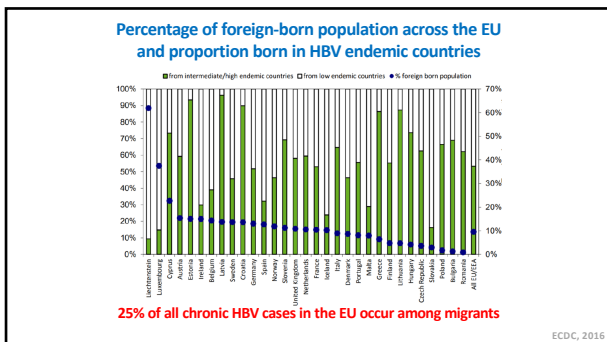
<sup>1</sup> Iuliu Haieganu University of Medicine and Pharmacy, 400340 Cluj-Napoca, Romania; d.mika@medcluj.ro  
<sup>2</sup> Department of Microbiology, Iuliu Haieganu University of Medicine and Pharmacy, 400340 Cluj-Napoca, Romania; vlad.neculicic@medcluj.ro (V.N.); ioana.cofan@medcluj.ro (I.A.C.)  
<sup>3</sup> Department of Medical Education, Division of Medical Informatics and Biostatistics, Iuliu Haieganu University of Medicine and Pharmacy, 400340 Cluj-Napoca, Romania; hcolosi@medcluj.ro  
<sup>4</sup> Correspondence: carmen.costache@medcluj.ro; Tel.: +40-723-872-701

Received: 29 April 2019; Accepted: 14 June 2019; Published: 17 June 2019

**Out of 452 persons interviewed, 30.3% expressed vaccine hesitancy**

**11.7% of parents refused to vaccinate their children**

MIKO D. et al. Medicina 2019;55:pii: E282



**Liver-related health issues among asylum seekers**

- >80% of first-time asylum seekers in the EU-28 in 2017 were <35 years old (source: EUROSTAT)
- Asylum seekers are in general healthy young males
- Hospitalization rates of migrant patients due to chronic medical conditions is statistically significantly lower to non-migrant patients

**HOWEVER, asylum seekers are at risk of:**

- Hepatitis A outbreaks due to overcrowding and poor sanitation in host facilities
- Sexual abuse and STD, including HBV and HIV
- Social marginalization, mental health issues and substance abuse

SERRE-DELICOR et al. Am J Trop Med Hyg 2018;98:300-7  
 TSITSAKIS et al. Health policy 2017;121:329-37  
 MELHEM et al. Eur J Epidemiol 2016;31:711-4; MELLOU et al. Euro Surveill 2017;22:30448  
 CASTAGNA et al. 2018;132:1357-304; PANNETIER et al. Lancet Public Health 2018;3:e16-e23  
 MICHAELIS et al. Emerg Microbes Infect 2017;6:e26  
 DE SCHRIJVER et al. Int J Environ Res Public Health 2018;15:61979; OLIVEIRA et al. Global Health 2018;14:48  
 CASTAGNA et al. 2018;132:1357-304; PANNETIER et al. Lancet Public Health 2018;3:e16-e23  
 QURESHI et al. Am J Addict 2014;23:337-42; ANAGNOSTOPOULOS et al. Int J Soc Psychiatry 2017;63:352-8

### Viral hepatitis among migrants to the EU

- Out of 14 HBsAg prevalence estimates in the general migrant population:
  - 57% were lower than the in-country estimate in the general population
  - 36% were comparable
  - 7% (one study) was higher
- Out of 10 anti-HCV prevalence estimates in the general migrant population
  - 70% were comparable to the in-country prevalence
  - 30% were lower

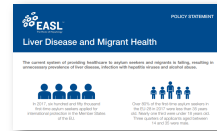
Epidemiological assessment of hepatitis B and C among migrants in the EU/EEA, ECDC, Stockholm, July 2016  
 FALLA et al, BMC Infect Dis 2018;18:34  
 FALLA et al, BMC Infect Dis 2018;18:32

- Children and young adults may have **missed out on vaccination programmes** for hepatitis B

<https://www.doctorsoftheworld.org.uk/Handlers/Download.ashx?IDMF=7d8c2ef9-403a-402d-8571-e8cefbec8d00>

### EASL Statement on Migrant Health (2019)

- Migrants should be offered affordable healthcare, treatment and referrals to specialist services
- Migrant screening programmes should be expanded to include HBV and HCV
- Healthcare professionals should be trained to treat migrants and asylum seekers with respect and in a culturally sensitive manner
- Governments must not require healthcare workers to report undocumented migrants to the police or immigration authorities, and should put in place rules that safeguard people from such violations of their privacy and confidentiality
- Specialized training should be put into place (migrant medicine)

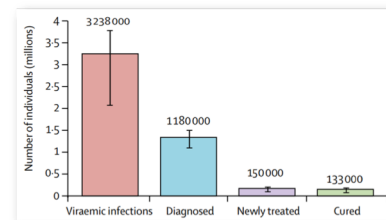


[https://journals.easl.eu/content/uploads/2019/04/EASL\\_POLICY\\_Liver\\_Disease\\_and\\_Migrant\\_Health\\_FINAL.pdf](https://journals.easl.eu/content/uploads/2019/04/EASL_POLICY_Liver_Disease_and_Migrant_Health_FINAL.pdf)

### Hepatitis C in Europe

- Epidemiology and continuum of care better characterized than for HBV
- Direct-acting antivirals are now available without restrictions in most Western countries, and prescribed by specialists according to EASL guidelines
- Challenges:
  - ✓ No vaccine available
  - ✓ Impact of immigrants significant
  - ✓ Restrictions to DAA use and reimbursement still apply to some EE countries

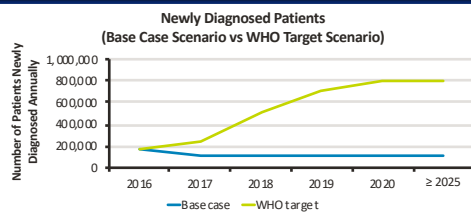
### Gaps in the hepatitis C continuum of care (Europe, 2015)



Lancet Gastroenterol Hepatol 2017;2:325-336

### Increased Screening Required in the WHO EURO Region to Meet WHO Targets

To achieve WHO goals by 2030, annual HCV diagnoses will need to increase from 171,000 (2016) to 800,000 by 2022



Robbins S, et al. J Hepatol 2018; 68(Suppl1):S447-S448 (abstract and poster presentation THU-057)

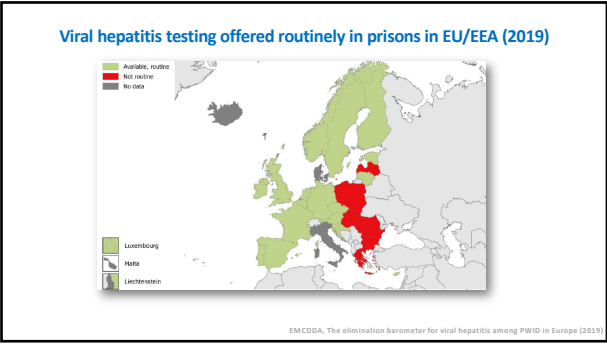
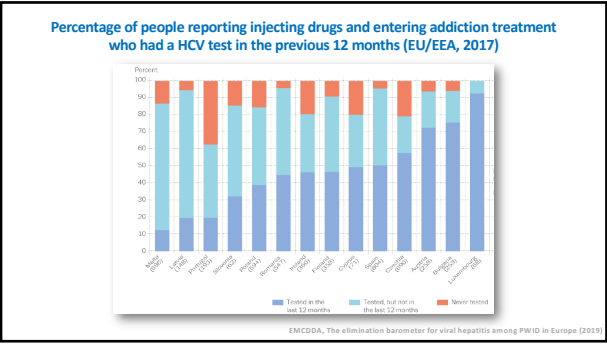
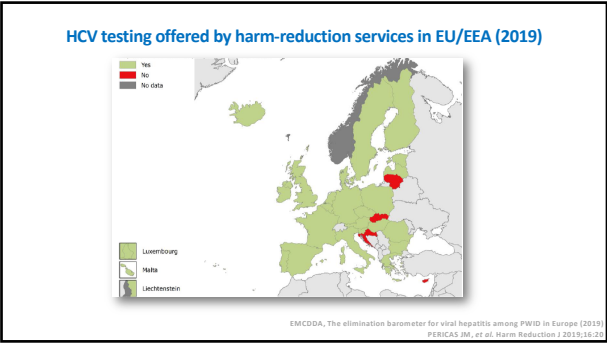
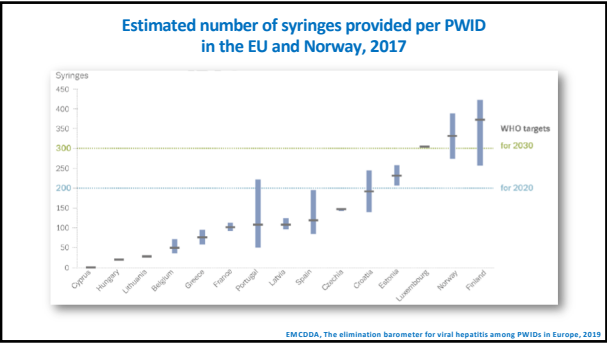
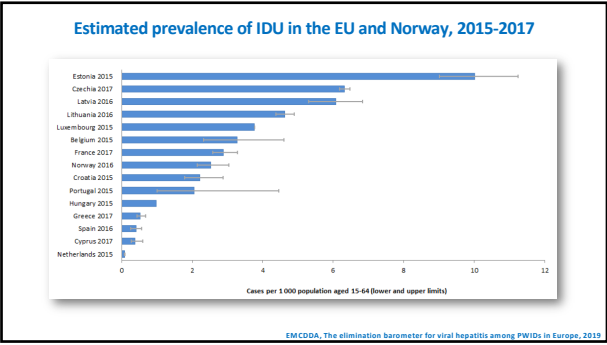
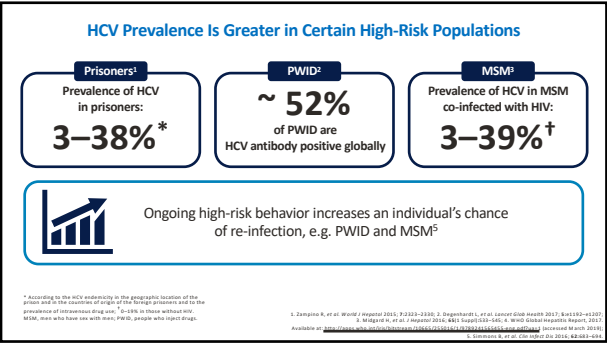
### Only six European countries are on track to HCV elimination by 2030

	Political will	Financial support	Harm reduction program	Expanded capacity	Restrictions	Monitoring	Awareness & screening	Linkage to care
France	Yes	Yes	Yes	Yes	No	Yes	Yes	Yes
Iceland	Yes	Yes	Yes	Not needed	No	Yes	N/r**	Yes
Italy	Yes	Yes	No	No	No	Yes	No	No
Spain	Yes	Yes	N/r	Yes	No	Yes	Yes	No
Switzerland	Partial	Partial	Yes	No	No	Yes	N/r***	No
UK	Yes*	Yes*	Yes*	Yes	No	Yes	Yes	Yes

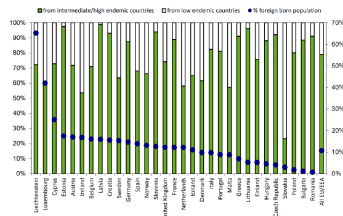
N/r, not relevant; \*Data for Scotland only; \*\*>90% of infections already diagnosed; \*\*\*Two thirds already diagnosed

Adapted from RAZAVI H, et al. Liver Int 2019





### Percentage of foreign-born population across the EU and proportion born in HCV endemic countries



14% of all chronic HCV cases occur among migrants

ECDC, 2016

### The dream: a vaccine to prevent HCV transmission

#### Meeting Coverage > IDWeek Hep C Vax Flops Among Injection Drug Users in Phase I/II Trial — But "a valiant effort" and "proof of principle" for drug users at high risk of infection

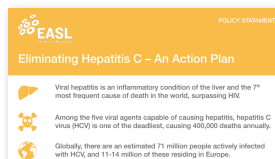
<https://www.medscape.com/meetingcoverage/idweek/82194>

- Phase I/II trial on 6-month chronic HCV outcome among 455 PWID randomized to receive HCV vaccine or placebo
- Two injections (0 and 8 weeks) of a vaccine designed to generate T cell immunity based on viral vectors (recombinant chimpanzee AV-3 vector vaccine prime followed by a recombinant modified vaccinia Ankara boost, both encoding HCV NS proteins)
- Well-tolerated
- T-cell response in 78% of vaccine recipients, but less robust and less broad than in healthy volunteers
- Incidence of 13 infections per 100 py (similar among vaccine or placebo recipients, vaccine efficacy -0.529, 95% CI -2.535 to 0.339)

PAGE K, et al. IDWeek, Washington, 6-8 October 2018, Late Breaker 10

### EASL HCV Elimination Policy Statement (2019)

- All countries should develop a **national plan**
- Plans should be **costed** and **comprehensive**, i.e. covering all steps of the continuum of care (awareness, prevention, testing, linkage to care, treatment and FU after cure)
- Public health approach** (to provide the best available treatment **and** to afford the widest benefit at the population level)
- To monitor progress** with robust data and refine efforts accordingly



<https://easl.eu/publication/policy-statement-eliminating-hepatitis-c-an-action-plan/>



### Georgia: the importance of partnership

- Prevalence of 5.4% (150,000 viremic cases)
- The first national HCV elimination program in the world (2015)
- MOU with Gilead to provide free DAA
- MOU with the US CDC to provide technical assistance plus a monitoring and evaluation plan, and to perform research
- Further partnership with Abbott

\*Current 2020 goals are 90% diagnosed, of whom 95% are treated, of whom 95% are cured



### Georgia: results and challenges

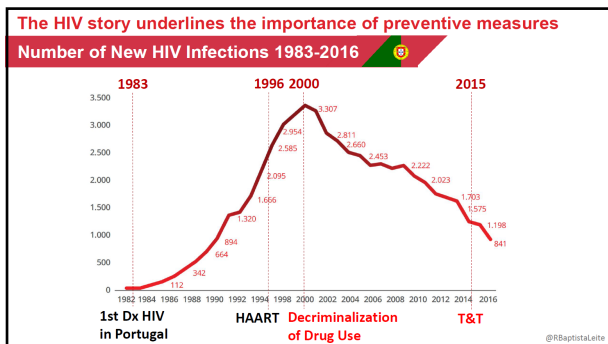
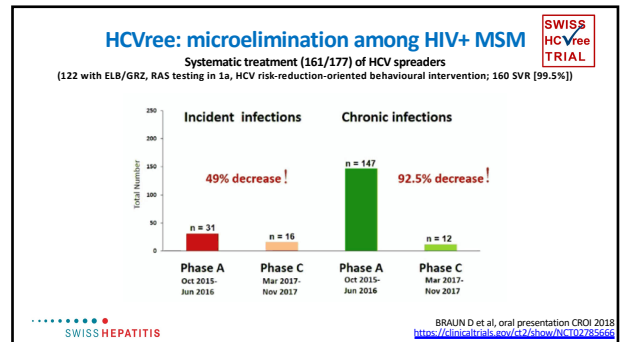
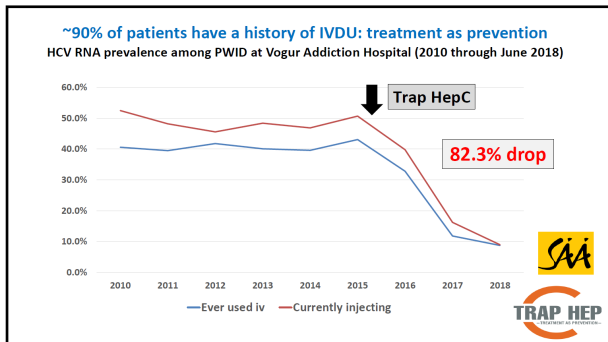
- Strong points:**
  - Political commitment, advocacy, partnership with industry (Gilead, Abbott) + CDC
  - Total screened: ~1,200,000 (~1/3 of the population)
  - Establishment of a unique ID allowing linkage among databases to monitor the progression
- Challenges ahead:**
  - Gaps in cascade of care (~20% of anti-HCV+, hospital-based screened persons did not undergo a confirmatory test)
  - Many patients unaware of their seropositivity
  - Out-of-pocket expenses deemed important by ~60% of patients



### The Iceland success story

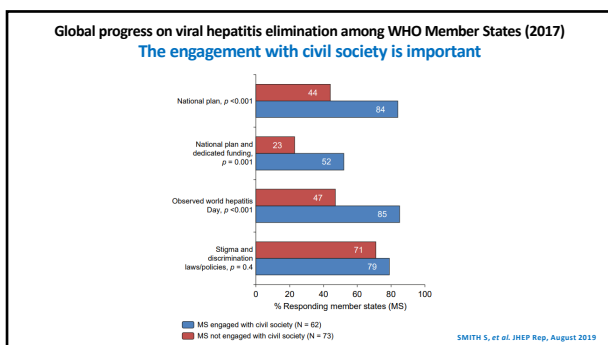
- Estimated HCV prevalence (2015): ~800 viremic out of 340,000 inhabitants (**>80% diagnosed, 88% IVDU**)
- Nationwide elimination programme (TraP HepC) launched in 2016 with **strong government support**
- No restrictions to DAA (with emphasis on case finding and treatment of advanced fibrosis, IVDU, prison inmates)
- As of November 2018, **709 patients have initiated therapy**
- Overall SVR12 (June 2018): 494/558 (89%)

OLAFSSON et al. J Intern Med 2018;283:500-507  
OLAFSSON et al. Global Hepatitis Summit 2018



#### To build successful viral hepatitis elimination national strategies

- Political will, leading to costed and comprehensive plans
- Timely and strong advocacy
- Partnership with the industry to reach price deals (diagnostics and drugs)
- General population screening (financial incentives, penalties for inaction)
- National registries (eCRF)
- Extend the number of prescribers
- Decentralize diagnosis and treatment
- Simplify procedures



#### Expanded screening strategies?

##### Risk-based screening is a failure

- Providers do not ask about risk factors / Patients do not volunteer this information
- If limited to high-risk settings, it may only partially affect liver-related mortality

##### Birth cohort-based strategies

- Proposed for HCV, it may miss patients with advanced liver disease

##### Migrants from high endemicity countries

- It may also identify persons to be vaccinated against HBV

##### Pregnant women (or WOCA)

- For HBV, to offer prophylaxis
- For HCV, this is often the only contact with health services

- Cost-effective at a HCV prevalence of 0.07%, the lowest estimated prevalence in the US
- JHAVERI R, et al. Clin Infect Dis 2018;67:1493-7  
CHAILLON A, et al. Clin Infect Dis 2019;69:1888-95


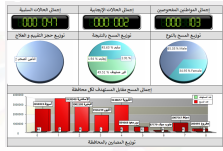


**HEALTH**

## Why Egypt Is at the Forefront of Hepatitis C Treatment

Despite the availability of revolutionary new drugs, countries with more resources haven't made as much progress against the disease.

**TEO ALCOHOL MAY 29, 2018**

**Case registry data**

Egyptian workers line up near a van for an examination check-up for hepatitis C (see connection, right)

**100 Million Healthy Lives**

- Launched in October 2018 under the auspices of President Abdel Fatah al-Sisi
- Aimed at screening for HCV 52,000,000 18-59 years old adults (using of the National Elections Commission)
- Awareness SMS sent to the eligible persons to locate screening sites
- Web-based database to monitor the progress
- 2019: >49,000,000 screened, ~2,200,000 anti-HCV+, ~1,800,000 treatments started
- Target: eliminating hepatitis C by 2022

**2<sup>ND</sup> CONFERENCE ON LIVER DISEASE IN AFRICA**

CAIRO, EGYPT • 6-8 SEPTEMBER 2019



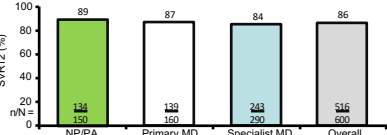
Egypt and the private partner PHARCO committed to providing free or low cost HCV medications for up to 18 African countries and treat one million persons (already ongoing programs: South Sudan, Eritrea, Djibouti, Chad)

Sharing the package of essential components from the Egyptian model of care together with these medications will leverage action to increase testing and treatment in Africa

Health systems will be strengthened to improve also hepatitis B care


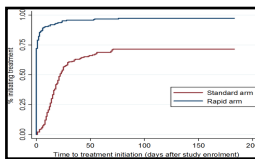
**Non-specialists can effectively treat HCV infection (The ASCEND Study)**

Nonrandomized phase IV trial of HCV treatment outcomes by DAA prescriber type  
n = 600 from 13 urban hospitals in DC, all treated with LDV/SOF per FDA prescribing info  
All providers given a 3-hr training in AASLD/IDSA HCV guidance



KATTANUZHNY S, et al. Ann Intern Med 2017;167:311-318

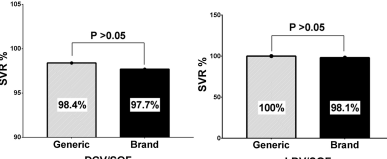
**Starting treatment the same day as the diagnosis is possible**  
A lesson learned from the HIV field

**WHO recommendation (July 2017)**

- Start within 7 days of an HIV diagnosis
- Consider same day start

**Similar efficacy of brand vs. generic DAAs in the Egypt HCV elimination plan (n=971, non randomized)**



Patients' groups were comparable regarding baseline age, liver enzymes, creatinine, platelet count, MELD score, HCV RNA and transient elastography values

ABOZEID M, et al. Intern J Infect Dis 2018;75:189-194

## Can technology help?

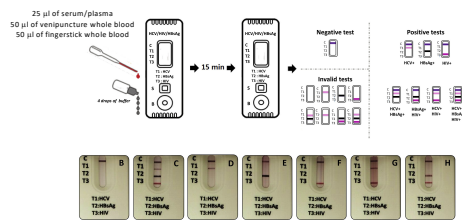
### Anti-HCV Rapid Diagnostic Test: the OraQuick™

- Simple, non-instrumented, rapid (20 min), point-of-care test developed by OraSure Technologies Inc. (Bethlehem, PA, USA)
- Can be used on serum, whole venous blood, fingerstick blood or crevicular fluid
- Sensitivity is 97.8-99.2% (saliva), 100% (serum), specificity is 100%  
LEE et al, J Viral Methods. 2011;172:27-31; CHA et al, Ann Lab Med 2013;33:184-9
- Licensed by FDA for use on whole blood (2010) or fingerstick blood (2011)
- WHO prequalified

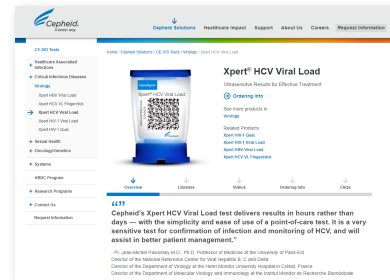


[http://www.who.int/diagnostics\\_laboratory/evaluations/pq-list/hcv/170301\\_final\\_pq\\_report\\_PQDx\\_0244\\_055\\_00.pdf?ua=1](http://www.who.int/diagnostics_laboratory/evaluations/pq-list/hcv/170301_final_pq_report_PQDx_0244_055_00.pdf?ua=1)

### Rapid POC assays: a multiplex POC for simultaneous screening of HIV, HBsAg and anti-HCV



ROBIN L. et al. J. Virological Methods 2010;253:1-4



LOD 4.0 UI/mL (plasma)  
LOD 6.1 UI/mL (serum)  
No requirements for strict  
PCR room settings  
1-min hands-on  
90-min hands off  
345 viral load results/8 h



2005

2013



credit: nbcsnews.com

### Science Translational Medicine

**Antibody assay: HIV, syphilis**  
**2 µl of blood by fingerprick**  
**Sensitivity 92%**  
**Specificity 79-100%**  
**15 minutes**  
**1.6 mW per test**  
**Audio jack powered**  
**1.4 USD per triplex**



