

HIV and HCV coinfection - Barriers in Central and Eastern Europe

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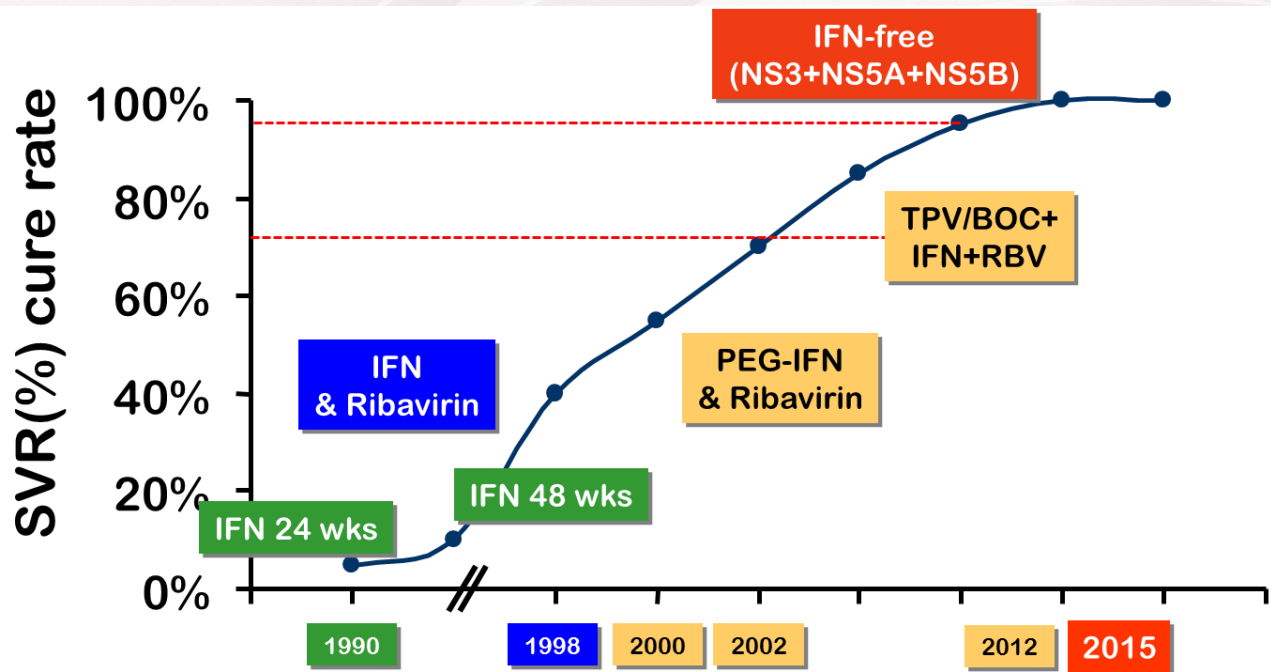
Potential conflicts of interest

Honoraria or consulting fees: Abbvie, Gilead, BMS, Roche, MSD

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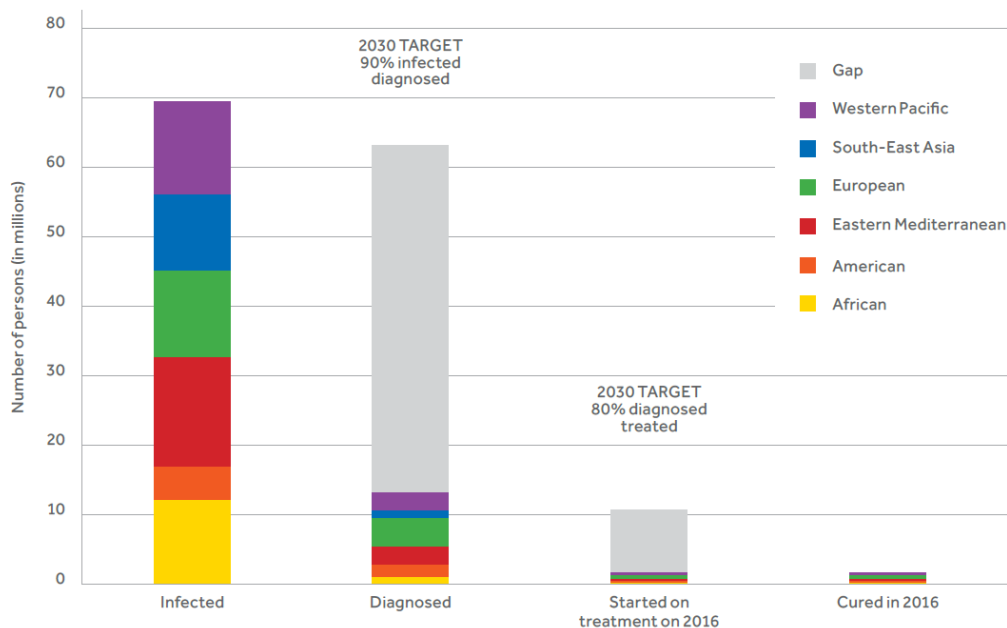
(R)Evolution of chronic hepatitis C treatement



**25 of intensive research and progress of molecular medicine
Unique progress of therapy of chronic disorder!**

WHO viral hepatitis elimination plan – Are we on track?

Fig. 1. Cascade of care for people living with HCV infection, by WHO region, 2016



WHO data from 2016:

- 1.76 mln anti-HCV+ started on therapy (2015r: 1.1 mln)
- Proportion of treated increased from 7% in 2015 to 13% in 2016r.
- Over 80% of infected still without diagnosis

The context: HCV-prevalence in Central and Eastern Europe

Anti-HCV prevalence:

Russia: 4.1%

Romania: 3.2%

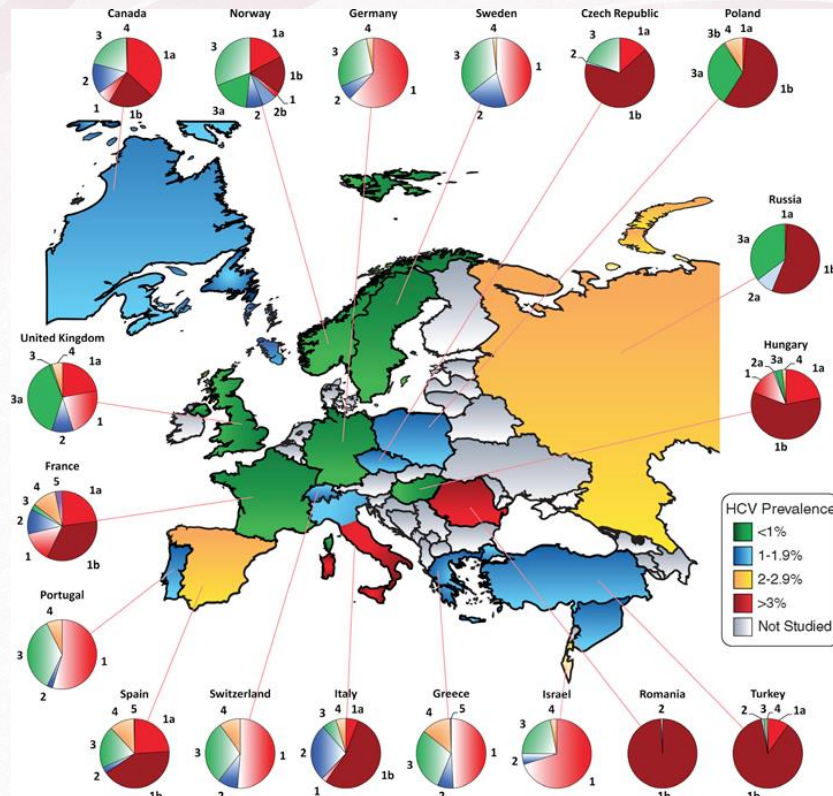
Slovakia: 1.5%

Bulgaria: 1.3%

Poland: 0.9%

Hungary: 0.8%

Czech R: 0.7%



Prevalence and burden of HCV co-infection in people living with HIV: a global systematic review and meta-analysis

Lucy Platt, Philippa Easterbrook, Erin Gower, Bethan McDonald, Keith Sabin, Catherine McGowan, Irini Yanny, Homie Razavi, Peter Vickerman



- **Systematic review and meta-analysis** of MEDLINE, Embase, CINAHL+, POPLINE, Africawide Information, Global Health, Web of Science, and the Cochrane Library and WHO databases
- Odds of HCV infection **were six times higher** in people living with HIV
- Worldwide, there are appr. **2,278,400 HIV–HCV co-infections** of which 1,362,700 are in PWID, equaling an overall co-infection prevalence in **HIV-infected individuals of 6.2%** (3.4–11.9).

	HIV-infected individuals (excluding PWID)			HIV-infected PWID				Total HIV-infected individuals* (including PWID)		
	HIV-infected individuals	HCV co-infection		HIV-infected individuals	HCV co-infection			HIV-infected individuals	HCV co-infection	
	n	Median prevalence (IQR)	Estimates (IQR)	n	PWID (%)†	Median prevalence (IQR)	Estimates (IQR)	n	Estimates (range)	Percentage of regional distribution
Africa (south, west, east, central)	25 860 100	1% (1–8)	361 300 (154 800–2 064 500)	92 300	<1%	74% (48–99)	68 300 (44 300–91 400)	25 899 000	429 600 (199 100–2 155 900)	19%
Latin America (South and Central America, Caribbean)	1 688 200	7% (3–16)	116 500 (43 900–270 100)	72 900	4%	82% (24–88)	60 100 (17 600–64 400)	1 761 100	176 600 (61 500–334 500)	8%
North America	1 411 600	12% (6–16)	163 700 (87 500–221 600)	187 000	12%	83% (61–94)	153 300 (114 900–175 100)	1 598 700	319 000 (202 400–396 700)	14%
South and Southeast Asia	2 899 800	3% (2–7)	89 900 (52 200–200 100)	234 600	7%	83% (72–88)	195 700 (168 900–206 400)	3 134 400	285 600 (221 100–406 500)	13%
Eastern Europe and central Asia	832 500	4.8% (2–9)‡	40 000 (16 700–74 900)	688 100	45%	83% (56–98)	567 700 (387 400–671 600)	1 520 600	607 700 (404 100–746 500)	27%
Europe (west, central)	940 200	7% (4–11)	66 800 (34 800–106 200)	53 000	5%	70% (37–91)	37 000 (19 300–48 200)	993 200	103 800 (54 100–154 500)	5%
North Africa and Middle East	185 400	4% (2–6)	7 000 (3 000–10 800)	52 600	22%	88%	46 500	238 000	53 500 (49 500–57 300)	2%
Western Pacific (Asia Pacific, Australasia)	653 000	6% (3–6)	41 800 (18 300–41 800)	88 300	12%	82% (55–88)	72 700 (48 700–78 100)	741 300	114 500 (67 000–119 900)	2%
East Asia	653 900	4% (2–7)	28 800 (12 400–45 100)	166 100	20%	96%§	159 500§	820 000	188 300 (171 900–204 600)	8%
Total	35 237 400	4.8% (2–9)	915 700 (423 600–3 035 200)	1 635 100	4%	82% (55–88)	1 362 700 (847 700–1 381 800)	36 663 400	2 278 400 (1 271 300–4 417 000)	100%

HCV=hepatitis C virus. PWID=people who inject drugs. *Estimates of HIV-infected individuals in each country were measured through spectrum and published by UNAIDS and UNODC.^{1,2} †Proportion of HIV cases in PWID. ‡No regional estimate available, so global median used as a proxy. §No range is reported because there is only one country estimate for PWID in east Asia.

Table 2: Global estimates of HCV infection in HIV-infected individuals by global burden of disease region

Key challenges in CEE

- Insufficient epidemiologic data
- Screening
- Simplification of diagnostics algorithm
- Linkage to care
- Therapeutic restrictions
- Prevention of reinfection

HIV/HCV coinfection in Central Europe

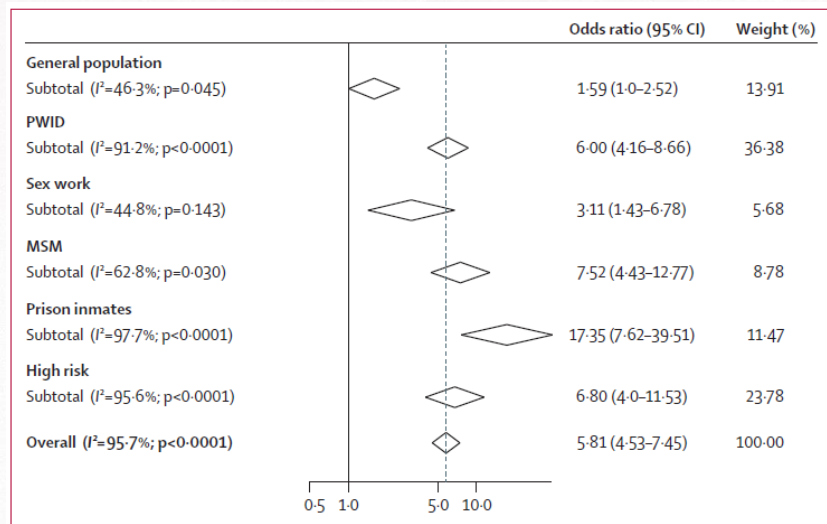
General population						Heterosexual or pregnant HIV-infected individual						PWID						MSM					
Total studies		Best estimate				Total studies		Best estimate				Total studies		Best estimate				Total studies		Best estimate			
n	Range*	%	Score	n	Year	n	Range*	%	Score†	n	Year	n	Range*	%	Score†	n	Year	n	Range*	%	Score	n	Year
(Continued from previous page)																							
Central Europe																							
Hungary	1	3-9	3-9%	C1	78	2004
Poland	1	29-2	29-2%	B0	120	2011	2	76-6-96-1	76-6%	C2	470	2013
Romania	1	3-7	3-7%	C1	107	2004	1	40-4	40-4%	C0	193	2012
Slovenia	1	7-6	7-6%	C3	576	2013
Total‡	3	3-7-29-2	3-9%	3	40-4-76-6	58-5%	1	7-6	7-6%	C3

HIV/HCV coinfection in Eastern Europe

	General population						Heterosexual or pregnant HIV-infected individual						PWID						MSM					
	Total studies		Best estimate				Total studies		Best estimate				Total studies		Best estimate				Total studies		Best estimate			
	n	Range*	%	Score	n	Year	n	Range*	%	Score†	n	Year	n	Range*	%	Score†	n	Year	n	Range*	%	Score	n	Year
Eastern Europe and central Asia																								
Estonia	1	56·3	56·3%	C2	80	2004
Kazakhstan	1	82·5	82·5%	B0	183	2012
Latvia	2	85·0–87·5	85·0%	C0	97	2008
Lithuania	1	51·3	51·3%	C2	80	2004
Russia	7	19·0–93·0	60·0%	B3	113	2010
Tajikistan	1	98·3	98·3%	B2	59	2004
Ukraine	2	71·3–97·6	97·6%	C2	82	2004
Total‡	15	56·3–97·6	82·5%

Various risk factors of HIV/HCV coinfection in Central and Eastern Europe

Odds of anti-HCV+ in HIV(+) vs (-) worldwide



Platt L et al. Lancet Infect Dis. 2016 Jul;16(7):797-808

HIV transmission in selected CEE countries

Main routes of HIV transmission by country.

Injecting drug use	Heterosexual contact	Sex between men
Azerbaijan	Albania	Czech Republic
Georgia	Armenia	Serbia
Kazakhstan	Bosnia and Herzegovina	Slovenia
Kyrgyz Republic	Kosovo	Hungary
Russian Federation	Estonia	Slovak Republic
	Moldova	FYR of Macedonia
	Romania	Bulgaria
	Turkey	Montenegro
	Uzbekistan	Croatia
		Poland

FYR, Former Yugoslav Republic.

Gokengin D et al., International Journal of Infectious Diseases 70 (2018) 121–130

Risk factors for anti-HCV positivity in Poland



N=26 057, anti-HCV: 1.94%, HCV-RNA: 0.6%, diagnosis rate in Poland ~15%

Table 6 Multivariate analysis of risk factors for anti-hepatitis C virus positivity

	OR (95% CI)	P
Sex male vs. female	1.74 (1.32, 2.29)	<0.001
Age > median	0.77 (0.59, 1.02)	0.07
Number of hospital admissions > median	1.75 (1.31, 2.34)	<0.001
Endoscopic procedures	–	>0.1
Dialysis	–	>0.1
Surgical procedures	–	>0.1
Blood transfusions before 1992	2.88 (2.08, 3.98)	<0.001
History of tattooing and/or piercing	–	>0.1
Intravenous drug use	6.13 (3.8, 10.0)	<0.001

Nosocomial

PWIDs

CI, confidence interval; OR, odds ratio.

Anti-HCV in healthcare workers 1.42% vs 1.92% in patients (P=0.008)

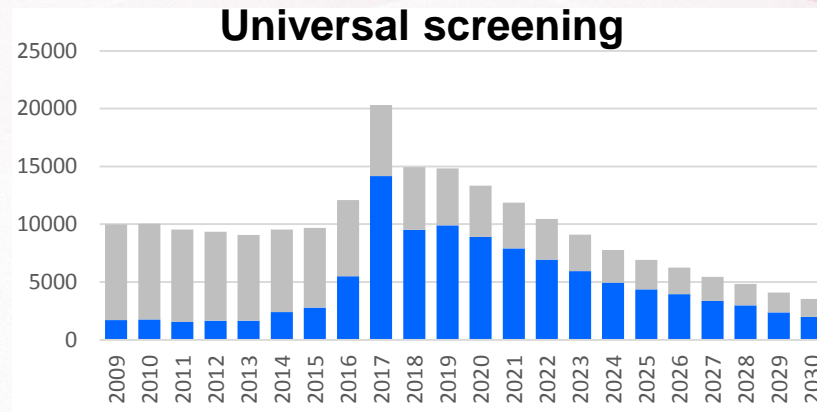
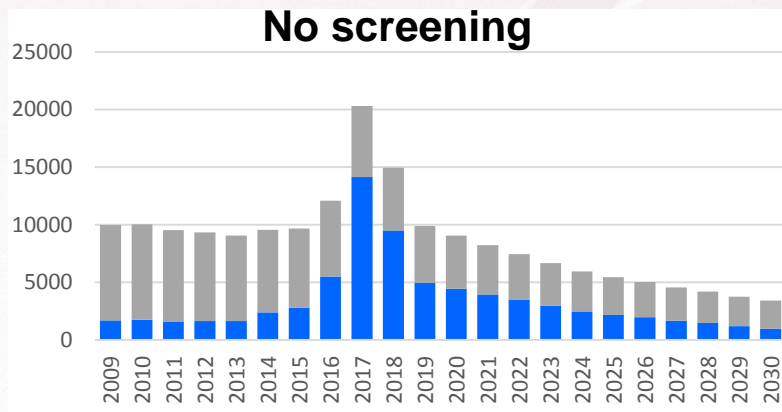
Screening for HCV in Poland - reality



- Pilot screening actions show limited coverage
(primary healthcare n=22,659, anti-HCV 1.1%, pregnant women n=8006, anti-HCV 0.95%, PWIDs n=1219, 65% anti-HCV)*
- National Elimination Plan for HCV in Poland although created in 2005 is still not implemented by Ministry of Health !
- Among important barriers in screening is lack of reimbursement of anti-HCV testing in primary health settings
- Nationwide screening campaign urgently needed

* Data by National Institute of Public Health

The impact of lack of screening programs on hepatitis C mortality



 Cured  Deaths from HCV infection

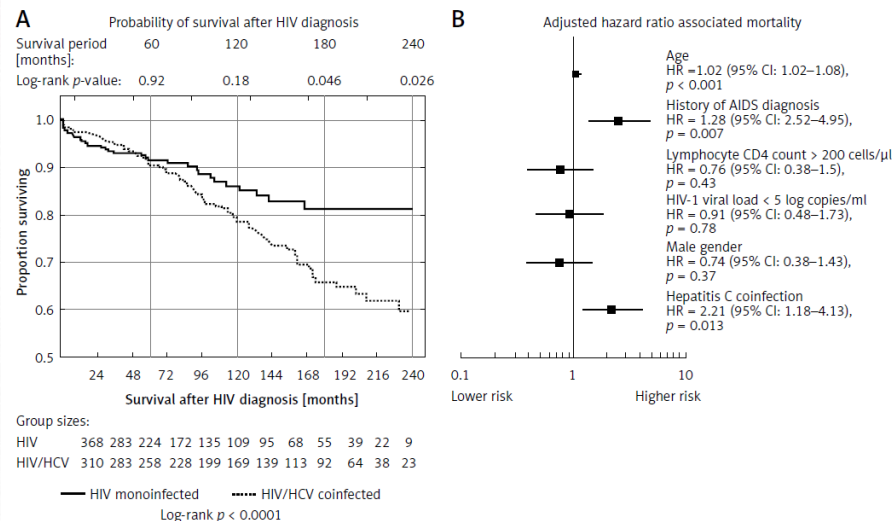
- Universal screening will lead to a greater reduction in new infections
 - We need to do more to reduce mortality

HIV/HCV is associated with reduced life expectancy

N=701, follow-up 1996-2014, 3 university centers

Parameter	HIV mono-infected	HIV/HCV coinfectd	P-value	Total
Male, n (%)	262 (71.2)	247 (74.2)	0.37	509 (72.6)
Age at HIV diagnosis, median (IQR) [years]	34.0 (27.1–43.4)	28.1 (23.7–34.1)	< 0.001	30.9 (25.5–38.3)
HIV infection stage at genotyping, n (%)*:				
A	122 (38.1)	136 (45.5)	< 0.001	258 (41.7)
B	102 (31.9)	113 (37.8)		215 (34.7)
C	96 (30.0)	50 (16.7)		146 (23.6)
Dominant transmission route, n (% of total)*:				
IDU (intravenous drug use)	22 (6.8)	257 (83.7)	< 0.001	279 (44.2)
MSM (men having sex with men)	143 (44.0)	19 (6.2)		162 (25.6)
HET (heterosexual)	160 (49.2)	31 (10.1)		191 (30.2)
Lymphocyte CD4+ T cell count at care entry, median (IQR)	250 (70–519)	283 (116–475)	0.169	277 (93–496)
HIV viral load at care entry, mean log copies/ml (SD)	4.98 (4.31–5.61)	4.15 (4.72–5.2)	0.003	4.91 (4.21–5.52)

*CDC category not available for 82 individuals, transmission route not available for 69 cases.



Cost-Effectiveness of One-Time Hepatitis C Screening Strategies Among Adolescents and Young Adults in Primary Care Settings

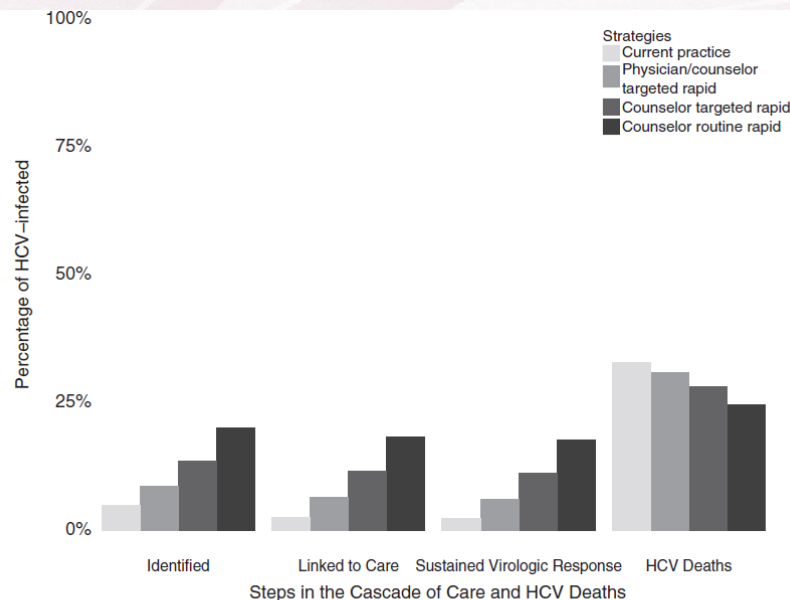


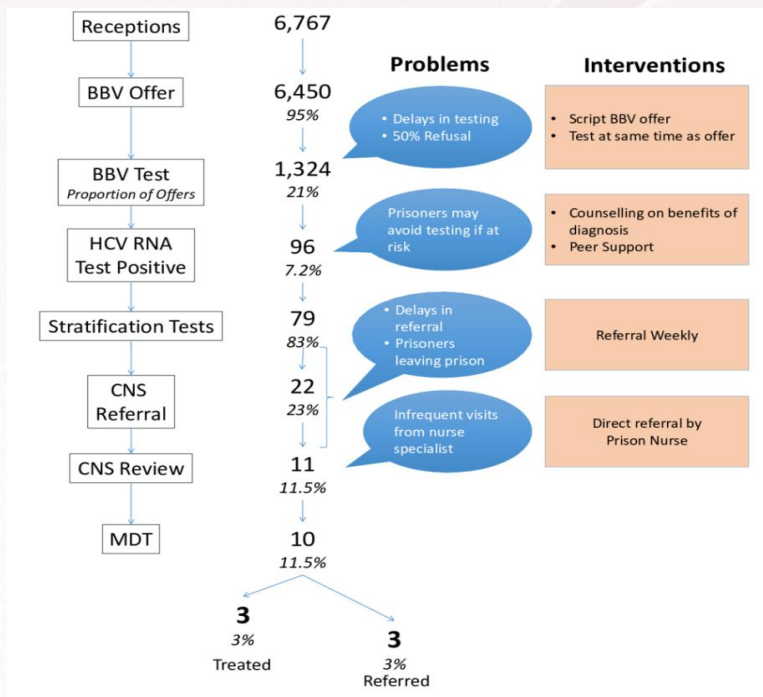
Figure 2. Outcomes for strategies that were not dominated. The bar graph shows the percentage of hepatitis C virus (HCV)-infected individuals who reached HCV cascade of care outcomes and the percentage of HCV-related deaths. Each bar represents a specific strategy. Abbreviation: HCV, hepatitis C virus.

Routine rapid HCV testing among 15- to 30-year-olds may be cost-effective when the prevalence of PWID is >0.59%. computer simulation model; cost-effectiveness; hepatitis C testing; adolescents and young adults; injection drug use.

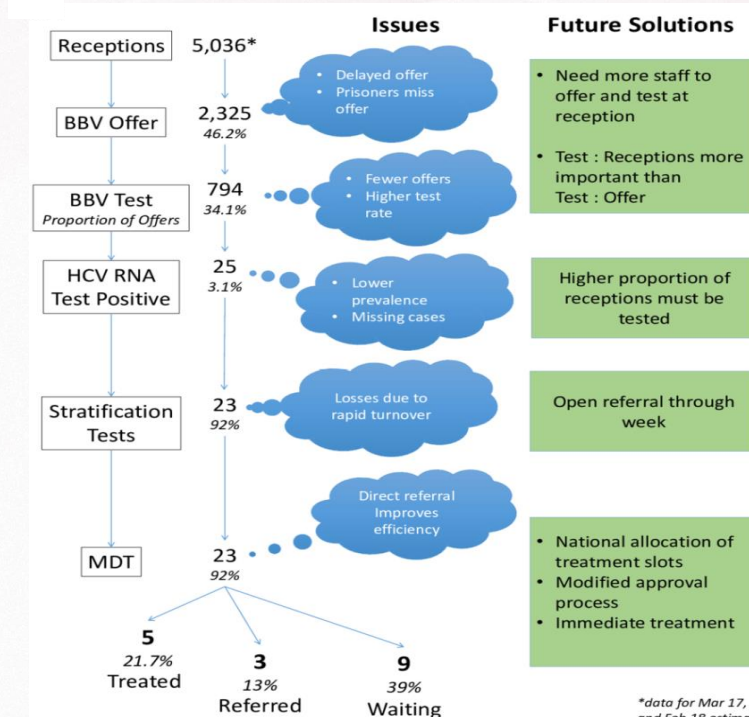
Reaching special populations may not be easy (e.g. prisoners) – screening not enough



Original pathway: Dec 2015–Feb 2017



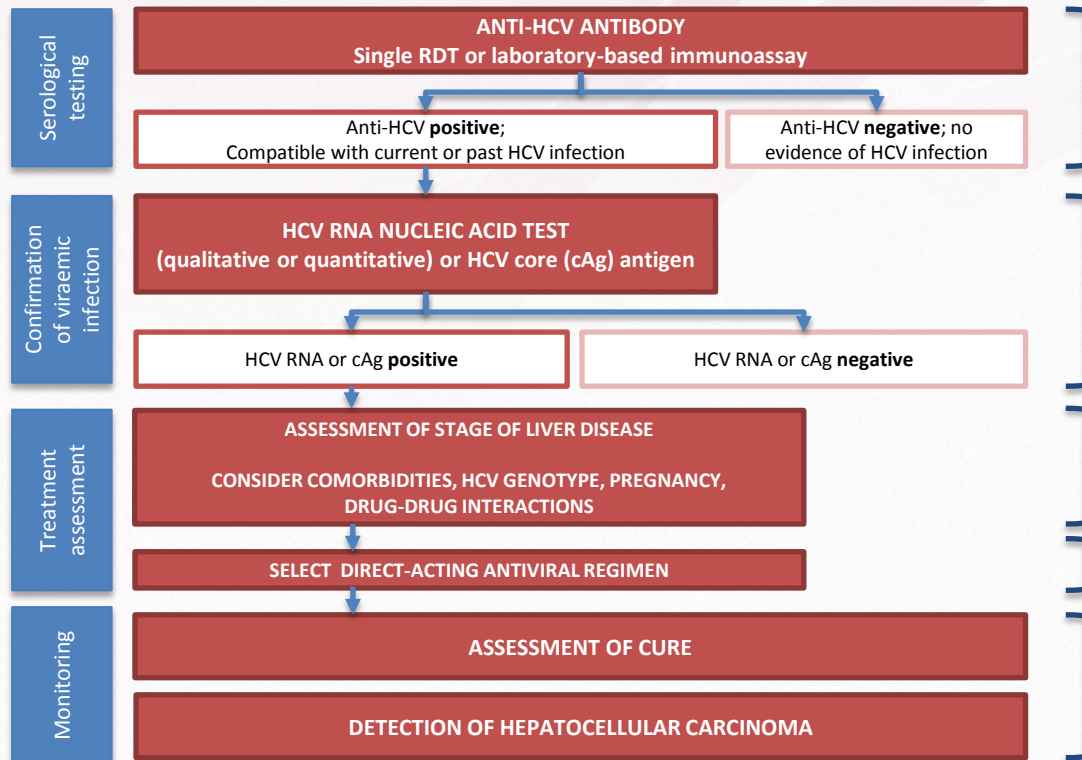
Revised pathway: Mar 2017–Mar 2018



*data for Mar 17, Jan and Feb 18 estimated

Can the WHO diagnostic algorithm be implemented in practice?

5 key steps



1. Single quality-assured rapid diagnostic test

2. Prompt or reflex HCV RNA or core antigen

3. Assess the stage liver disease using NITs (APRI, FIB4, TE)

4. Treat all with pan-genotypic regimens

5. One-step monitoring; one test of cure SVR12

Hepatitis C Reflex RNA Confirmatory Testing in New York City Implementation Guide



Reflex RNA testing for hepatitis C following a positive antibody test is the standard of care in New York City (NYC).
This guide provides background and case studies from four NYC hospitals on their implementation process.

Figure 1

Rates of HCV RNA testing at HepCX hospitals, 2016

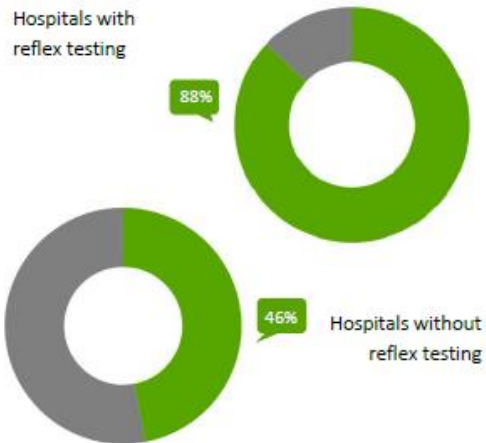


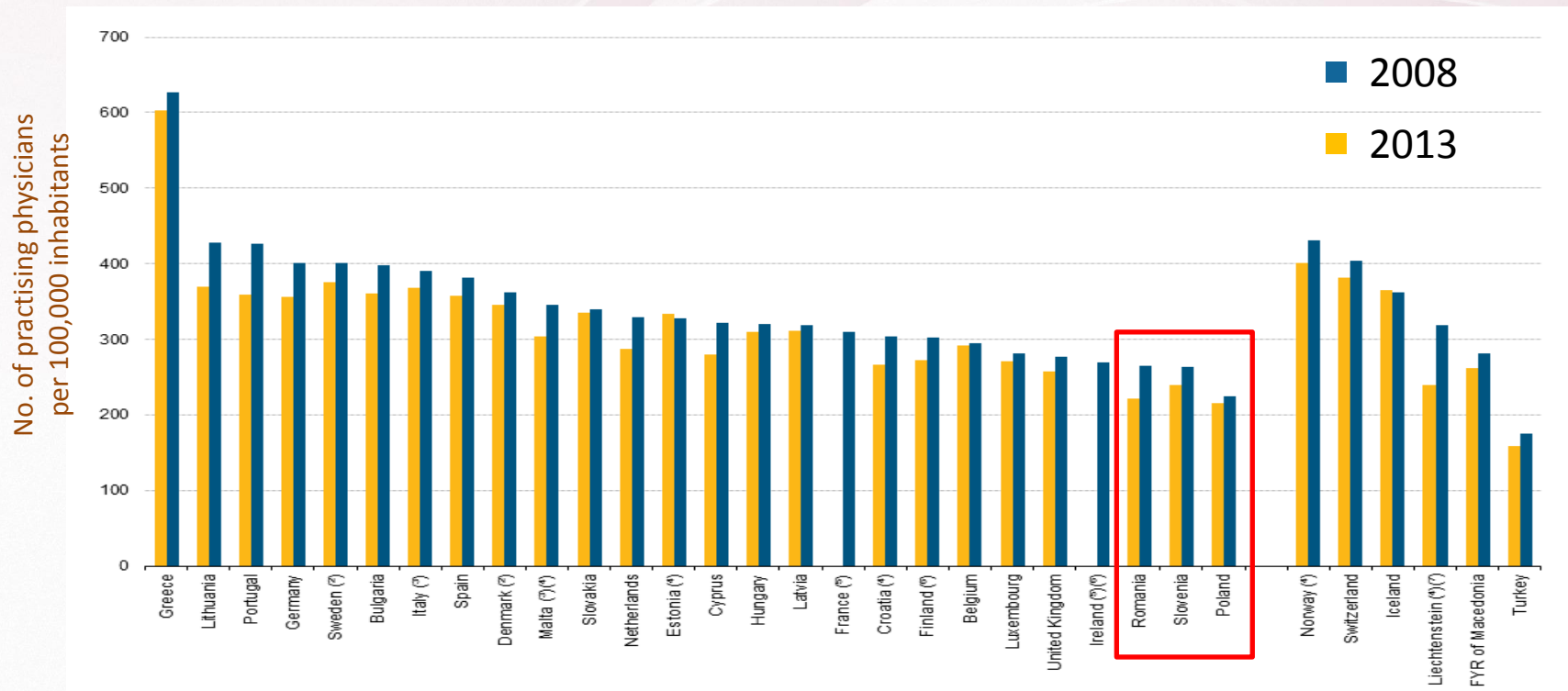
Figure 2

Number of HepCX hospitals with reflex testing, 2017



At the time of this report, of the 39 hospitals in the HepCX network, 22 currently conduct reflex testing.

Shortage of physicians in CEE region is a major problem

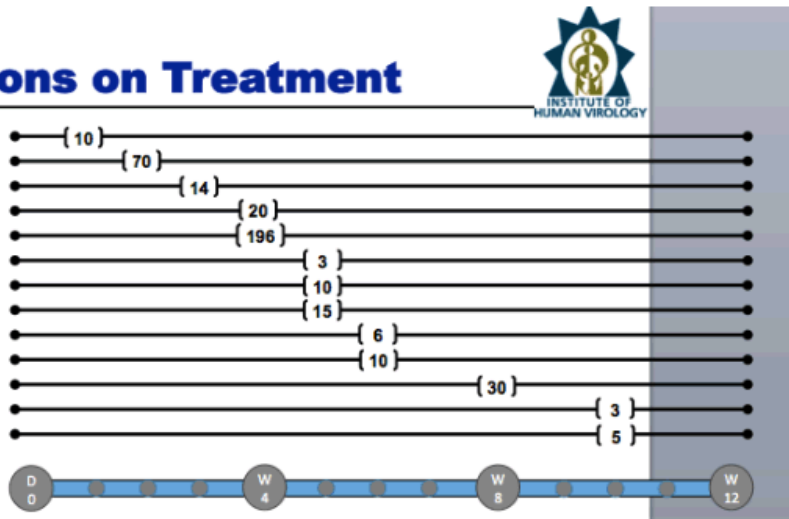


Education: Sofosbuvir/Velapatasvir for 12 wk shows high efficacy in active PWID – ANCHOR study

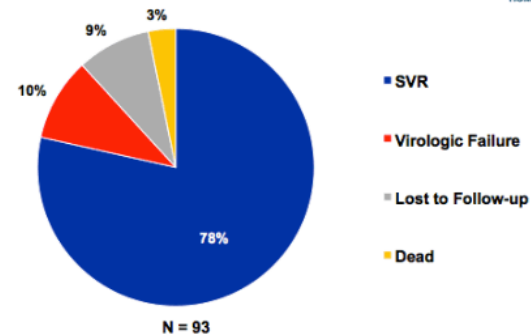
N=100, treated in harm reduction center in Washington, simplified diagnostic algorithm
Cirrhosis – 33%, unstably housed 51%, prior incarceration 92%, no income 92%, drinking 40%

Interruptions on Treatment

- Stolen = 3
- Did not take = 3
- Hospitalized = 2
- Inpatient drug treatment = 2
- Incarceration = 2
- Lost medication = 1



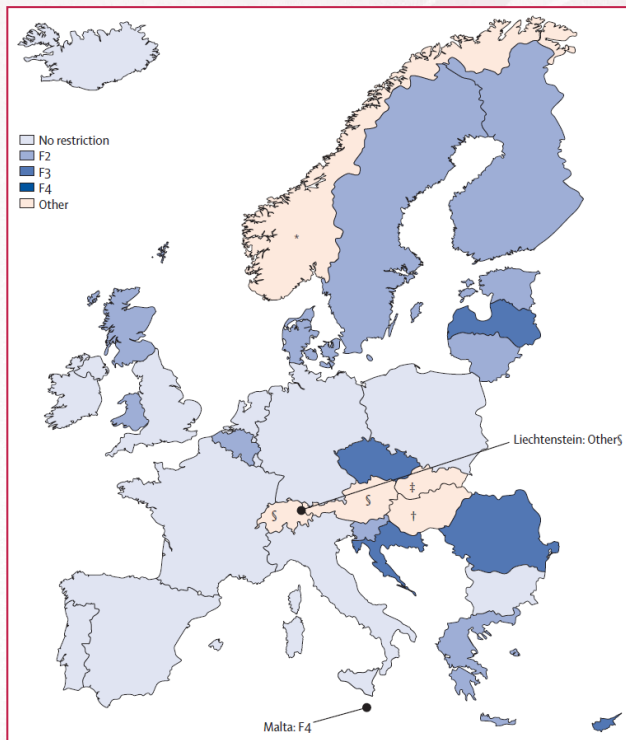
SVR – Intention to Treat



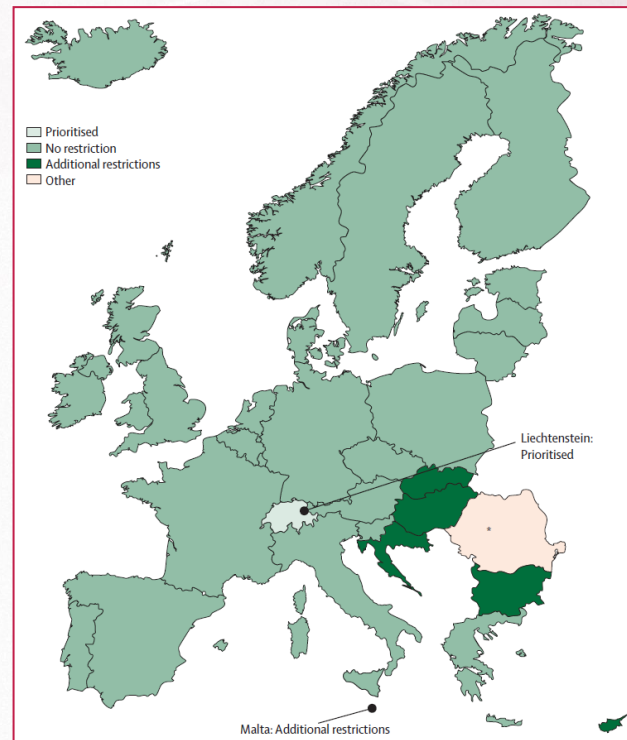
Per protocol SVR = 89%

Restrictions for reimbursement for HCV DAAs in Europe

Minimum fibrosis stage

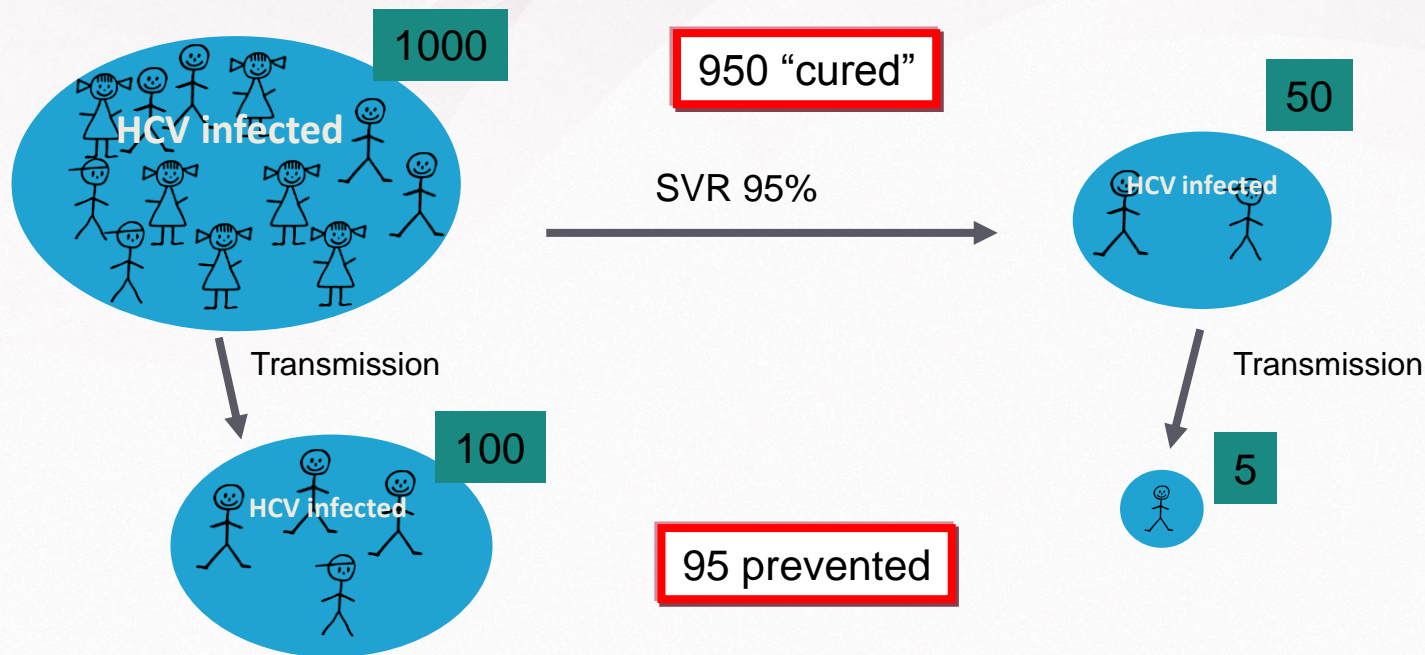


Recent drug/alcohol dependence



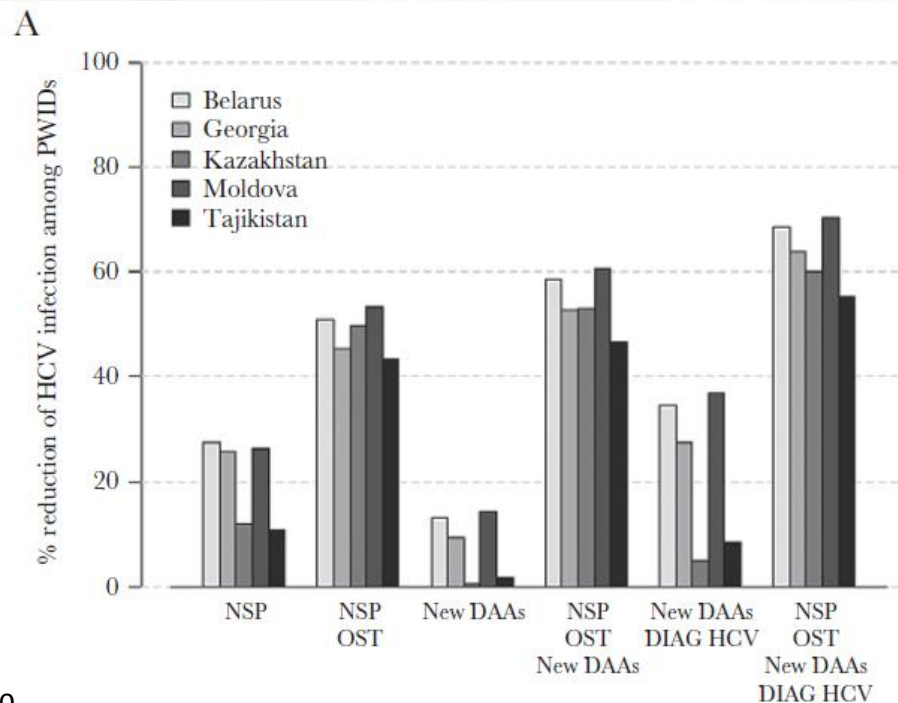
In PWID in CEE, treatment as prevention might not be sufficient to control HCV

1000 treated = 1045 infections cured / prevented (SVR=104.5%)



Intervention Packages to Reduce the Impact of HIV and HCV Infections Among People Who Inject Drugs in Eastern Europe and Central Asia: A Modeling and Cost-effectiveness Study

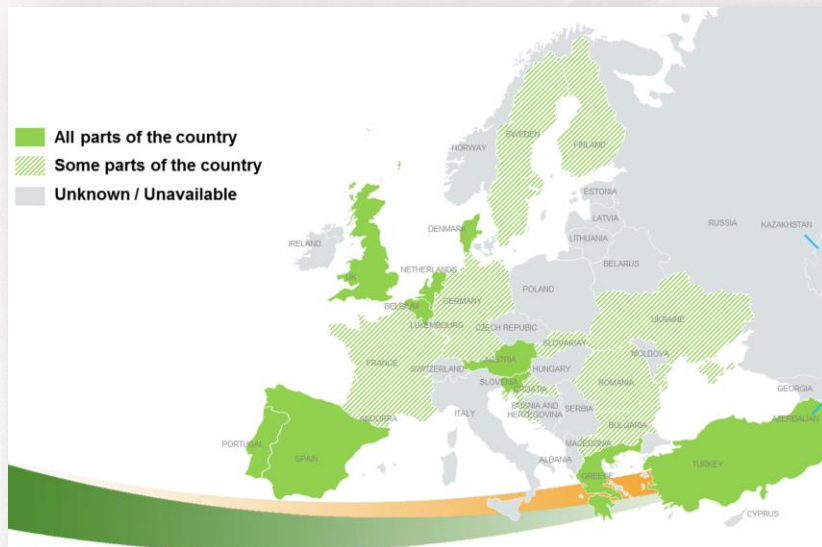
Guillaume Mabileau,^{1,2} Otilia Scutelniciuc,³ Maia Tsereteli,⁴ Ivan Konorazov,⁵ Alla Yelizaryeva,⁶ Svetlana Popovici,⁷ Karimov Saifuddin,⁸ Elena Losina,⁹ Manoela Manova,¹⁰ Vinay Saldanha,¹⁰ Jean-Elie Malkin,¹¹ and Yazdan Yazdanpanah^{1,2,12}



Harm reduction services for PWID in CEE



Needle and syringe programmes (NSP)



Opioid substitution therapy (OST)



- ELPA Hep-CORE report, 2017. <https://epha.org/wp-content/uploads/2017/03/1.ELPA-Hep-CORE-Report-Alimena.pdf>

One solution for all barriers

Smart and implemented National Elimination Plan

Conclusions

- There is still a lot to do to meet WHO targets
- Adequately resourced National Control Programmes are essential
- Priority needs to be given to the challenges around hard-to-reach populations
- Cooperation between HCPs and NGOs is essential to leverage different skill sets
- We need to share best practice