Identification and prevention of new infections in at risk-groups

HCV symposium, CDC Atlanta, December 2nd 2011

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Identification and prevention of new HCV infections

1. Today's global and local epidemiology

2. Decreasing the incidence

   a. Preventing infections in the uninfected population

   b. Preventing transmission by the infected population

   c. Preventing re-infection following spontaneous clearance or successful therapy

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Today's HCV situation in high income countries

People who inject drugs account for the majority of new HCV infections

New at-risk groups

- Men having sex with men (MSM)
- Migrants from HCV endemic countries

Migration patterns and HCV

Migrants account for 5%-31% of HCV prevalent cases in high income countries

Increasing migration flows from middle or high HCV prevalence countries to low prevalence countries might increase HCV prevalence in the general population

Migration also diversifies HCV genotype distribution as has been shown in several studies/countries

Large proportion still undiagnosed

Today's HCV situation in people who inject drugs (PWID)

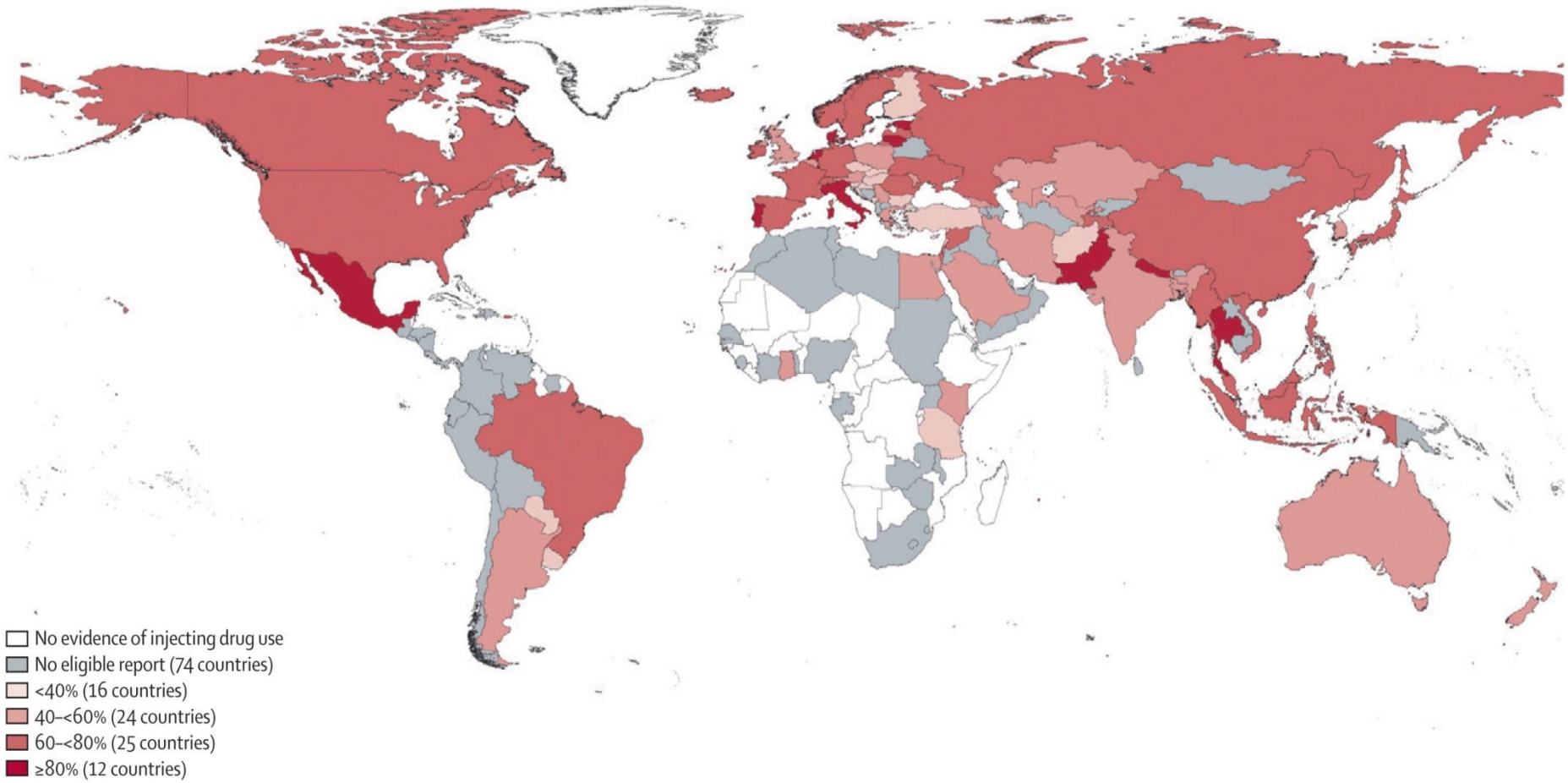
- IDU is prevalent worldwide

- Global HCV estimates (ever-injectors/incidental injectors excluded) and using updated IDU prevalence data (*Nelson et al, Lancet 2011)*

10 million PWID in 2010 were anti-HCV positive (range 6.0-15.2)

Midpoint anti-HCV prevalence: 67.0%

Prevalence of anti-HCV in people who inject drugs



Nelson et al, Lancet 2011

What about trends in HCV incidence in PWID?

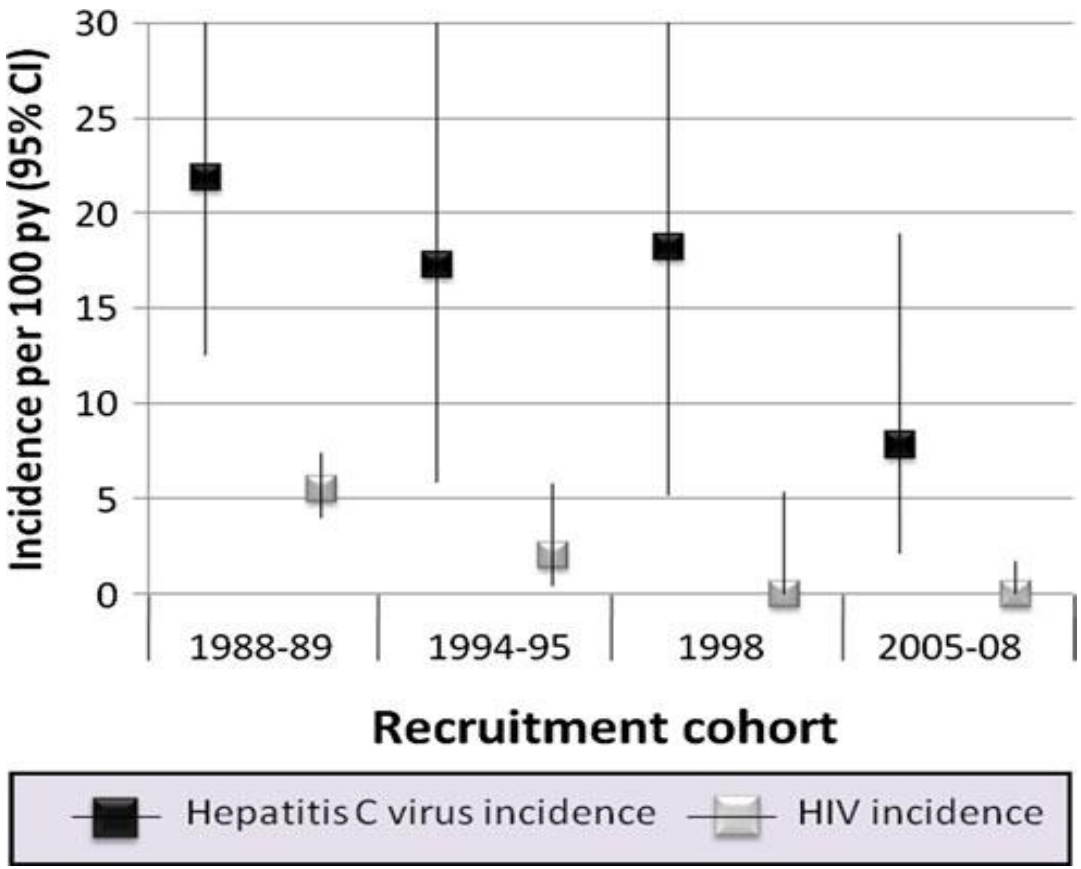
~ 5 - 40 per 100 years, exceeds HIV incidence

Meta-analysis: Lengthening in time to HCV infection since onset of injecting:
Mean fitted cumulative incidence was 27.6% (95% CI: 16.9-41.7) at 1 year of drug injection (*Hagan et al, Am J Epidemiol 2008*)

Cohort studies: Evidence for declining trends in HCV incidence in North-America and EU (*e.g. Berg at al, Eur j Epidemiol 2007, Mehta al al JID 2011)*

HIV and HCV incidence by recruitment cohort

ALIVE cohort, Baltimore

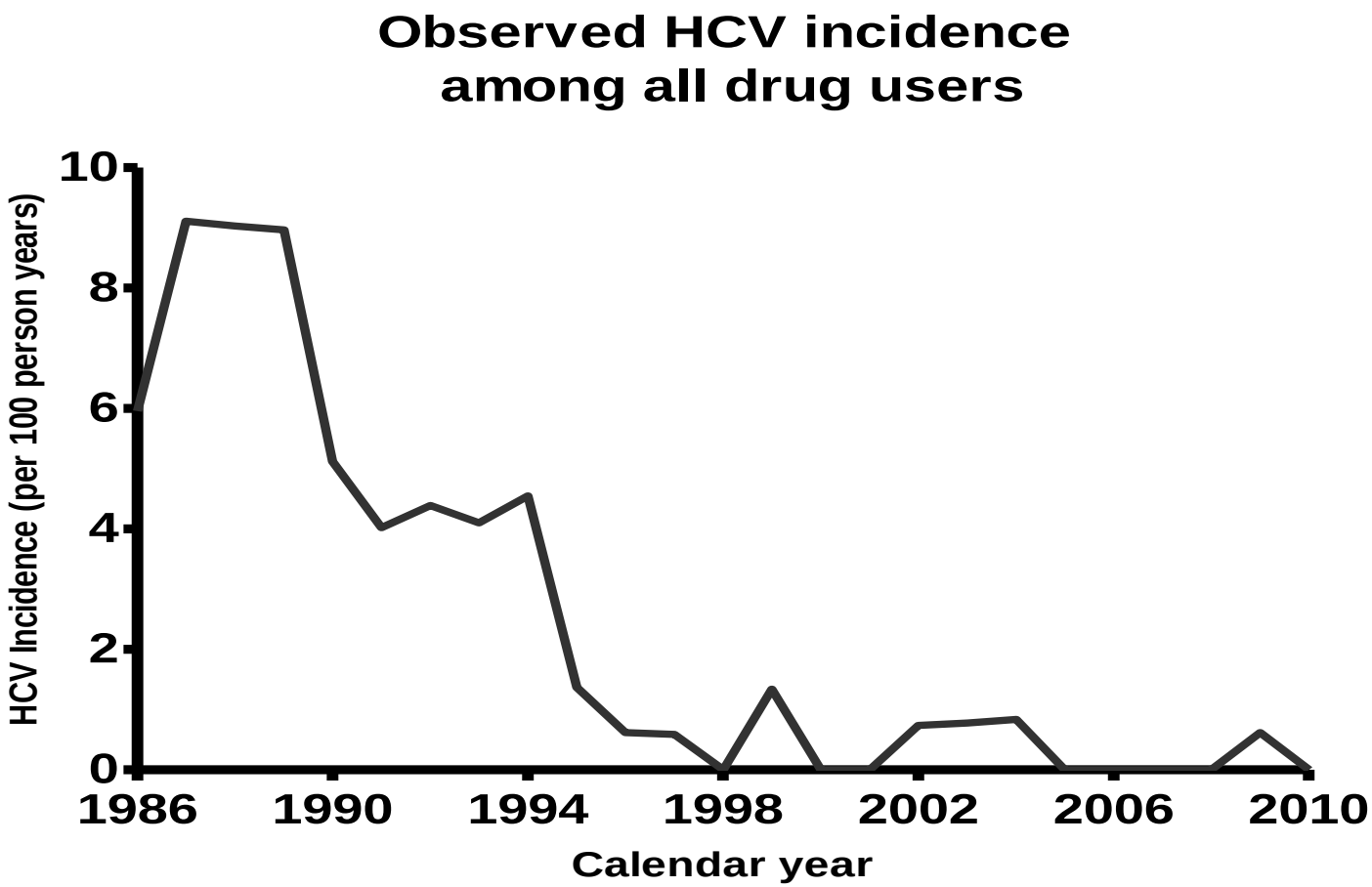


Mehta et et al, JID 2011

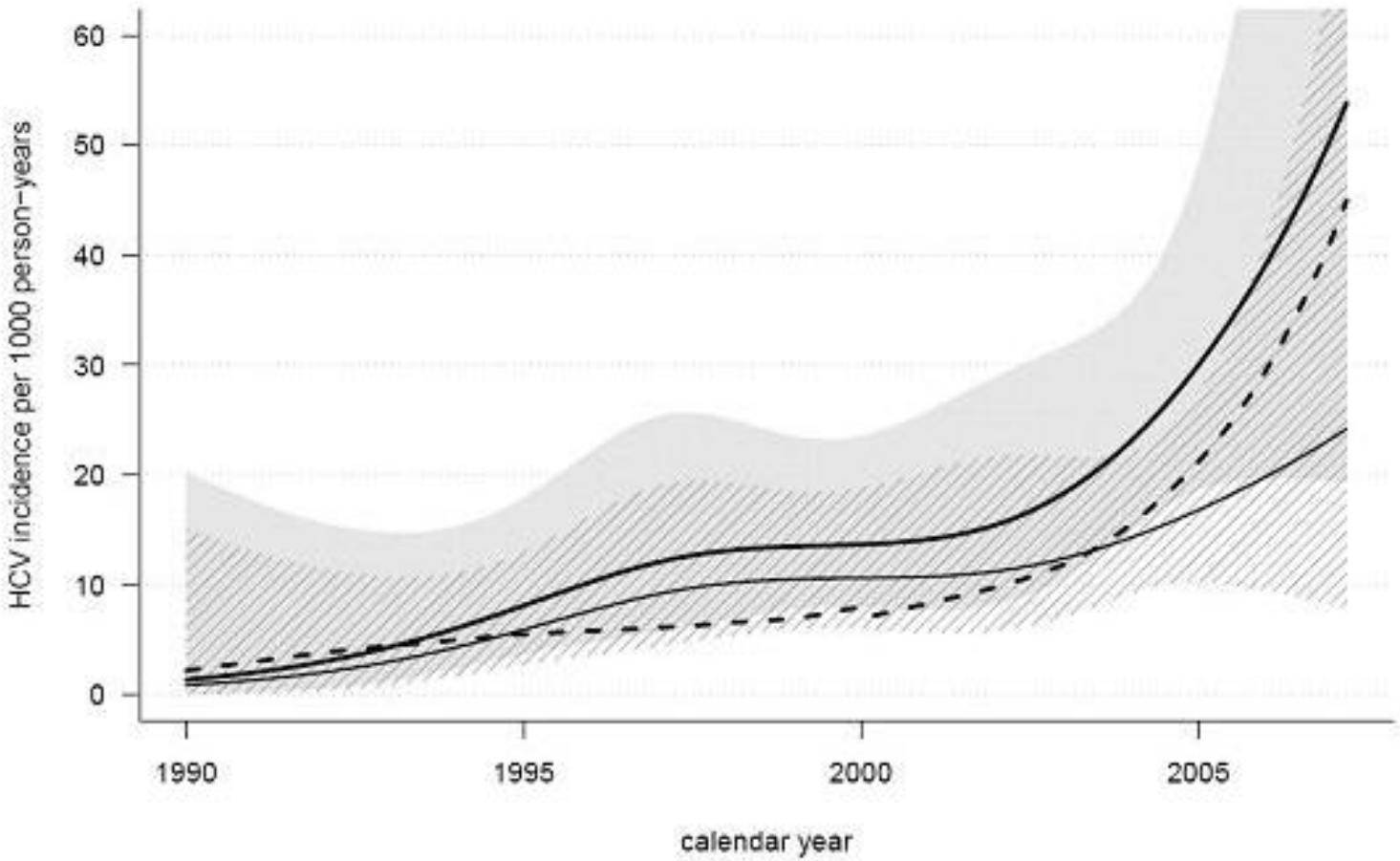
Today's Dutch HCV situation

- Very limited number of new infections in PWID
- Men who have sex with men account for the majority of new HCV inflections
- Migrants born in HCV middle and high prevalence countries account for the majority of all infections: Phylogenetic analysis and the low prevalence among 2nd generation migrants suggest they that they had acquired HCV before moving to the Netherlands (*van de Laar et al, Transfusion 2006, de Bruijne et al J Med Vir 2009, Urbanus et al J Hepatol 2011*).

Amsterdam Cohort Studies



HCV incidence among MSM with documented dates of HIV seroconversion: CASCADE in Eurocoord study



Each line represents a different method for estimating HCV incidence

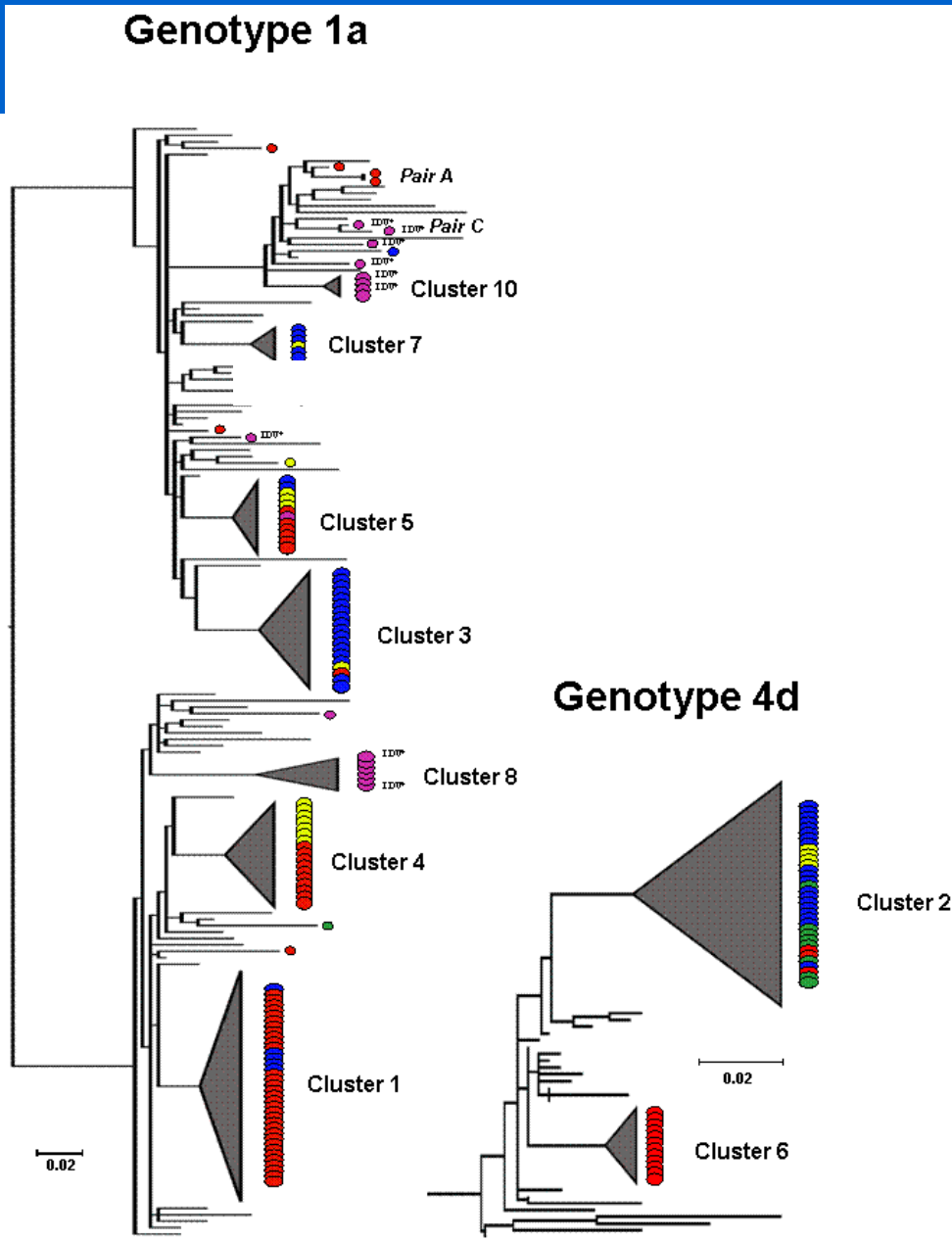
v.d. Helm et al, AIDS 2011

European HCV network among HIV-infected MSM

- UK
- The Netherlands
- Germany
- France
- Australia

Genotypes 1 and 4

MSM specific clustering of HCV strains support sexual transmission



v.d. Laar et al, Gastroenterol 2009

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~~Vaccination~~

Reducing risk behavior (e.g. by harm reduction measures)

Testing

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Harm reduction programmes for people who inject drugs

Key components:

- Drug dependency treatment: opiate substitution programs (OST)
- Provision of needles and syringes and other injecting equipment
- Health promotion and education
- Condom provision
- Social care

- Regular testing for bloodborne infections and STI in groups at risk

  - Public health resources: HCV antibodies

Evaluation of Harm reduction measures

<u>Effect of a single intervention</u>

Good evidence that opiate substitution therapy (OST) and needle exchange programmes (NEP) reduce self-reported injecting risk behaviour

Prevention of HIV transmission Sufficient/tentative evidence

Prevention of HCV transmission: Weak/insufficient evidence

Report Institute of Medicine 2007, Palmateer et al Addiction 2010

<u>Effect of combined interventions</u>

Mounting evidence that comprehensive harm reductions programmes work, also to reduce HCV transmission

van den Berg et al Addiction 2007, Craine et al Epidemiology and infection 2009, Turner et al Addiction 2011, Hagen et al JID 2011

amsterdam cohort studies

Effect of harm reduction participation on HIV and HCV incidence: Amsterdam Cohort Studies among drug users

	HIV			HCV		
	IRR	95% CI	p value	IRR	95% CI	p value
No harm reduction	1		<0.001	1		<0.001
Incomplete harm reduction	0.87	(0.50-1.52)		1.17	(0.59-2.31)	
Full harm reduction	0.43	(0.21-0.87)		0.36	(0.13-1.03)	
-Limited dependence	0.046	(0.006-0.35)		0.044	(0.006-0.35)	
-No dependence	0.20	(0.078-0.50)		0.13	(0.044-0.40)	

Adjusted for injection duration, HIV status steady partner (for HIV only)

:

v.d. Berg et al, Addiction 2007

Meta-analysis and pooled analysis of six UK-based studies

Full harm reduction (OST plus high NSP coverage) reduces the odds of new HCV infection by nearly 80%

aOR=0.21, 95% CI: 0.08-0.52.

Turner et al, Addiction 2010

Systematic review and meta-analysis of interventions to prevent HCV infection: published and unpublished studies

26 eligible studies of behavioral interventions, substance-use treatment, syringe access, syringe disinfection, and multicomponent interventions

- Effects of single-method interventions: pooled relative risk of 0.6 to 1.6.
- Interventions using multiple combined strategies reduced risk of HCV seroconversion by 75% (pooled relative risk, 0.25, 95% CI 0.07-0.83)

Hagan et al, JID 2011

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Testing negative; being aware of negative status

Evidence from review of published reviews (RoR) in effectiveness of testing in reducing incidence

- Injecting risk behaviour: +/- (insufficient evidence)
- HIV transmission: ?
- HCV transmission: ?

?: No core or supplementary reviews of the topic identified, possibly due to a lack of primary studies

Source: Prevention and Control of infectious diseases among person who inject drugs, ECDC-EMCDDA Guidance, October 2011, ISBN 978-92-9193-313-6

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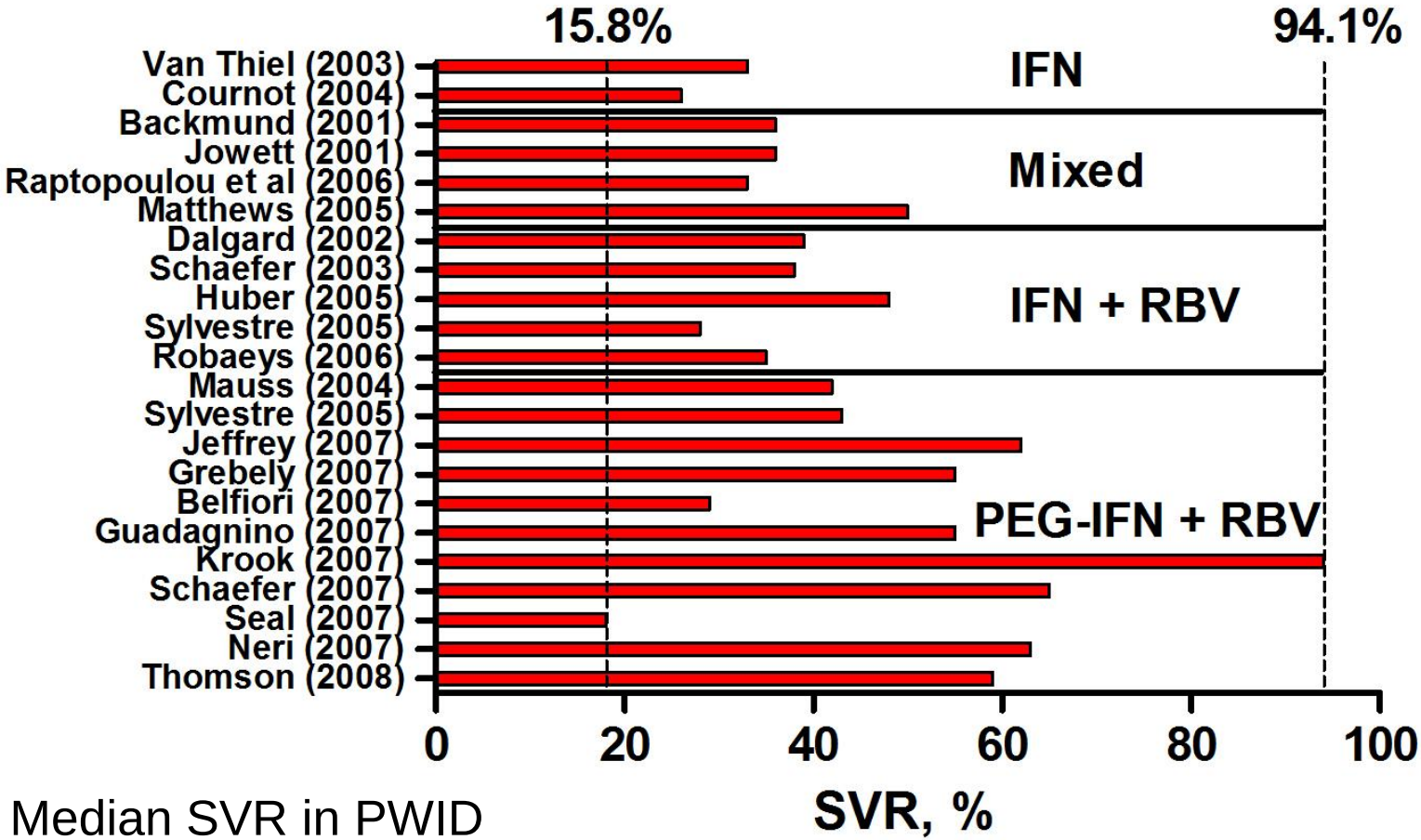
Early detection: testing

No reviews identified on effect (via decreasing HCV risk behaviour) on transmission

Observational studies and modelling studies suggest that in PWID efficient linkage to treatment access reduces forward transmission

Source: Prevention and Control of infectious diseases among person who inject drugs, ECDC-EMCDDA Guidance, October 2011, ISBN 978-92-9193-313-6



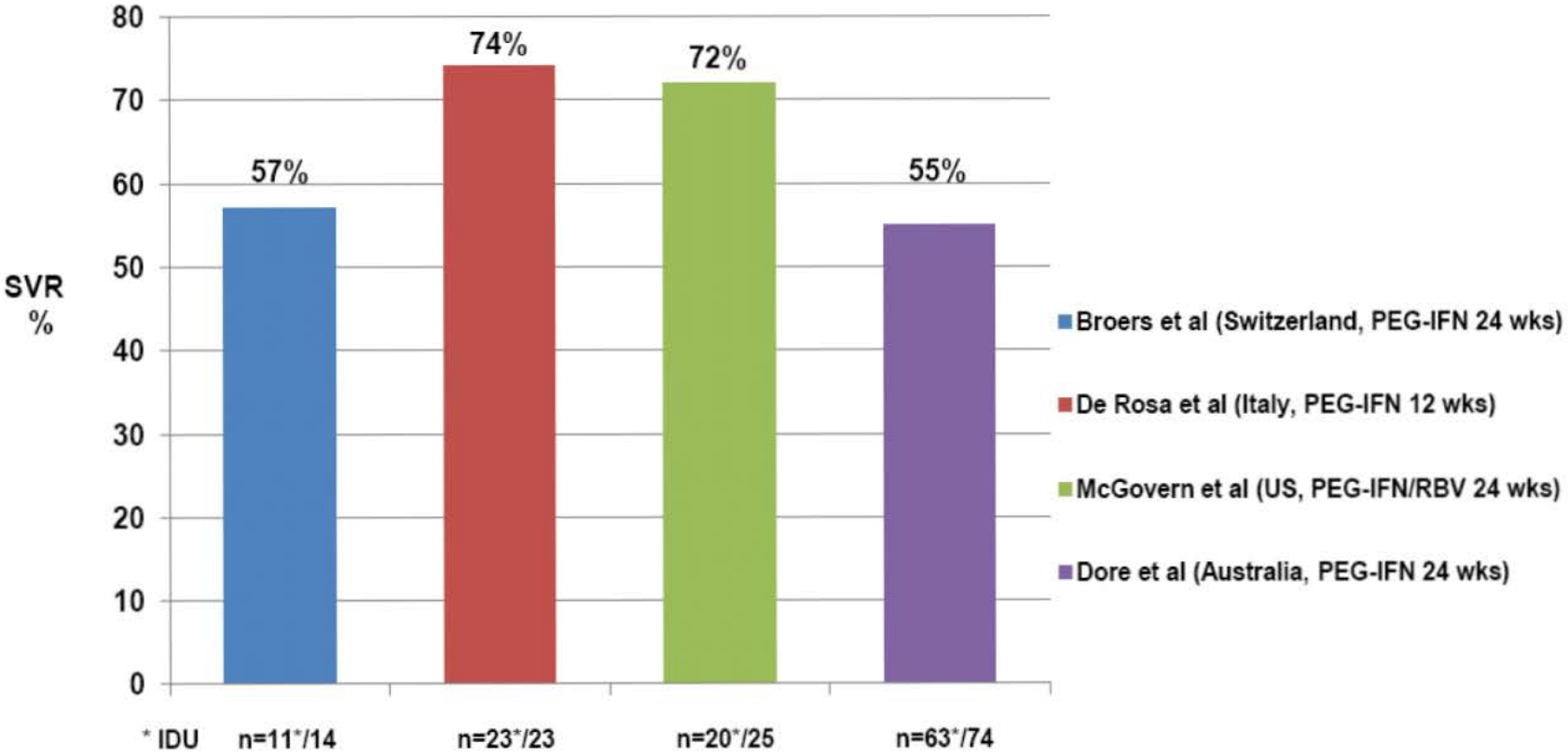
- Median SVR in PWID
  - Regardless of treatment regimen: 40.6%
  - Peg-IFN alfa + RBV: 54.3% (range 18.1-94.1)

Hellard M, et al. Clinical Infectious Diseases 2009.

Kirby Institute UNSW

Acute hepatitis C treatment: IDUs

81% in non drug-using populations



Broers B et al. J Hepatol 2005;42:323-328. De Rosa et al. Clin Infect Dis 2007;45:583-588. McGovern BH et al. J Infect Dis 2009;200:877-881. Dore GJ et al. Gastroenterology 2010;138:123-135.

Treatment uptake among people who use drugs is low

	n	Cohort	HCV Treatment Uptake/Year
Canada (Vancouver)[1]	1,360	Community-based inner city residents	<1%
United States (Baltimore)[2]	597	Community-based IDUs	<1%
Australia[3]	2,500	Needle exchange participants	1%

1) Grebely J, et al. J Viral Hepatitis 2009; 16:352-358; 2) Mehta S, *et al* J Community Health 2008; 33:126-133; 3) National Centre in HIV Epidemiology and Clinical Research 2010.

Testing and treatment uptake in drug user settings

Amsterdam: Dutch-C (Drug Users Treatment for Chronic Hepatitis C) unit

- Multidisciplinary approach including DOT, integrated with methadone treatment
- Test uptake: 90%
- Treatment uptake 16% overall, 33% among HIV negative individuals
- Patients attended 95% of scheduled visits
- SVR (HCV RNA negative 24 weeks after end of treatment) 65%

Lindenburg et al Eur J Gastro 2011

Australia: ETHOS

- HCV treatment provided in primarily opiate substitution therapy clinics
- Treatment uptake: 19%.

Alavi M, et al. 2nd ISHCSU, Brussels, Belgium 2011

Treatment of chronic infections in PWID

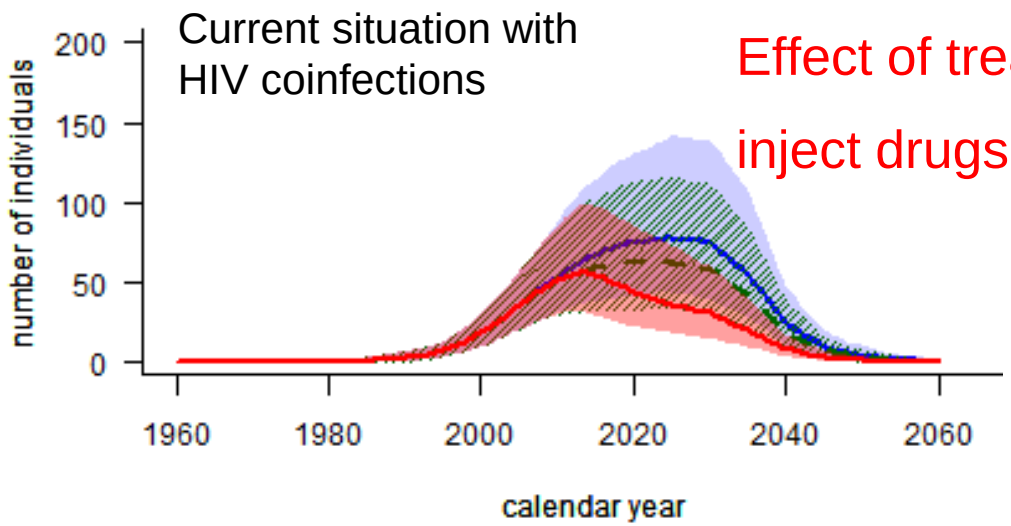
Treatment reduces future burden of disease in people who inject drugs

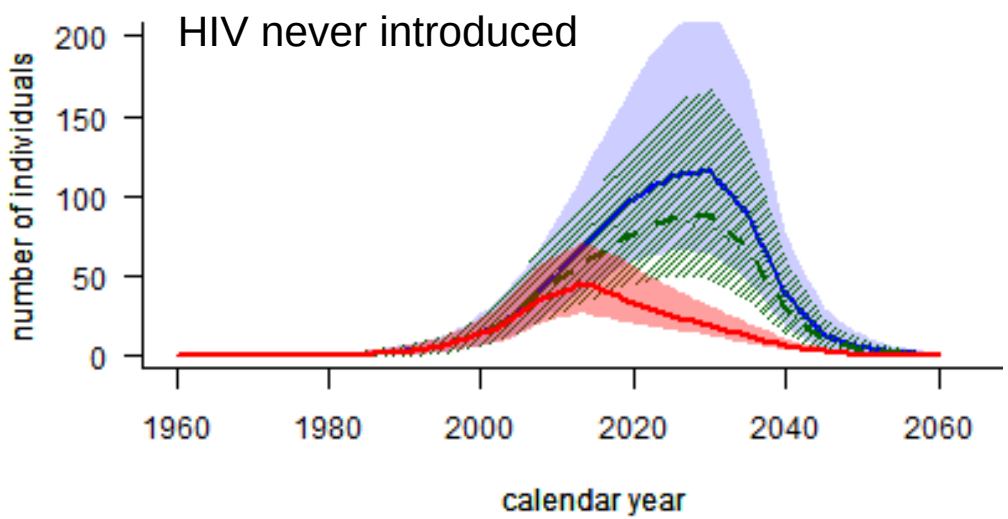
(*Hutchinson et al Hepatology 2005; Matser et al Addiction 2011)*

Modelling studies suggest that treatment could reduce forward transmission

(*Zeiler et al Drug Alcohol Depend 2010, Vickerrman et l Drug Alcohol Depend 2011, Martin et l J Hepatolgy 2011)*

Effect of treatment on HCV burden in people who inject drugs In Amsterdam, the Netherlands





Med. n of prevalent cases with HCV-related disease (No treatment)

Med. n of prevalent cases with HCV-related disease (Treating 25% of HIV-)

Med. n of prevalent cases with HCV-related disease (Treating 95% of HIV-, 65% of HIV+)

Matser at al. Addiction ahead of print

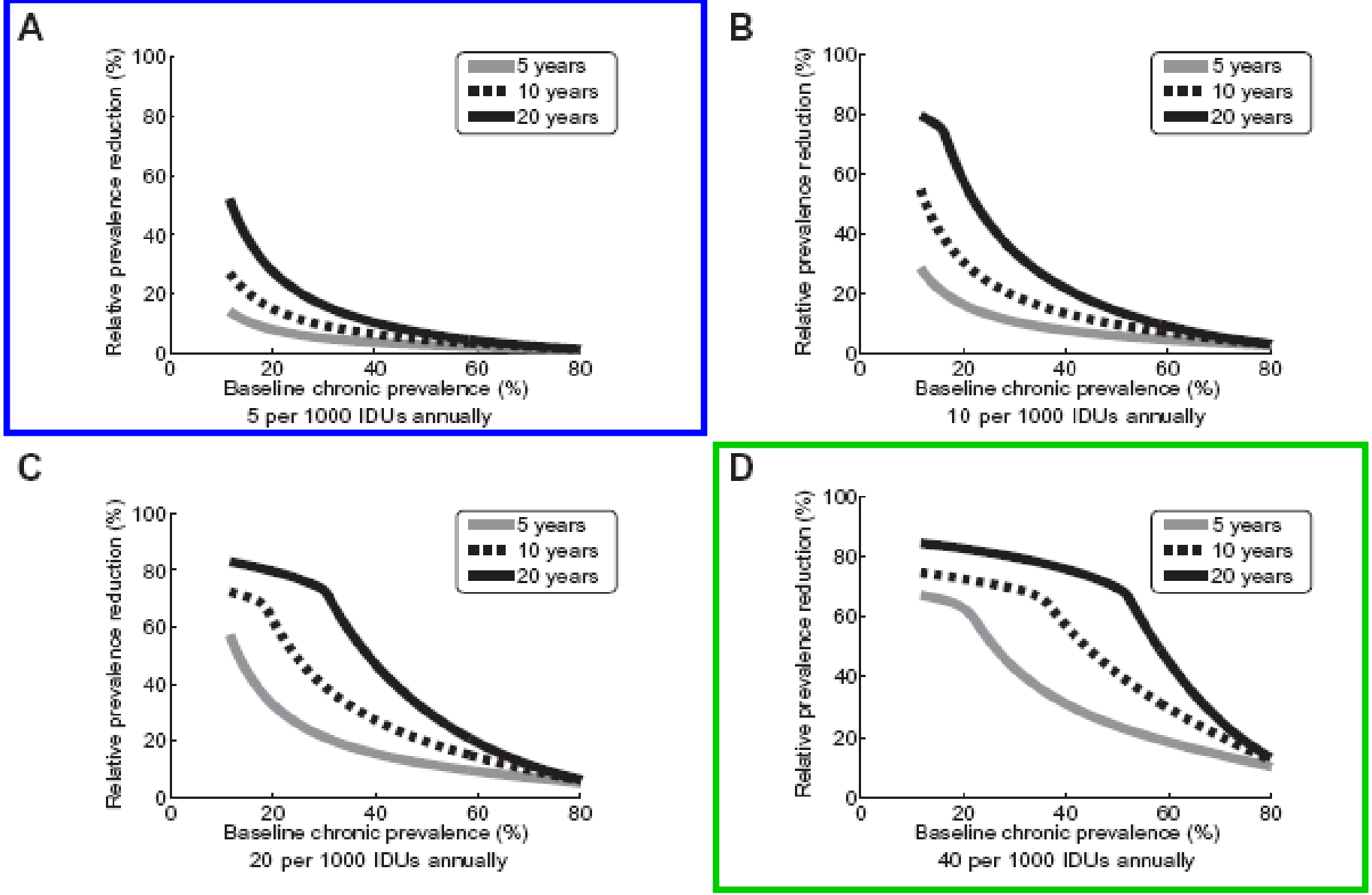


Fig. 3. Projected relative reduction in prevalence at 5, 10, and 20 years for the baseline scenario (no immunity, mixed genotype) at different baseline prevalences and treatment rates. The relative prevalence reduction from baseline chronic prevalence (vertical axis) is shown at 5 years (grey line), 10 years (black dashes), and 20 years (black line) for varying baseline untreated chronic prevalences (horizontal axis) and different treatment levels. Baseline chronic prevalence is defined as untreated endemic chronic infection prevalence.

Martin et al. J Hepatol. 2011.

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HCV reinfection following SVR in PWID

Study	Study Population	Median Age	IDU post-treatment	Median Follow-up (years)	New infection	HCV reinfection incidence rate
Backmund 2004	n=18	32	50%	2.8 (0.8-5.1)	2/18	4.1/100 py
Dalgard 2005	n=27	NA	33%	5.4 (1.1-6.8)	1/27	0.8/100 py
Currie 2008	n=9	46	22%	3.6 (3.2–6.0)	1/9	0.6/100 py
Grebely 2010	n=35	44	54%	2.0 (0.4-5.0)	2/35	3.2/100 py
Bate 2010	n=57	34	NA	3.4 (0.2-11.5)	5/57	NA
Grebely 2011*	n=87	36	NA	1.2 (0.1-3.0)	4/87	3.7/100 py
Grady 2011*	n=42	51	21%	2.5 (1.6-3.7)	1/42	0.8/100 py

** Abstracts 2nd ISHCSU Brussels, Belgium and AALSD, 2011*

Response to first reports of HCV outbreak in MSM

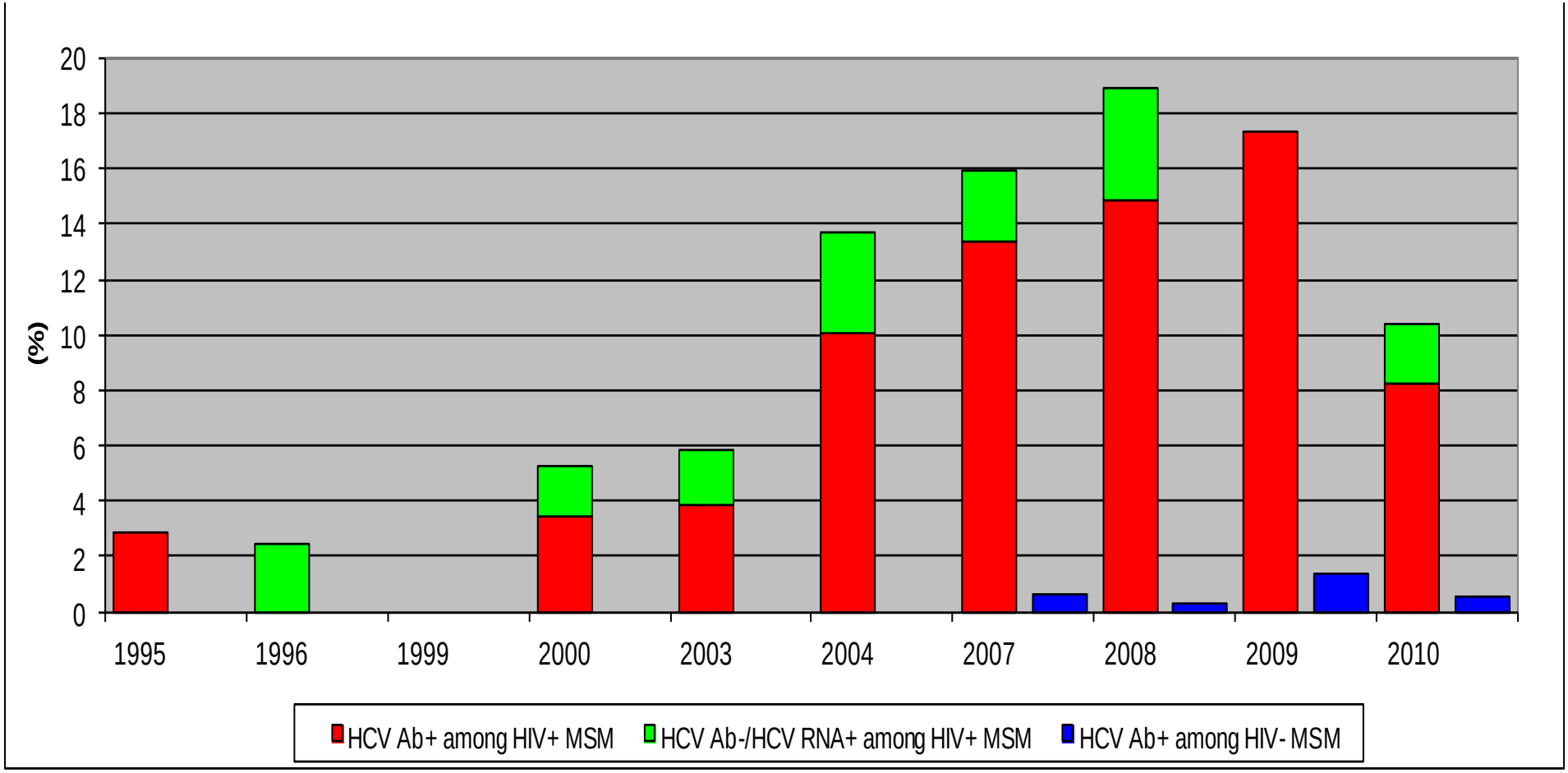
> Case reports from several western European countries (England, France, Germany, and the Netherlands) and soon after from Australia and the US

> HCV prevalence (15-18%) in 2007-2008 among HIV-infected MSM at a large STI outpatient Clinic (*Urbanus et al. AIDS 2009*)

Response:

- Increased awareness among HIV physicians: elevated ALT based screening
- Increased awareness and prevention materials for MSM (2008)
- Routine HCVab testing for uninfected HIV positive and HIV opt-out MSM including contact tracing at STI clinic (since 2008)

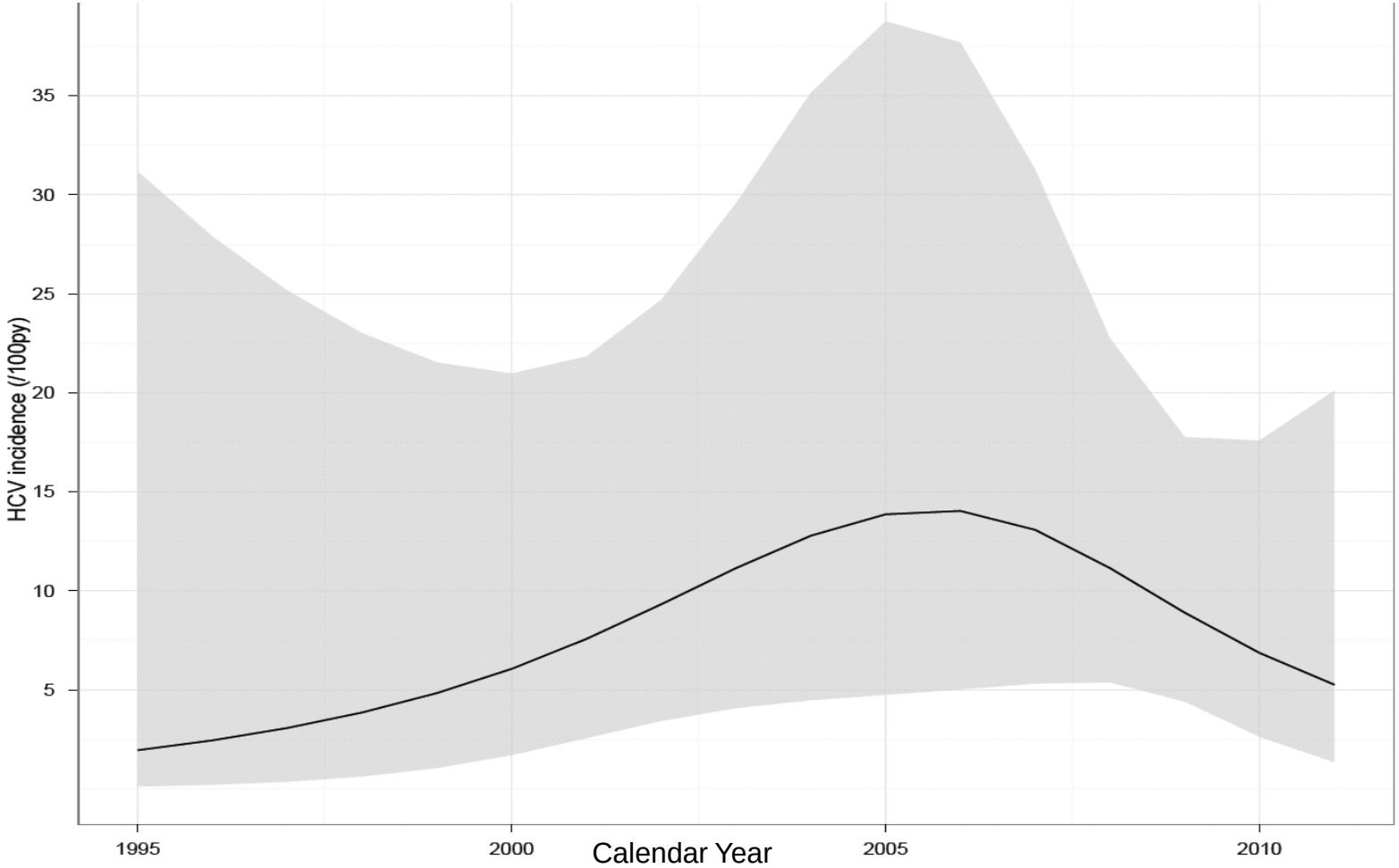
HCV prevalence in HIV+ and HIV- MSM participating in the bi-annual cross-sectional survey at Amsterdam STI clinic



Urbanus et al. AALSD 2011

Estimated HCV incidence among HIV-infected MSM

Amsterdam STI clinic, 1995-2010



HCV reinfection following primary acute HCV treatment in HIV-infected MSM

Study population: Fifty-six HIV coinfected MSM who became HCV RNA-negative during primary acute HCV treatment in two large hospitals

- 5/56 cases relapsed

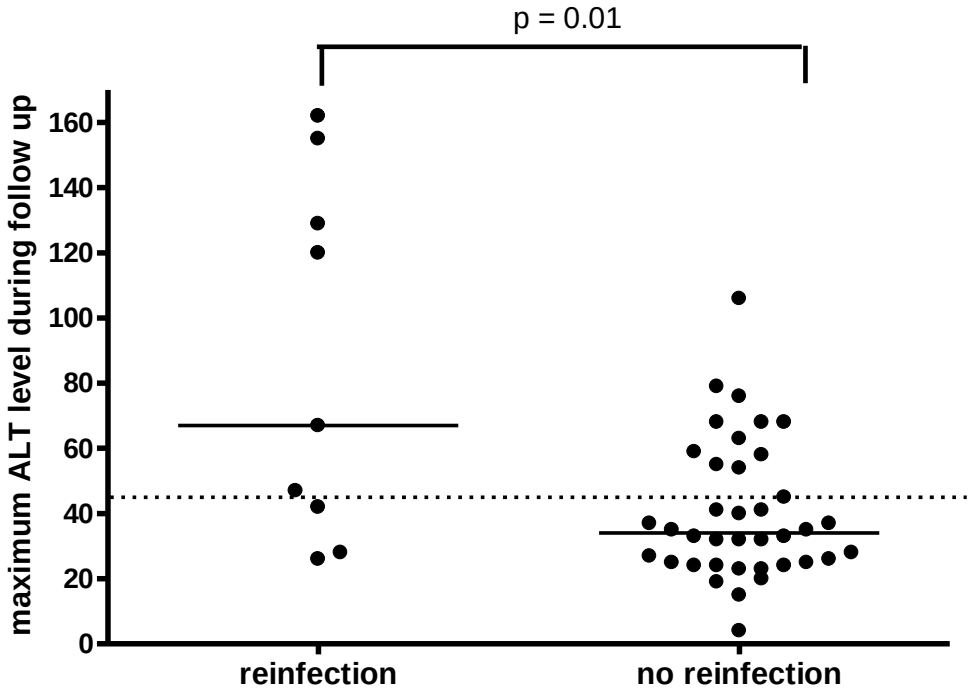
- 11/56 reinfected (defined as undetectable HCV RNA at the end of treatment accompanied by a switch in HCV genotype or clade)

Incidence of HCV re-infection: 15/100 person-years (95% CI 8.0-26.5).

Cumulative incidence: 33% within 2 years.

** Lambers et al, AIDS 2011*

Peak ALT levels during follow-up according to reinfection status



Legenda: peak ALT levels in U/L during the observation period (end of treatment until last negative or first positive time point). The dotted line represents the maximum normal ALT value.

Conclusions

- PWID
  - Declining trends in Amsterdam and other high income regions
  - Combined comprehensive harm reduction programmes reduce HCV transmission
  - Uptake of testing and treatment might reduce transmission: uptake treatment still limited!
  - Reinfection rate following SVR relatively low

- MSM
  - HCV prevalence and incidence in HIV-infected MSM seem to be leveling off in Amsterdam, possibly due to increased awareness and introducing routine frequent testing
  - HCV prevalence remained low among HIV negative MSM
  - MSM specific clustering of HCV strains support sexual transmission in an international network
  - Of concern: High reinfection rate

Key points

Routine surveillance, cohort studies and cross-sectional studies including molecular and behavioral network data are needed to track transmission

Some challenges:

1. Legal access and high coverage of comprehensive harm reduction programmes for PWID
2. Availability of rapid and oral tests and improved treatment:
   - Need for effective and innovative methods to identify undiagnosed chronic HCV infections: combining screening for various infections/diseases
   - Need for increased uptake of regular testing for acute infections in at-risk populations
   - Need for increased and early uptake of treatment; for marginalized populations treatment should be organized and delivered to their needs
3. Reinfection prevention and testing following spontaneous clearance or successful therapy

Thanks

- Colleagues (especially PhD fellows) at the Public Health Service and Academic Medical Center Amsterdam
- Colleagues at EMCDDA, Lisbon and ECDC, Stockholm
- Jason Grebely, Kirby Institute, NSW, Sydney, Australia
- Study participants

Organizers of the symposium

TO YOU: THE AUDIENCE