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
Speakers’ bureau: Abbvie, Gilead
Grants / research supports: Merz
(R)Evolution of chronic hepatitis C treatment

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?

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%

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).
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

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<tr>
<th></th>
<th>General population</th>
<th>Heterosexual or pregnant HIV-infected individual</th>
<th>PWID</th>
<th>MSM</th>
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<td>Poland</td>
<td>1 29.2</td>
<td>29.2% 80 120 2011</td>
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<td>Romania</td>
<td>1 3.7</td>
<td>3.7% C1 107 2004</td>
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<td>Slovenia</td>
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HIV/HCV coinfection in Eastern Europe

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Platt L et al. Lancet Infect Dis. 2016 Jul;16(7):797-808
Various risk factors of HIV/HCV coinfection in Central and Eastern Europe

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

HIV transmission in selected CEE countries

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

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

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

Flisiak R, Conference of Polish Association for the Study of Liver, 7–9 Jun 2018, abstracts in Clin Exp Hepatology 2/2018
HIV/HCV is associated with reduced life expectancy

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

Leszczyszyn-Pynka M et al., Arch Med. Sci 2018
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

- Receptions: 6,767
- BBV Offer: 6,450 (85%)
- BBV Test: 1,324 (21%)
- HCV RNA Test Positive: 96 (7.2%)
- Stratification Tests: 79 (83%)
- CNS Referral: 22 (23%)
- CNS Review: 11 (11.5%)
- MDT: 10 (11.5%)

Problems:
- Delays in testing
- 50% Refusal

Interventions:
- Script BBV offer
- Test at same time as offer
- Counselling on benefits of diagnosis
- Peer Support
- Referral Weekly
- Direct referral by Prison Nurse

Revised pathway: Mar 2017–Mar 2018

- Receptions: 5,036
- BBV Offer: 2,325 (46.2%)
- BBV Test: 794 (34.1%)
- HCV RNA Test Positive: 25 (3.1%)
- Stratification Tests: 23 (92%)
- MDT: 23 (92%)

Issues:
- Delayed offer
- Prisoners miss offer
- Fewer offers
- Higher test rate
- Lower prevalence
- Missing cases
- Losses due to rapid turnover
- Direct referral improves efficiency

Future Solutions:
- Need more staff to offer and test at reception
- Test: Receptions more important than Test: Offer
- Higher proportion of receptions must be tested
- Open referral through week
- National allocation of treatment slots
- Modified approval process
- Immediate treatment

*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

- Hospitals with reflex testing: 88%
- Hospitals without reflex testing: 46%

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%

Per protocol SVR = 89%

Kattakuzhy S et al., AASLD 2018
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 Mahieume,1,2 Ottelia Scalvini,3 Maia Tsarebli,4 Irina Konorova,5 Alla Yelizaryeva,6 Svetlana Popovici,7 Karimeh Saitulidin,8 Elena Leonova,9 Manuela Manova,10 Visva Saldanha,11 Jean-Elie Malim,12 and Vasilis Yotzianpanah13,14

A

<table>
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<tr>
<th>% reduction of HCV infection among PWIDs</th>
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<td>Georgia</td>
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% reduction of HCV infection among PWIDs

- NSP
- NSP OST
- New DAAs
- NSP OST New DAAs
- New DAAs DIAG HCV
- NSP OST New DAAs DIAG HCV

OFID 2018; DOI: 10.1093/ofid/ofy040
Harm reduction services for PWID in CEE

- Needle and syringe programmes (NSP)
- Opioid substitution therapy (OST)

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