A national multidisciplinary healthcare network for treatment of hepatitis C in PWID in Slovenia

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Disclosure

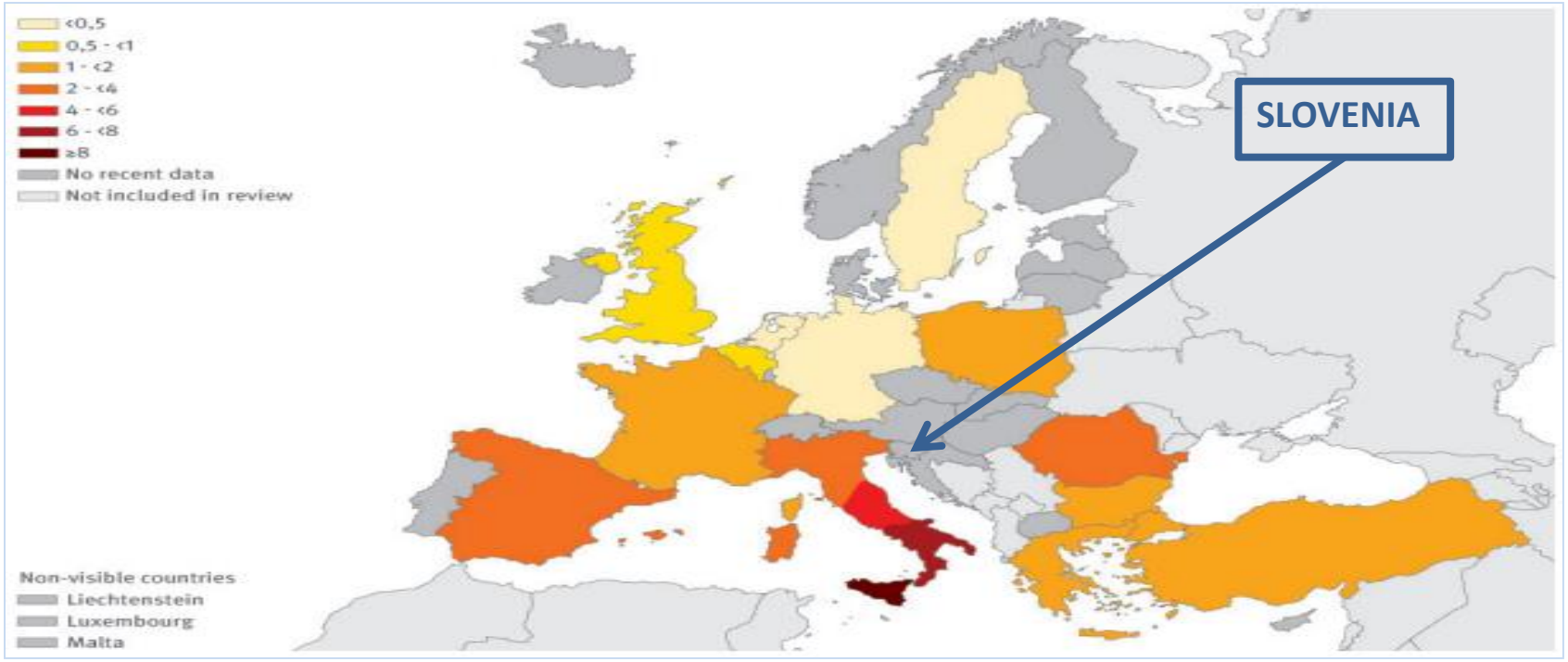
Within the last 36 months:

- Lecturer: Abbvie, Bayer, Boehringer-Ingelheim, Janssen, Merck, Roche
- Manuscript preparation: Abbvie, Gilead, Janssen, Merck, Roche
- Travel/accommodational meeting expences: Abbvie, Gilead, Janssen, Merck, Roche

No conflict of interest regarding this presentation

HCV prevalence in the general population of Europe

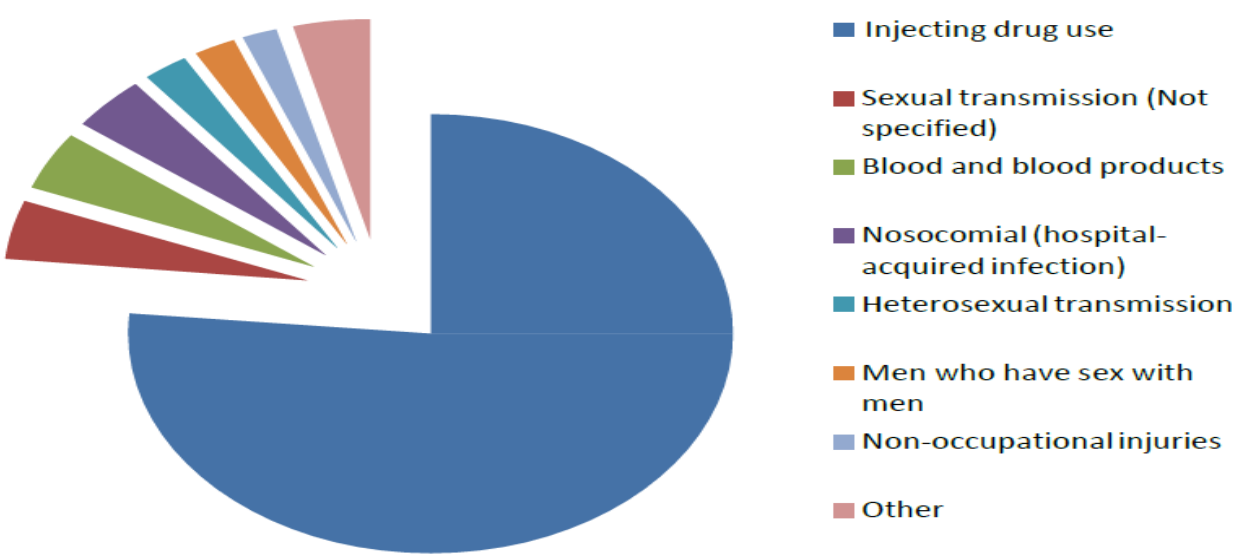
- WHO Evrope: **15 million** HCV RNA positive
- Anti-HCV prevalence in general population: **0.4 – 5.2%**
- Deaths related to HCV infection**: 86 000 / year**



ECDC Technical Report. Hepatitis B and C in the EU neighbourhood: prevalence, burden of disease and screening policies. 2010;1–26
Hope VD et al. Epidemiol Infect. 2014;142:270–286

Current treansmission route of HCV cases in EU/EEA countries, 2012

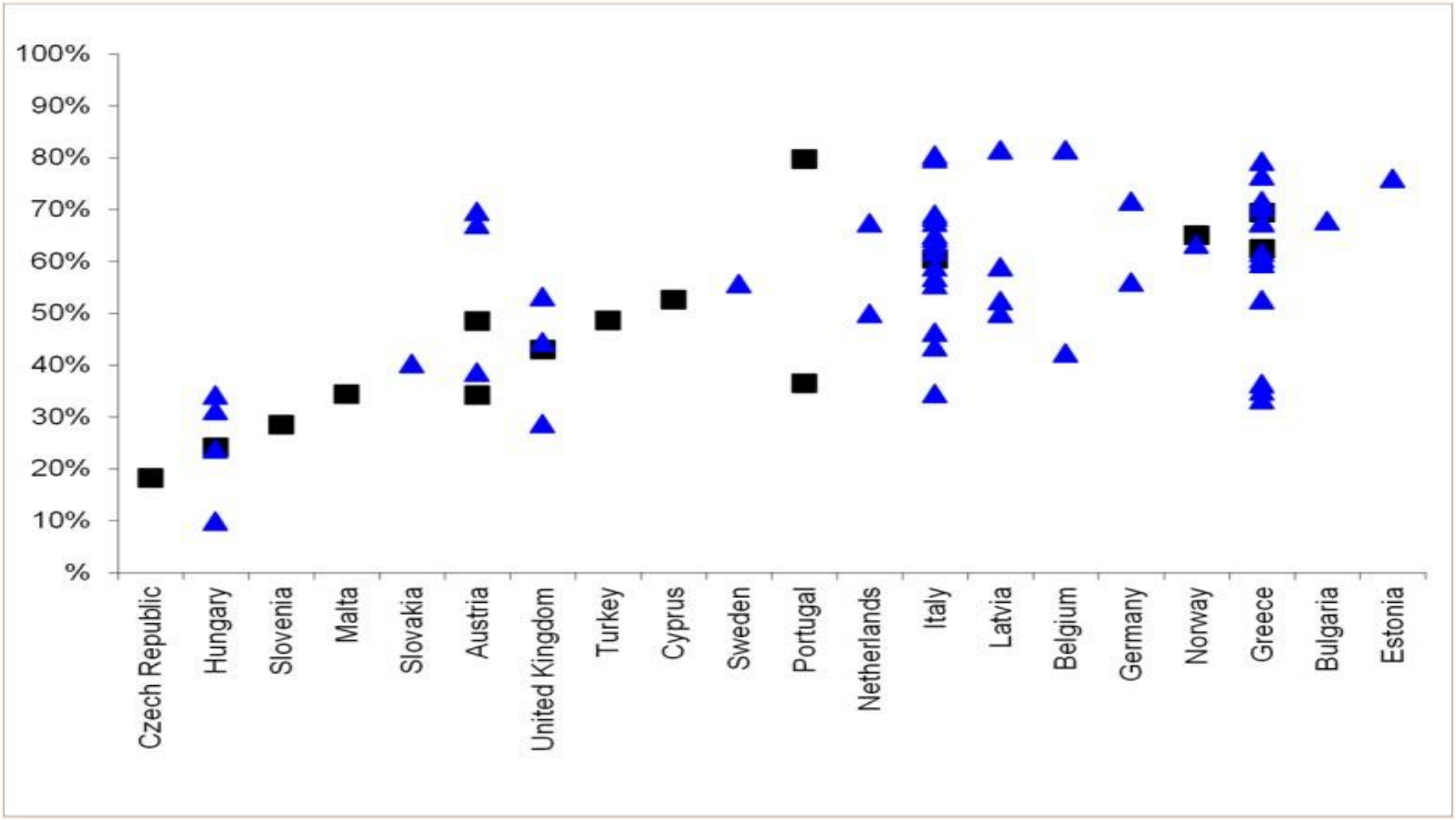
- In 2015: new infections **not** common in general population
  major problem people who inject drugs (PWID)



Route of transmission: injecting drug use 78.1%

Terrault NA, et al. Hepatology 2013;57:881–9
Thomas SL, et al. Int J Epidemiol 1998;27:108–17
Prati et al, J Hepatol 45 (2006) 607-616
Shepard CW, et al. Lancet Infect Dis 2005;5:558–67

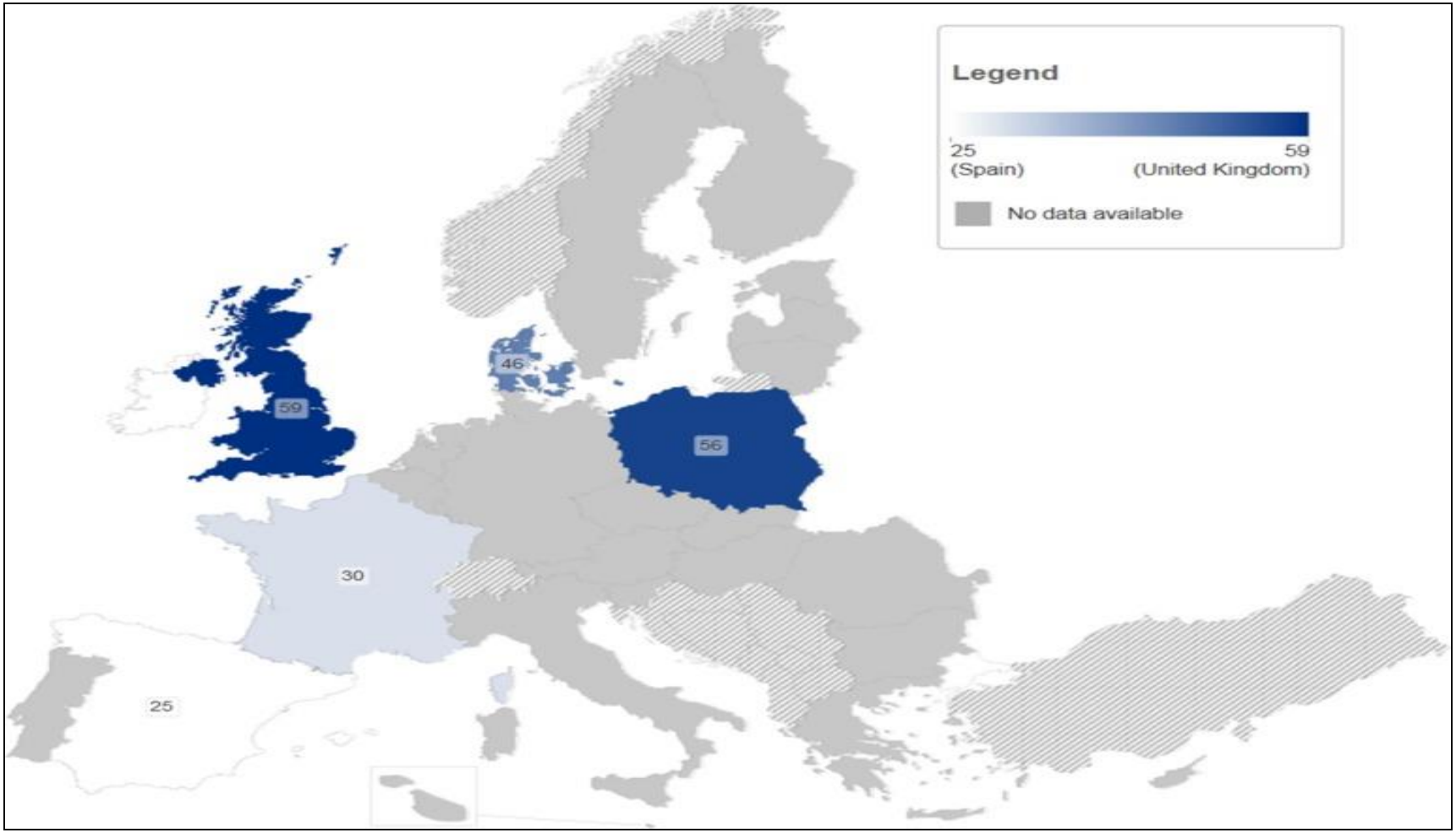
HCV seroprevalence among PWID in the EU 2006–2011



black squares are data with national coverage, blue triangles are data with sub-national (local, regional) coverage.

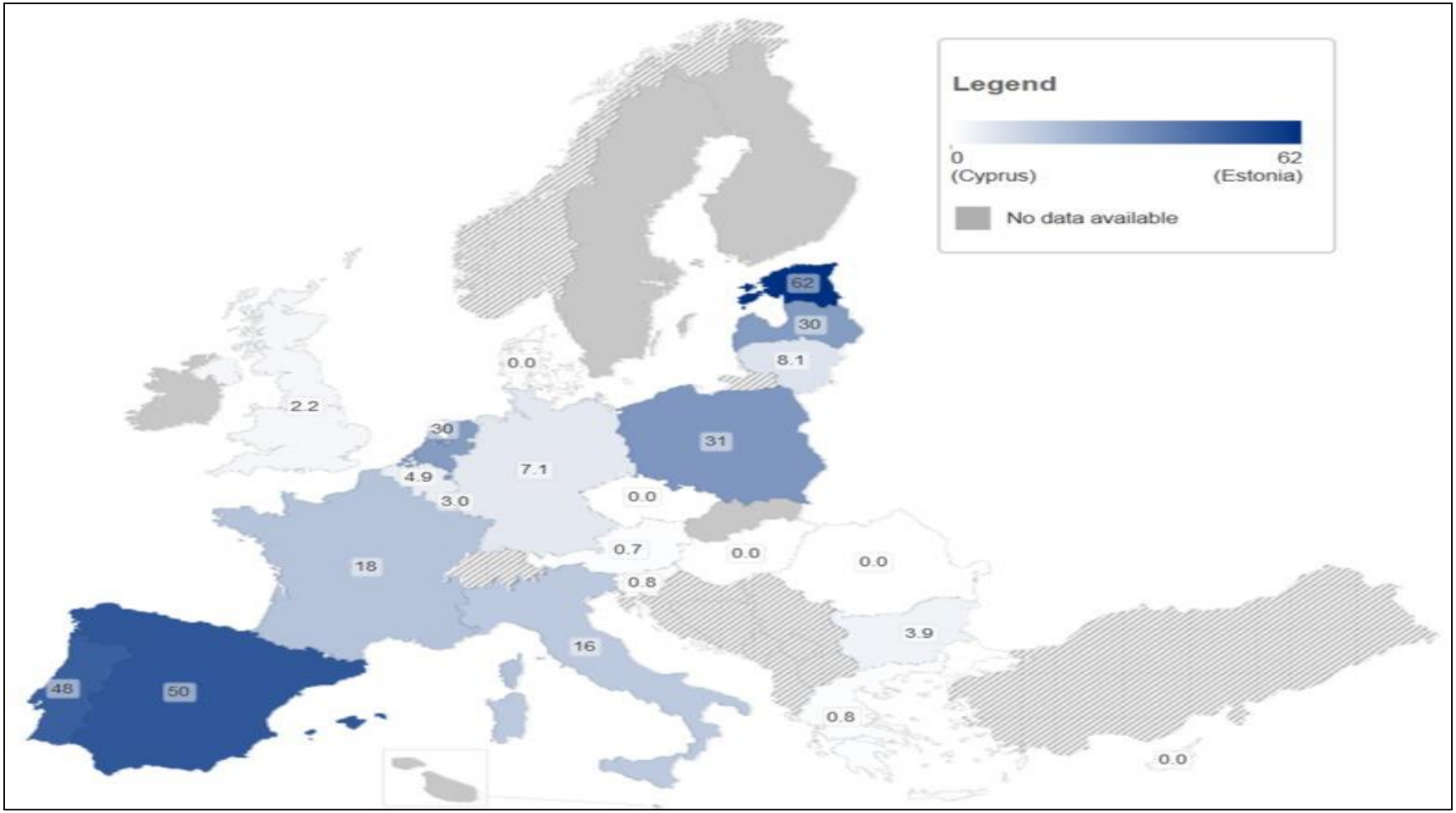
EMCDDA, 2013 (http://www.emcdda.europa.eu/stats13#inf:displayTables

Proportion (%) of HCV undiagnosed PWID in Europe



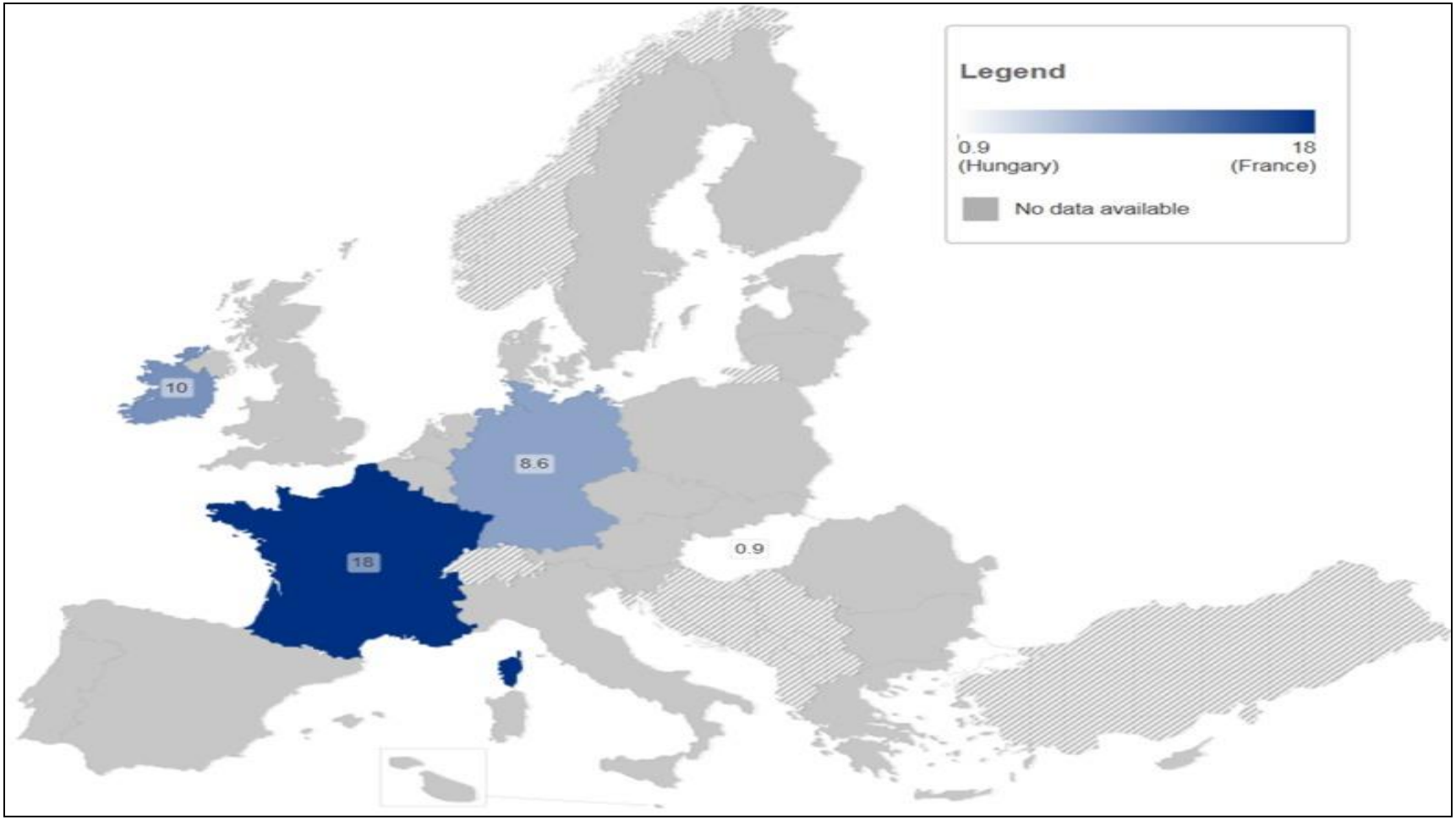
Wiessing L et al. PLoS One 2014; 9(7):e103345

Proportion (%) of PWID co-infected with HCV and HIV



Wiessing L et al. PLoS One 2014; 9(7):e103345.

Proportion (%) of HCV-infected PWID in Europe entering antiviral treatment in observational studies in non-clinical settings

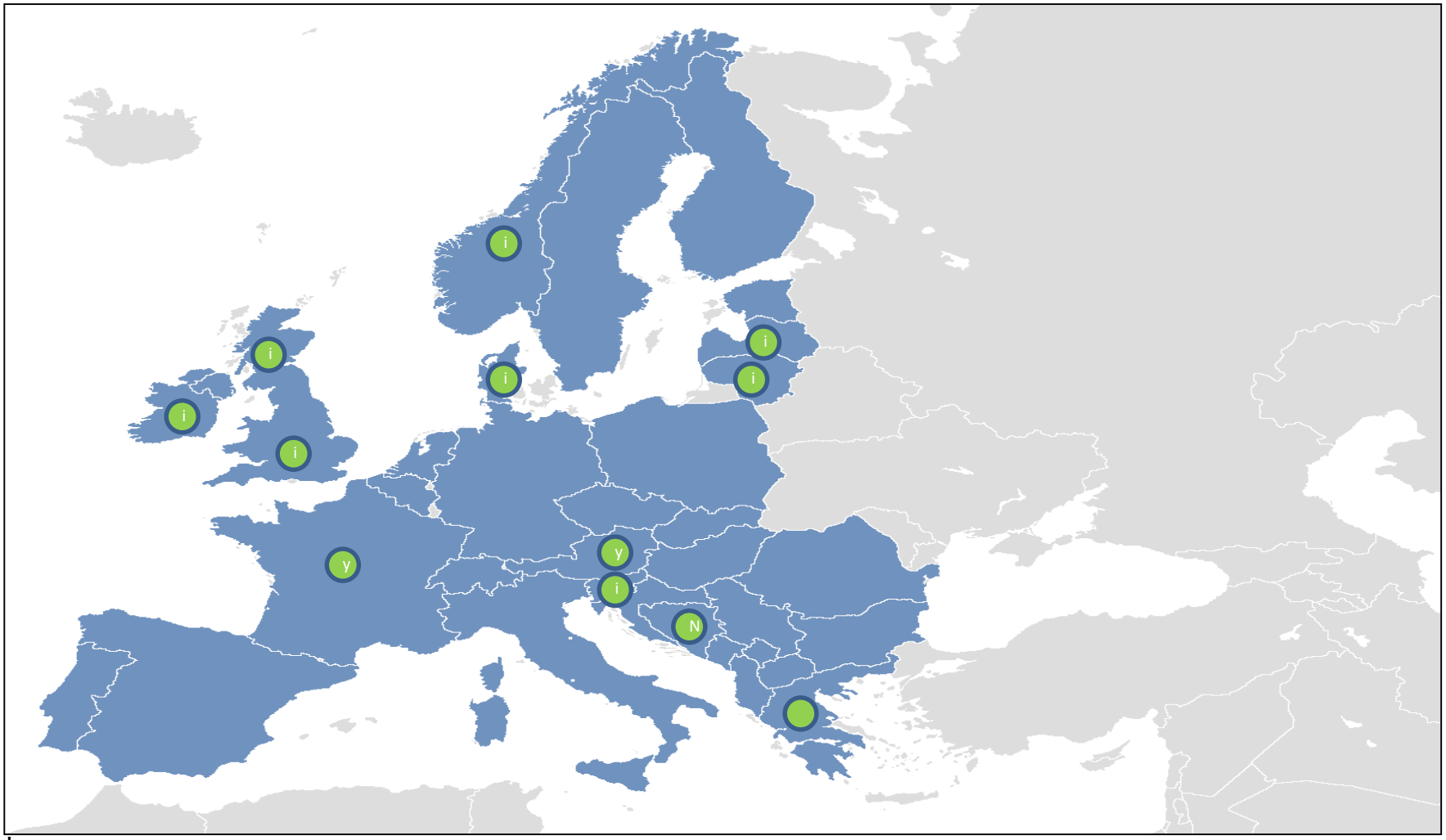


Wiessing L et al. PLoS One 2014; 9(7):e103345.

National level activities on HCV management

A survey of 33 European countries

National strategy , 12 (11 PWID)



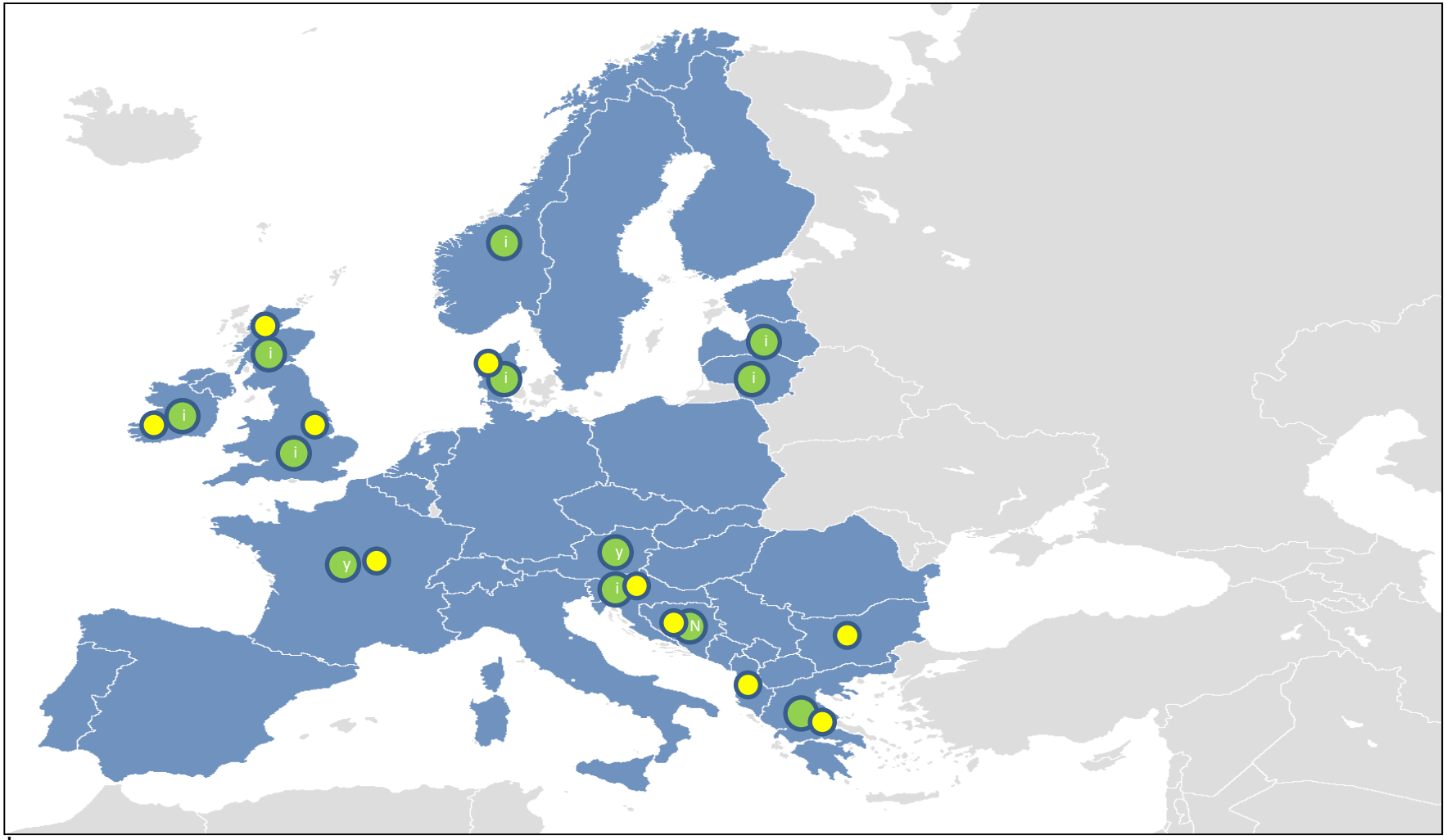
*Scotland was treated separately from UK

Maticic M et al. BMC Infect Dis 2014; 14(Suppl 6): 514-23.

National level activities on HCV management

A survey of 33 European countries

National strategy, 12 (7 PWID) **National action plan, 10 (7 PWID)**



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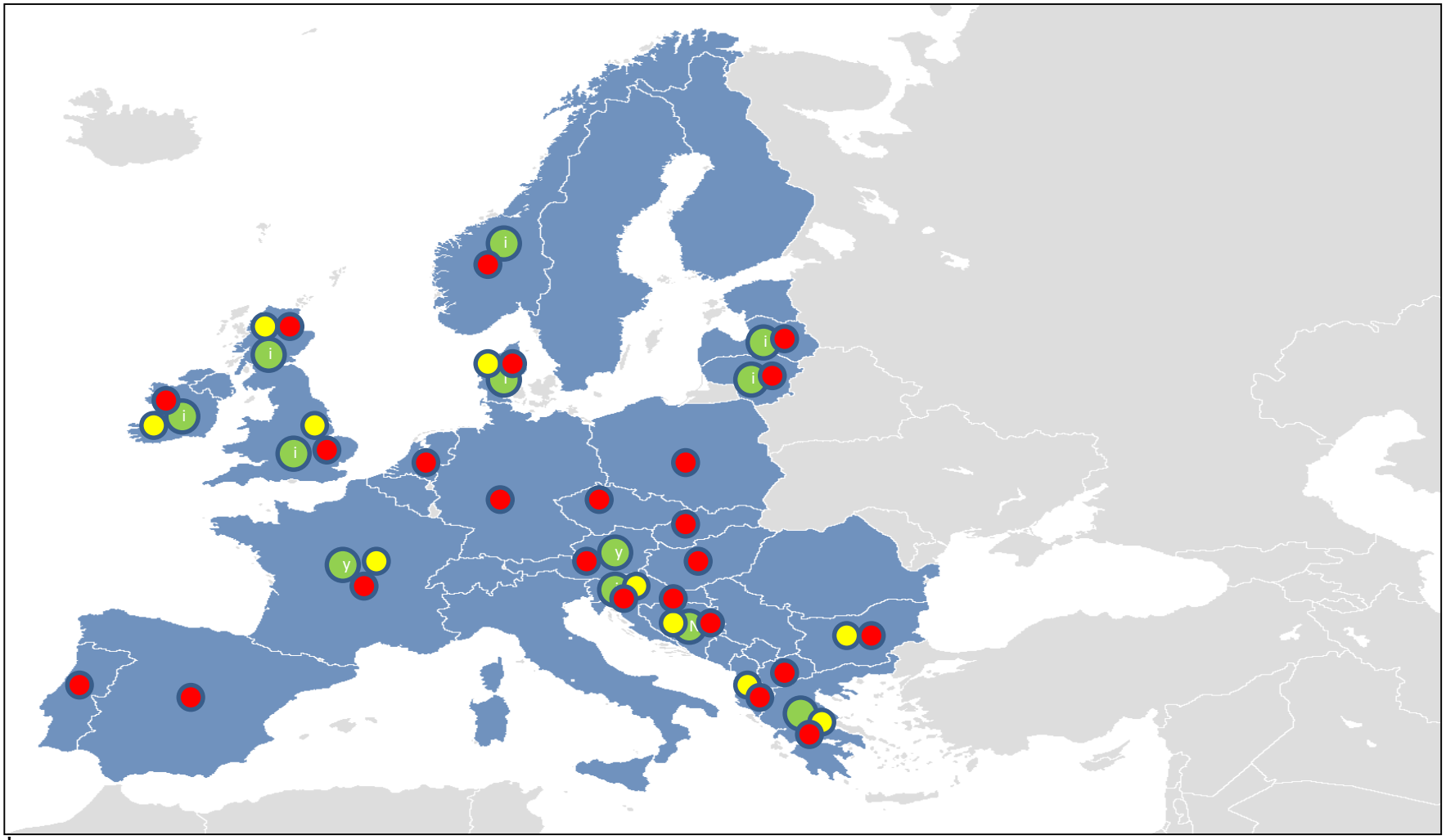
National level activities on HCV management

A survey of 33 European countries

National strategy, 12 (**10 PWID**) National action plan, 10 (**7 PWID**) National treatment guidelines, 24 (**20 PWID**)



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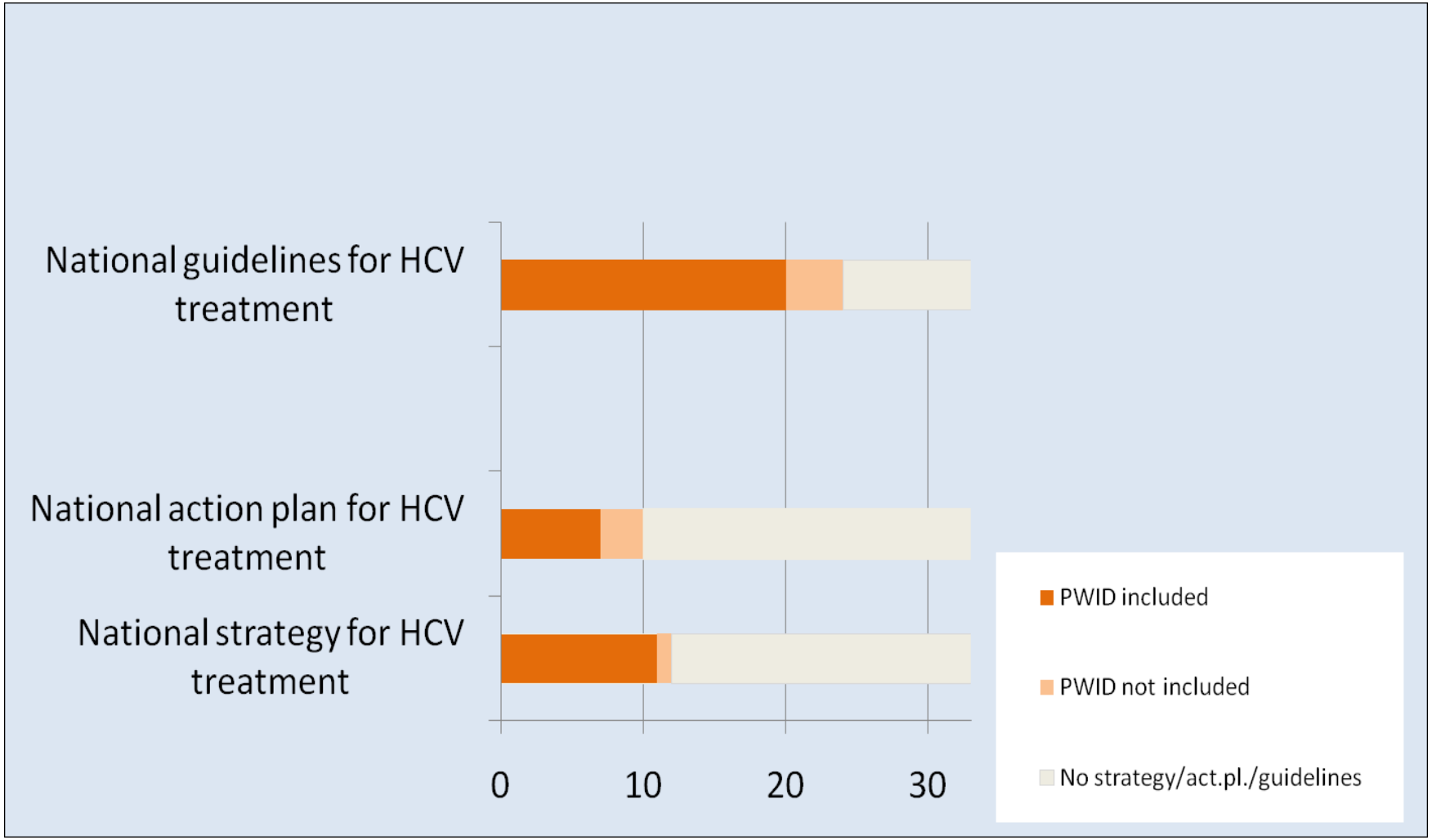


Maticic M, et al. BMC Infect Dis 2014; 14(Suppl 6): 514-23.

SLOVENIA

Gross national income per capita (2012):
27,240 $
Life expectancy at birth m/f (2011):
77 / 83 years
Probability of dying under five (2012):
3 / 100 000
Probability of dying between 15 and 60 years m/f (2011):
118/51 / 1 000
Total expenditure on health/capita (2011):
2,519 Intl $
Total expenditure on health as (2011):
9.1 % GDP

Inhabitants:
2 million

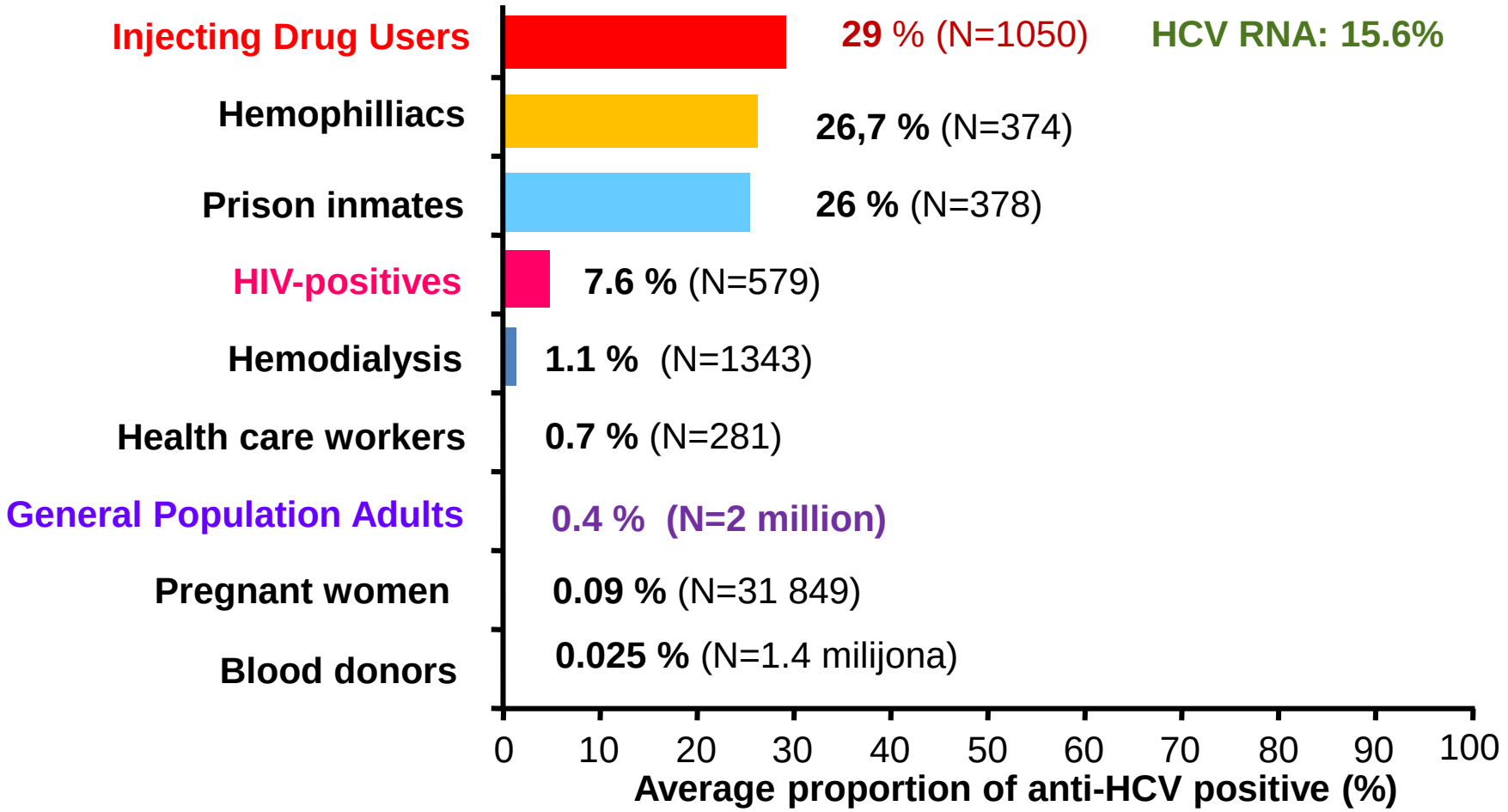
Drug users: est. 10 000

PWID: est. 6 000

http://www.who.int/countries/svn/en/ http://ecdc.europa.eu/en/publications/Publications/101012TERHepBandCsurvey.pdf
Hope VD et al. Epidemiol Infect. 2014;142:270–286. Seme K et al. J Med Virol 2009; 81: 634-9. Razavi H et al. J Viral Hep 2015 (in press).

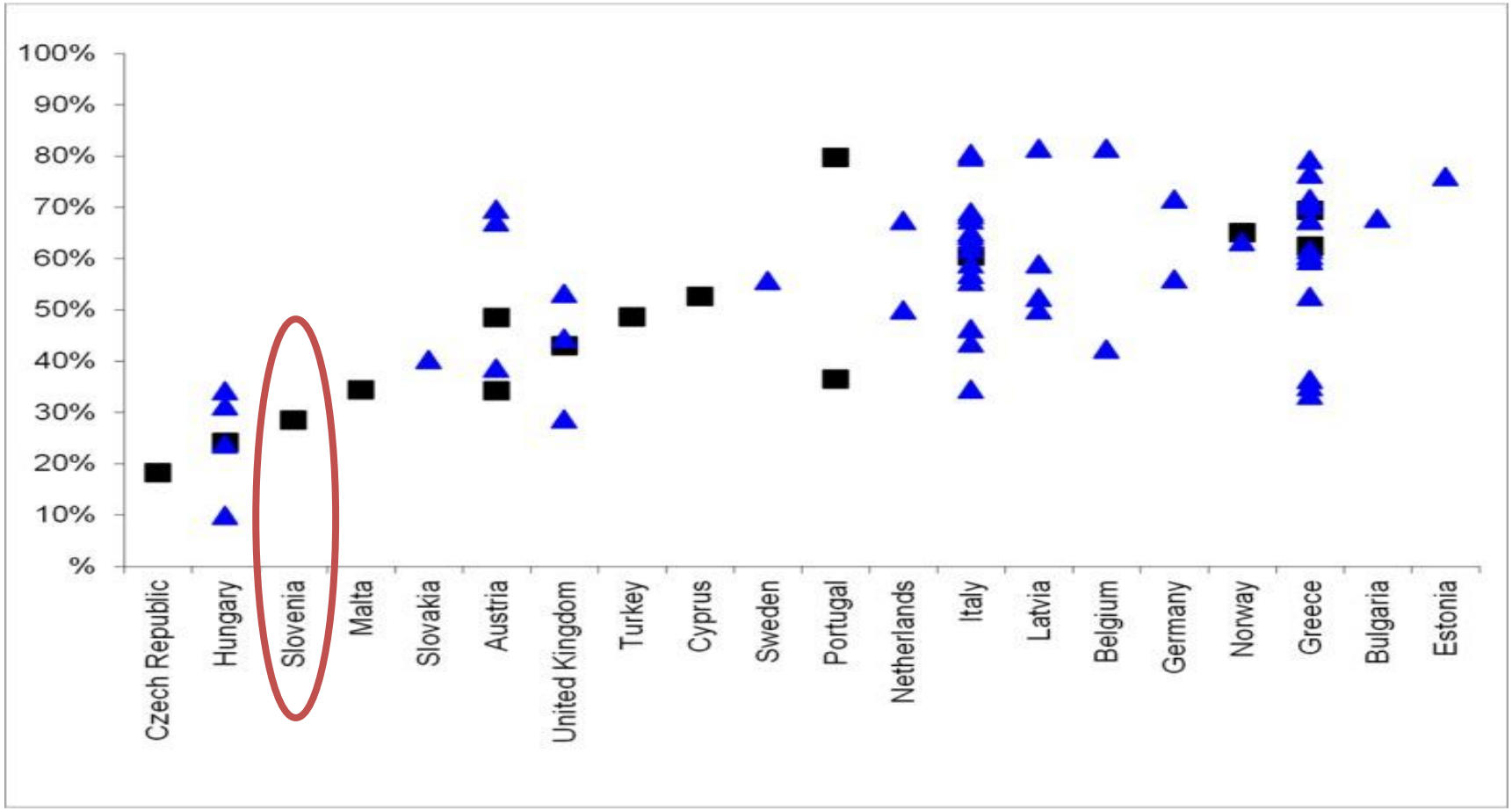
SLOVENIA 2000-2014

Anti-HCV prevalence by selected groups



Maticic M. JEADV 2008; Kastelic A et al. 2nd Slovenian Conference on HCV Infection in IVDU, March 2007; Baklan Z, et al. Wien Klin Wochenschr 2004; 116(2): 5-7. http://www.emcdda.europa.eu/publications/country-overviews/si; Kopilovic B et al. Euro Surveillo 2015; 20(22): pii=2144

HCV seroprevalence among PWID in the EU 2006–2011



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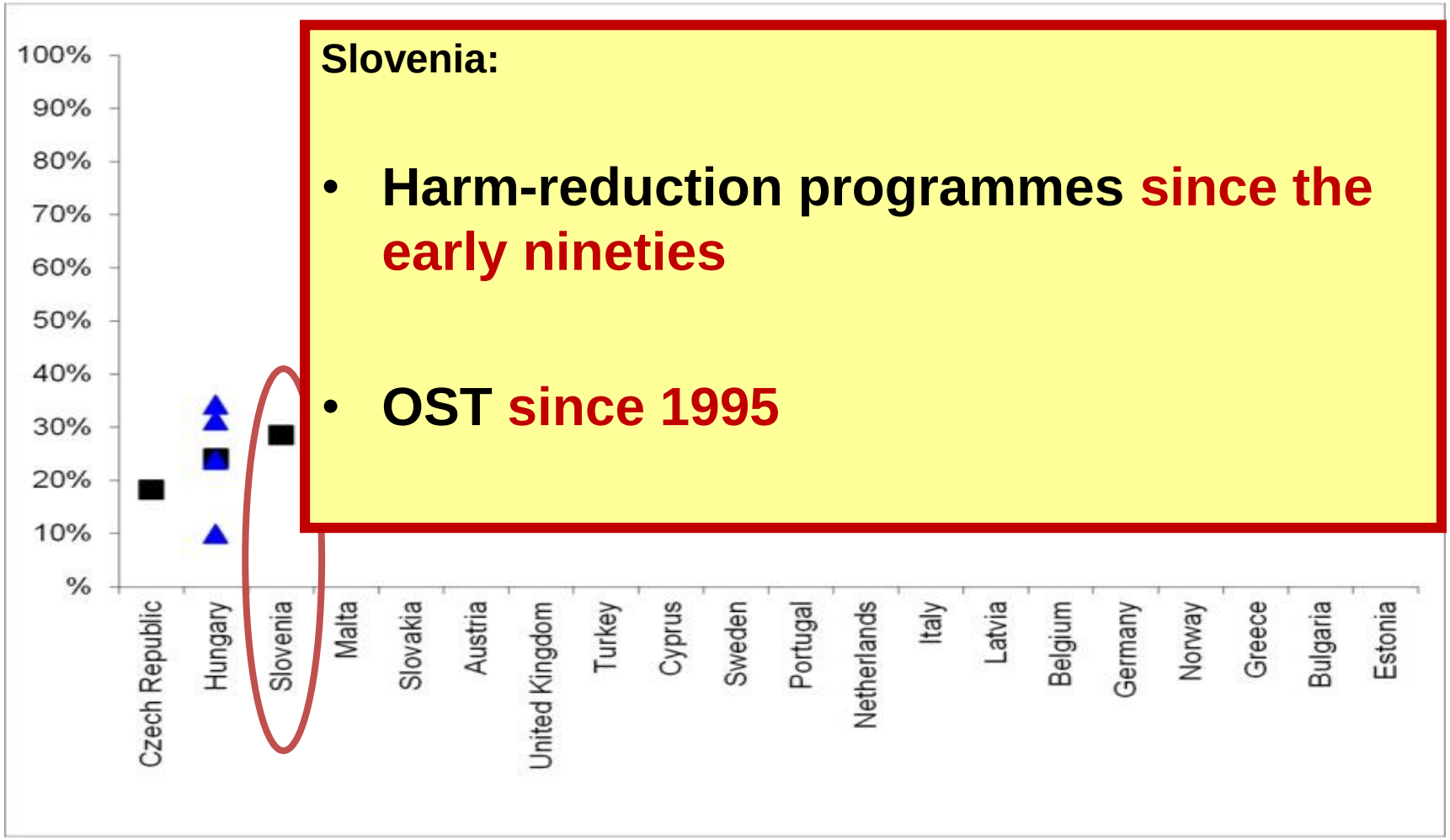


Slovenia:

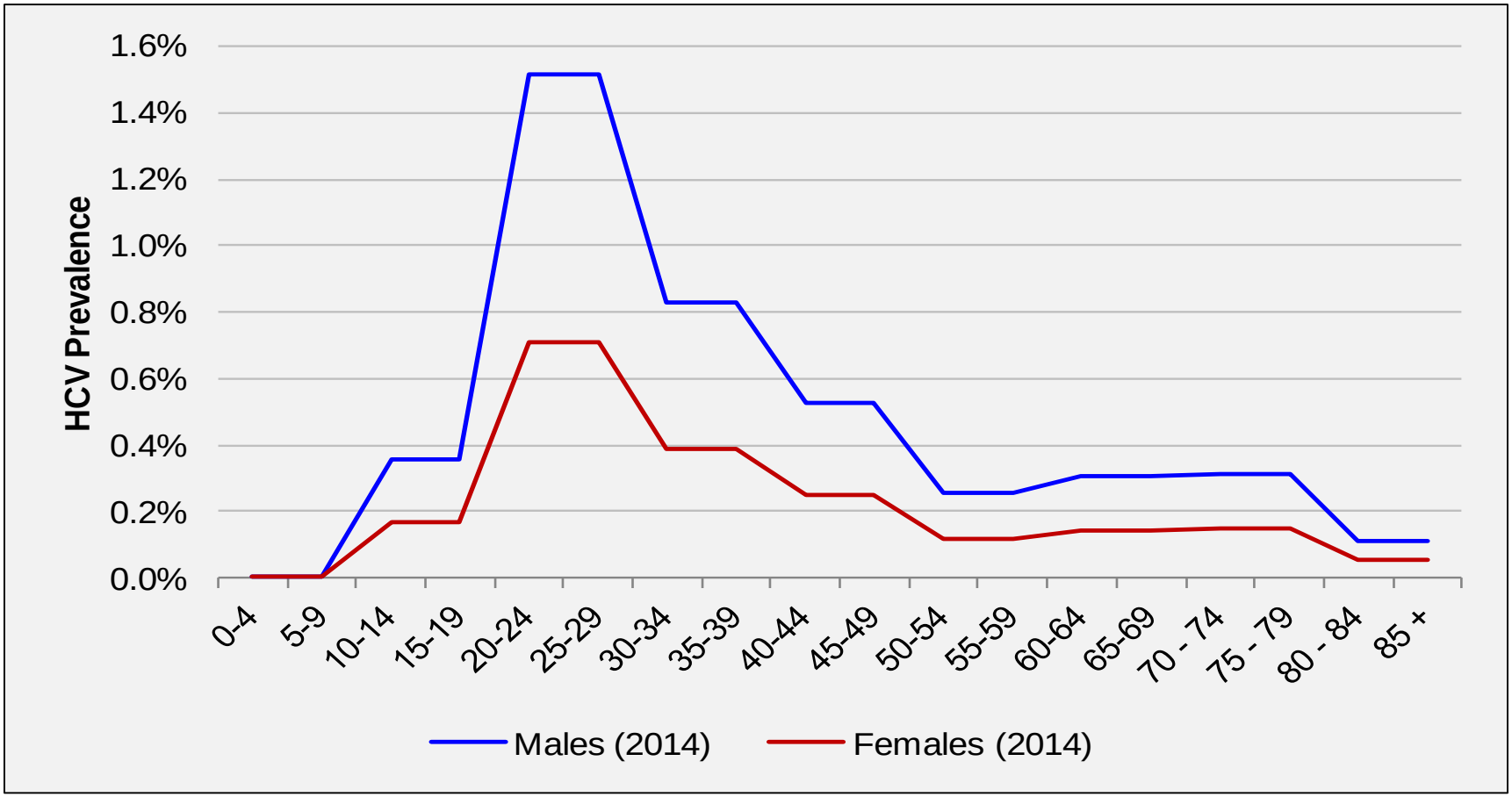
- **Harm-reduction programmes since the early nineties**
- **OST since 1995**

Kastelic A, Kostnapfel T. ZdravVestn 2010, 79: 575-81.
EMCDDA, 2013. http://www.emcdda.europa.eu/stats13#inf:displayTables

SLOVENIA 1993-2007

Anti- HCV seroprevalence according to gender and age

N=1504

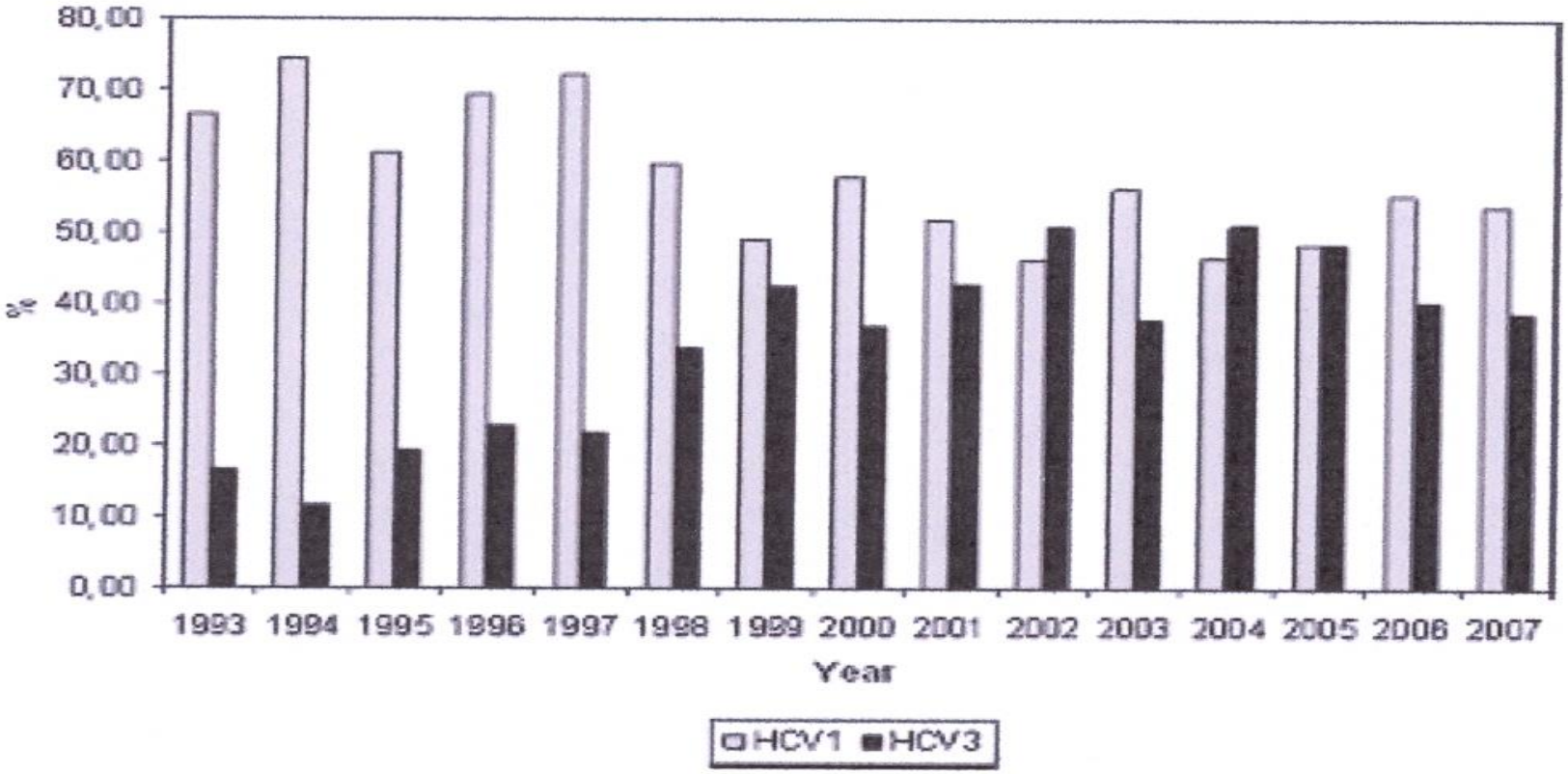


Seme K et al. J Med Virol 2009; 81: 634-9.

SLOVENIA 1993-2007

Dynamics of HCV-1 and HCV-3 genotypes

N=1504



Seme K et al. J Med Virol 2009; 81: 634-9.

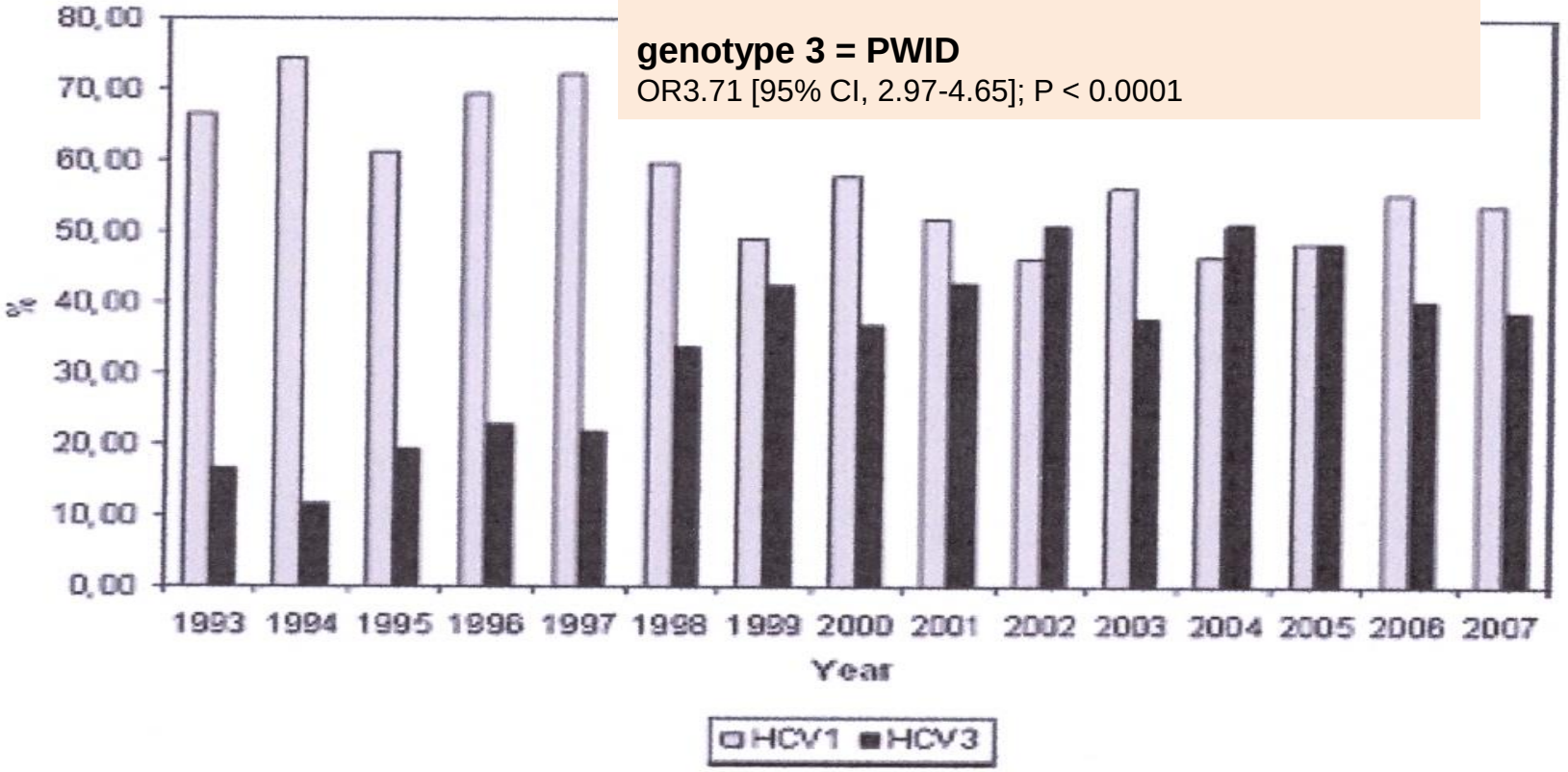
SLOVENIA 1993-2007

Dynamics of HCV-1 and HCV-3 genotypes

N=1504

genotype 1 = blood transfusion before 1992
OR, 3.28 [95% CI, 2.18-4.95]; P < 0.0001

genotype 3 = PWID
OR3.71 [95% CI, 2.97-4.65]; P < 0.0001



Seme K et al. J Med Virol 2009; 81: 634-9.

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Management of hepatitis C

An integrated approach

- **National Institute of Public Health of Republic Slovenia**

  (Ministry of Health: Law on communicable diseases)

  Surveillance of communicable diseases

  Strategies for reducing transmission and harm (drug use)

- **National Viral Hepatitis Expert Group**

  (Interdisciplinary team of highly involved proffessionals, self-founded in 1997)

  National strategy

  Action plan

  Consensus clinical guidelines

http://www.ivz.si/gradiva_nalezljive_bolezni

Matičič M et al. Isis 1999; 8: 49-51.
Matičič M, Kastelic A. Zdrav Vestn 2009; 78: 529-39.

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National Viral Hepatitis Expert Group

National strategy for complex management of HCV infection

- **Testing**: - special populations: case finding, surveillance
  - general population: **voluntary free-of-charge testing** (**routine** + campaigns)

- **Treatment**: - availability, access, process, follow-up
  - systematical **analysis** of treatment efficacy and safety (since 1997)

- National consensus **guidelines** on management of HCV infected

- **Research**
- **Education** (proffessionals, general population)
- **Mass media campaigns** (World Hepatitis Day, etc.)

Matičič M et al. Isis 1999; 8: 49-51. Matičič M et al. Zdrav Vestn 2010; 79: 599-608. Matičič M, Kastelic A. Zdrav Vestn 2009; 78: 529-39.

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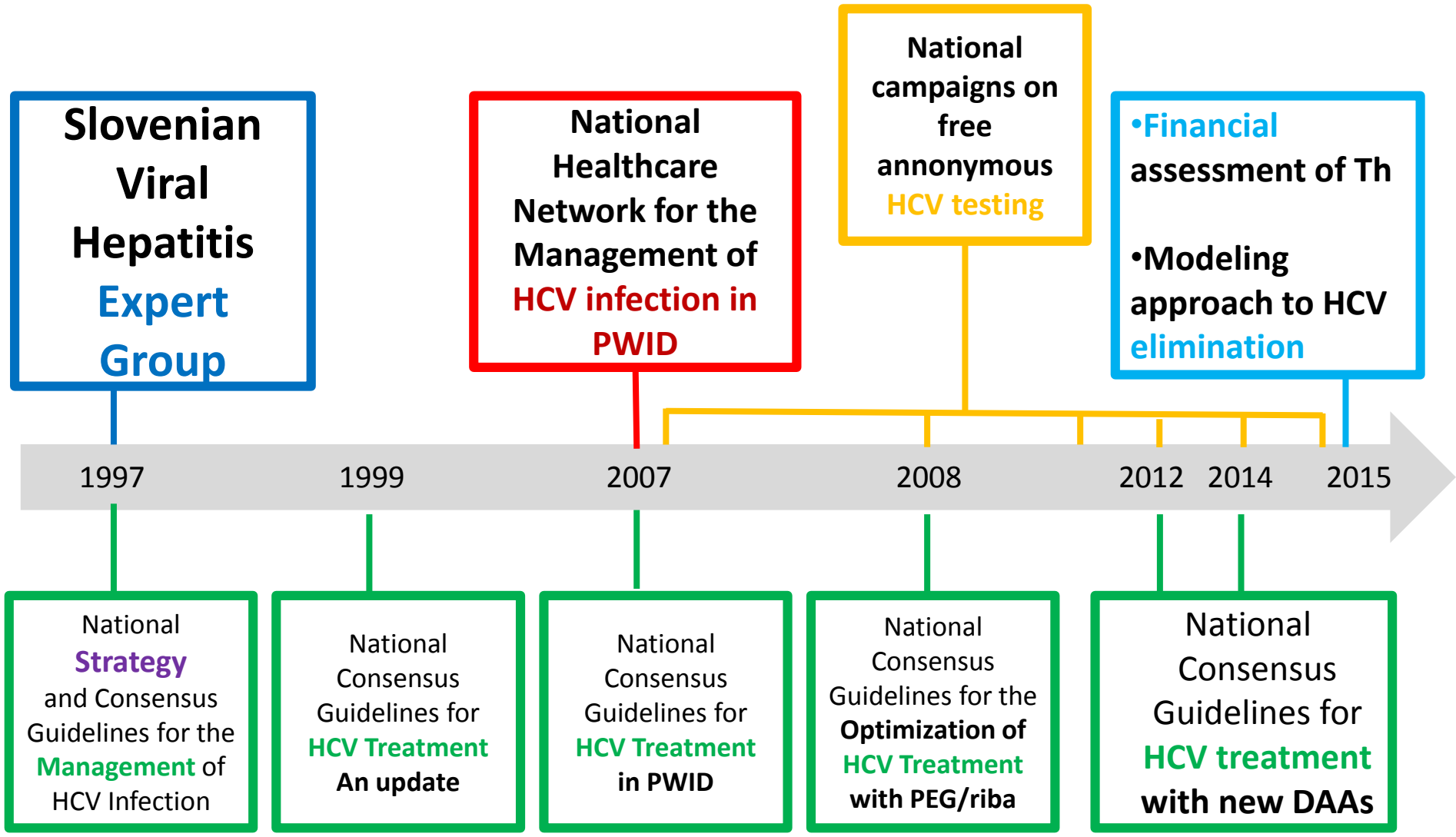
Management of HCV infection 1997 - 2015



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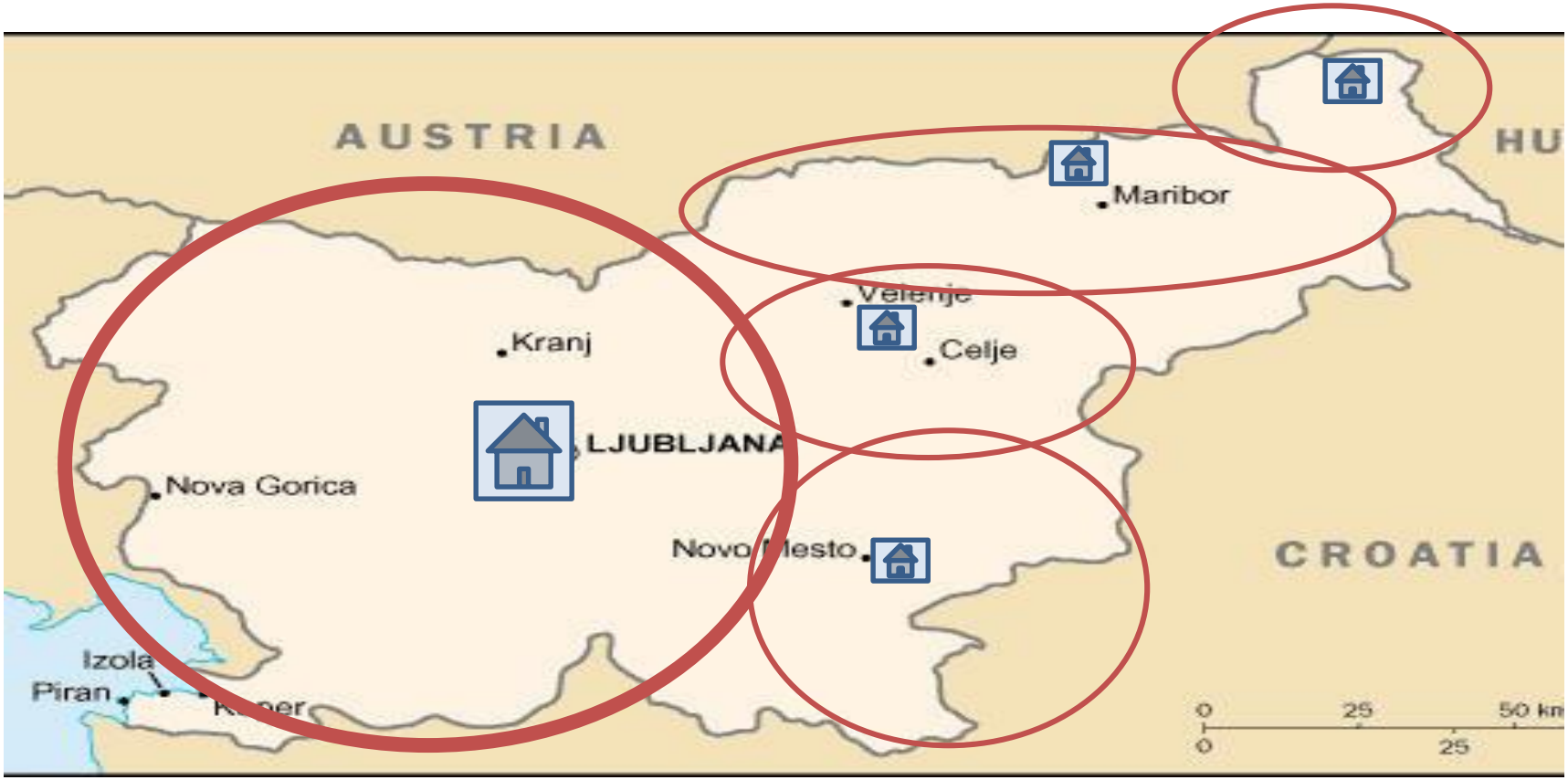
Clinical management of patients with HCV infection

- 5 clinical centers for viral hepatitis: infectologists, (hepatologists)



Refferential:
Clinic for Infectious Diseases nad Februle Illnesses, University Medical Centre Ljubljana

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Clinical management of patients with HCV infection

THERAPY for HCV:

- IFN (1993)
- IFN/RBV (1999)
- PEG/RBV (2001)
- BOC/TVP (2012)
- SIMEPREVIR (2014)
- SOFOSBUVIR (2015)
- 3D (2015)
- SOFOSBUVIR+LEDIPASVIR (2015)

- Liver transplantation (since 1998)

FINNANCING of HBV&HCV management :

- Public Health Insurance System:
  Nominated specialists to prescribe P/R, DAAs
  National consensus guidelines for the management of HCV infection

- **National register**: all the HCV treated patients (since 1997)

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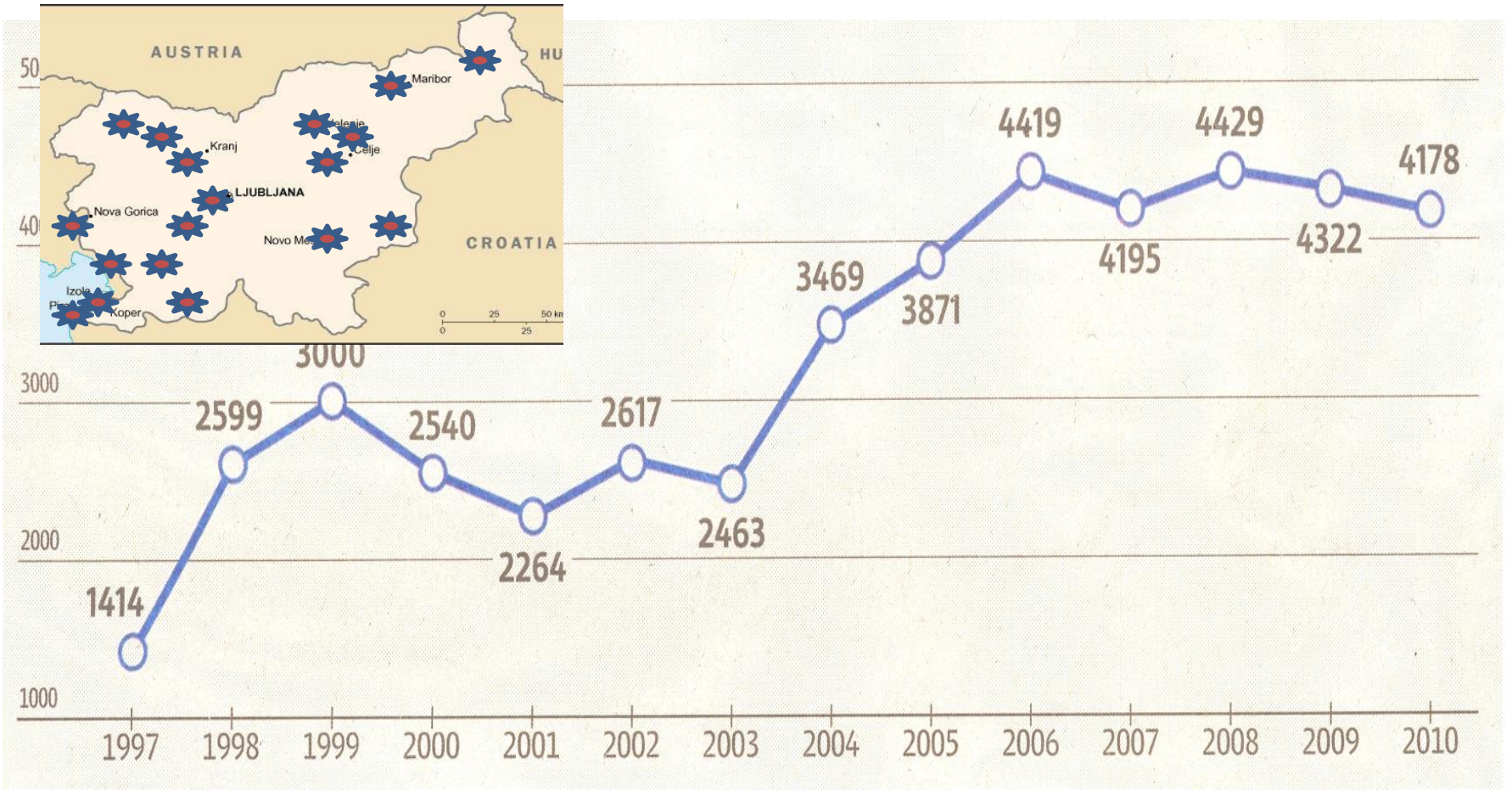
Centres for Prevention and Treatment of Drug Addiction

Number of PWID managed per year



Coordination of Centers for Prevention and Treatment of Illict Drug Abuse, Slovenia 2011.

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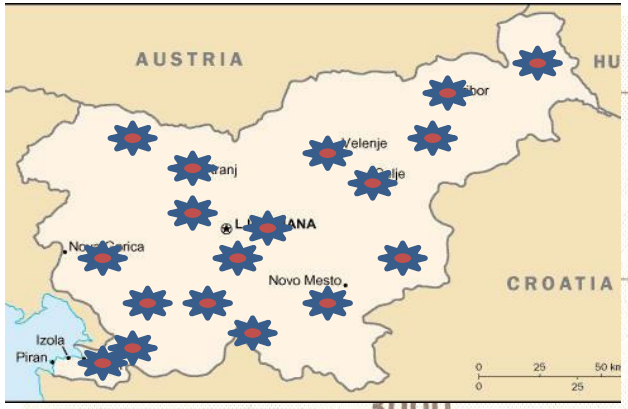
Centres for Prevention and Treatment of Drug Addiction

Number of PWID managed per year

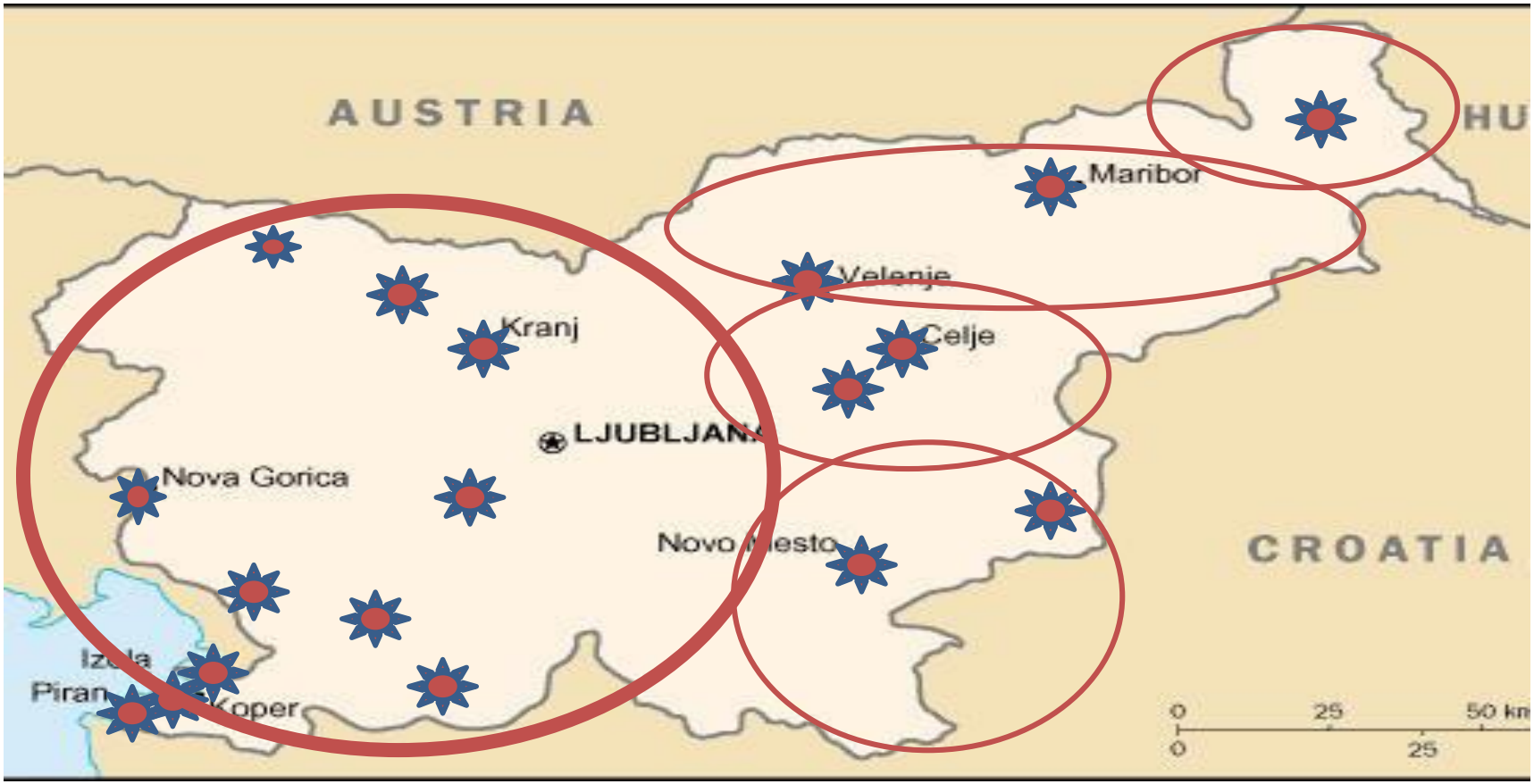


Coordination of Centers for Prevention and Treatment of Illict Drug Abuse, Slovenia 2011.
Kastelic A et al. 2nd Slovenian Conference on HCV Infection in IVDU, Ljubljana 2007

SLOVENIA 2007

National healthcare network for managing HCV in PWID

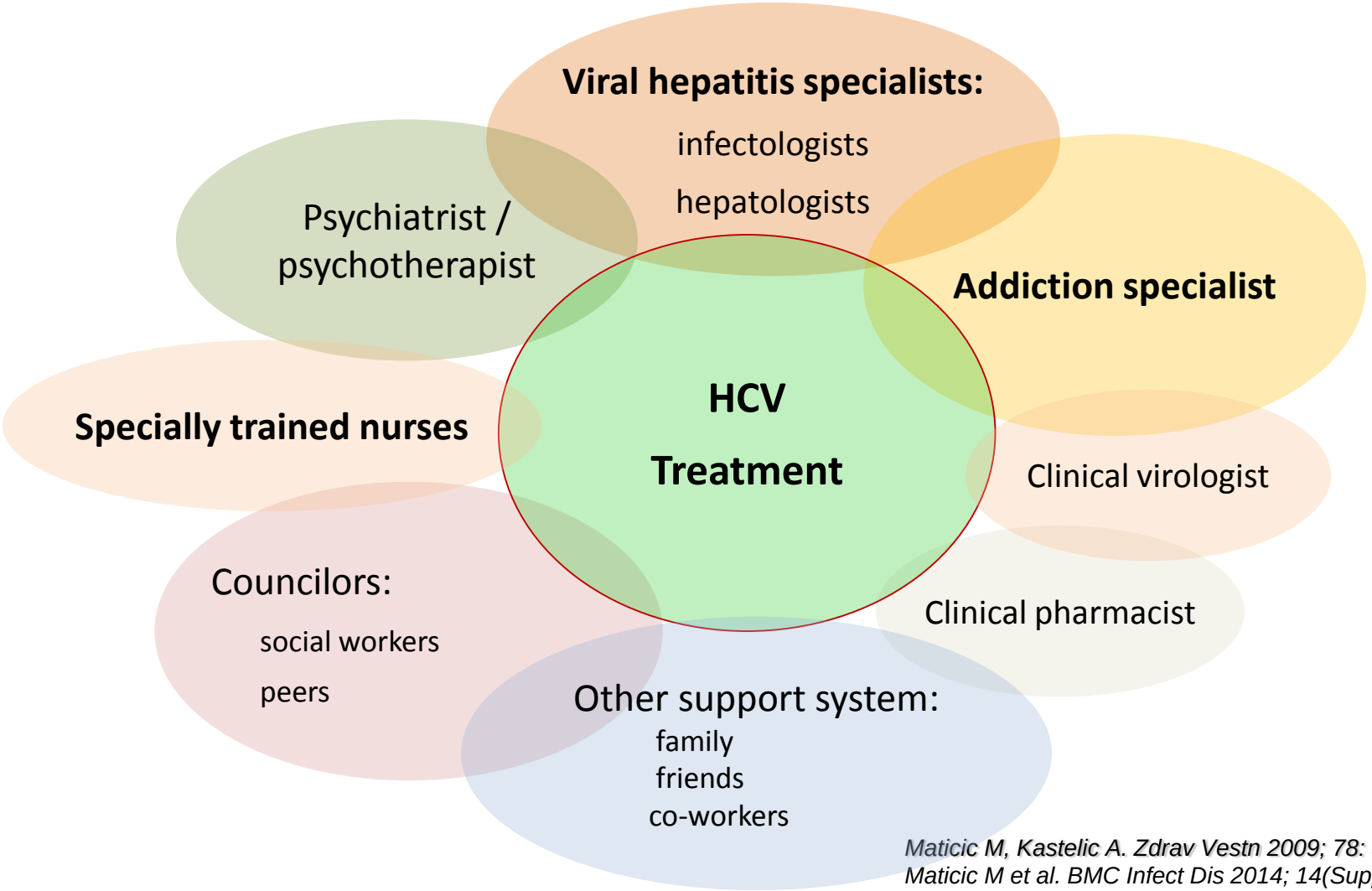
INTEGRATED already existing facilities: **18 Drug Treatment Centers**
5 Viral Hepatitis Centers



Maticic M, Kastelic A. Zdrav Vestn 2009; 78: 529-39
Maticic M et al. BMC Infect Dis 2014; 14(Suppl 6): 12-3.

SLOVENIA

A multidisciplinary team for HCV treatment in PWID



Maticic M, Kastelic A. Zdrav Vestn 2009; 78: 529-39
Maticic M et al. BMC Infect Dis 2014; 14(Suppl 6): 12-3.

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National Conferences "HCV in PWID"

for integrated providers of HCV treatment

- ***1st Slovenian Conference on HCV Infection in IVDU (Jan 2006):***
  basic medical and supportive education
  strategies, interventions
- ***2nd Slovenian Conference on HCV Infection in IVDU (Mar 2007):***
  set up National guidelines for the management of HCV in IVDUs
- ***3rd Slovenian Conference on HCV Infection in IVDU (Apr 2008):***
  vulnerable groups
- ***4th Slovenian Conference on HCV Infection in IVDU (Feb 2010):***
  experiences/improvements of the National guidelines
  future perspectives
- ***5th Slovenian Conference on HCV Infection in IVDU (Dec 2011):***
  role of addiction programmes, new drugs for HCV, HIV and IVDUs in Slovenia
- ***6th Slovenian Conference on HCV Infection in PWID (Mar2015):***
  new DAAs, increase HCV testing, Inauguration of Slovene Liver Patient Association

Maticic M, Kastelic A. Zdrav Vestn 2009; 78: 529-39
Maticic M et al. BMC Infect Dis 2014; 14(Suppl 6): 12-3.

SLOVENIA

Hepatitis C in drug users on substitution treatment:

National guidelines for clinical management and treatment

March 2007

Maticic M, Kastelic A. Zdrav Vestn 2009; 78: 529-39

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National healthcare network for managing HCV in PWID

An integrated approach

- **Un-infected:** counselling to **prevent** HCV infection
  testing for HCV infection (every 6-12 mths)
  HBV vaccination

Drug Tretment Centre

- **Acutely infected:** **testing** and quick diagnosis

Drug Treatment Centre

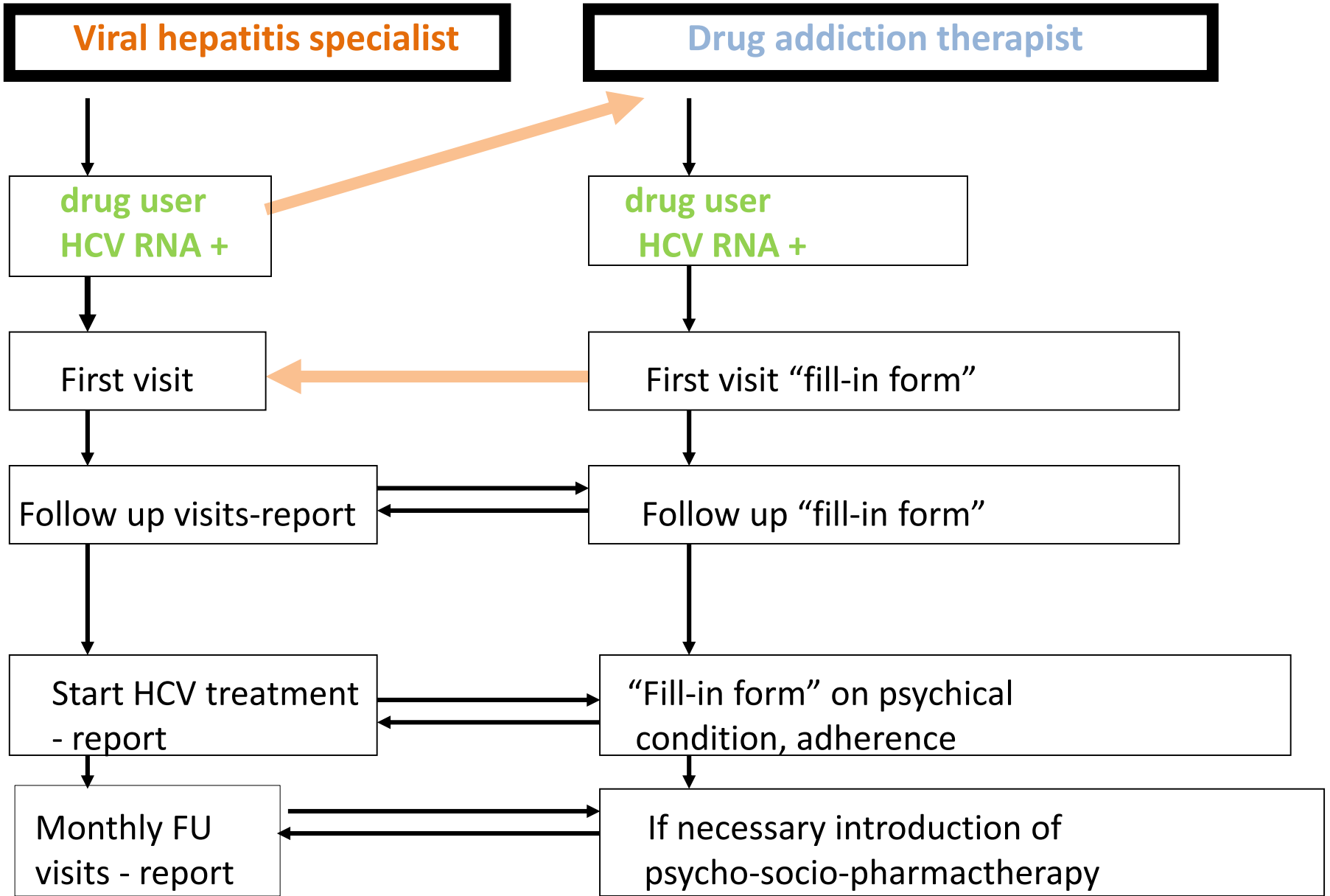
- **Chronically infected**: **treatment:**
  identification
  evaluation of readiness
  medical evaluation
  clinical management
  counselling
  motivation

Viral Hepatitis Centre + Drug Treatment Centre

Maticic M, Kastelic A. Zdrav Vestn 2009; 78: 529-39.

SLOVENIA

National healthcare network for managing HCV in PWID
An integrated approach



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National healthcare network for managing HCV in PWID

Written communication between viral hepatitis and drug addiction specialists

PODATKI O BOLNIKU

namenjeno specialistu za klinično obravnavo hepatitisa C

prvi pregled

Center za preprečevanje in zdravljenje odvisnosti od prepovedanih drog: _____

Center za zdravljenje odvisnih od prepovedanih drog, Psihiatrična klinika Ljubljana ☐

ime in priimek bolnika: _____ datum rojstva: _____

dovoljujem, da se podatki o mojem zdravljenju posredujejo specialistu za klinično obravnavo hepatitisa C

podpis bolnika: _____

trajanje uživanja drog leta: _____ meseci: _____ v zdravljenju odvisnosti od: _____

vrsta substitucijske terapije: _____ trenutni odmerek substitucijskega zdravila: _____

morebitno uživanje drog: _____ pogostnost: _____ način: _____

urinski test: _____ uživanje alkohola: _____

pridružene telesne bolezni: _____

pridružene duševne motnje: _____

prejemanje psihofarmakov / odmerek: _____

_____

terapevtski načrt: _____

_____

ima stalnega partnerja ☐ DA ☐ NE urejeno bivališče ☐ DA ☐ NE

zaposlitev: _____

okužba s HCV: anti-HCV pozitiven ☐ DA ☐ NE datum testa: _____ ☐ ni testirano

HCV RNA pozitiven ☐ DA ☐ NE datum testa: _____ ☐ ni testirano

ALT _____ µkat/L datum testa: _____ ☐ ni testirano

AST _____ µkat/L datum testa: _____ ☐ ni testirano

okužba s HBV: HBsAg pozitiven ☐ DA ☐ NE datum testa: _____ ☐ ni testirano

anti-HBs pozitiven ☐ DA ☐ NE datum testa: _____ ☐ ni testirano

anti-HBc pozitiven ☐ DA ☐ NE datum testa: _____ ☐ ni testirano

okužba s HIV: anti-HIV 1/2/0 pozitiven ☐ DA ☐ NE datum testa: _____ ☐ ni testirano

cepljenje proti HBV: ☐ DA datum zadnjega odmerka _____ št. odmerkov _____ anti-HBs _____ IU/ml

☐ NE ☐ NEZNANO

mnenje glede zmožnosti zdravljenja: _____

_____

_____

kontrolni pregled: _____ datum, podpis in žig zdravnika: _____

PODATKI O BOLNIKU

namenjeno specialistu za klinično obravnavo hepatitisa C

ponovni pregled

Center za preprečevanje in zdravljenje odvisnosti od prepovedanih drog: _____

Center za zdravljenje odvisnih od prepovedanih drog, Psihiatrična klinika Ljubljana ☐

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pridružene duševne motnje: _____

prejemanje psihofarmakov / odmerek: _____

_____

terapevtski načrt: _____

_____

pomembna nova opažanja

splošna: _____

sprememba somatskega stanja: _____

sprememba psihičnega stanja: _____

drugo: _____

terapevtski načrt: _____

_____

na novo uvedeno zdravilo / ukinjeno zdravilo / odmerek: _____

_____

_____

mnenje glede zmožnosti zdravljenja: _____

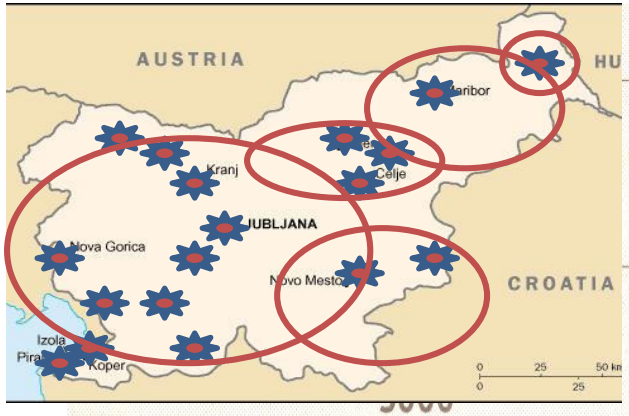
_____

_____

kontrolni pregled: _____ datum, podpis in žig zdravnika: _____

SLOVENIA

National healthcare network for managing HCV in PWID



16% HCV RNA positive
3% treated for HCV

13% treated for HCV

Strategy
Network
Guidelines

Coordination of Centers for Prevention and Treatment of Illict Drug Abuse, Slovenia 2011.
Maticic M, Kastelic A. Zdrav Vestn 2009; 78: 529-39.
Maticic M et al. Suchtmed 2013; 15: 245. Maticic M et al. BMC Infect Dis 2014; 14(Suppl 6): 12-3.

SLOVENIA

Four prospective national studies on currently recommended treatment of all naive patients with chronic hepatitis C

Standard of care treatment	Period	% of treated PWID Among all the treated patients in Slovenia
Interferon	1997-1999	**5 %**
Interferon/ ribavirin	1999-2001	**16 %**
Peginterferon/ribavirin	2001-2004	**36 %**
National healthcare network for PWID	**2007**	
Optimised peginterferon/ribavirin	2008-2010	

Brinovec V et al. Hepatogastroenterology 2002; 49: 1320-25.

Brinovec V et al. Hepatogastroenterology 2004; 51: 506-11.

SLOVENIA

Four prospective national studies on currently recommended treatment of all naive patients with chronic hepatitis C

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National healthcare network for PWID	**2007**	
Optimised peginterferon/ribavirin	2008-2010	**78 %**

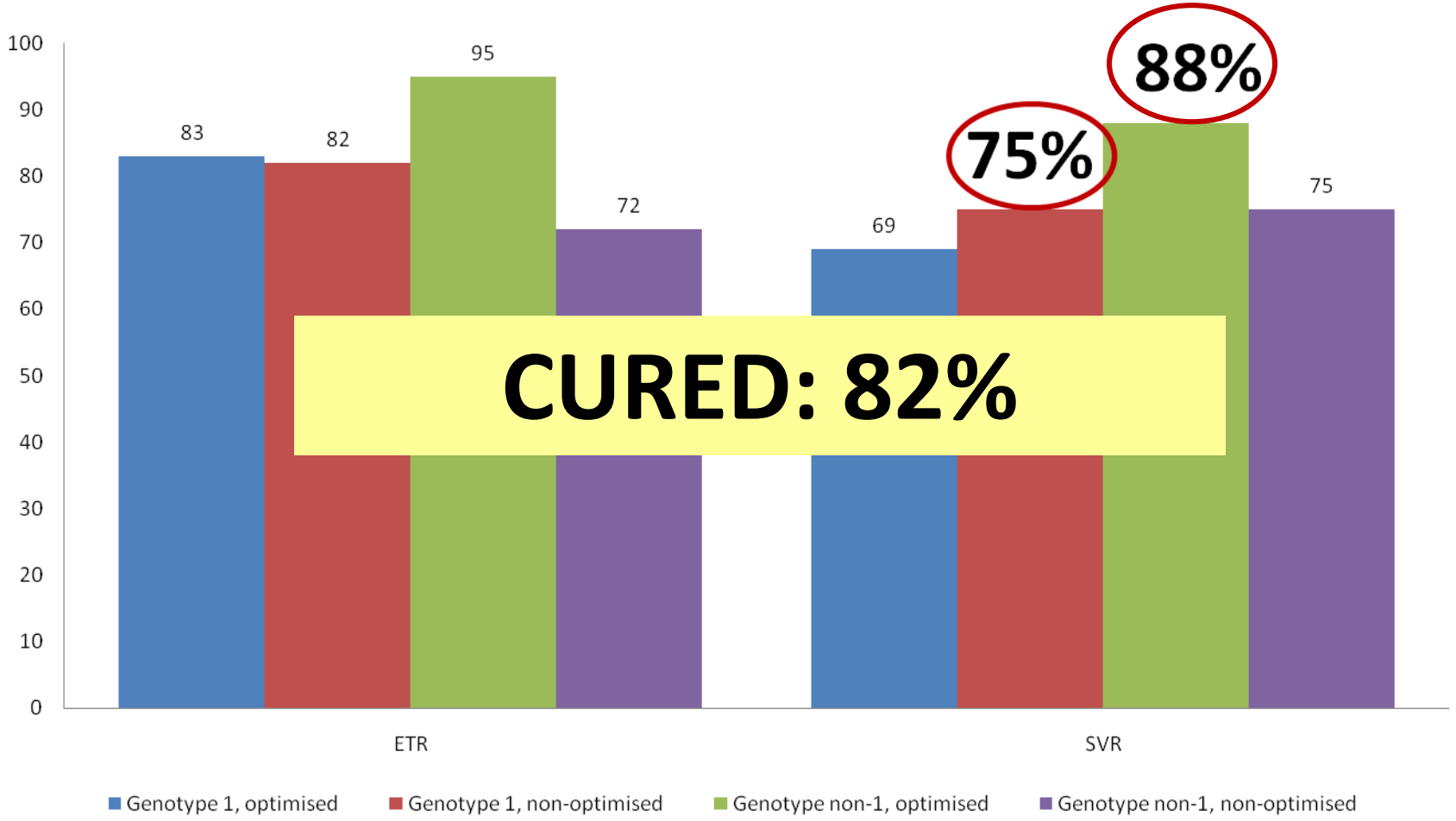
Brinovec V et al. Hepatogastroenterology 2002; 49: 1320-25.
Maticic M et al. Suchtmed 2013; 15: 245.

Brinovec V et al. Hepatogastroenterology 2004; 51: 506-11.
Selic-Kurincic T, et al. Intervirology 2014; 57:23-30 .

SLOVENIA 2008 – 2010

HCV treatment success in PWID

Optimised PegIFN/RBV



Matičič M, et al.. Suchtmed 2013: 15: 245.

SLOVENIA 2008 – 2010

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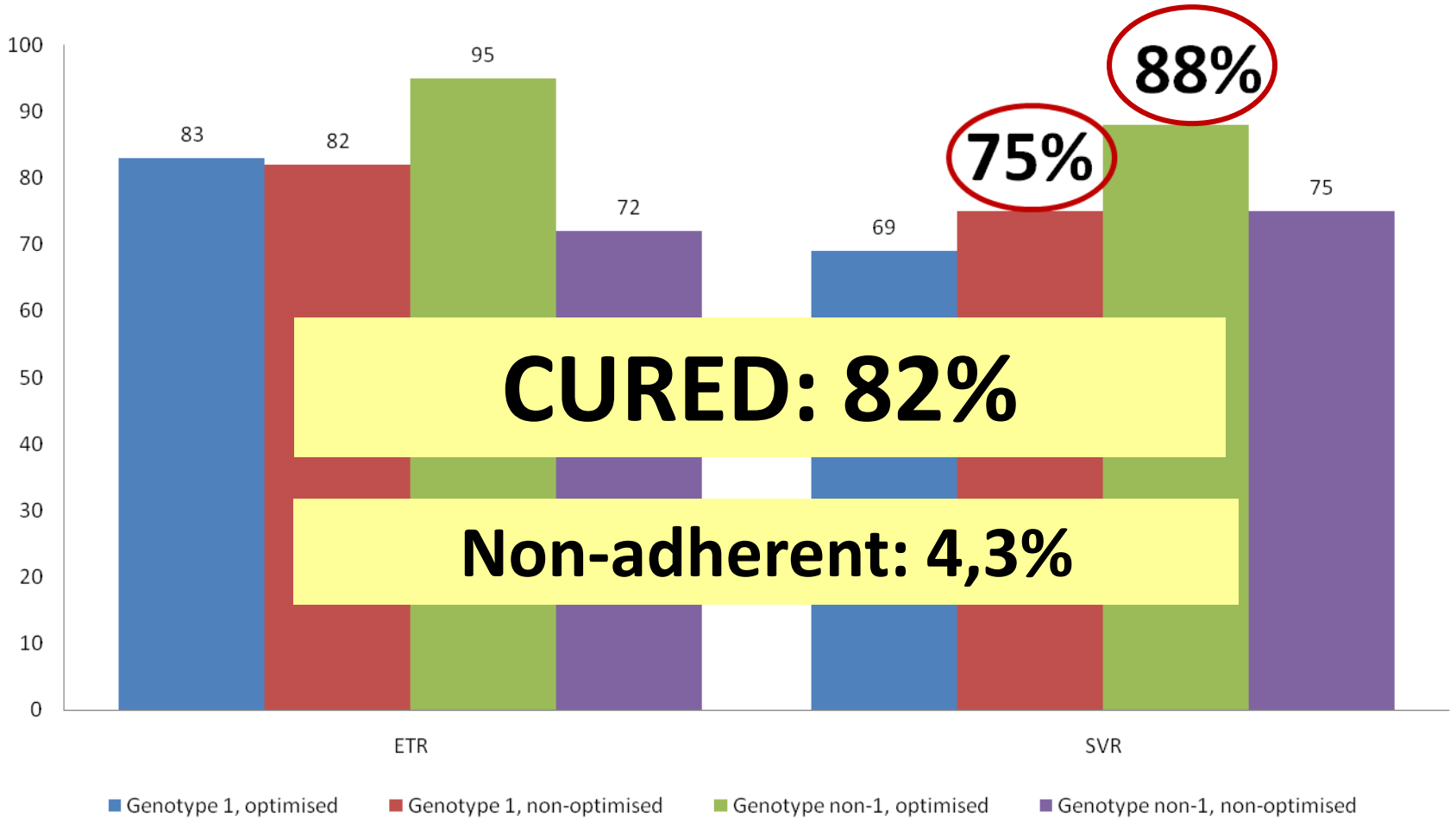

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Different models for HCV treatment in PWID (Peg/riba)

Study	HCV Treated at:	No of IDUs initiating Th	SVR All	SVR Gen 1	SVR Gen 3	Non-adherent
Wilkinson 2008 (London)	Drug Th Center	58	51 %	45 %	-	19 %
Litwin 2009 (USA)	Drug Th Center	73	45 %	40 %	36 %	NR
Curcio 2010 (Italy)	**Multidisciplinary**	**16**	**68 %**	**50 %**	**87 %**	**7 %**
Sasadeusz 2011 (Australia)	Hepatitis Th Center	53	57 %	36 %	71 %	15 %
Maticic 2013 (Slovenia)	**Multidisciplinary (National)**	**88**	**82 %**	**80 %**	**91 %**	**4,3 %**

Wilkinson et al. Aliment Pharmacol Ther 2009; 29: 29-37. Litwin et al. J Subst Abuse Treat 2009; 37: 32-40. Curcio et al. J Addict Med 2010; 4: 223-32. Sasadeusz et al. Addiction 2011; 106: 977-84. Maticic et al. Suchtmed 2013: 15: 245.

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DAAs – A game changer

2011-2013

2015

Conclusions

- National healthcare network for HCV treatment in PWID increases HCV screening among PWID, improves identification of HCV treatment eligible PWID and motivates others, increases proportion of PWID beeing treated for HCV and gains satisfactory HCV treatment adherence, efficacy and safety.

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- Close cooperation of a multidisciplinary team is crucial

- A comprehensive national policy is needed to set up national strategies, action plans and clinical guidelines for the integrated management of HCV infection in PWID

Thank you !