

The global hepatitis C elimination goal and EASL recommendations for a complex management of HCV in people who inject drugs

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EASL Policy and Public Health Committee Member

EHRA, EASL, WHO Europe Webinar: April 22, 2021

Disclosure

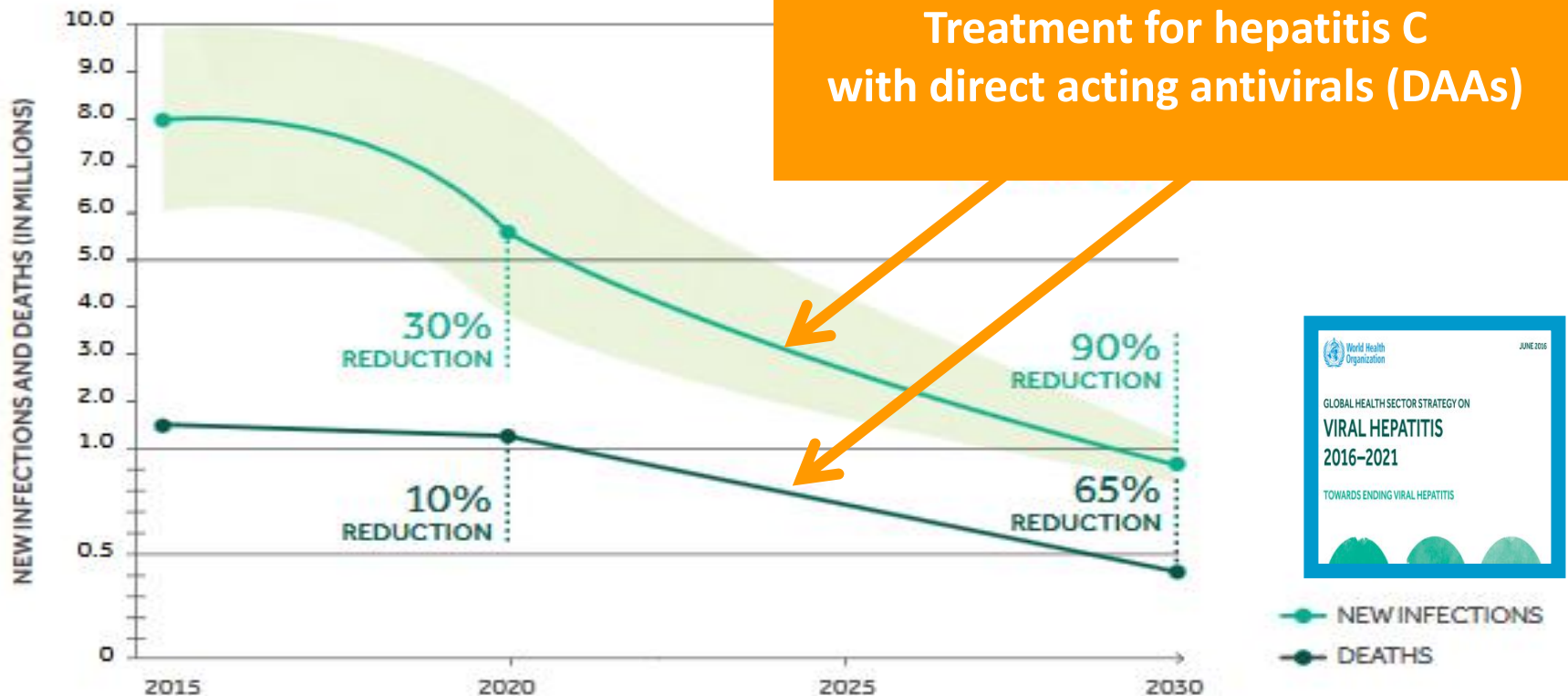
Within the last 36 months:

- Lecturer: Abbvie, Bayer, Gilead, Merck, Sandoz
- Manuscript preparation: Abbvie, Gilead, Merck
- Travel/accommodational meeting expences: Abbvie, Gilead, Merck

No conflict of interest regarding this presentation

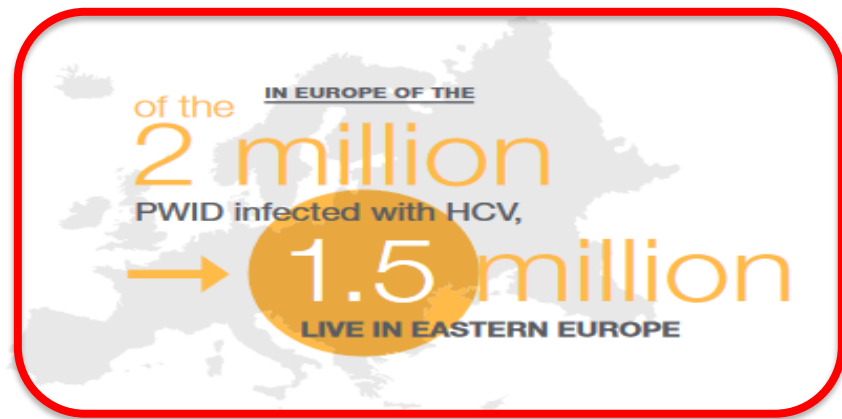
WHO strategy towards elimination of viral hepatitis as a public health threat

GOALS



Why focus on people who inject drugs to eliminate hepatitis C?

8.5% **of all HCV infections occur amongst persons aged 15-64 WHO HAVE INJECTED DRUGS within the last 12 months**



16% **IT IS ESTIMATED THAT** of all people living with **VIRAEMIC HCV INFECTION IN THE EU AND NORWAY** were **PWID**

DEATH FROM LIVER DISEASE (INCLUDING HCV) is as equally common AS DEATH FROM OVERDOSE, IN THOSE AGED OVER 50

IN THE LAST DECADE, MORTALITY DUE TO UNTREATED HCV INFECTION has been increasing, particularly due to late presentation by PWID

WHO. Available at: <https://www.who.int/hepatitis/publications/global-hepatitis-report2017/en/>

Grebely J, et al. *Addiction* 2019; 114(1): 150-66. Kielland KB, et al. *J Hepatol* 2013; 58: 31-7.

EMCDDA. Available at: https://www.emcdda.europa.eu/system/files/publications/13091/Technical-report_DRID2020.pdf

Why focus on people who inject drugs to eliminate hepatitis C?

8.5% of all HCV infections occur amongst persons aged 15-64
WHO HAVE INJECTED DRUGS
within the last 12 months

of the **2 million** PWID infected with HCV,
1.5 million LIVE IN EASTERN EUROPE

16%
of all people living with **VIRAEMIC HCV INFECTION IN THE EU AND NORWAY** were PWID

DEATH FROM LIVER DISEASE (INCLUDING HCV)
is as equally common
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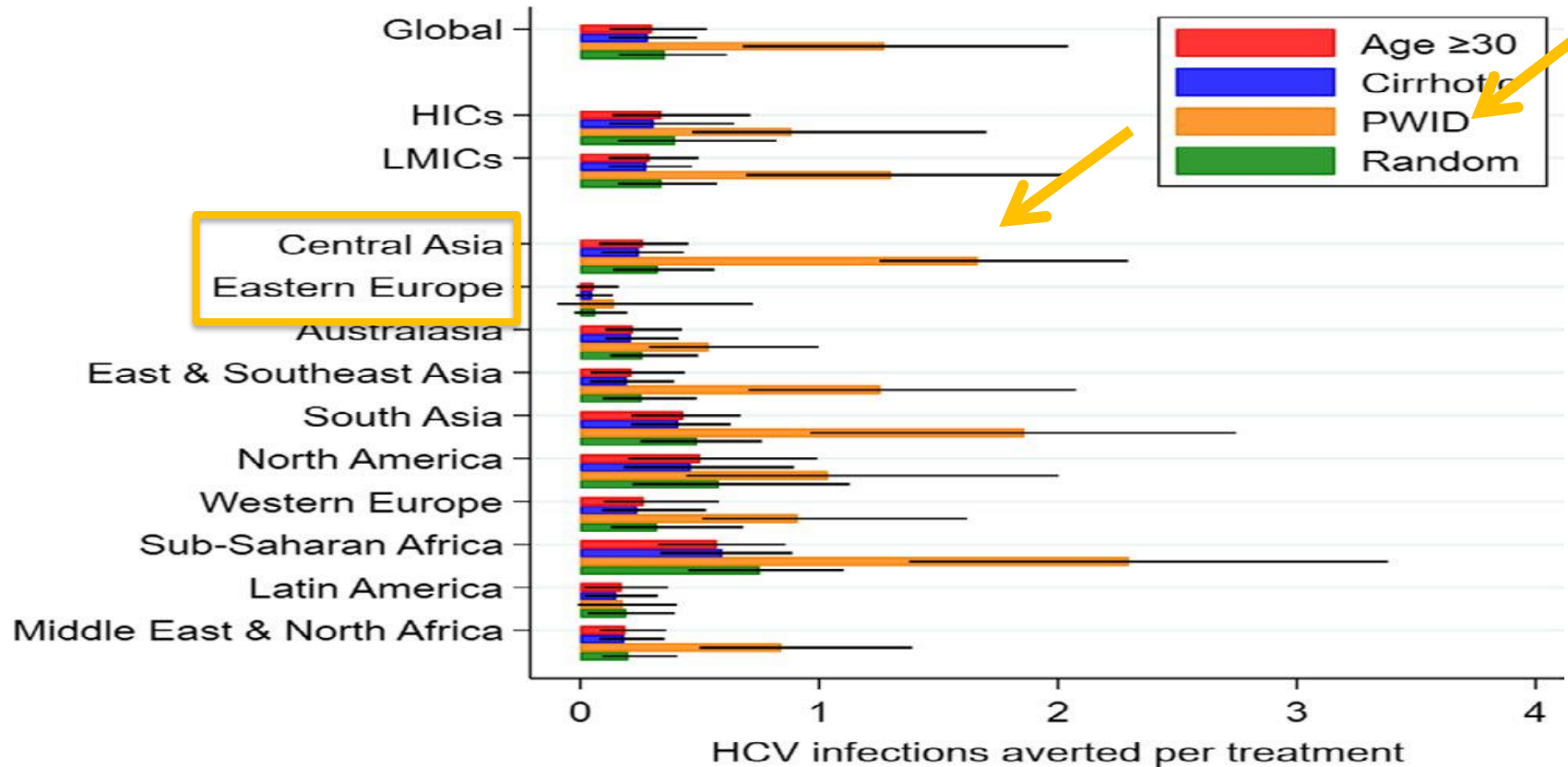
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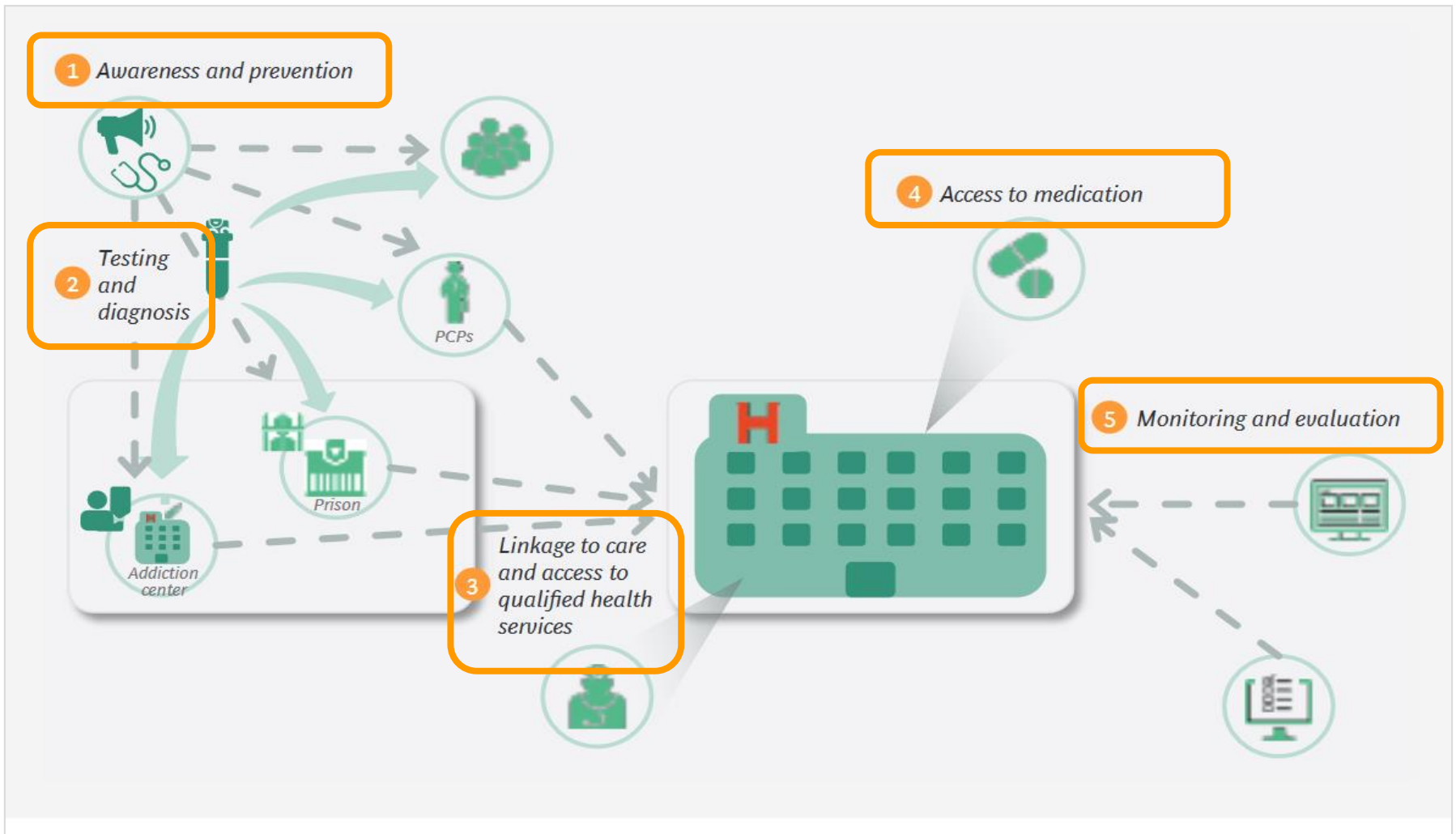
Treatment-as-prevention

Modelling the potential prevention benefits of a **treat-all** HCV treatment strategy at global, regional and country levels

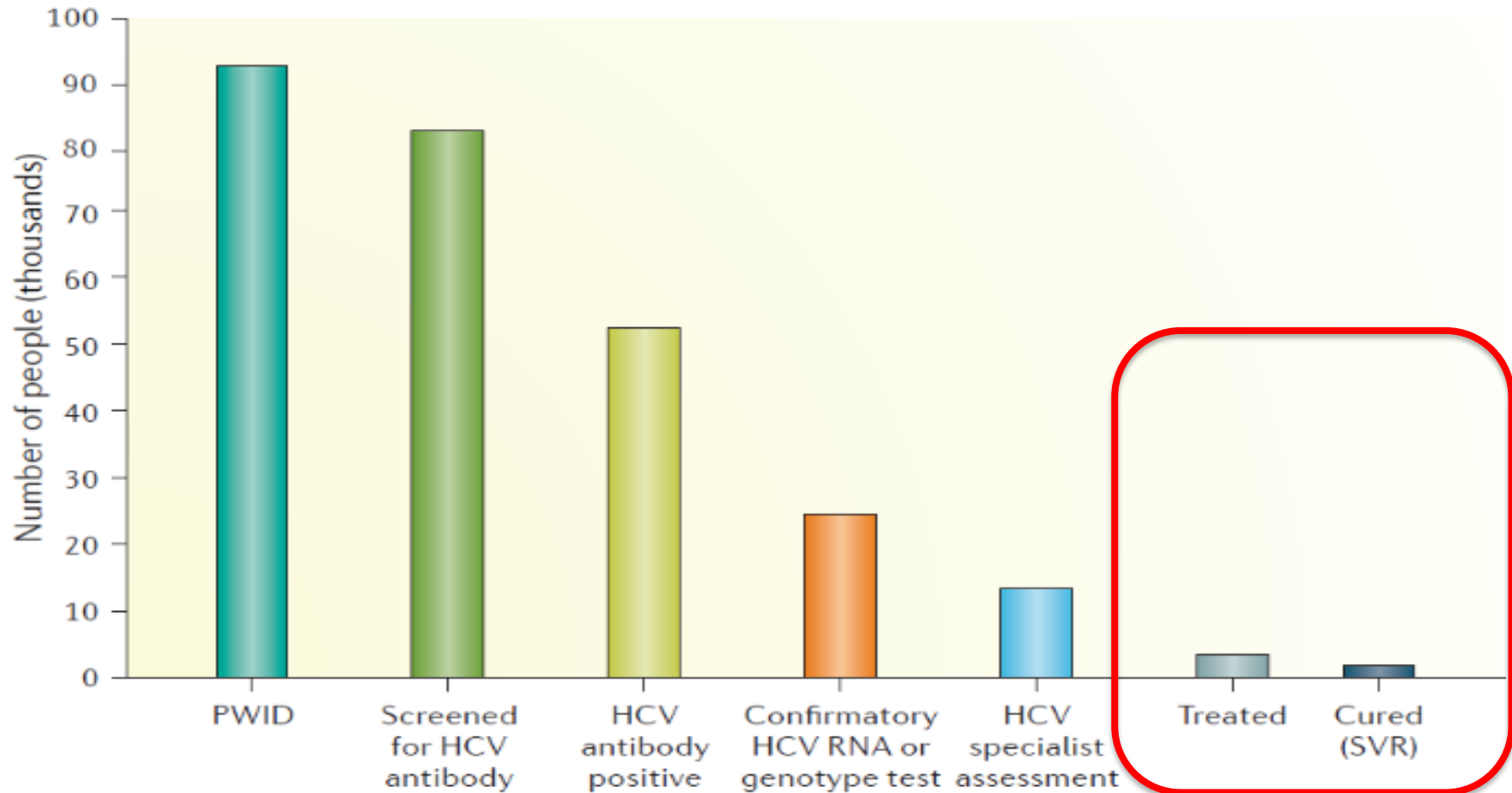


WHO's treat-all strategy could bring about appreciable prevention benefits, although greater benefits per treatment can be achieved through **targeting PWID**.

The road to HCV elimination is complex: a continuum-of-services



A continuum of services: A real-life cascade of HCV care in PWID



Grebely J, et al. *Nat Rev Gastroenterol Hepatol* 2017; 14: 651-61.
Iversen J et al. *Int J Drug Pol* 2017; 42: 1-6.

Barriers and gaps to elimination of viral hepatitis in PWID



Patient



Practitioner



System



Policy

Overcomming barriers: A PATIENT centered care for HCV

Simplification:

- Diagnostic and treatment algorithms – a “one-stop-shop”

Decentralisation:

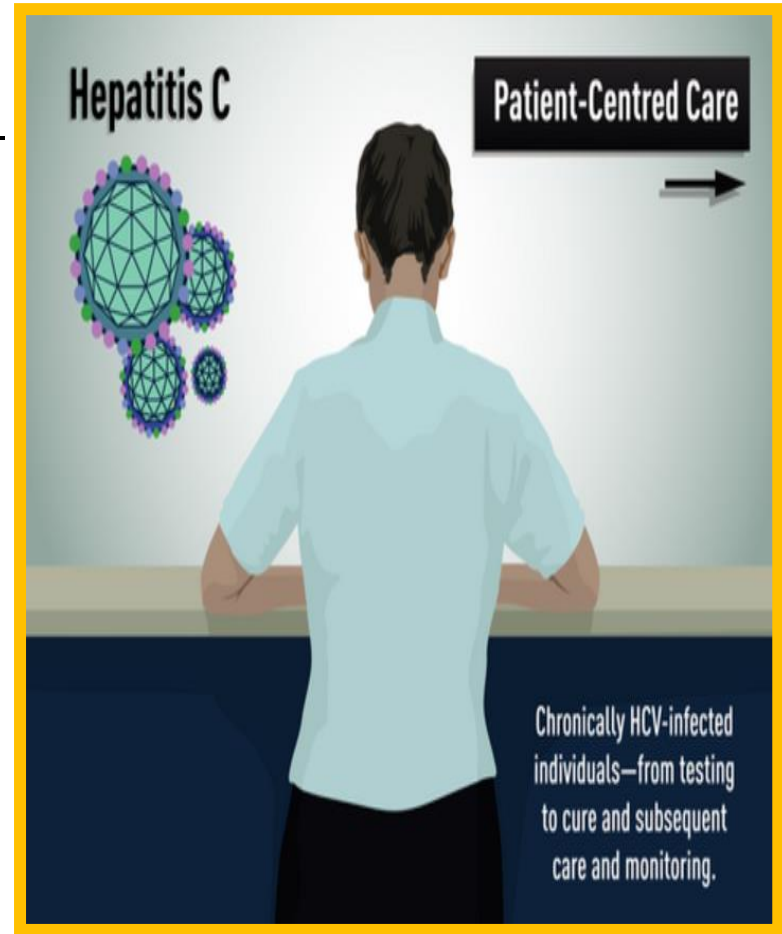
- HCV services put out of hospitals to regional and local level

Task-sharing:

- Involve GPs and nurses to manage uncomplicated HCV cases

Integration:

- HCV testing and treatment performed in primary care, harm-reduction services and other outreach services



EASL Hepatitis strategies in the framework of elimination of viral hepatitis as a public health treat



Patient



Practitioner

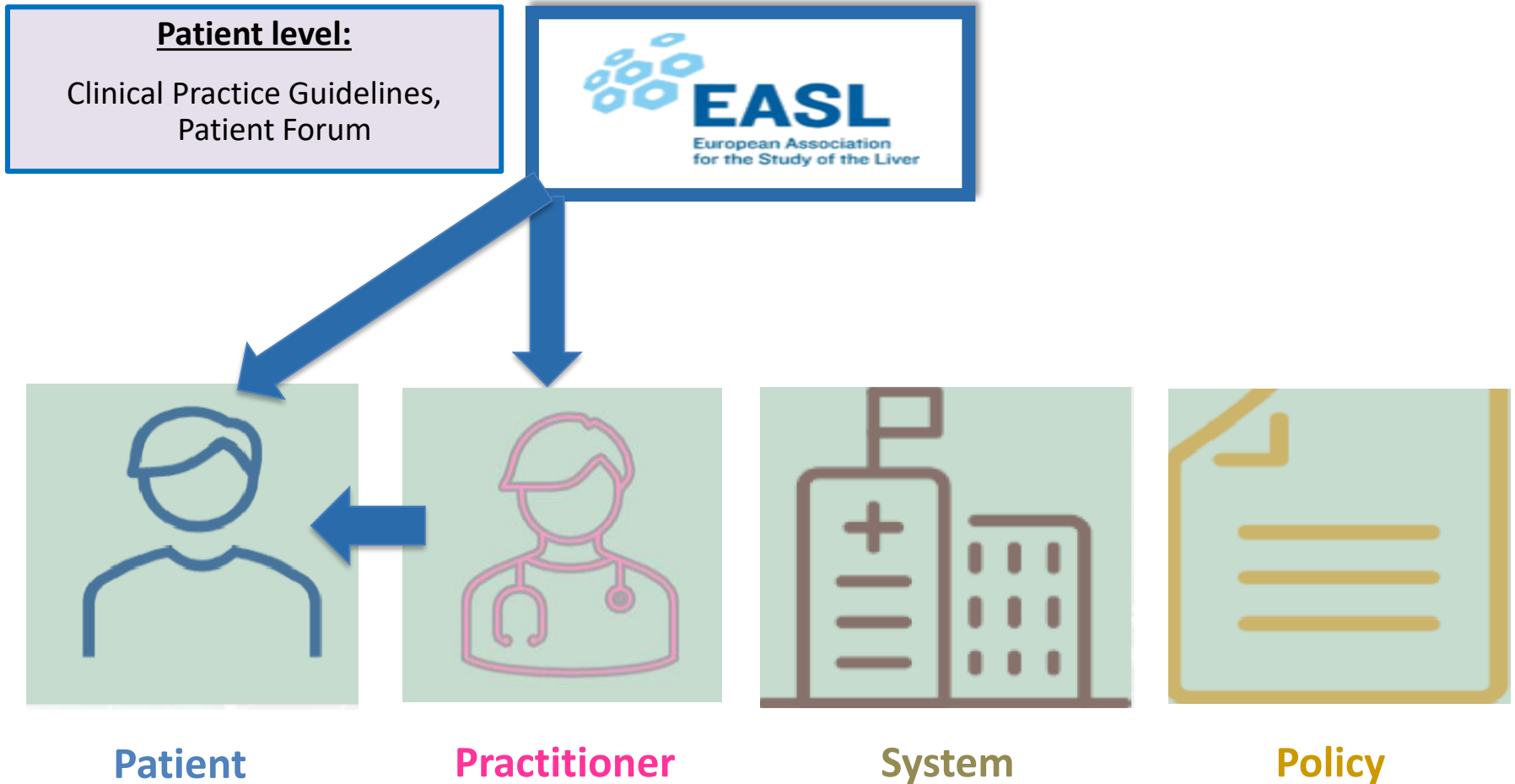


System

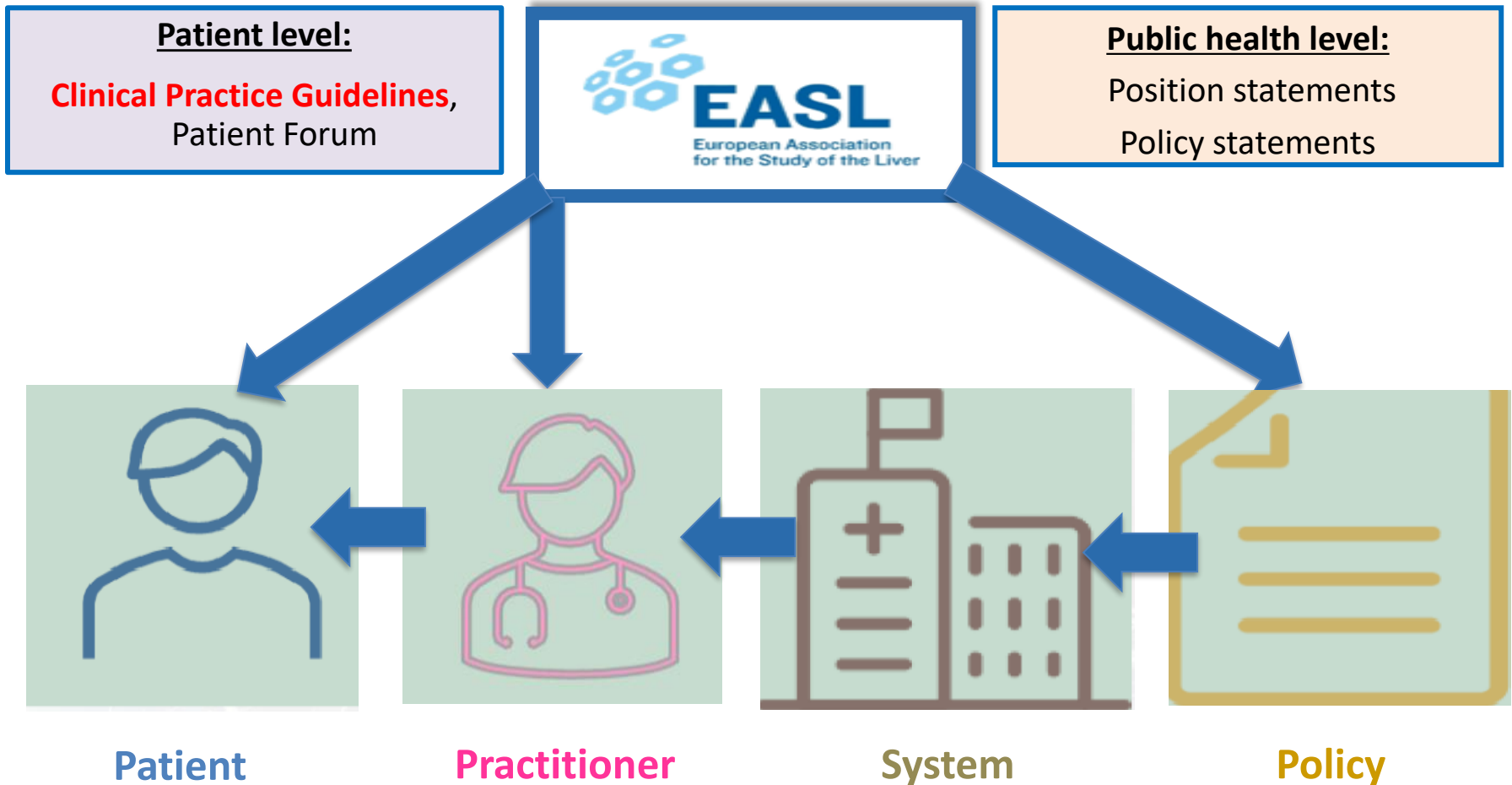


Policy

EASL Hepatitis strategies in the framework of elimination of viral hepatitis as a public health treat



EASL Hepatitis strategies in the framework of elimination of viral hepatitis as a public health treat



EASL 2020: CPG

Treatment of hepatitis C

- **All** treatment-naïve and treatment-experienced patients with **recently acquired** or **chronic** HCV infection must be offered treatment without delay.

Urgent treatment should be considered in patients with:

- ...
- in individuals at risk of transmitting HCV:
PWID,
MSM with high-risk sexual practices,
women of child-bearing age who wish to get pregnant,
haemodialysis patients,
incarcerated individuals.

EASL 2020: CPG

Treatment of hepatitis C

PWID include:

- former injectors who have ceased injecting
- recent/current injectors on OST

- PWID should be **routinely tested** (anti-HCV antibodies, HCV RNA) at least annually and following high-risk episodes

- PWID should be provided with appropriate **access to OST** and clean drug-injecting equipment as part of **harm-reduction programmes**, including in prisons

- **All PWID**, regardless of whether they have recently injected or are on OST, are candidates for DAA and **should be treated** according to the general recommendations

EASL 2020: CPG

Treatment of hepatitis C

| Product | Presentation | Posology |
|-------------|--|--|
| SOF | Tablets containing: 400 mg SOF Half-strength tablets containing: 200 mg SOF* | 1 tablet QD 1 tablet QD |
| SOF/VEL | Tablets containing: 400 mg SOF, 100 mg VEL Half-strength tablets containing: 200 mg SOF, 50 mg VEL* [†] Granules containing: 50 mg SOF, 12.5 mg VEL* [†] | 1 tablet QD 1 tablet QD 3 or 4 granules QD [¶] |
| SOF/VEL/VOX | Tablets containing: 400 mg SOF, 100 mg VEL, 100 mg VOX | 1 tablet QD with food |
| GLE/PIB | Tablets containing: 100 mg GLE, 40 mg PIB Film-coated granules in sachets containing: 50 mg GLE, 20 mg PIB | 3 tablets QD with food 3–5 sachets QD [¶] mixed in a small amount of food |
| GZR/EBR | Tablets containing: 100 mg GZR, 50 mg EBR | 1 tablet QD |

EASL 2020: CPG

Treatment of hepatitis C

Pangenotypic HCV drug regimens

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EASL 2020: CPG

PWID: **Simplified HCV care**

Pre-treatment:

- ✓ Proof of viraemia (HCV RNA, HCV cAg)
- ✗ **HCV genotype / subtype** ←
- ✓ Stage of liver disease
- ✓ Drug-drug interactions
- ✓ Co-morbidities
- ✓ HBV/HIV co-infection
- ✓ HCV treatment experience

When genotype/subtype determination is **not available, not affordable** and/or **limits access**, simplified treatment should be used to facilitate the cascade of care.

On-treatment

Post-treatment:

- Testing for SVR

EASL 2020: CPG

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Fibrosis stage must initially be assessed by non-invasive methods, such as **liver stiffness** measurement and serum biomarkers, including **APRI and FIB-4** (inexpensive, reliable biomarker panels). Cirrhosis **must be identified**, as some treatment regimens must be adjusted and post-treatment surveillance for HCC is mandatory.

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EASL 2020: CPG

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Pangenotypic treatment regimens

On-treatment

Post-treatment:

- Testing for SVR

**Simplified treatment algorithm
(no genotype/subtype determination)**



| Genotype | Cirrhosis status | Treatment history | SOF/VEL | GLE/PIB | SOF/VEL/VOX | GZR/EBR |
|---------------|-------------------------------|-----------------------|----------|----------|-------------|---------|
| All genotypes | No cirrhosis | Treatment-naïve | 12 weeks | 8 weeks | No | No |
| | | Treatment-experienced | | | | |
| | Compensated cirrhosis (CTP A) | Treatment-naïve | | | | |
| | | Treatment-experienced | | 12 weeks | | |

EASL 2020: CPG

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Pangenotypic treatment regimens

On-treatment

Post-treatment:

- ✗ **Testing for SVR**

Testing for SVR12 **can be omitted** in all adherent patients except those with high-risk behaviours and risk of re-infection who **require SVR12 testing** and monitoring for HCV re-infection

PWID: Can we omit testing for SVR12?

SIMPLIFY study:

- PWID, who recently injected
- N=103
- SOF/VEL for 12 weeks

SVR: 93%

Not achieving SVR:

- lost to follow up: 4
- died: 1
- re-infection: 1

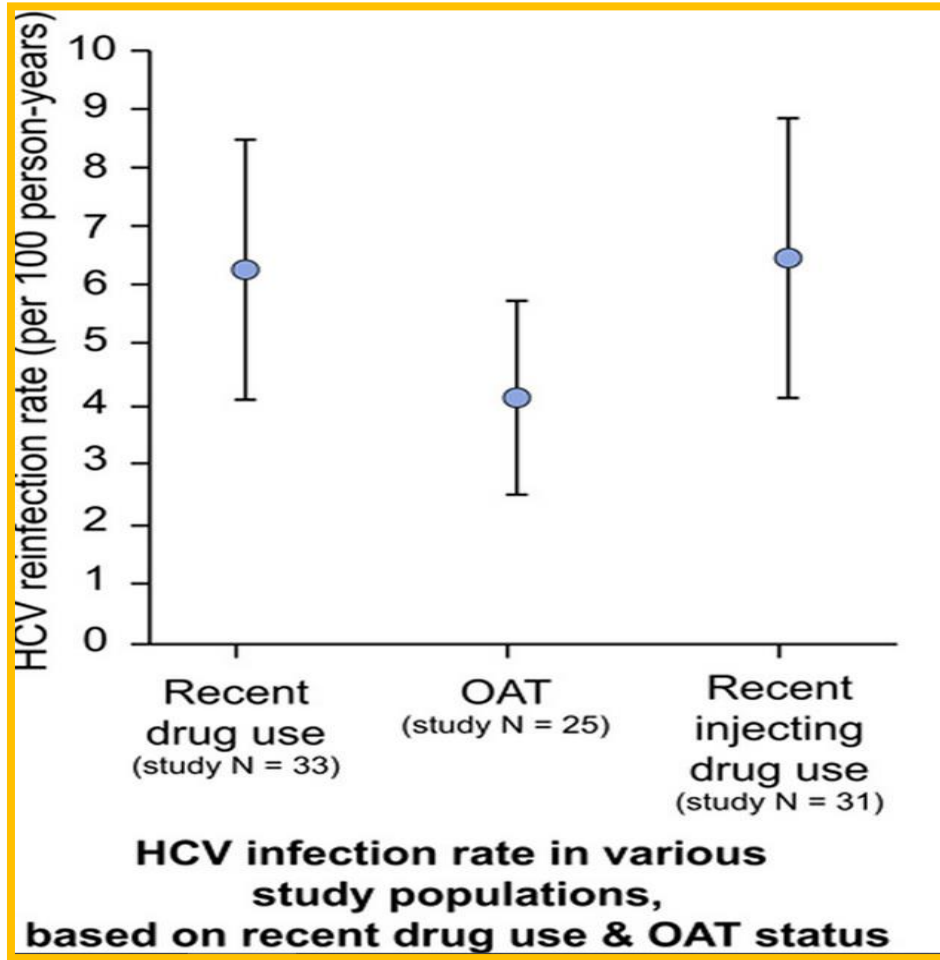
Adverse events:

- fatigue, headache, nausea: most frequent
- treatment discontinuation: 1 (1%)

Adherence: 94%

PWID:

Hepatitis C re-infection after successful antiviral treatment



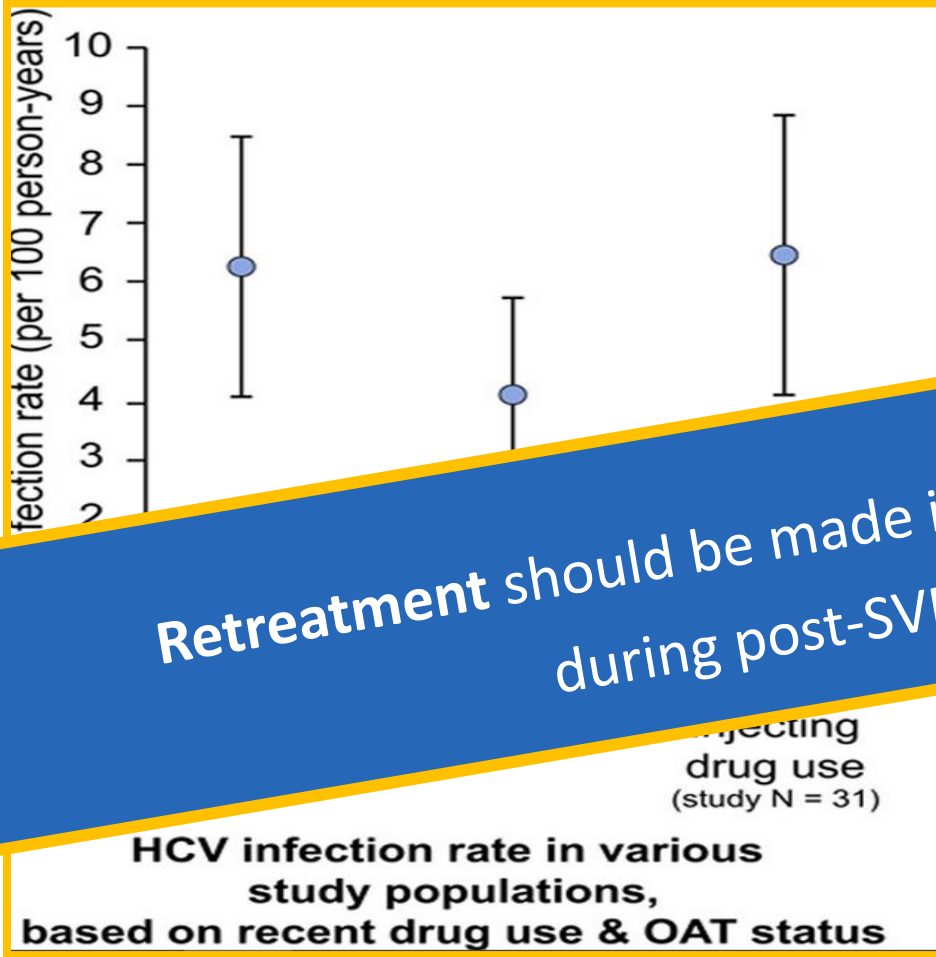
- A meta-analysis of 36 studies
- Follow-up of 6.311 p-y

Overall rate of re-infection:

- recent drug use: **5.9/100 p-y**
- recent injecting: **6.2/100 p-y**
- on OAT: **3.8/100 p-y**

PWID:

Hepatitis C re-infection after successful antiviral treatment



- A meta-analysis of 36 studies
- Follow-up of 6.311 p-y

Retreatment should be made if re-infection is identified during post-SVR follow-up

- on OAT: **3.8/100 p-y**
- recent injecting: **6.2/100 p-y**

Patients with **decompensated cirrhosis** with/without an indication for liver transplantation

- Patients with decompensated cirrhosis (CTP B or C) should be **treated in experienced centres** with easy **access to liver transplantation**.
- **Protease inhibitor-containing regimens** are **contraindicated** in patients with decompensated cirrhosis and in patients with compensated cirrhosis with previous episodes of decompensation.

Current care for hepatitis C in PWID

- **Broad accessibility to direct acting antivirals (DAA) can reduce HCV prevalence among PWID.**
- **Combination of OST and high-coverage needle/syringe exchange programmes can reduce HCV incidence by more than 70%.**

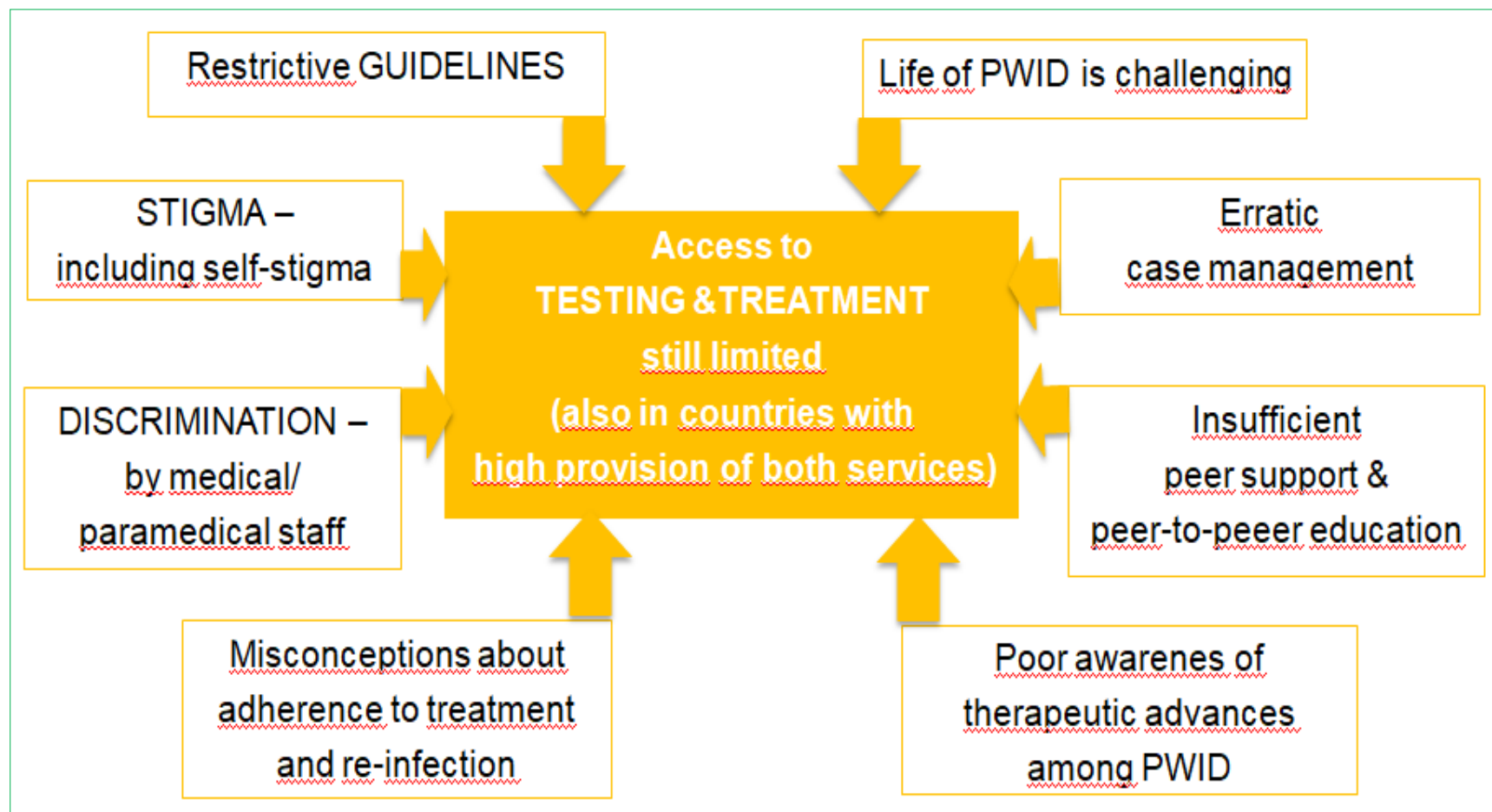
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179 countries:

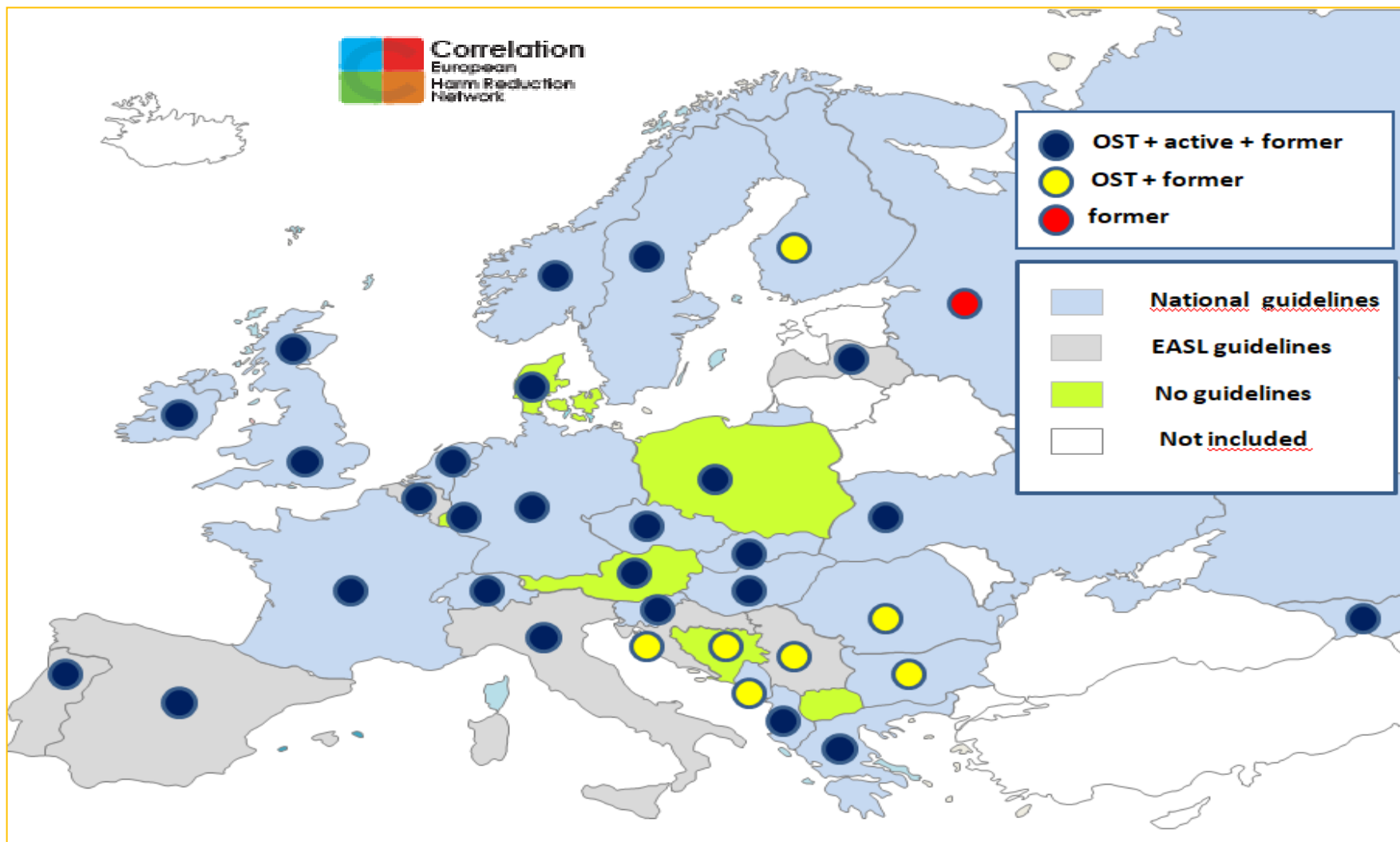
- **48%** (86/179) implemented OST
- **52%** (93/179) adopted needle/syringe exchange programs
- **High provision of HCV testing and treatment realised only in 1%** of PWID

Current care for hepatitis C in PWID

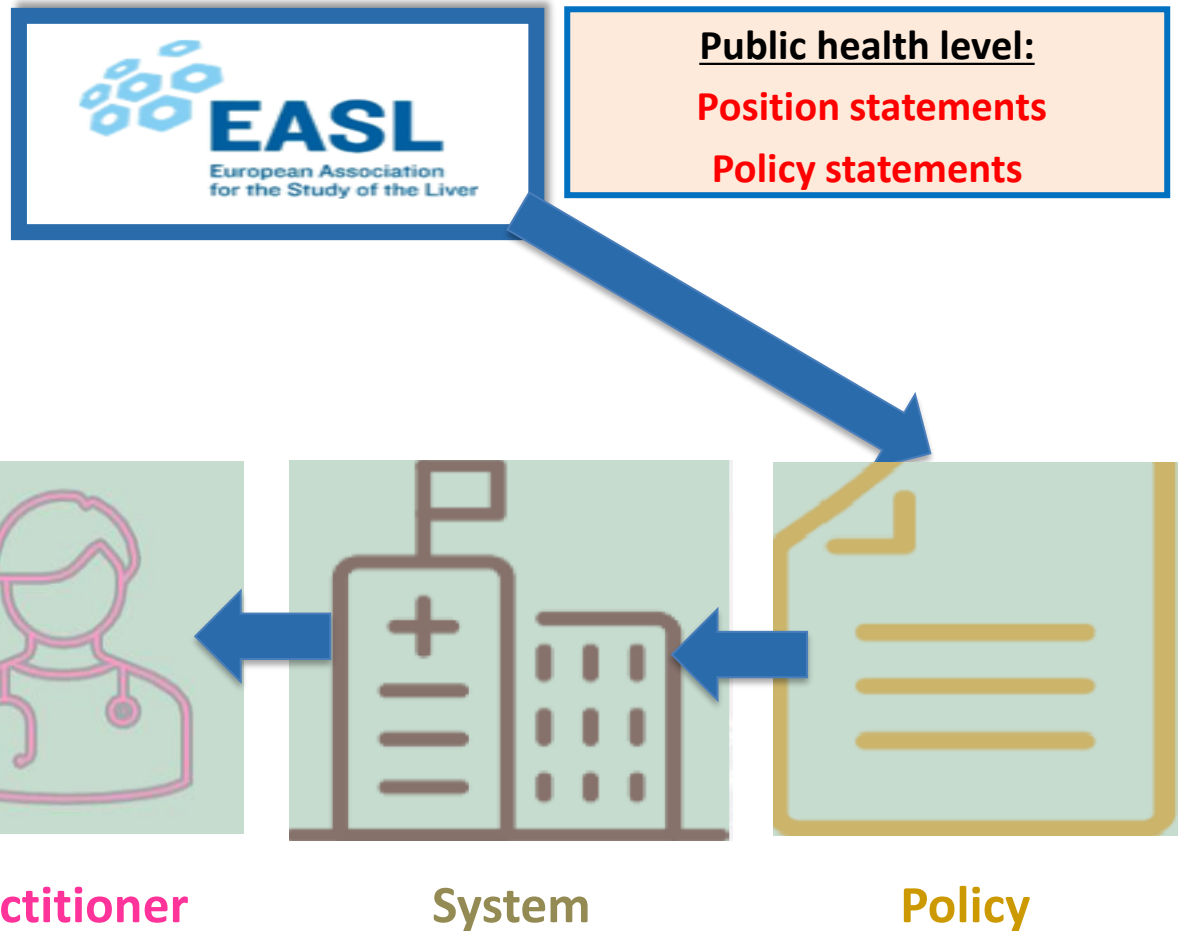


Marcias J, et al. *J Hepatol* 2019; 71: 45-51. Iversen J, et al *J Hepatol* 2019; 70: 33-9.
Platt L, et al. *The Cochrane Database of Systematic Reviews* 2016; 2017: CD012021.
Maticic M, et al. *Harm Reduct J* 2019; 16: 32.

Reported indications for treatment in different groups of PWID and use of most relevant guidelines for the treatment of hepatitis C in 35 European countries



EASL Hepatitis strategies in the framework of elimination of viral hepatitis as a public health treat



In april 2019:

Position statement on elimination of hepatitis C

Key messages

EASL recommends that:

- All European countries develop a comprehensive hepatitis C national strategy or action plan to: increase awareness throughout the population and to ensure appropriate preventive measures; offer testing; provide linkage to care, treatment and follow-up of patients in line with the WHO Global Health Sector Strategy on Viral Hepatitis and the WHO Action Plan for the health sector response to viral hepatitis in the WHO European Region (2017);
- All European countries adopt EASL recommendations on the management of hepatitis C, where it is stated that every hepatitis C patient should be considered for treatment, and that treatment should be initiated with DAAs;
- DAAs be globally available at reasonable prices, to avoid any further reimbursement restrictions, and to allow governments to implement a comprehensive elimination strategy.

Eliminating Hepatitis C - An Action Plan



Globally, there are an estimated 71 million people actively infected with HCV, and 11-14 million of these reside in Europe

EASL Recommends:

1

Increasing awareness amongst HCPs, patients, policy-makers, the media and the public (especially high risk groups), whilst combating the stigma and discrimination that is associated with HCV infection

2

Implementing harm reduction strategies, such as access to opioid substitution therapy, safe injecting equipment for drug users and safe sex education

3

Making DAAs available at reasonable prices, to avoid any further reimbursement restrictions and to allow governments to implement a comprehensive elimination strategy

4

Improving access to treatment and care by increasing the number of authorised prescribers, promoting telemedicine and by increasing input from AHPs during and after treatment

5

Treating every Hepatitis C patient at the earliest opportunity, especially those at high risk

6

Providing rapid testing, in all relevant settings, with priority given to high-risk persons

In August **2020**:
Policy statement:
Drug use and the global hepatitis C elimination goal

European countries:

- most of them have laws that criminalize the possession and distribution of drugs
- policies differ regarding offences and penalties

EASL/ILC 2020. Digital, August 27, 2020.

Armenta A, et al. Available at: <https://www.tni.org/en/publication/the-un-drug-control-conventions>
EMCDDA. Available at: http://www.emcdda.europa.eu/publications/pods/legal-supply-of-cannabis_en

Drug use policy - a direct barrier to achieving the goal of HCV elimination

- Prohibiting the possession of drug paraphernalia hinders harm reduction service delivery and uptake
- Many national laws impose severe custodial sentences for minor, non-violent drug offenses, such as drug use and possession
- As a result, PWID are frequently imprisoned or detained, without access to prevention and other harm reduction services, and often forced to interrupt ongoing HCV treatment
- Laws criminalising drug use reinforce stigmatisation and discrimination of PWID

Drug use and the global hepatitis C elimination goal

A time for change - EASL call to action

In order to achieve the 2030 WHO viral hepatitis elimination goals, EASL recommends: **that all barriers to the uptake of healthcare services by PWID be removed by changing policies and discrimination that hinder access. This includes the decriminalisation of minor, non-violent drug offences and the adoption of an approach based on public health promotion, respect for human rights and evidence.**

www.easl.eu

To eliminate HCV in PWID, combining activities is required

DECRIMINALISATION
of personal drug consumption
and possession

INTEGRATED interventions:
HCV
Testing & Treatment & Counselling

**PWID can freely access centers of assistance –
regardless of their drug consumption**

EASL/ILC 2020. Digital, August 27, 2020.

EMCDDA 2015. Available at: https://www-wmcdda-europa.eu/attachments.cfm/att_240836_EN_TDAU14007ENN.pdf

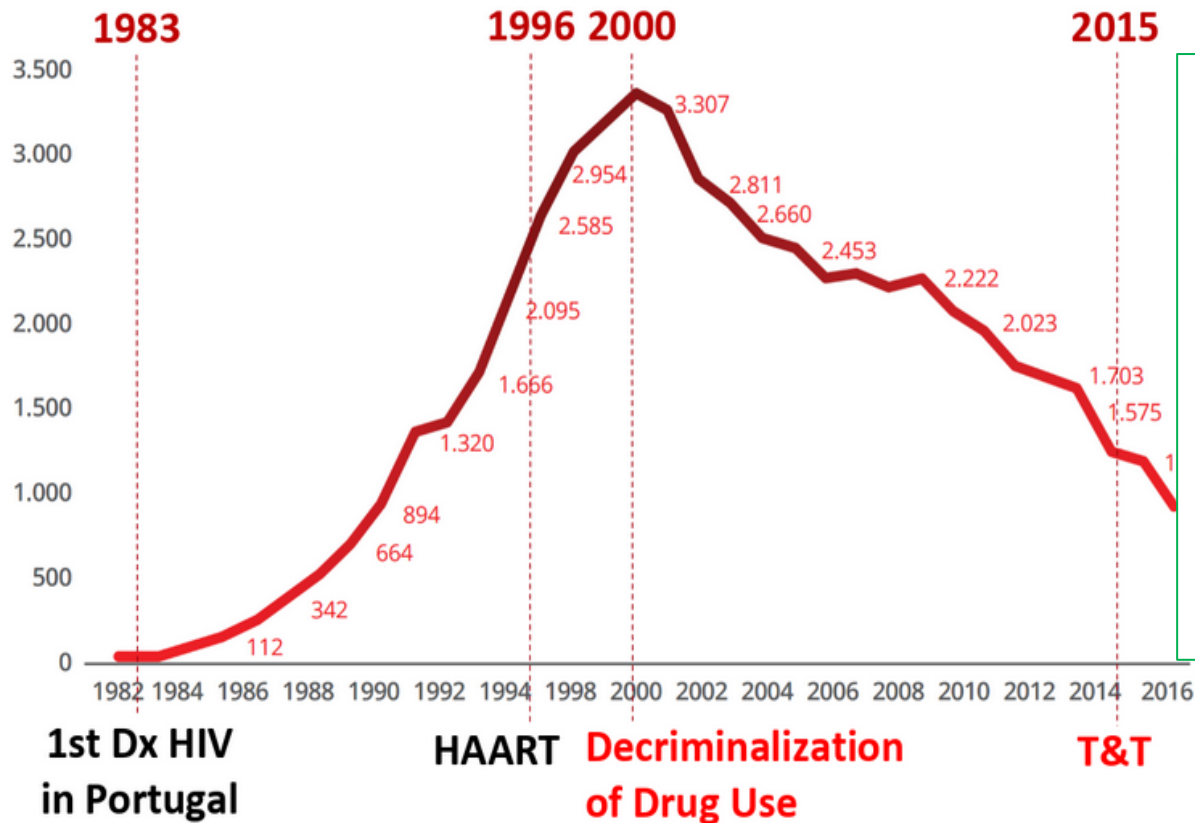
European Commission 2016. Available at: https://ec.europa.eu/home-affairs/sites/homeaffairs/files/what-we-do/policies/organized-crime-and-human-trafficking/drug-control/eu-response-to-drugs/docs/acs_final_report_new_ec_template_en.pdf

EMCDDA 2013. Available at: http://www.emcdda.europa.eu/attachements.cfm/att_218205_EN_PDU%20revision.pdf

A good practice example: PORTUGAL



Number of New HIV Infections 1983-2016



OUTCOME:

Reductions in:

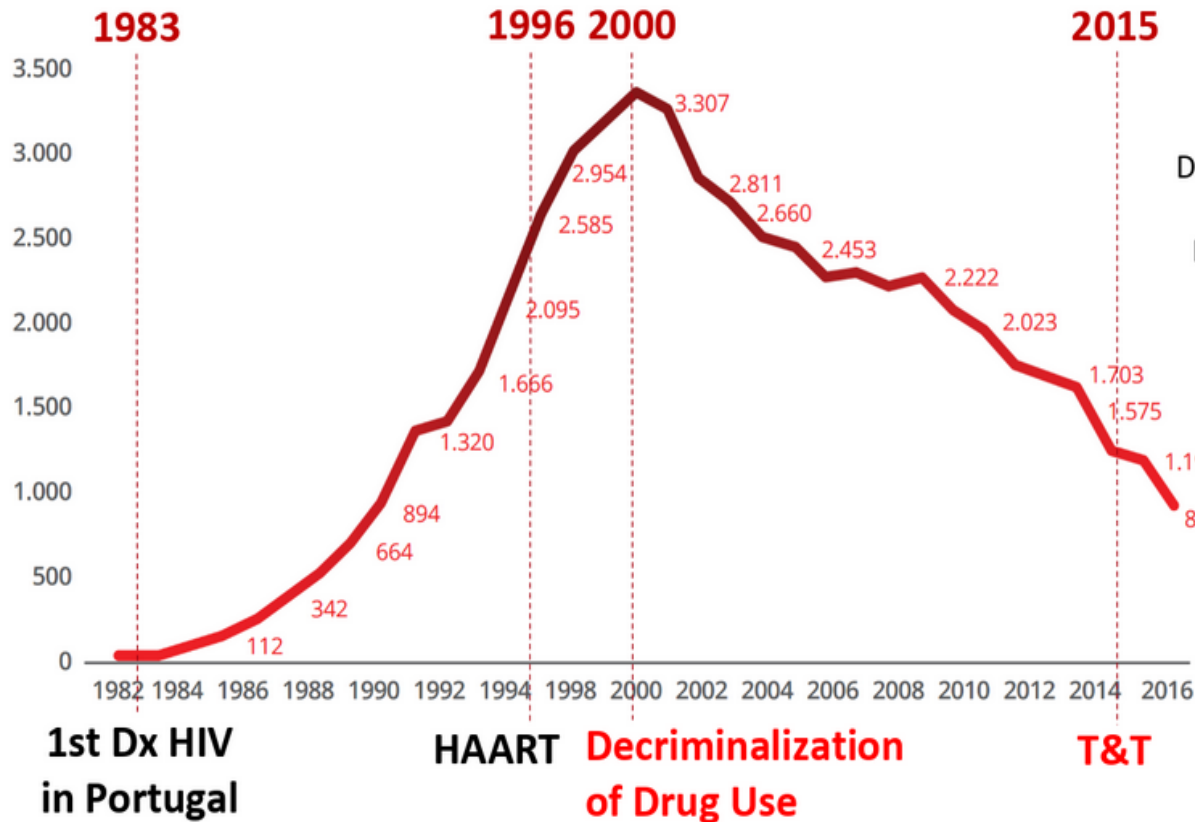
- problematic drug use
- drug-related harms
- criminal justice overcrowding

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A good practice example: PORTUGAL



Number of New HIV Infections 1983-2016



Drug use-related deaths (2001-2008) **-84%**

New drug use-related HIV diagnoses (2000-2008) **-75%**

In 2017, **only 2.2%** of new HIV infections were related to drug use

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Management of hepatitis C in the era of COVID-19

Review



JHEP|Reports

Care of patients with liver disease during the COVID-19 pandemic: EASL-ESCMID position paper



Tobias Boettler,¹ Philip N. Newsome,^{2,3} Mario U. Mondelli,⁴ Mojca Maticic,^{5,6} Elisa Cordero,⁷ Markus Cornberg,^{8,9} Thomas Berg^{10,*}

Review



JHEP|Reports

Impact of COVID-19 on the care of patients with liver disease: EASL-ESCMID position paper after 6 months of the pandemic



Tobias Boettler,^{1,†} Thomas Marjot,^{2,†} Philip N. Newsome,^{3,4} Mario U. Mondelli,⁵ Mojca Maticic,^{6,7} Elisa Cordero,⁸ Rajiv Jalan,⁹ Richard Moreau,^{10,11} Markus Cornberg,^{12,13} Thomas Berg^{14,*}

Position Paper



JOURNAL
OF HEPATOLOGY

EASL position paper on the use of COVID-19 vaccines in patients with chronic liver diseases, hepatobiliary cancer and liver transplant recipients

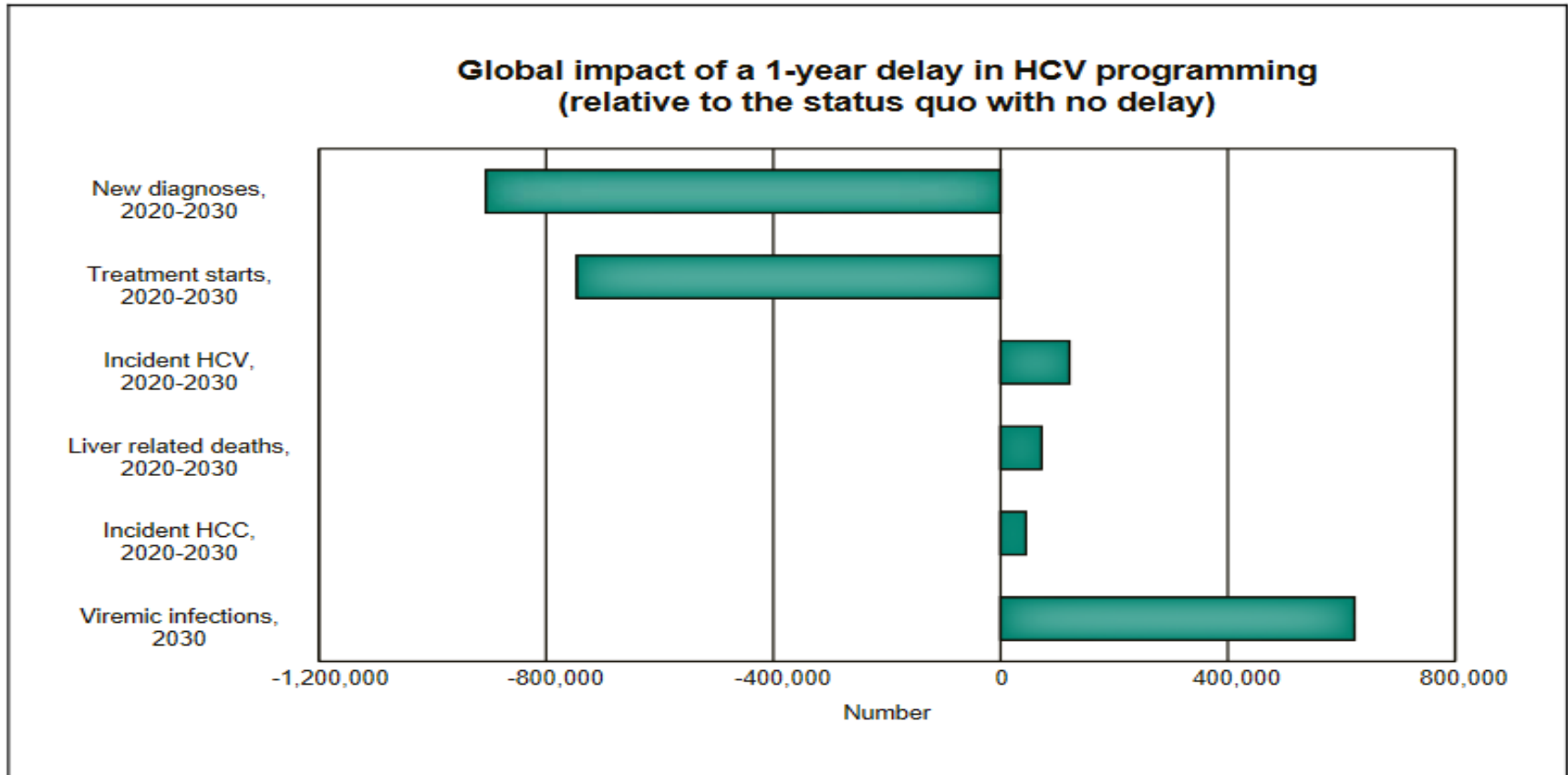
Markus Cornberg^{1,2,3,*}, Maria Buti⁴, Christiane S. Eberhardt⁵, Paolo Antonio Grossi^{6,7}, Daniel Shouval⁸

Boettler T et al. JHEP Reports April 2, 2020.

Boettler T, et al. JHEP Reports, August 8, 2020.

Cornberg M, et al. J Hepaol February 2021, 2021.

COVID-19: Impact on global HCV elimination efforts



Immediate action to improve HCV screening and treatment is needed to make the WHO's elimination targets attainable by 2030.

Medicine Nobel 2020 honors three scientists for discoveries on hepatitis C virus



A call to end the journey started by these Nobel Laureates