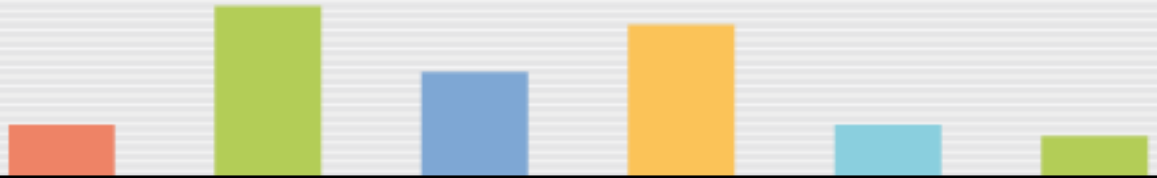
European Monitoring Centre
for Drugs and Drug Addiction

The European Monitoring Centre for Drugs and Drug Addiction (EMCDDA) – HCV in people who inject drugs (PWID) in Europe
+
A systematic review of prevalence and cost-effectiveness of screening hepatitis B and C in Europe *(Hahné et al. 2013)*

Lucas Wiessing, EMCDDA

VHPB meeting, 10 March 2016, Ljubljana



Two main messages

- PWID are a key group, perhaps the largest group, at risk for HCV in Europe. Prevention (harm reduction) needs strengthening

- Clinicians and liver specialists need to collaborate more closely with drug specialists and drug service providers, to improve diagnosis and treatment referral rates in PWID (‘outreach’)

EMCDDA first warning: 1997 (+ annually since)

Annual Report on the State of the Drugs Problem in the European Union

1997

Table 12 • Prevalence of antibodies against hepatitis B and C among injecting drug users in EU countr

COUNTRY	HEPATITIS B Year	Data	% infected	HEPATITIS C Year	Data	% infected	Numb infect
AUSTRIA							750(
BELGIUM							7500–10
DENMARK	1995	Estimate	21[1]	1995	Estimate	50[1]	750(
FINLAND				1994	Drug-positive traffic controls (IDUs[5])	65	300(
FRANCE				1995	Survey treatment centres, self-reports	53–70	70,000–1(
GERMANY	1993	Drug deaths/emergencies	37[1]	1993	Drug deaths/emergencies	44[1]	35,000–75,000
GREECE	1995–96	Athens: methadone treatment	9[4]	1995–96	Athens: methadone treatment	87[4]	24,000–32,000
IRELAND				1995	Dublin: treatment	84[4]	
ITALY	1996	Treatment	44	1996	Treatment serosurveys	>50	140,000
LUXEMBOURG							500
The NETHERLANDS	1994	Rotterdam: treatment serosurvey	61[4]	1994	Rotterdam: treatment serosurvey	84[4]	6000
PORTUGAL	1995	Treatment	56	1995	Treatment	85	35,000–58,000
SPAIN	1996	Treatment	59	1996	Treatment	83	
SWEDEN	1992	Estimate	2	1992	Estimate	32	6000–36,000[3]
UNITED KINGDOM	1995	Unlinked anonymous, England & Wales	22	1994	Survey treatment centres, UK	48–77	75,000

2. Due to lack of data these estimates are necessarily very global. Source estimates a total of 417,000 to 550,500 infected "drug addicts" in the EU. Almost all will be injecting drug users.
3. The upper limit of this estimate is probably too high – compare with table 5.
4. Not national.
5. Injecting drug users.

Eurosurveillance, Volume 5, Issue 31, 02 August 2001

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The access of injecting drug users to hepatitis C treatment is low and should be improved

Two recent American articles discuss the indications for hepatitis C treatment for injecting drug users (IDUs) (1,2). Although IDUs are a major risk group for infection with hepatitis C virus (HCV), guidelines in the United States (US) recommend not treating active injectors (3). Reasons include poor adherence, side effects, risk of reinfection, cost-benefits, and lack of urgency given the greater risks of drug use. These arguments, however, are not necessarily valid for all IDUs, and in the articles an individualised approach, rather than exclusion of injecting drug users as a group, is recommended.

As in the US, HCV infection in IDUs is a major public health problem in the European Union (EU). At least 500 000 drug injectors in the EU are seropositive for HCV (4), and this does not include a possible large number of infections in former drug users. The prevalence of HCV infection in IDUs

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(2003)

Drugs in focus

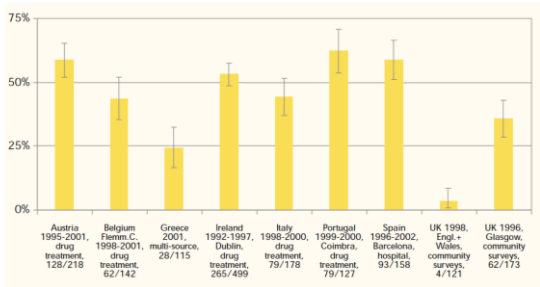
Bimonthly briefing of the European Monitoring Centre for Drugs and Drug Addiction

Hepatitis C: A hidden epidemic

A major challenge to public

Over the past few years hepatitis C has emerged as a major threat to public health worldwide. Within the European Union the total number of people infected is unknown but it is likely to exceed one million and could be considerably higher.

HCV prevalence in IDUs injecting less than 2 years

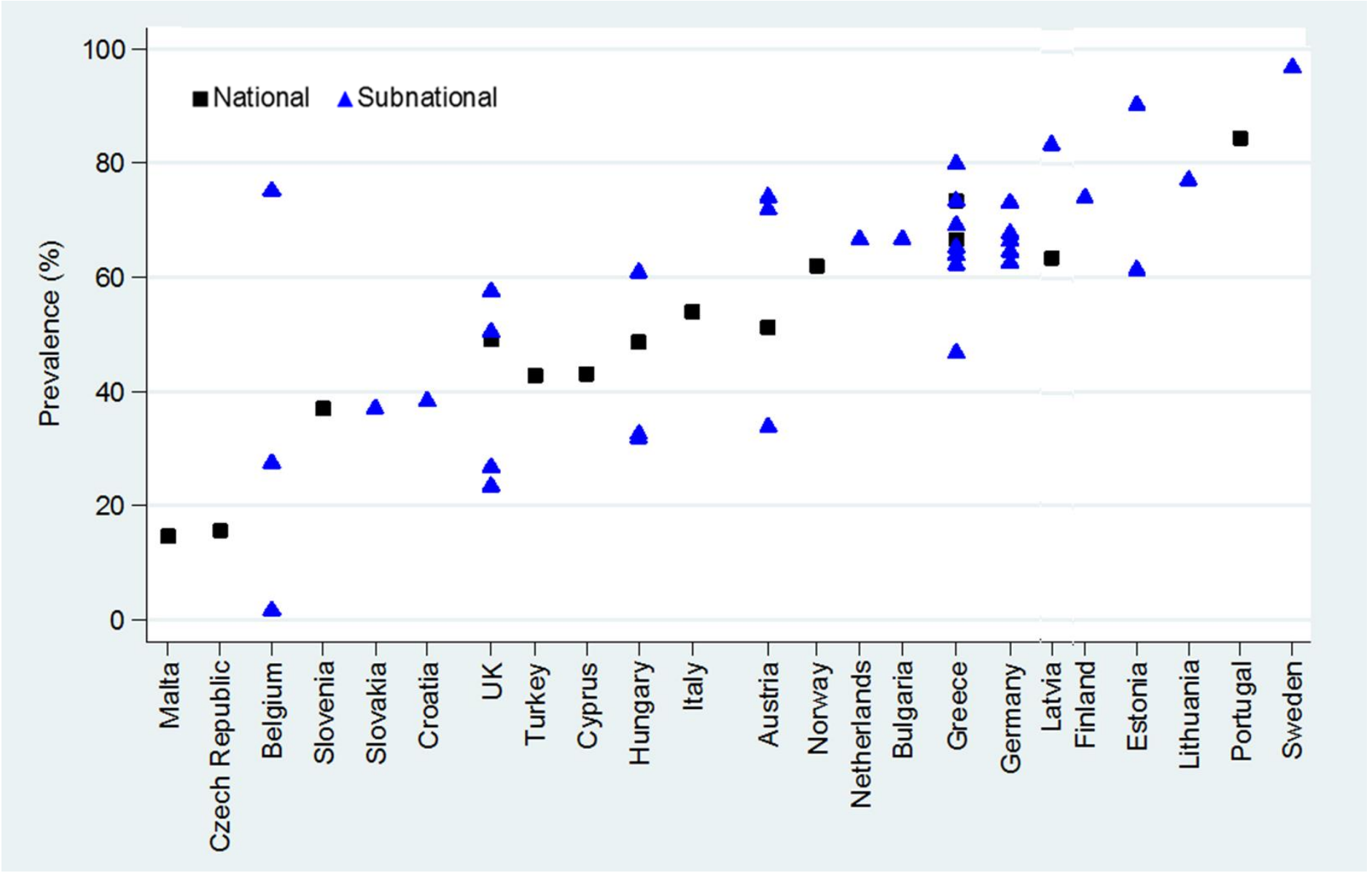


PWID the main risk category in Europe? HCV notifications 2014 (ECDC)

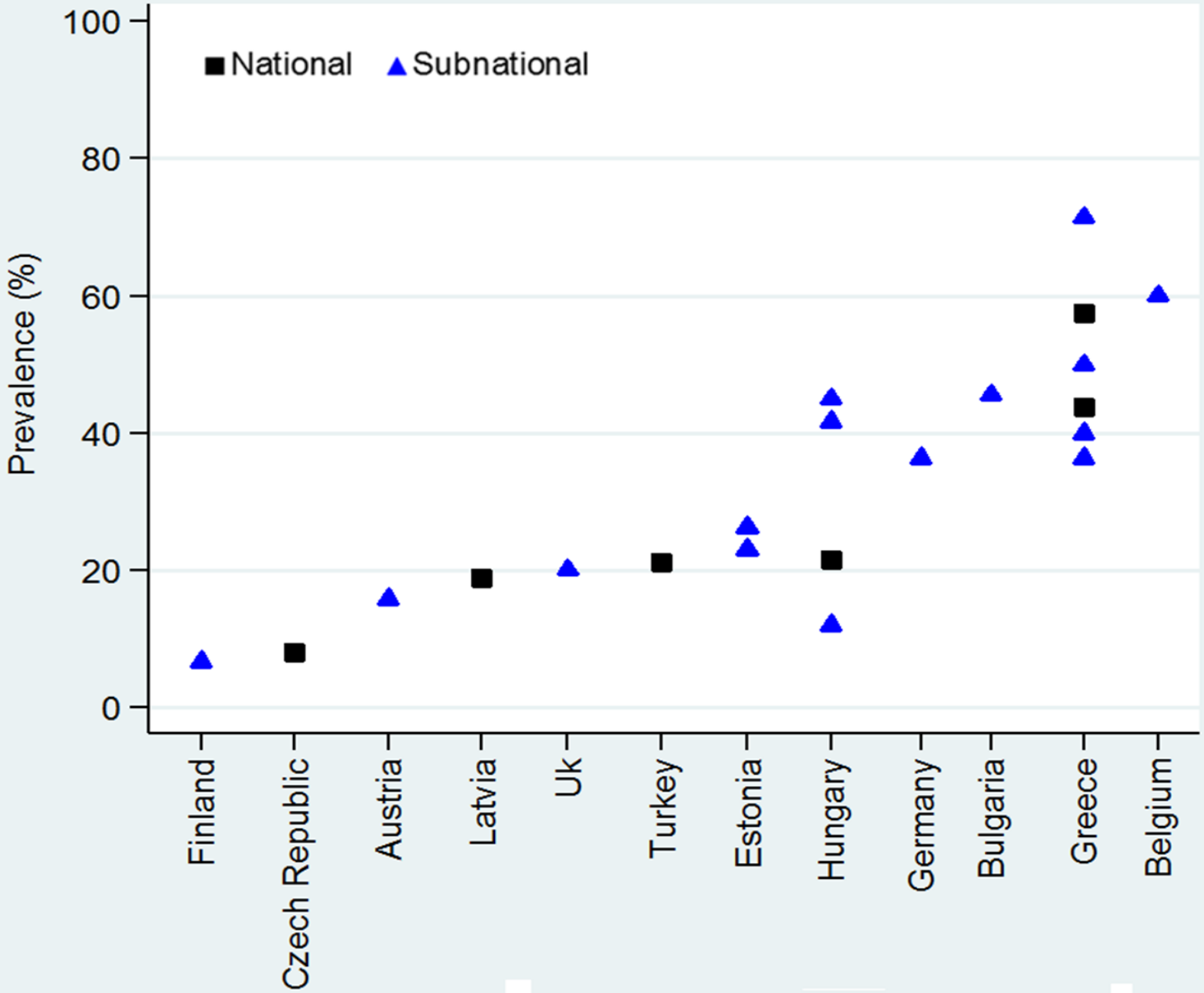
- 22 361 cases of hepatitis C were reported in the EU/EEA in 2014 (ECDC 2015)
- Of these only 5616 (25.1%) had information on exposure category
- Of these 4386 were PWID (78.1%)

Note: the large proportion with no exposure information makes the data unreliable

HCV antibody prevalence among injecting drug users – studies with national and subnational coverage 2013-2014



HCV-ab prevalence in samples of new injecting drug users (injecting <2 years), national & subnational studies 2013-2014



Trends in HCV prevalence among PWID at national or subnational level, EU+2, 2008-2014

Declining HCV ab prevalence in PWID recorded in 5 countries:
Belgium, Malta, Netherlands(?), Norway, Slovakia

Increases reported from 9 countries: Austria, Bulgaria, Greece, Hungary, Latvia, Slovenia, Turkey, UK

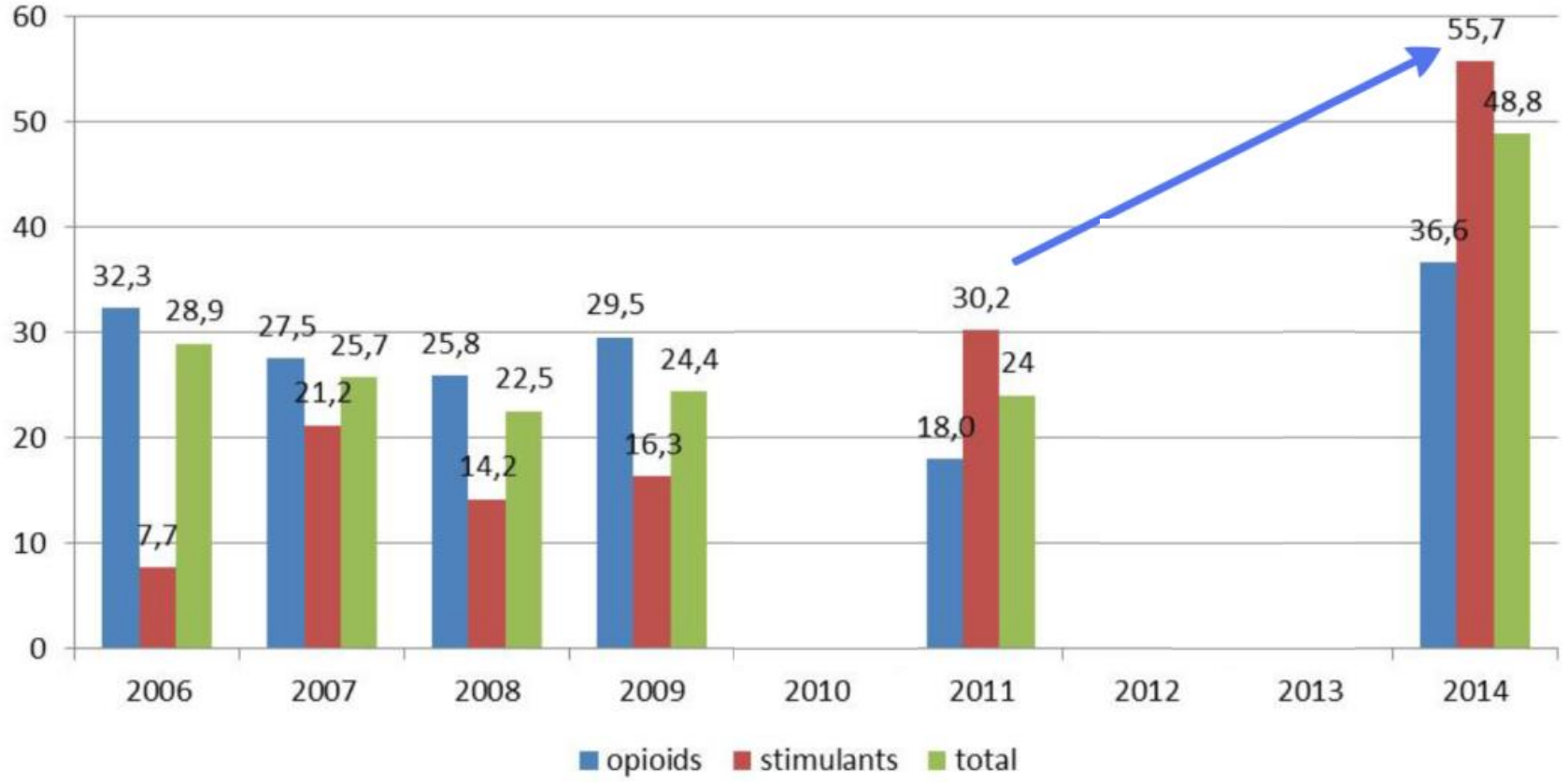
Increases **among young IDUs** (age < 25): Austria, Czech Republic(?), Greece, Hungary (declines: Bulgaria, Turkey)

Increases **among new IDUs** (injecting < 2 yrs): Greece, Hungary (decline: Turkey)

Note: no trend data available for 14 out of 30 countries

EMCDDA 2016; Wiessing etal. Eurosurveillance 2011

HCV prevalence 2006-2014 among ever PWID in Hungary, by primary drug injected



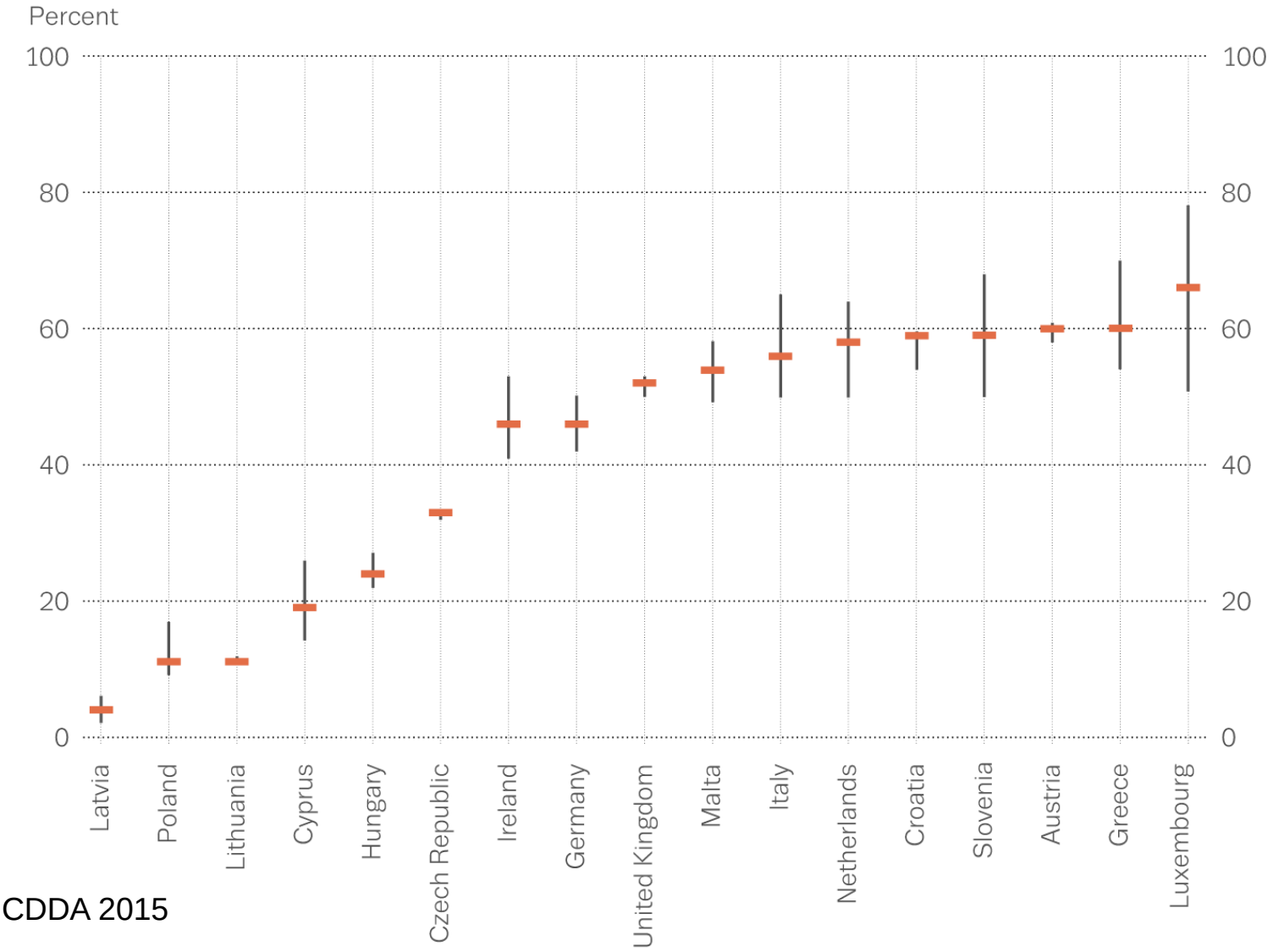
Tarjan A. National Focal Point, 2015

Can we reduce HCV in PWID?

Europe has been successful in reducing new HIV infections among PWID through evidence-based policies and interventions

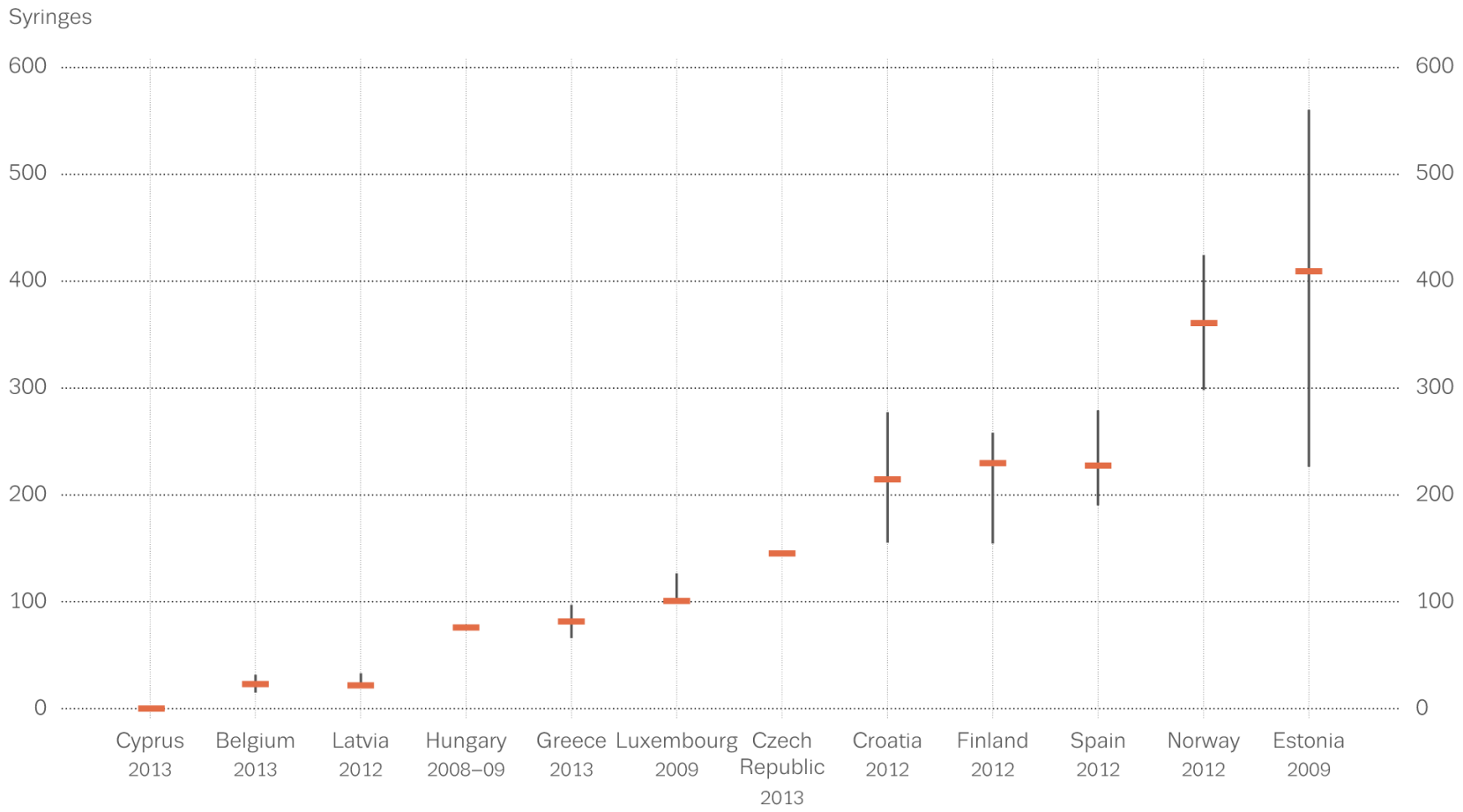
- We know what works: *Joint European guidance: Prevention and control of infectious diseases among people who inject drugs (ECDC/EMCDDA,* 2011).
- Prevention and harm reduction efforts need to be strengthened;
- Models show HCV treatment and harm reduction are complementary, and have the potential to reduce prevalence among PWID and keep it low
- High price of medications is a barrier to widespread scale-up of HCV treatment (2-3 x cost previous generation).

Percentage of problem opioid users receiving opioid substitution treatment (estimate based on 2013 or most recent data)



EMCDDA 2015

Number of syringes provided by specialised programmes per injecting drug user (estimate, based on 2013 or most recent data)



NB: Data displayed as point estimates and uncertainty intervals.

EMCDDA 2015

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PLOS ONE

Hepatitis C Virus Infection Epidemiology among People Who Inject Drugs in Europe: A Systematic Review of Data for Scaling Up Treatment and Prevention

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Abstract

Background: People who inject drugs (PWID) are a key population affected by hepatitis C virus (HCV). Treatment options are improving and may enhance prevention; however access for PWID may be poor. The availability in the literature of information on seven main topic areas (incidence, chronicity, genotypes, HIV co-infection, diagnosis and treatment uptake, and burden of disease) to guide HCV treatment and prevention scale-up for PWID in the 27 countries of the European Union is systematically reviewed.

Methods and Findings: We searched MEDLINE, EMBASE and Cochrane Library for publications between 1 January 2000 and 31 December 2012, with a search strategy of general keywords regarding viral hepatitis, substance abuse and geographic scope, as well as topic-specific keywords. Additional articles were found through structured email consultations with a large European expert network. Data availability was highly variable and important limitations existed in comparability and representativeness. Nine of 27 countries had data on HCV incidence among PWID, which was often high (2.7-66/100 person-

Hepatitis C virus infection epidemiology among people who inject drugs in Europe: a systematic review…

- **Data availability (27 EU countries) highly variable and with limited comparability and representativeness**
- Incidence median 13/100 person-years (range 2.7-66, 9 countries)
- Most common HCV genotypes were G1 and G3 (but G4 may be increasing). The proportion of traditionally ‘difficult to treat’ genotypes (G1+G4) showed large variation (median 53, IQR 43–62)
- 12 countries reported on HCV chronicity (median 72, IQR 64–81)
- 22 countries on HIV prevalence in HCV-infected PWID (median 3.9%, IQR 0.2–28)
- **Undiagnosed infection was high (median 49%, IQR 38–64, 5 countries)**
- **Of those diagnosed, the proportion entering treatment was low (median 9.5%, IQR 3.5–15, 11 countries)**
- Burden of disease where assessed (4 countries), was high and will rise in the next decade.

Wiessing et al. 2014

Drug facilities can help to improve access to HCV testing and treatment

Key-partners

- They reach out to PWID with information and testing offers;
- They may be key for referral to further diagnostics and treatment pathways for those in need.

Drugs agency staff needs ongoing training.

Collaboration with clinical/hepatology services must be improved.

- EASL treatment guidelines: ‘multidisciplinary team setting’ (cooperation hepatologists & addiction specialists)
- Liver treatment services should be re-designed to be drug user-’friendly’ and co-location with specialist drug services for PWID should be considered.

In conclusion (two main messages)

- PWID are a key group, perhaps the largest group, at risk for HCV in Europe. Prevention (harm reduction) needs strengthening

- Clinicians and liver specialists need to collaborate closely with drug specialists and drug services, to improve diagnosis and treatment referral rates of PWID

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Hahné *et al. BMC Infectious Diseases* 2013, **13**:181
http://www.biomedcentral.com/1471-2334/13/181

BMC Infectious Diseases

RESEARCH ARTICLE Open Access

Infection with hepatitis B and C virus in Europe: a systematic review of prevalence and cost-effectiveness of screening

Susan JM Hahné[1*], Irene K Veldhuijzen[2], Lucas Wiessing[4], Tek-Ang Lim[3], Mika Salminen[3] and Marita van de Laar[3]

Abstract

Background: Treatment for chronic hepatitis B virus (HBV) and hepatitis C virus (HCV) infection is improving but not benefiting individuals unaware to be infected. To inform screening policies we assessed (1) the hepatitis B surface antigen (HBsAg) and anti-hepatitis C virus antibody (anti-HCV-Ab) prevalence for 34 European countries; and (2) the cost-effectiveness of screening for chronic HBV and HCV infection.

Methods: We searched peer-reviewed literature for data on HBsAg and anti-HCV-Ab prevalence and cost-effectiveness of screening of the general population and five subgroups, and used data for people who inject drugs (PWID) and blood donors from two European organizations. Of 1759 and 468 papers found in the prevalence and cost-effectiveness searches respectively, we included 124 and 29 papers after assessing their quality. We used decision rules to calculate

Methods Prevalence

- Searched studies prevalence HBsAg, anti-HCV-Ab, 34 countries
- Medline, Embase, and SciSearch for English-language, peer-reviewed literature published between 1 January 2000 and 27 July 2009
- General population, pregnant women, first-time blood donors, MSM, migrants
- Plus data from: Council of Europe (donors), EMCDDA (PWID)
- Extracted: year, country population of the study, the sampling method, laboratory test used, participation rate, number of participants, HBsAg and anti-HCV-Ab results
- Quality assessed: sampling method, standardisation age, sex (gen pop.)
- Estimate of number people in country likely positive

1759 citations, 244 papers (13%) full text, 124 included, 81 used for prevalence estimates

Hahné et al. 2013

General Population

- Only 9/34 countries had information on both diseases
- **Prevalence gradient for both infections increasing from low in north-west to high in south and south-east**

HBsAg

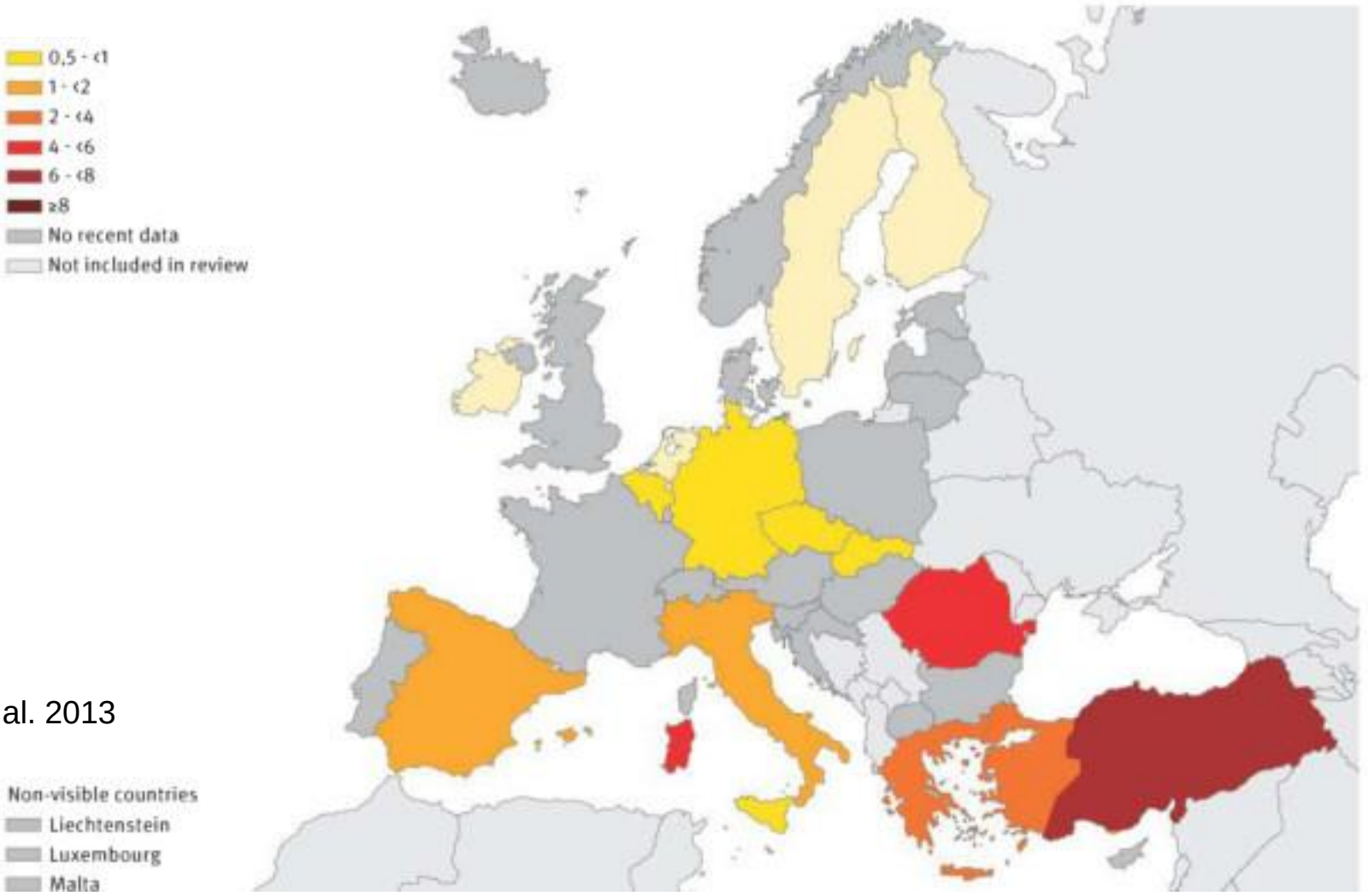
- 13 of the 34 countries
- 0.1% to 5.6%
- N= 3,718,889 in Turkey to 4,466 in Ireland

Anti-HCV-Ab

- 13 of the 34 countries
- 0.4% to 5.2%
- N= 3,122,779 in Italy to 37,025 in Sweden

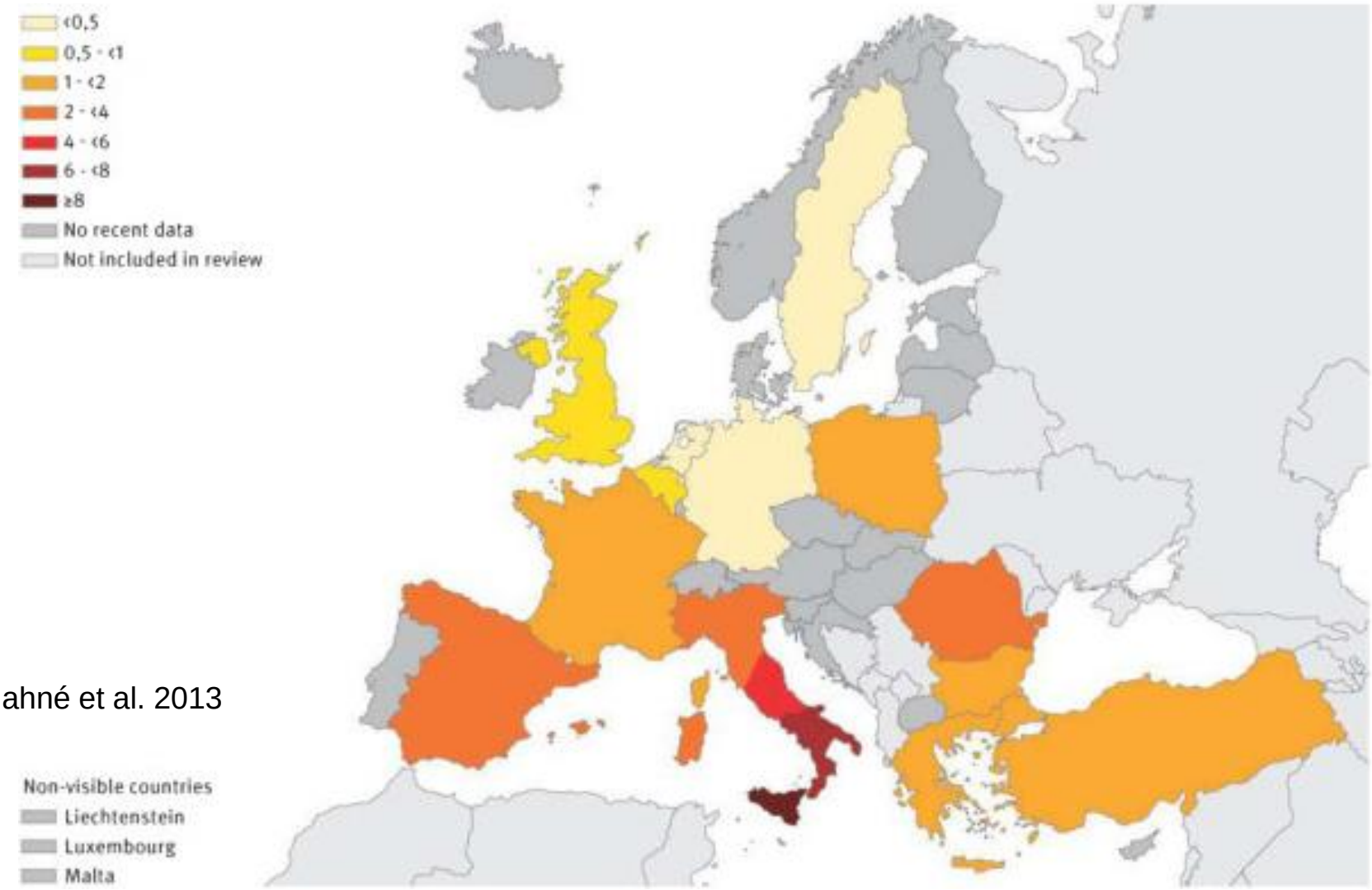
Hahné et al. 2013

Hepatitis B surface antigen (HBsAg) prevalence (%) in the general population by country, Europe, 2000–2009



Hahné et al. 2013

Hepatitis C (anti-HCV-antibody) prevalence (%) in the general population by country, Europe, 2000–2009



Hahné et al. 2013

Migrants

HBV prevalence 6x higher (4 countries) and
HCV prevalence 2x higher (3 countries, not in Italy)
than corresponding prevalence for general population

HBsAg
5 countries
1.0% to 15.4%

anti-HCV-Ab
5 countries,
0% to 23.4%

Hahné et al. 2013

Blood donors

HBV prevalence 3x lower (12 countries) and **HCV prevalence 4x lower** (11 countries) than corresponding prevalence for general population

HBsAg

- 24 countries
- 0.0% to 5.2%

Anti-HCV-Ab

- 23 countries,
- 0.02% to 3.3%

Hahné et al. 2013

Pregnant women

HBV prevalence 3x higher than corresponding prevalence for general population (6/7 countries, except in Spain, due to vaccination adolescents?)

HCV prevalence varied compared to general population

HBsAg

- 11 countries
- 0.1% to 4.4%

anti-HCV-Ab

- 6 countries
- 0% to 1.7%

Hahné et al. 2013

People who inject drugs (PWID)

HBV prevalence 9x higher in than corresponding prevalence for general population (6/8 countries, not in Romania, Ireland)
HCV prevalence 47x higher (13 countries)

HBsAg
21 of the 34 countries
0% to 21.3%

anti-HCV-Ab
29 of the 34 countries
5.3% to 90%

Hahné et al. 2013

Men who have sex with men (MSM)

HBV prevalence 22x higher (2 countries) and **HCV prevalence 3x higher** (1 country) higher than corresponding prevalence for general population

HBsAg

- 3 countries,
- <1% to 4%

anti-HCV-Ab

- 3 countries
- 0.07% to 2.9%

Hahné et al. 2013

Methods Cost-effectiveness

- Cost-effectiveness screening chronic HBV and/or HCV infection
- Medline, Scopus, NHS Economic Evaluation Database (EED)
- Studies English-language, peer-reviewed, between 1 January 2000 and 31 December 2012
- Reporting estimated costs per additional chronic infection identified and/or costs per life year (LY) gained (quality or disability adjusted) – Euro converted
- Extracted: year, country of study, target population, screening scenario, model used, outcome measure(s), monetary value and year, discounting percentage (costs/effects), results, and conclusions

Hahné et al. 2013

Results cost-effectiveness of HBV and/or HCV screening

- 468 publications identified
- full text for 41 publications (9%).
- **29 publications included**
- No paper studied combined screening for HBV and HCV
- 23 used a Markov model (**21 used hypothetical data**)
- 6 studies did not model but presented costs per case identified or infection prevented
- **None used dynamic modelling** (to take account of effects of reducing transmission by lowering viral load through treatment, behaviour change, or HBV vaccination)

Hahné et al. 2013

General population

HBsAg 1 study

- Base case: 35 year old males with a 2% prevalence) found this **was cost-effective** (ICER) €23.966/quality adjusted life year (QALY))

HCV-ab 6 studies

- 2 studies costs per life year gained by screening and subsequent treatment: **both cost-effective**
- 4 USA studies estimated cost per QALY gained: **3 / 4 concluded cost-effective**

Hahné et al. 2013

Antenatal screening

HBsAg 5 studies

- costs per LY gained, costs per case detected and per infant carrier prevented and costs per case detected
- universal screening of all pregnant women, with vaccination of infants born to HBsAg positive mothers
- none considered antiviral treatment
- ICERs ranged from €2,032 to €26,181 per LY gained – **all studies concluded it was cost-effective**

HCV-ab 1 study

- Universal antenatal HCV screening and treatment of HCV infection with or without elective caesarean delivery
- **Neither scenario was considered cost-effective**

Hahné et al. 2013

People who inject drugs (PWID)

HBsAg – no studies found

HCV 10 studies

- HCV screening and treatment
- 7 / 10 reported estimated costs per QALY
- studies varied widely, including different screening settings, treatments considered, and discount rates
- Nevertheless, **all 7 studies concluded that HCV screening of PWID was likely to be cost-effective**
- ICERs €3.328 - €41,874 per QALY

Hahné et al. 2013

Discussion cost-effectiveness general population

- “The only study found that considered general population screening for HBsAg, suggested this would be cost-effective in populations with a prevalence above 0.3%. This includes nearly all European countries. However, the study considered only men, included no costs for the screening programme (except for a blood test and consultation) and made unrealistic assumptions regarding compliance with treatment”
- “Screening for anti-HCV: recent studies mainly from the USA suggest this is cost-effective, particularly when targeted at high-prevalence birth cohorts, the so-called baby-boomers”
- CDC has recommended these cohorts to be offered screening
- More evidence on general population HCV screening is needed for European countries, especially for those with a relatively high prevalence.

Hahné et al. 2013

Limitations

Comparability prevalence estimates

- Different laboratory tests used
- Prevalence estimates not standardised (age, sex)
- Definition and sampling of the high risk population groups differ

Comparability cost-effectiveness studies

- Methods, assumptions, and quality varied between studies (guidance needed as existing for economic analysis vaccination)
- Markov models can overestimate the effects of screening and treatment by being too optimistic on life expectancy (PWID, HIV)
- Markov models do not allow for the effect of reduced transmission by lowering viral load (dynamic models needed)

Hahné et al. 2013

Conclusions

- Available data suggest a wide variation in prevalence of chronic HBV and HCV infection between countries in Europe
- Countries in the south and east of the European Union and in Turkey have a much higher prevalence for chronic HBV and HCV than countries in northwestern Europe
- For the majority of countries data on the general population prevalence of HBV or HCV are lacking
- Within countries, the prevalence of HBsAg and anti-HCV-Ab among PWID, MSM, and migrants is generally much higher than the general population prevalence

Hahné et al. 2013

Conclusions (2)

- Considerable health benefits can be gained cost-effectively by anti-HCV-Ab screening of PWID
- HBsAg screening of pregnant women and migrants is also very likely cost-effective
- Appraisals of the evidence for screening the general population in mid- and highly endemic countries in Europe and of combined HBV/HCV screening are needed
- Future cost-effectiveness analyses may need to take the effect of antiviral treatment on preventing HBV and HCV transmission into account

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Thank you for your attention

Acknowledgements

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