
EACS European AIDS Clinical Society MEETING

# STANDARD of CARE for **HIV** and **COINFECTIONS** in **EUROPE**

Chairs: *A. Antinori, A. d'Arminio Monforte, C. Mussini*

# HIV/HCV co-infection in Europe

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# 170 million people infected with HCV
# 3–4 million new infections each year

universitäts klinikum bonn

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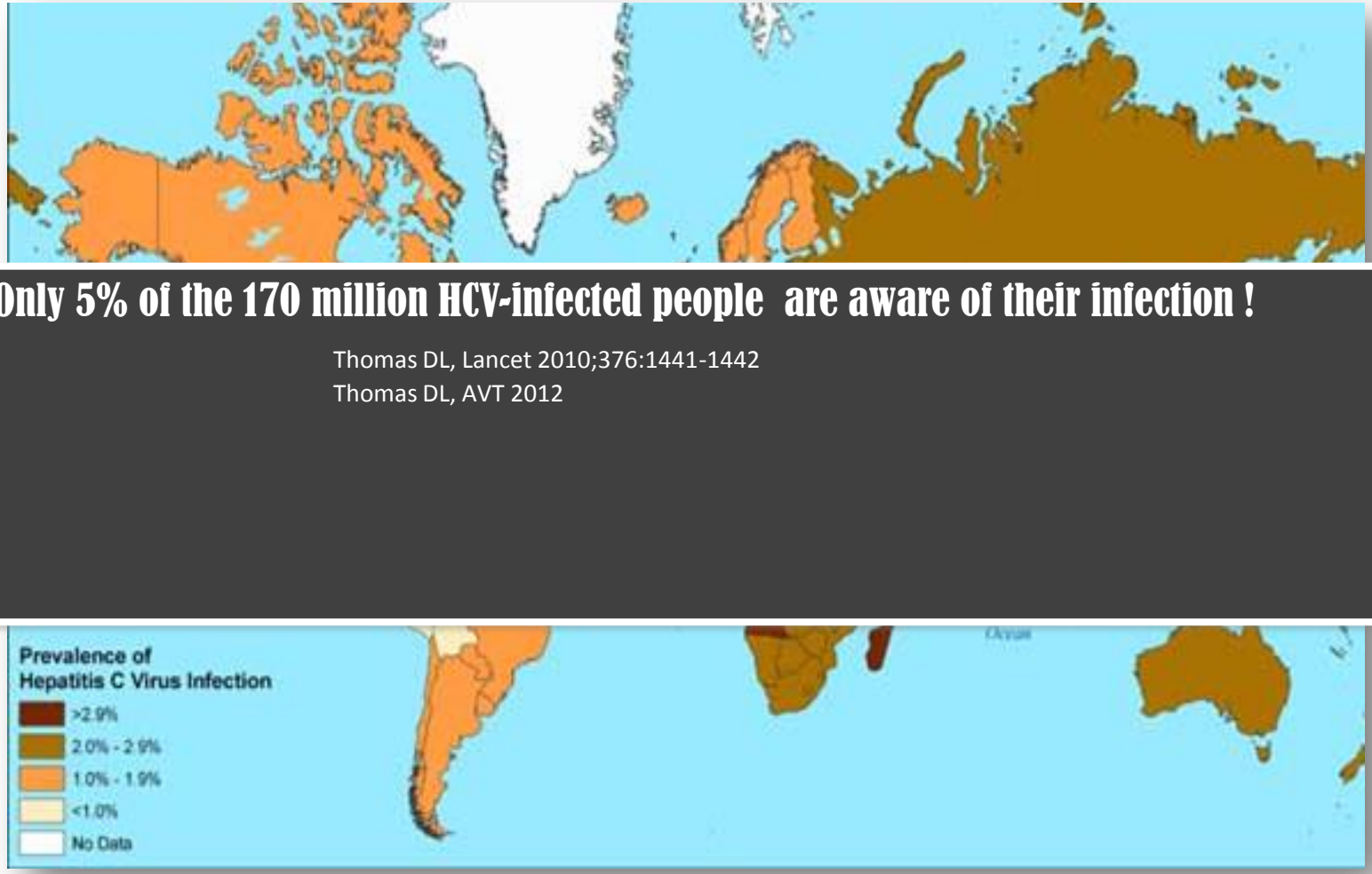



**Only 5% of the 170 million HCV-infected people are aware of their infection !**

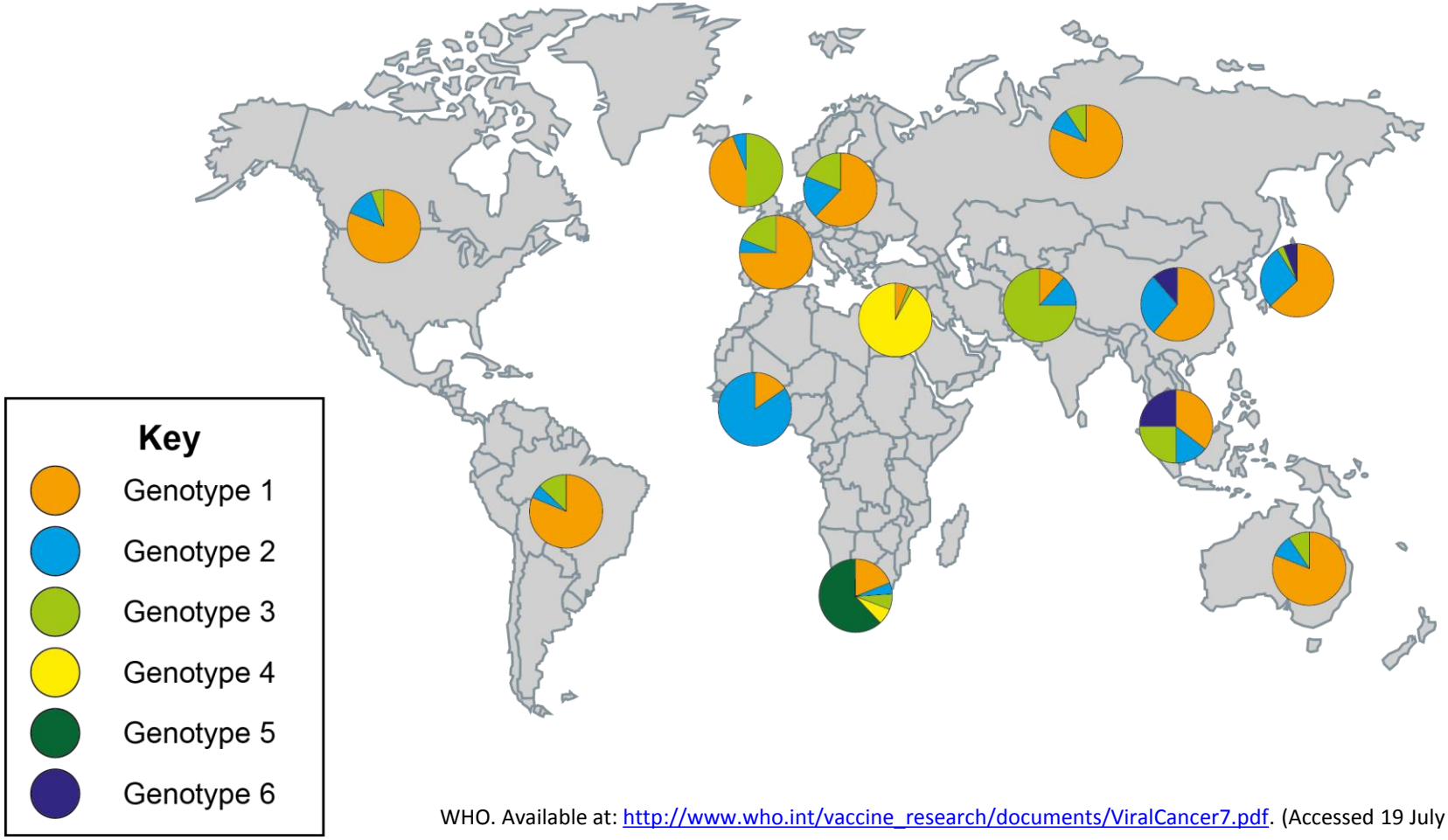
Thomas DL, Lancet 2010;376:1441-1442
Thomas DL, AVT 2012



Jules L, N Engl J Med 2008; Lavanchy D. Clin Microbiol Infect 2011;17:107–15

# Global distribution of HCV genotypes



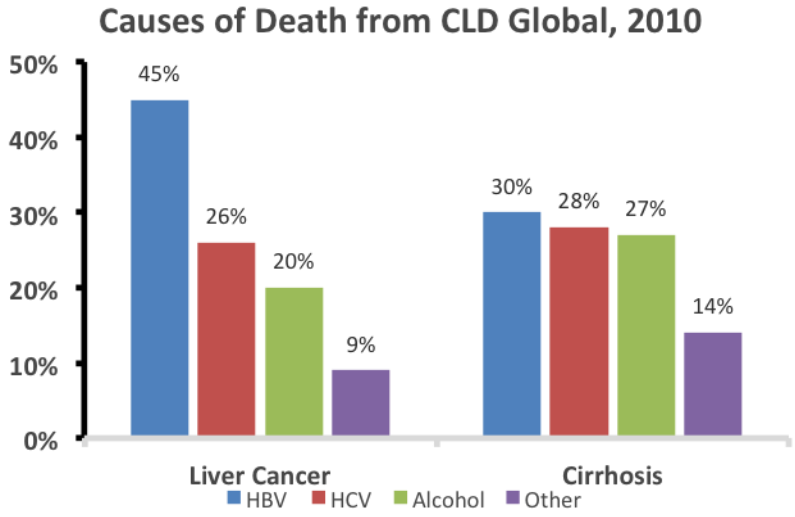


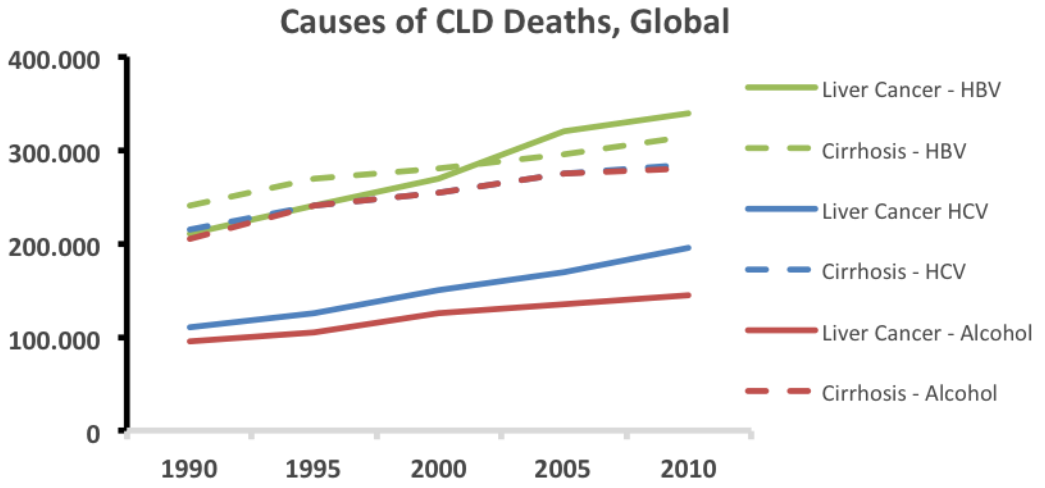

WHO. Available at: http://www.who.int/vaccine_research/documents/ViralCancer7.pdf. (Accessed 19 July 2013).

# Global Burden of Liver Disease: Deaths, Cirrhosis and Liver Cancer - 2010



- 750,000 liver cancer deaths and 1.03 million cirrhosis deaths
- Total deaths increased from 1.25 to 1.75 million per year
- An increasing proportion due to liver cancer
- HBV associated with 45% of liver cancer and 30% of cirrhosis
- HCV and alcohol each cause approximately 25% of deaths






Cowie B, et al. 64th AASLD; Washington, DC; November 1-5, 2013. Abst. 23.

# Epidemiology of hepatitis C

- 27000 to 29000 newly diagnosed cases per year in EU/EEA*
- Most affected age group: 22-44 year, followed by 15-24 yr; men twice more affected than women
- Clustered in sub-populations: injecting drug users, people with HIV infection, inmates, haemodialysis patients, immigrants from high endemic region
- Sexual transmission is considered to be rare, some data indicate that high risk sexual behaviour could enhance a risk for HCV transmission via per mucosal route (i.e. MSM)

Source: ECDC Annual Epidemiological Report; ECDC Hepatitis in EU neighbourhood

# Epidemiology of hepatitis C

- Prevalence of HCV infection (HCV-Ab) in the general population varies widely between countries
  - Range: 0.4% to 22%
  - Prevalence is higher in Southern Europe
  - Variation across the countries:

    Low: ≤0.5% in Belgium, Germany, Netherlands, Sweden, UK

    Intermediate: 0,5 – 2% in Bulgaria, France, Hungary, Romania

    High: ≥2% in (parts of) Italy

- Particularly Italy has a high general population prevalence of HCV, much higher than the estimated HBV prevalence
  - Epidemiologic and phylogenetic assessments suggest this is caused by a period of increased iatrogenic transmission around the 1950s

Source: ECDC Hepatitis in EU neighbourhood

# Epidemiology of hepatitis B and C

## Migrants: HBV and HCV prevalence studies are limited

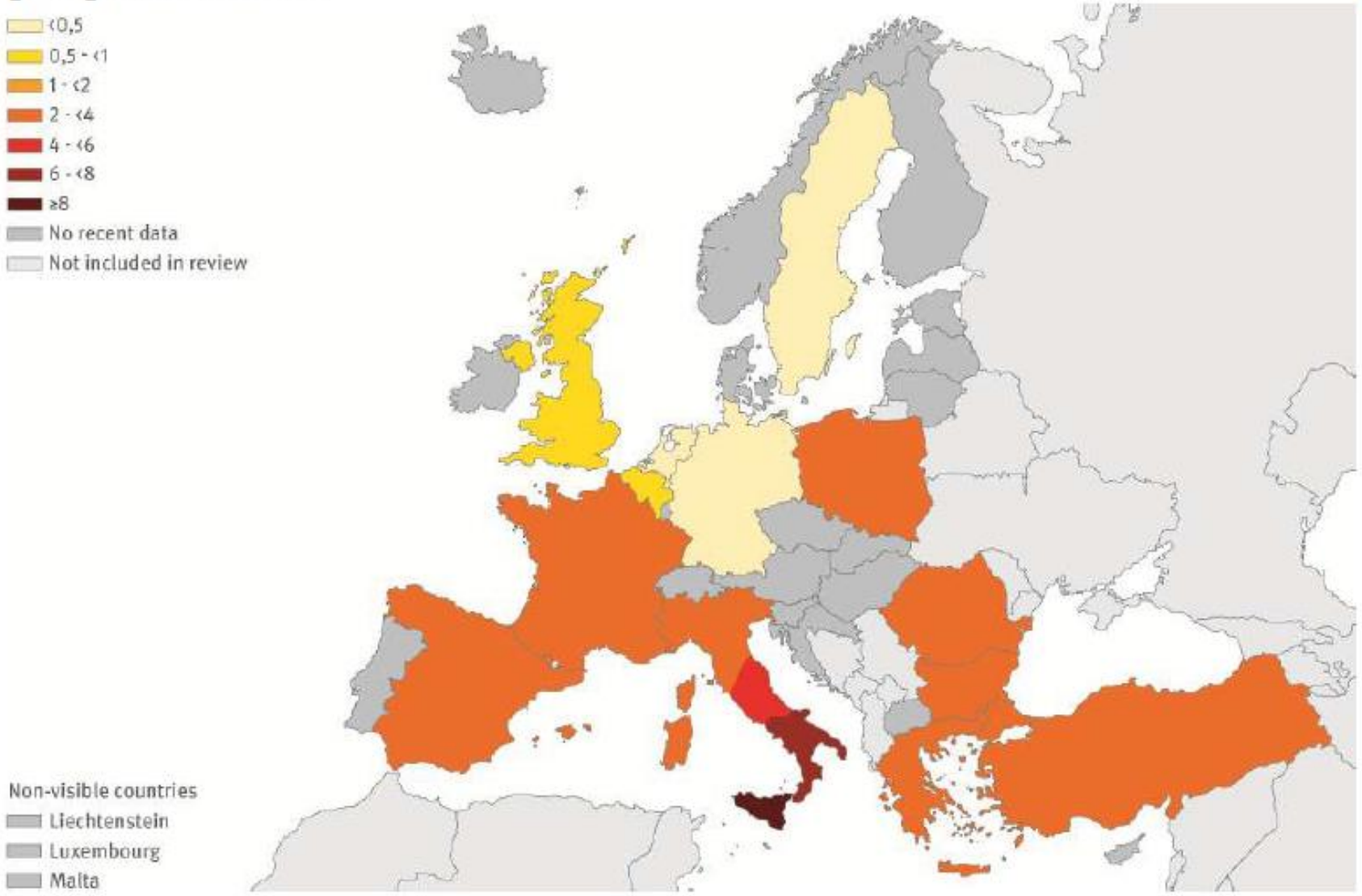
- In nearly all countries the estimated prevalence of HBV and HCV is higher among migrants compared to the general population
- Large estimated numbers of chronically HBV and HCV infected migrants in Western European countries (Germany, Spain, France, Italy, UK)

## Injecting drug users: large number of HCV prevalence studies

- Representativeness of studied populations is variable
- HCV is highly prevalent among IDUs in Europe
- HBV prevalence among IDUs is much lower than that of HCV

Source: ECDC Hepatitis in EU neighbourhood

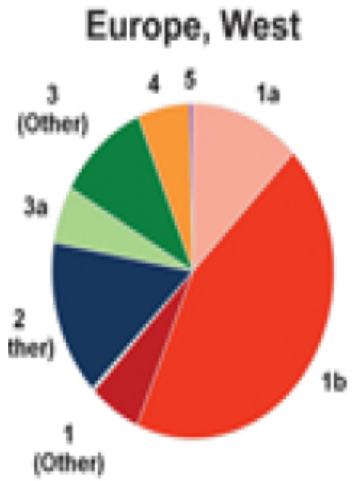
# The prevalence of anti-HCV in the general population

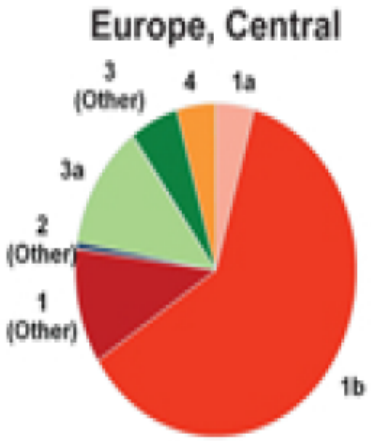



Source: ECDC Hepatitis in EU neighbourhood

# Distribution of HCV Genotypes in Europe



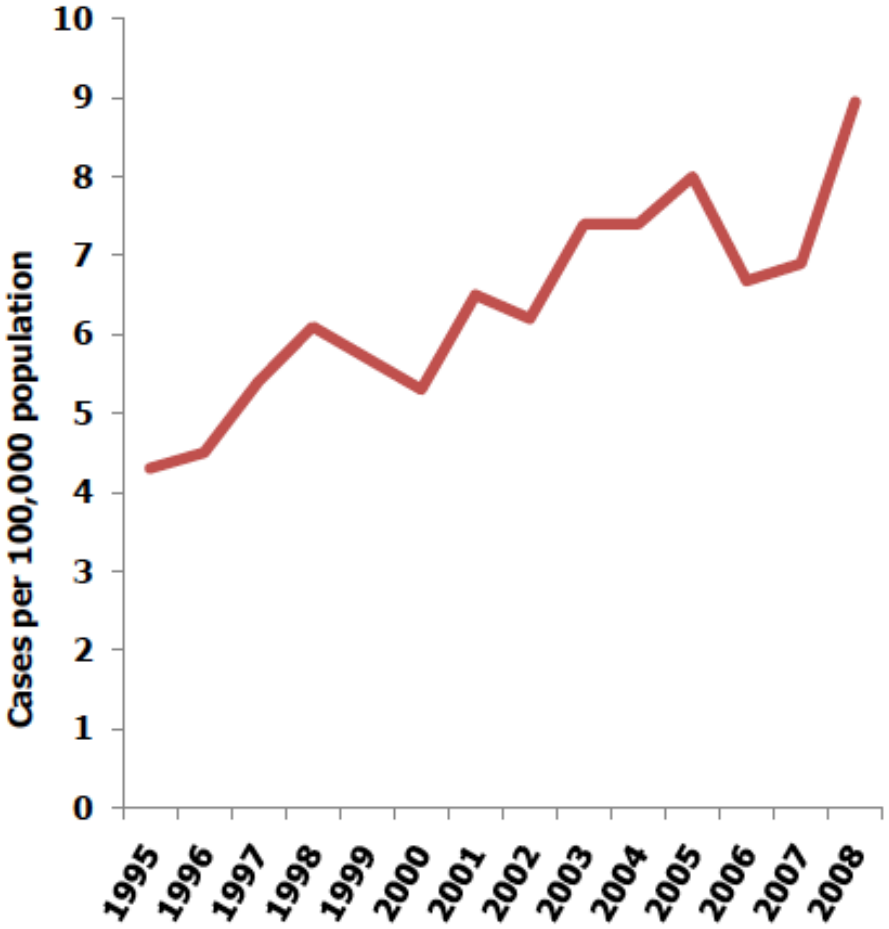




*Razavi et al, AASDL 2013*

# Epidemiology of hepatitis C




Increasing trend of hepatitis C in EU/EEA countries

Interpretation is hampered:

1. Reflects testing and screening practices

2. Large heterogeneity in reporting systems
   - geographical coverage
   - mix of acute and chronic cases
   - use of different case definitions

Source: ECDC Annual Epidemiological Report

# HCV: two different epidemics



**Non sterile injections**
**Medical procedures**

**IVDU**
**Sexual contacts**

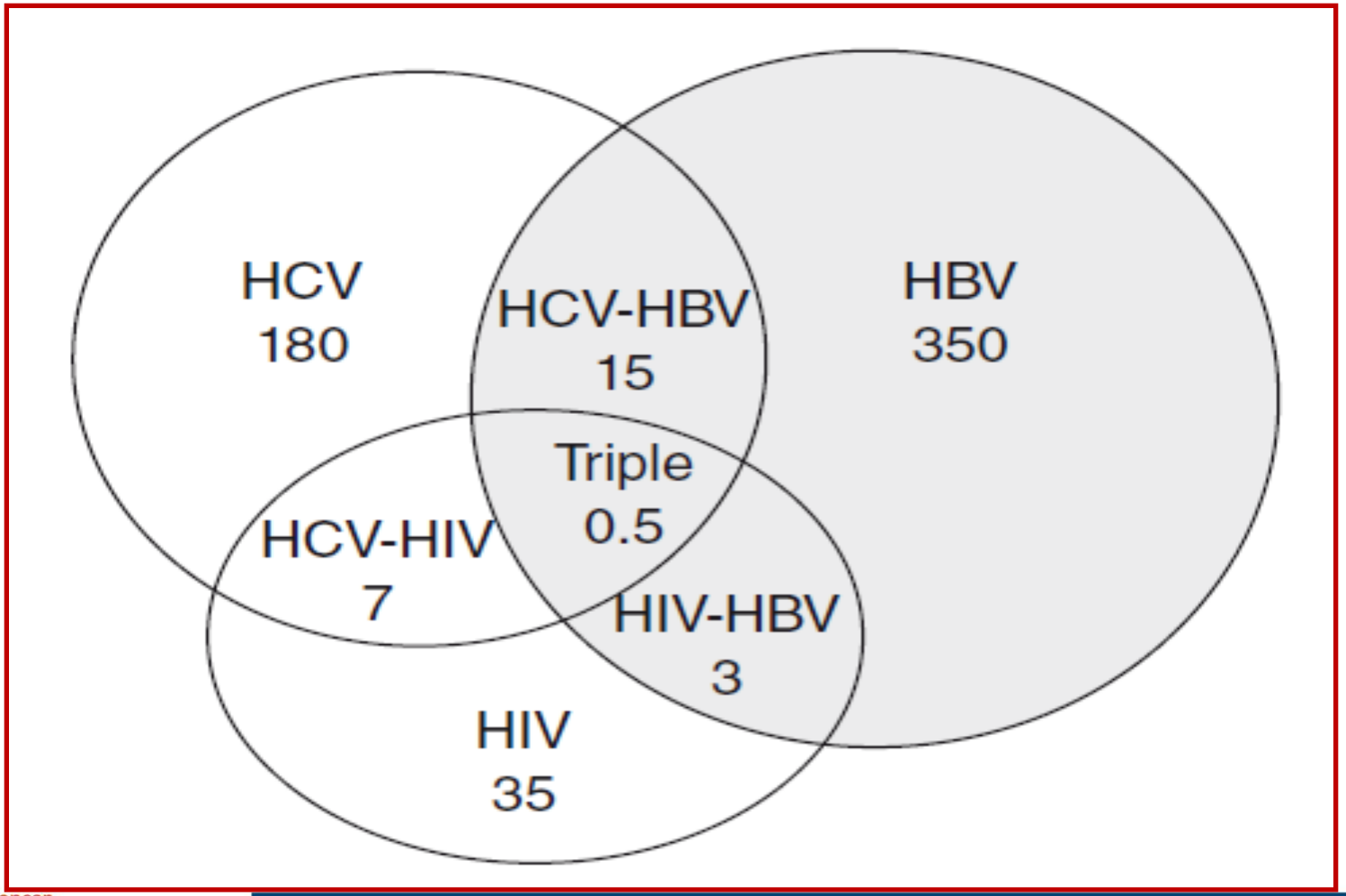
**older**
**not linked to HIV**

**younger**
**often HIV co-infection**

# Estimated number of individuals with HBV, HCV and HIV worldwide



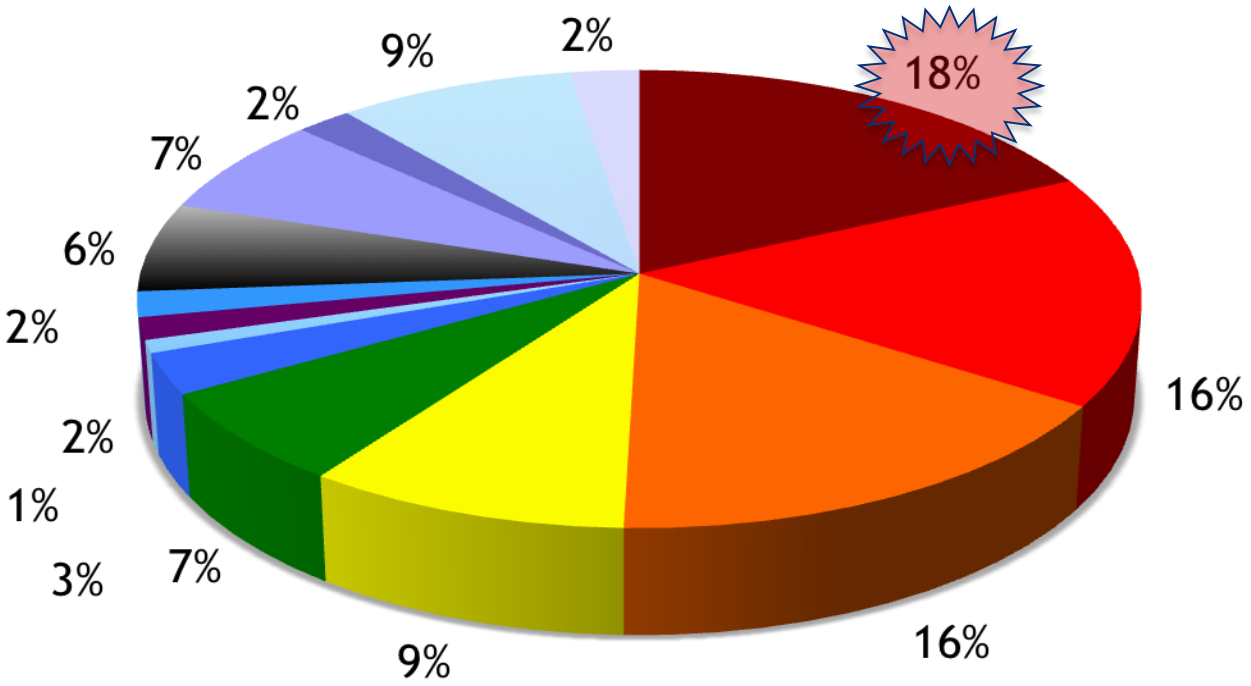
- **Of the 35 million people living with HIV worldwide, around 20% (~7 million) had chronic hepatitis C and 3 million are chronically infected with HBV**






Soriano V et al., AIDS REV 2013

# Causes of death in the Swiss HIV Cohort study 2005-09




- Liver diseases
- AIDS
- Non AIDS Malignancies
- Non AIDS infections/ sepsis
- Heart diseases
- CNS
- Kidney
- Gastro/pancreas
- Lung
- Suicide or psych.
- Substance use
- Accident or Homicide
- Other or not classified
- Unknown

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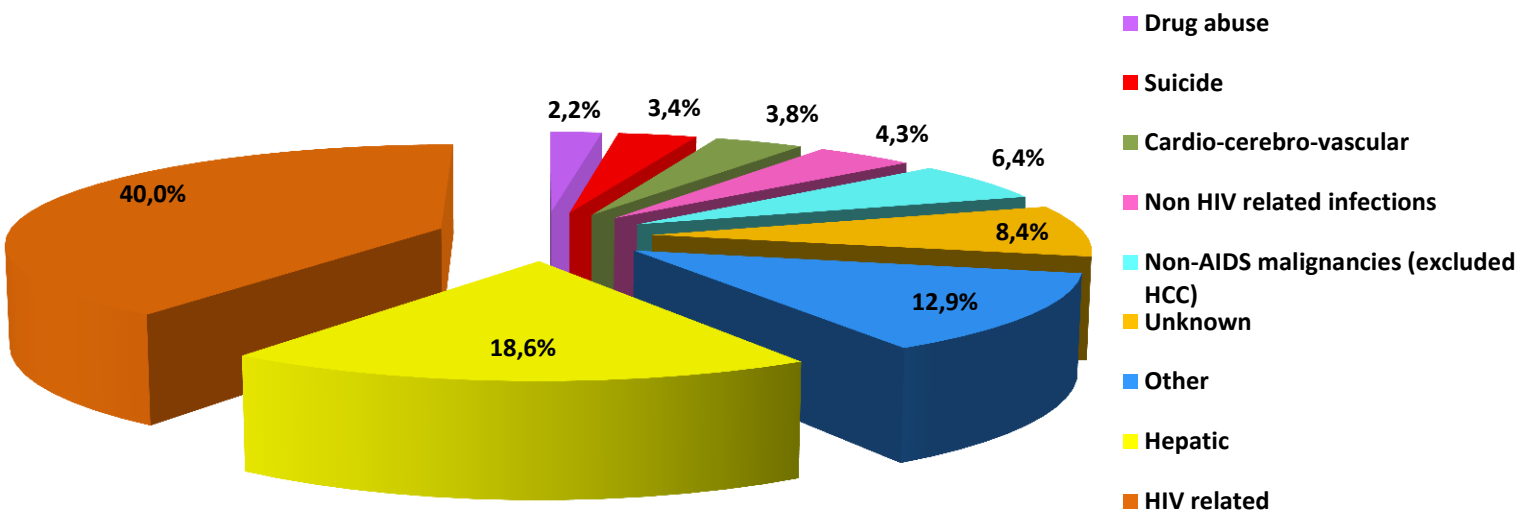
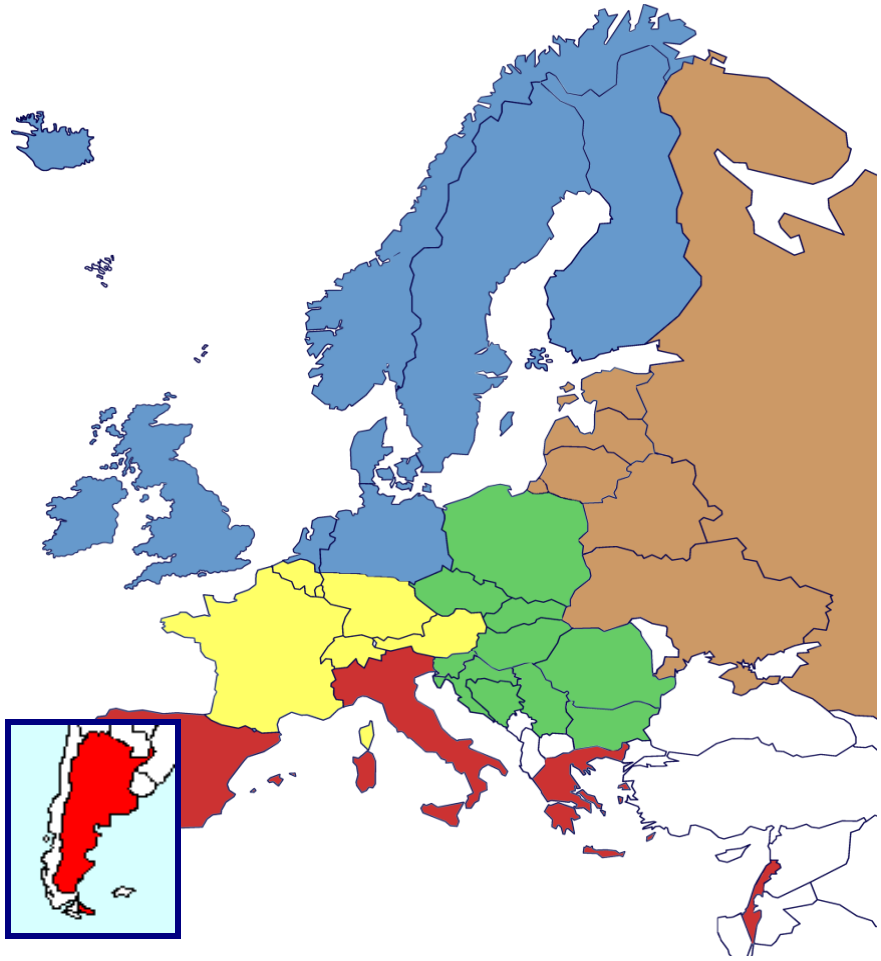
Weber R et al HIV Medicine (2013), 14, 195–207

# Cause of death in the Icona cohort, n=677



# Anti-HCV antibody prevalence in HIV positive individuals from different EuroSIDA regions





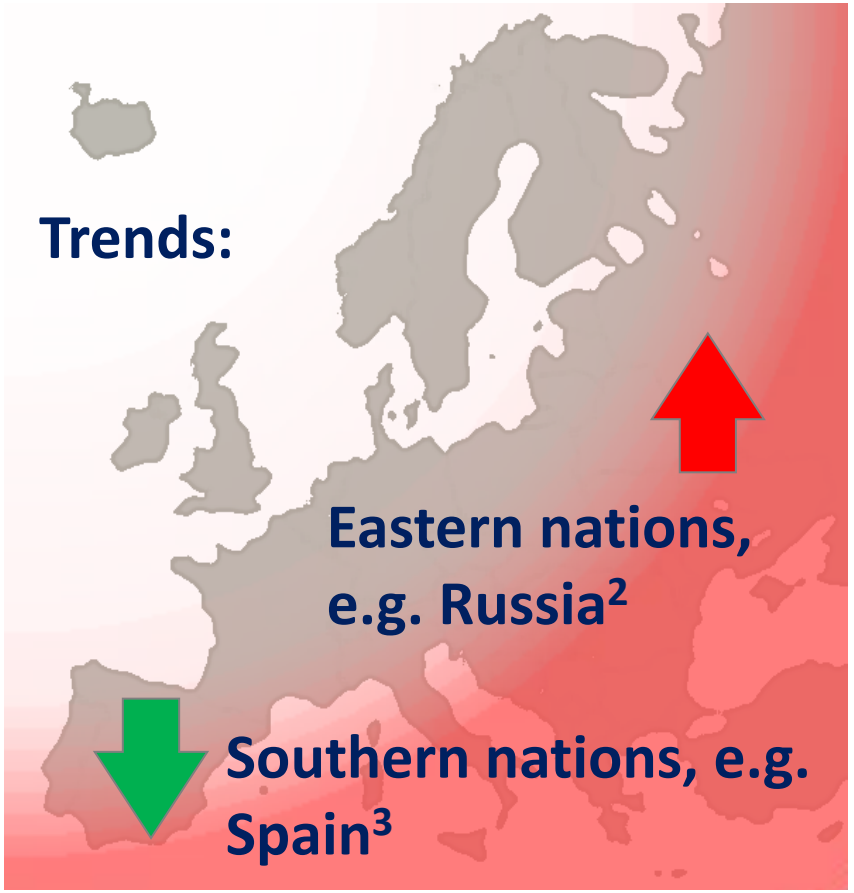
- South: 28.8%
- West: 20.1%
- North: 17.3%
- East Central: 34.0%
- East: 57.7%
- Argentina: 20.6%

Peters et al, BMC Infect Dis, 2014

# Wide regional and intra-national variation in prevalence



- Greater prevalence in east and south Europe (~45% of HIV+ patients)[1]
- Greater prevalence in urban areas (50–90% of HIV+ patients)[1]




Peters et al, BMC Infect Dis, 2014

1. World Health Organization. Protocol 6. Management of hepatitis C and HIV coinfection. WHO Regional Office for Europe; 2007; 2. Wiessing L, et al. Euro Surveill 2011;16:pii:20031; 3. Perez Cachafeiro S, et al. Clin Infect Dis 2009;48:1467–70.

# Prevalence of HBV and HCV in HIV infected subjects from Eastern Europe



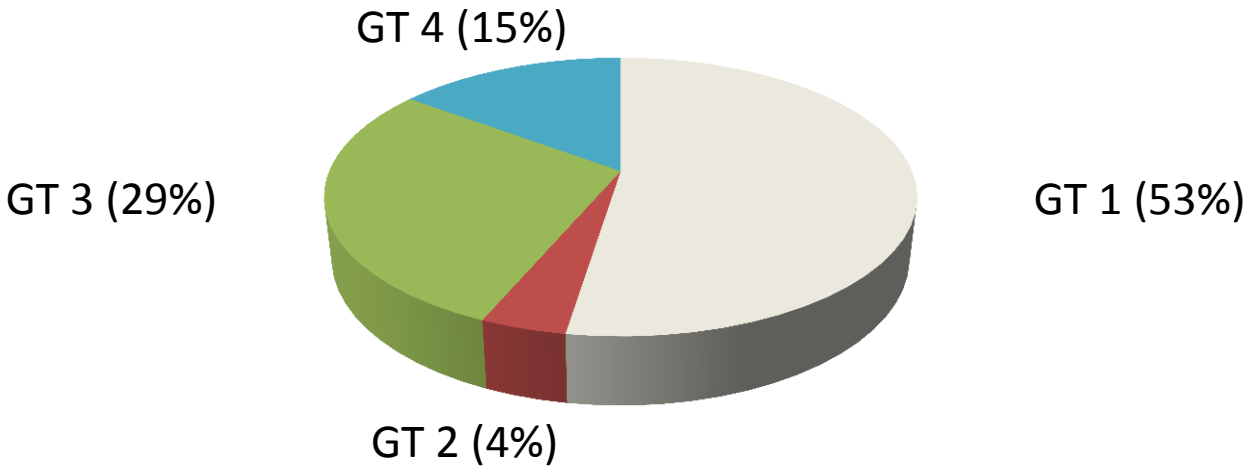
| | HBsAg | anti-HCV |
|---|---|---|
| Poland | 1-2 % | 99% ivdu, 2% others |
| Croatia | 4-5% | 10% |
| Bulgaria | NA | NA |
| Slovakia | 5 of 59 patients (8,5%) | 1 of 59 patients (1,7%) |
| Hungary | 5% | 4 - 5% |
| Czech Republic | 2-3 % | 10-15 % |
| Romania | 30-40% children , 8-10 % other | 98-100% IDUs 2-3% other |
| Serbia | 10-15% | 25% |
| Albania | 15% | 5% |

***C Oprea, Survey 2014***

# Trends in HCV viral genotype distribution



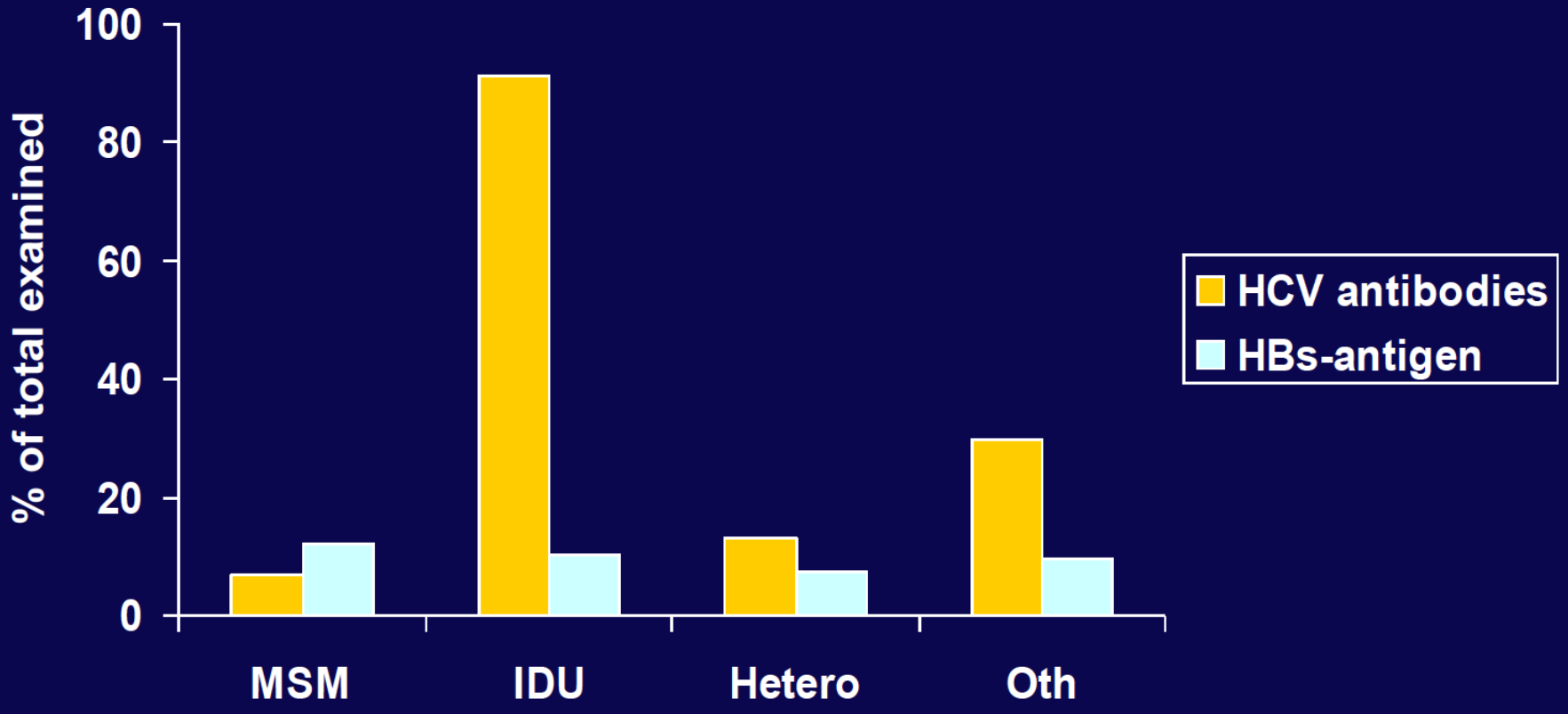
- HCV GT 1 and GT 3 are most commonly identified in co-infections in Europe[1,2]




- GT4 becoming increasingly prevalent in some regions due to immigration[3]
- GT 1 and GT 4 are usually considered the most difficult to cure[4,5]

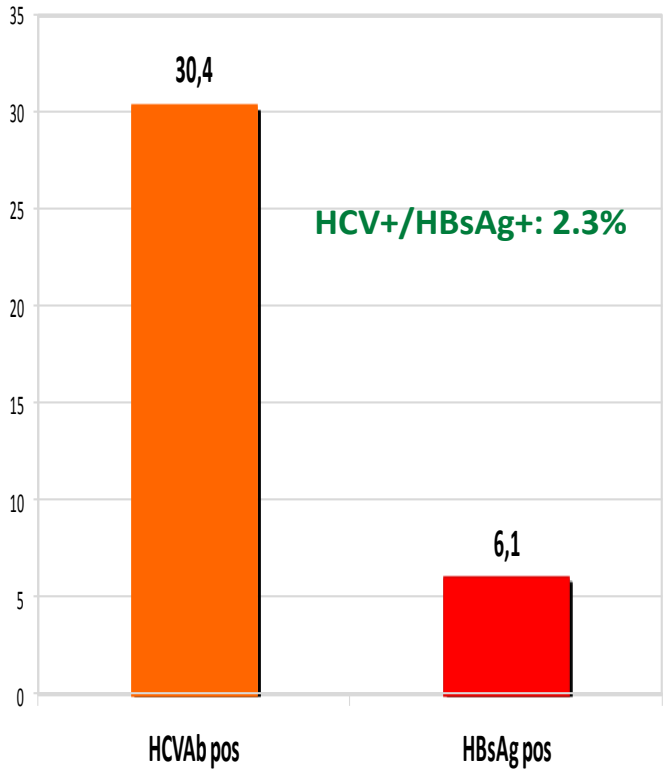
1. Esteban JI, et al. J Hepatol 2008;48:148–62; 2. Soriano V, et al. J Infect Dis 2008;198:1337–44; 3. de Bruijne J, et al. J Clin Microbiol 2009;47: 3832–8; 4. European Association for the Study of the Liver. J Hepatol 2014;60:392–492 http://www.easl.eu/assets/application/files/bdb06ff135c7ccb_file.pdf; 5. European AIDS Clinical Society (EACS). Guidelines Version 7.0. EACS, 2013. http://www.eacsociety.org/Portals/0/Guidelines_Online_131014.pdf.

# Prevalence of hepatitis

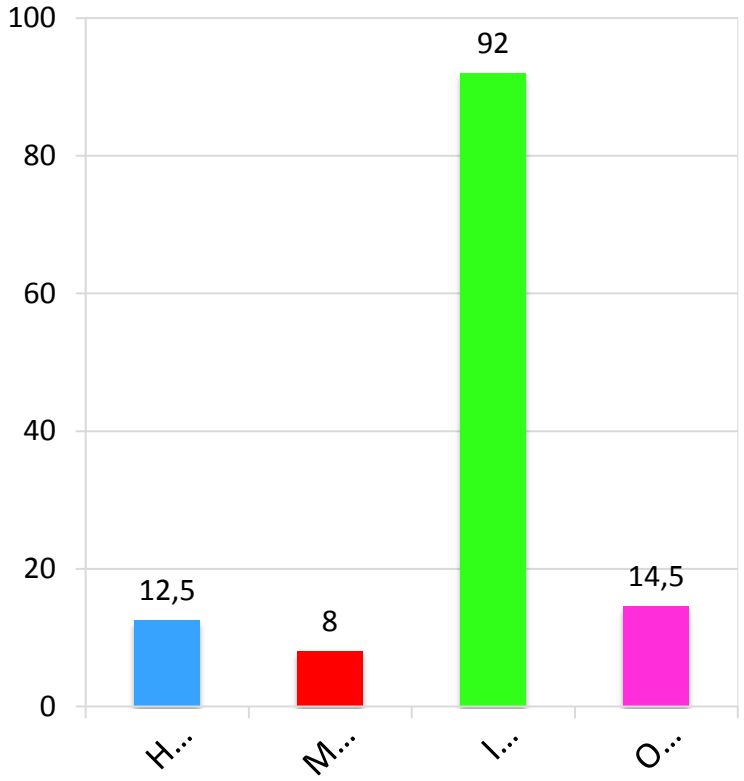


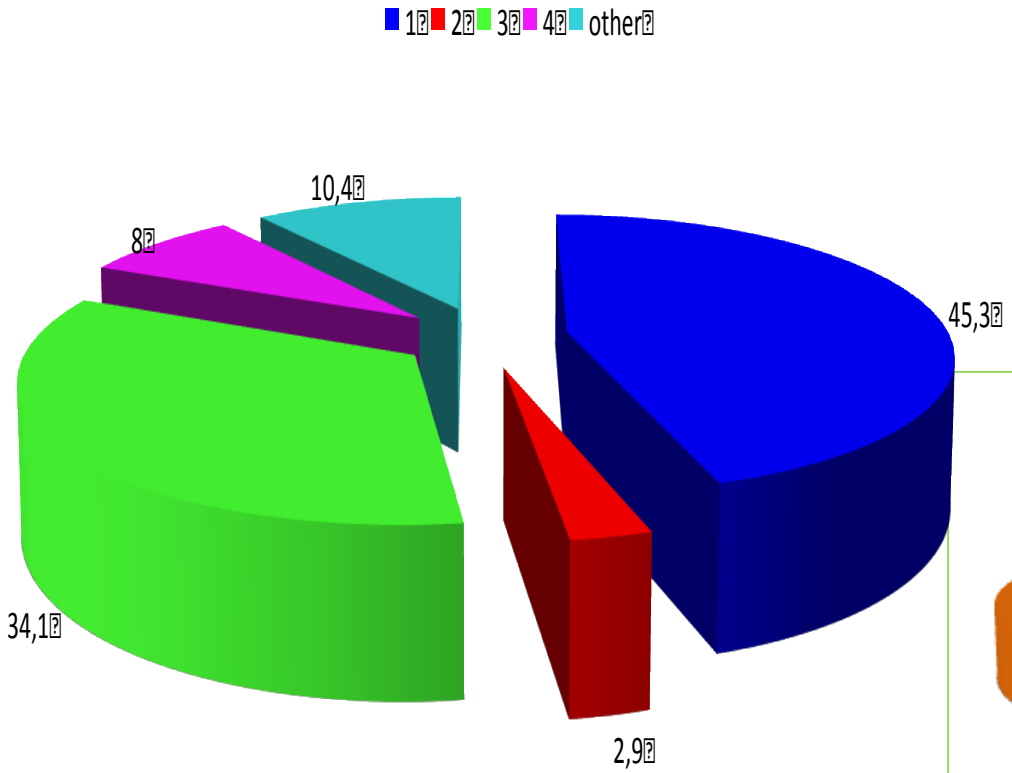

EuroSIDA: Soriano *et al*, JID 2002

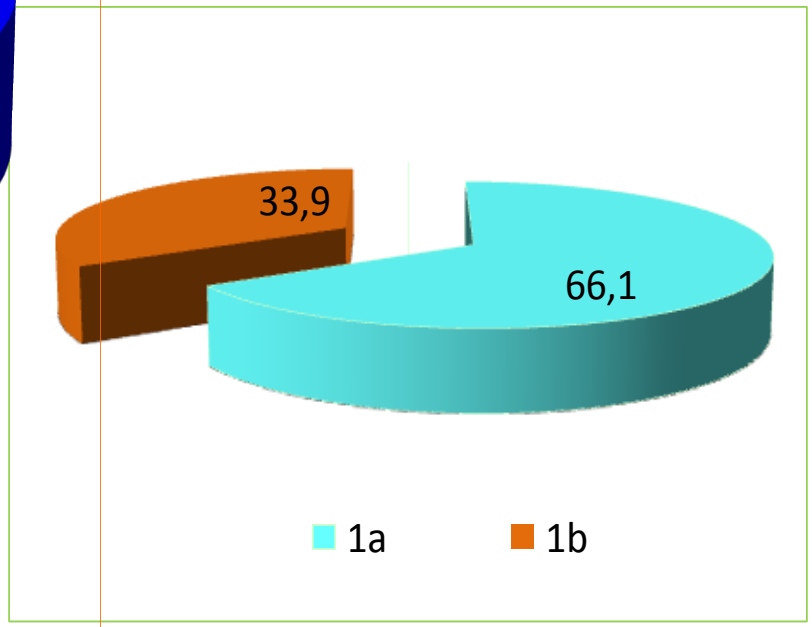
## HBsAg and HCV Ab positivity in 10,665 patients




## Mode of HIV transmission according to HCV Ab status N=10665





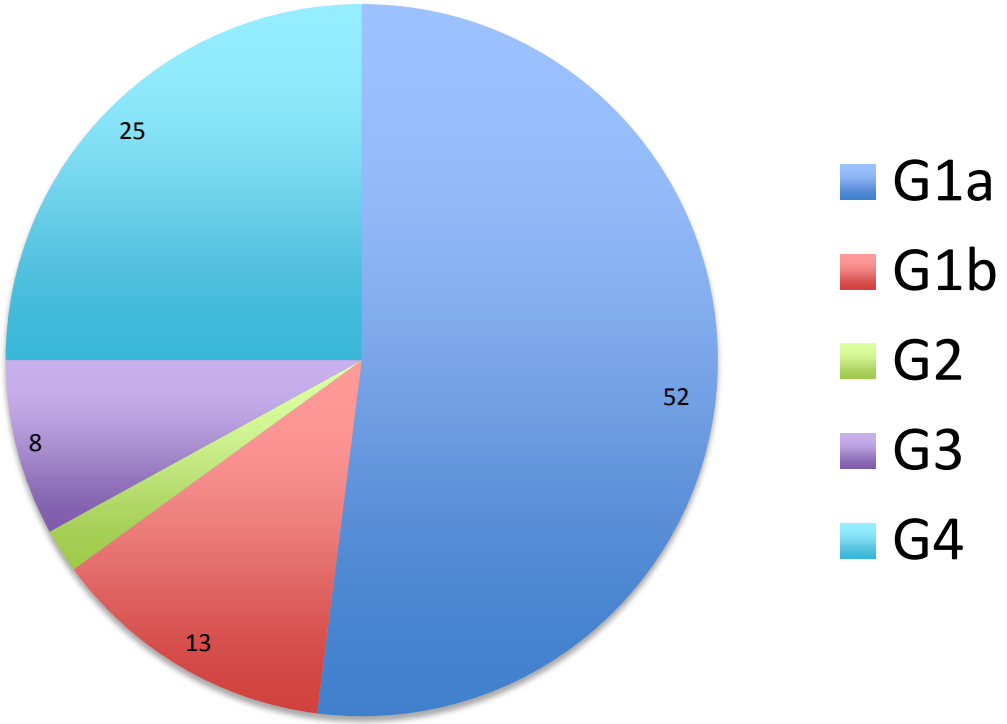






for 2014, 6 months

# Royal Free Hospital, London – HCV genotypes



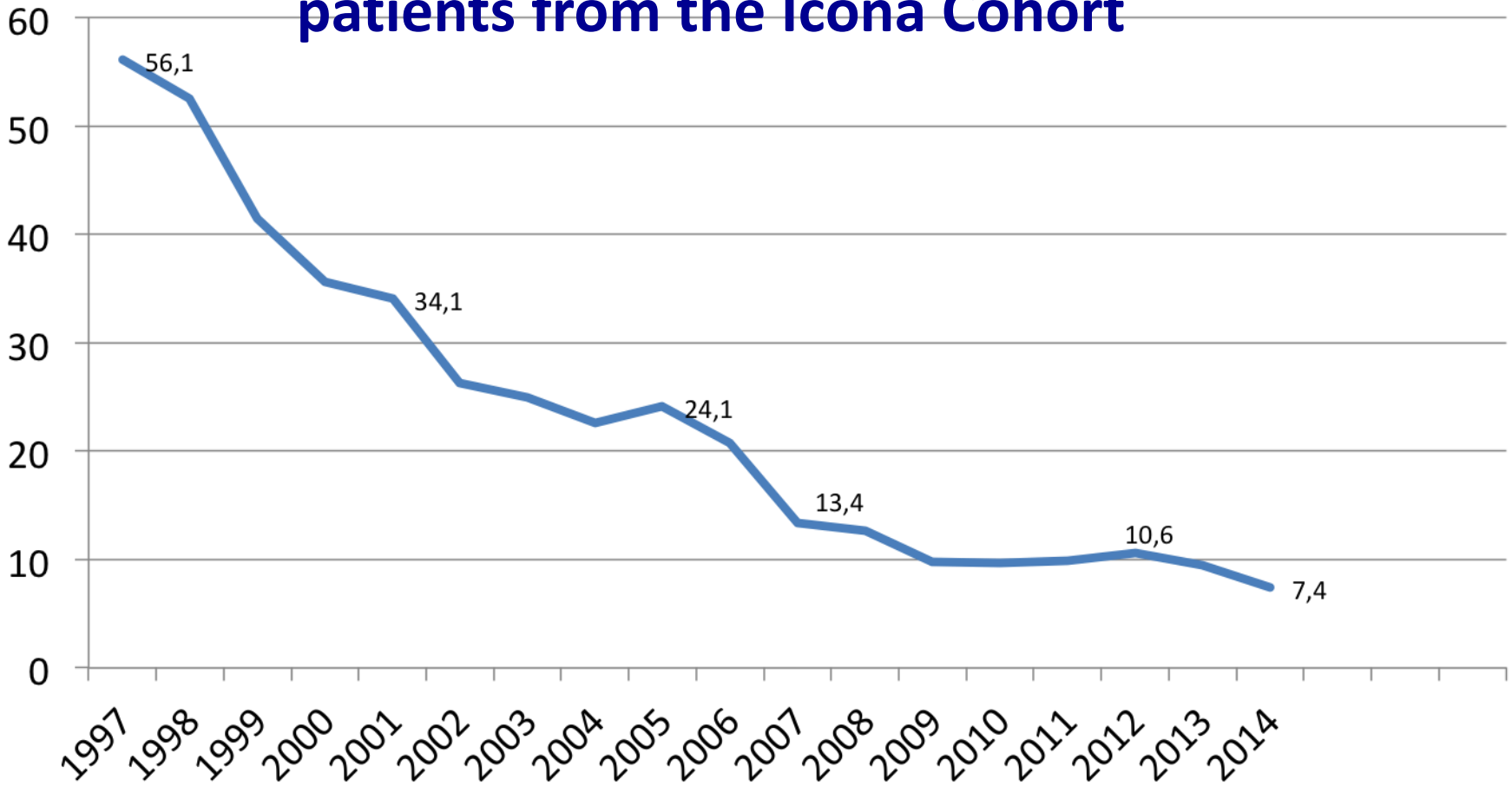



Increasing GT 4 infections

GT 1a >> GT 1b

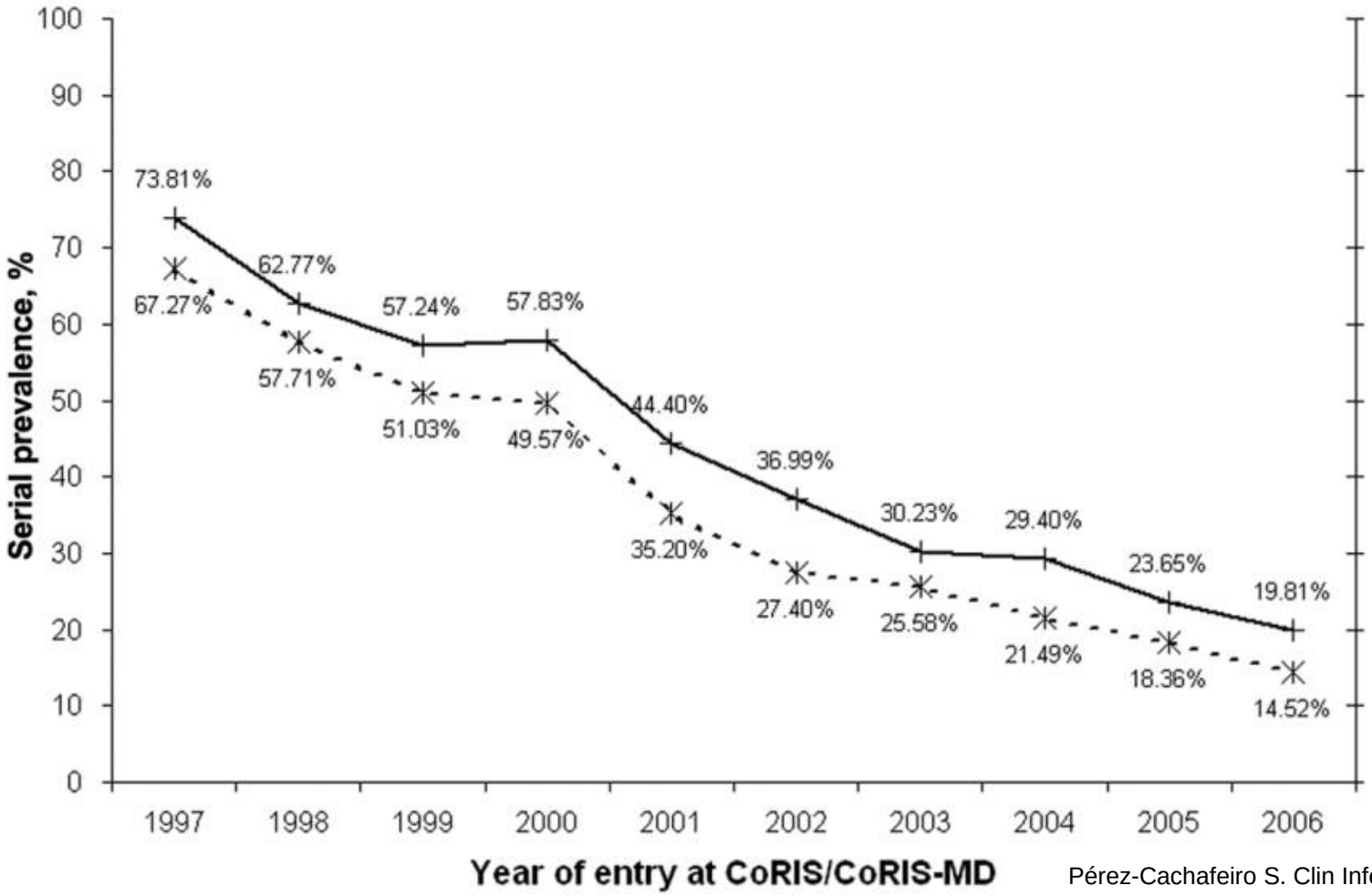
Bhagani S, personal communication

# Decreasing frequency of HCVAb positive in 10,665 patients from the Icona Cohort



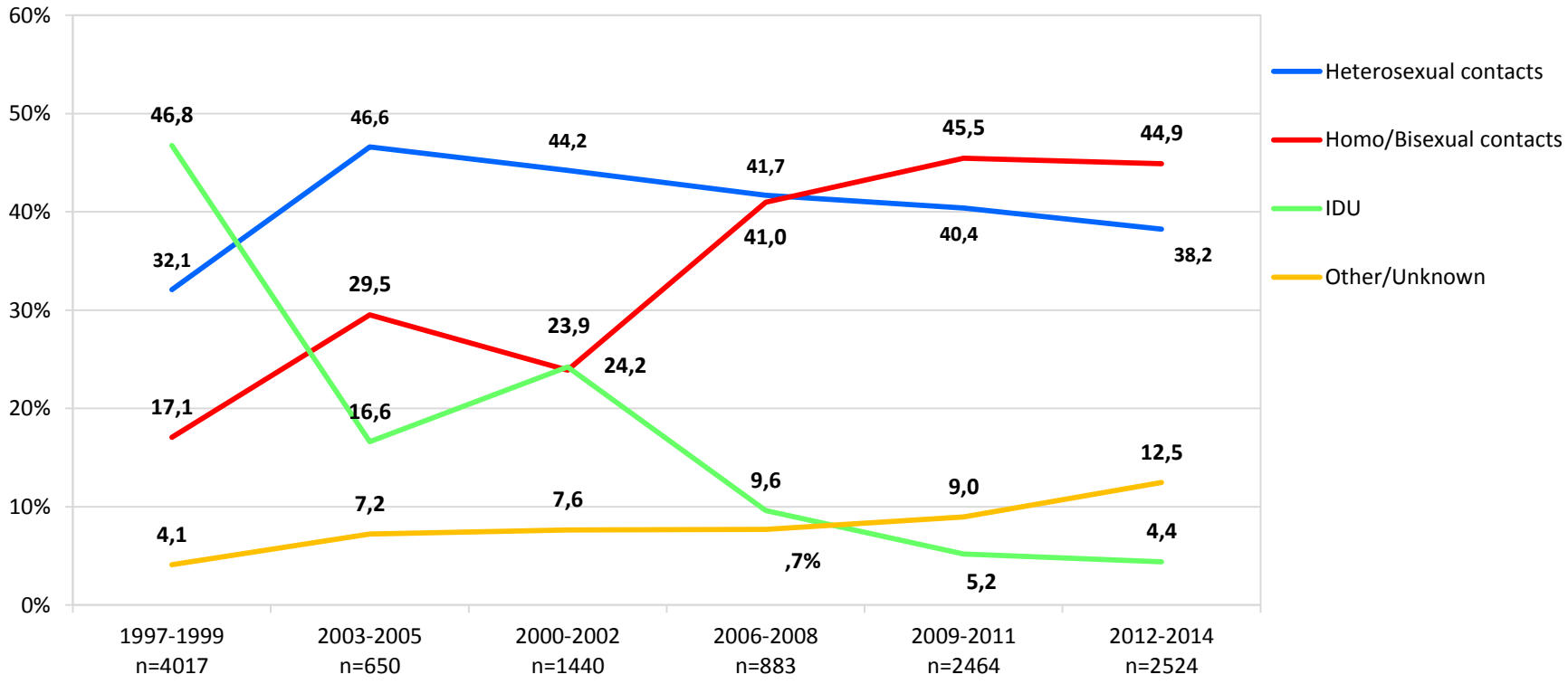
# Decrease in Serial Prevalence of Coinfection with Hepatitis C Virus among HIV-Infected Patients in Spain, 1997–2006





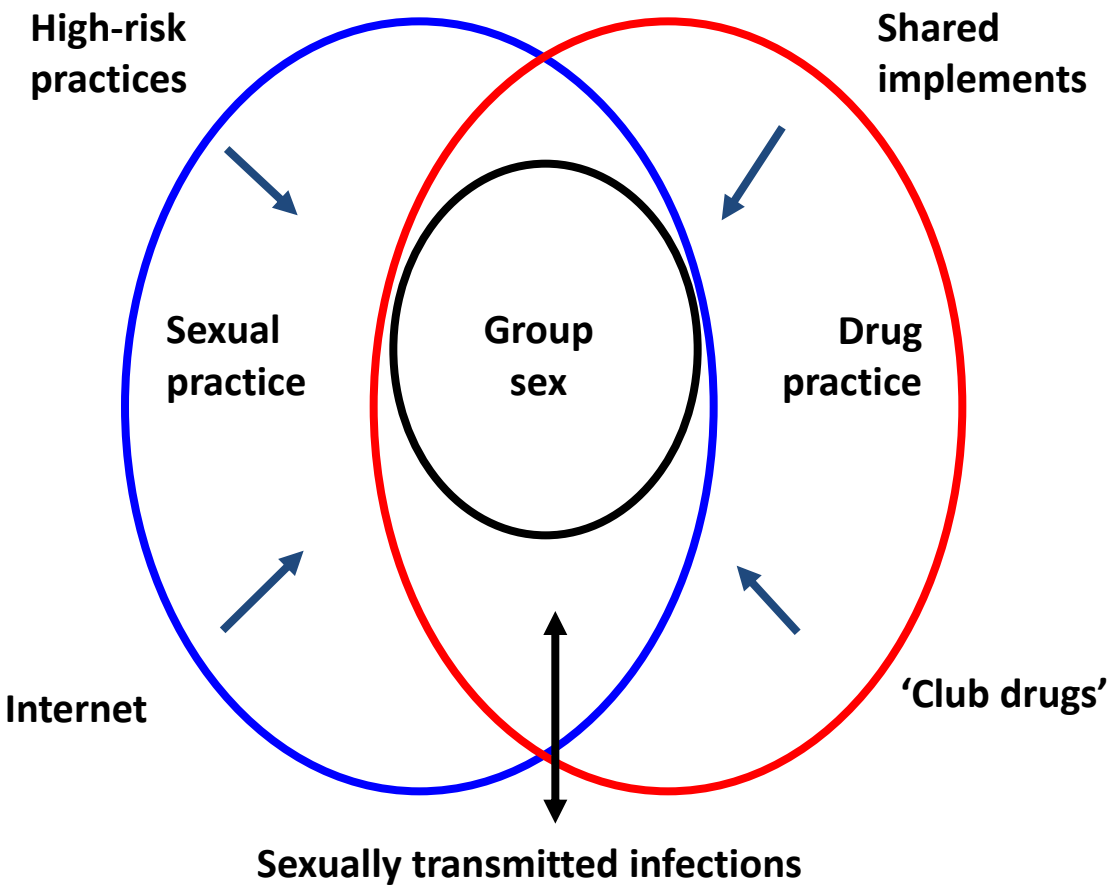

Pérez-Cachafeiro S. Clin Infect Dis 2009.

## Mode of HIV transmission according to calendar year of enrollment



# Changing epidemiology and pattern of transmission in Northern Europe






Danta M, et al. AIDS 2007;21:983–91.

# HCV co-infection: Athena cohort



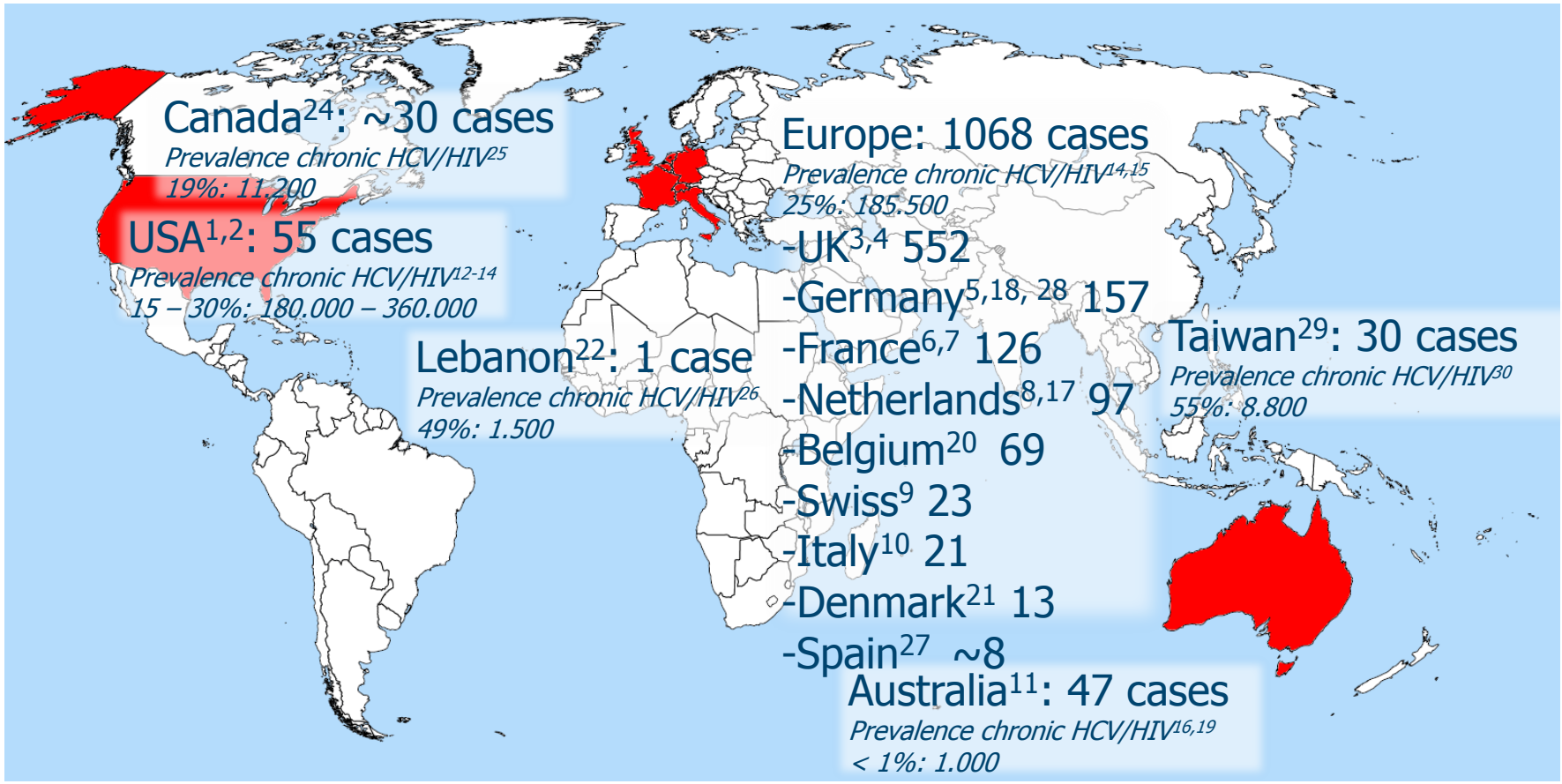
Screened at least once 18,718

HCV antibody/RNA positive 2,235 (12%)

- Confirmed chronic 987
- Confirmed acute 120

| HCV co-infection | Chronic (N=987) | | Acute (N=120) | |
|---|---|---|---|---|
| | N | % | N | % |
| Male | 814 | 82 | 120 | 100 |
| Origin | | | | |
| Netherlands | 641 | 65 | 98 | 82 |
| Europe | 171 | 17 | 13 | 11 |
| Transmission route | | | | |
| MSM | 431 | 44 | 114 | 95 |
| Heterosexual | 101 | 10 | 3 | 3 |
| IDU | 341 | 35 | 1 | 1 |

# Acute HCV among HIV+ MSM

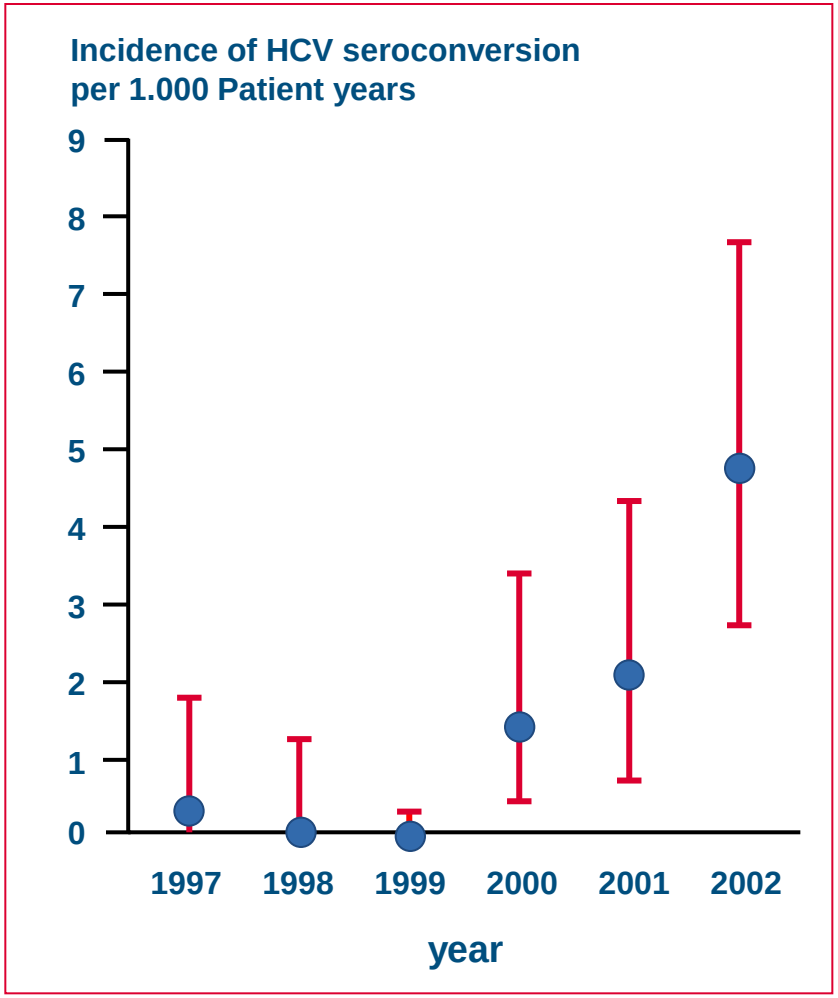



1:Luetkemeyer JAIDS 2006; 2:Cox Gastroenterology 2008; 3:Giraudon Sex Transm Infect 2008; 4:Ruf Eurosurveill 2008; 5:Vogel CID 2009; 6:Gambotti Euro Surveill 2005; 7:Morin Eur J Gastro Hepat 2010; 8:Urbanus AIDS 2009; 9:Rauch CID 2005; 10:Gallotta 4th Works. HIV & Hep. Coinf. 2008; 11:Matthews CID 2009; 12:Sherman CID 2002; 13:Backus JAIDS 2005; 14:UNAIDS Report 2008; 15:Soriano JID 2008; 16:Matthews CID 2011; 17:Arends Neth J Med 2011; 18:Neukam HIV Med 2011; 19:Pfafferott PLoS One 2011; 20:Bottieau Euro Surveill 2010; 21:Barfod Scand JID 2011; 22:Dionne-Odom Lancet Infect Dis 2009; 23:Taylor Gastroenterology 2009; 24:Hull personal conversation 2011; 25:Remis 1st Canadian HCV Conference 2001; 26:UNGASS Country progress Report 2010; 27:Soriano personal conversation 2011; 28:Boesecke 18thCROI Boston 2011 abstract #113; 29:Sun Liver International 2011; 30:Lee J F Med Assoc 2008

# Acute HCV-Epidemic in Europe



- London Chelsea qnd Westminster:
  - 27 cases 1997 - 2002
  - 26 male
  - 25 HIV+
- Risk factors
  - Unprotected anal or vaginal sex (n=21)
  - i.v. drug use (n=2)
  - Recent syphilis infection (n=9)



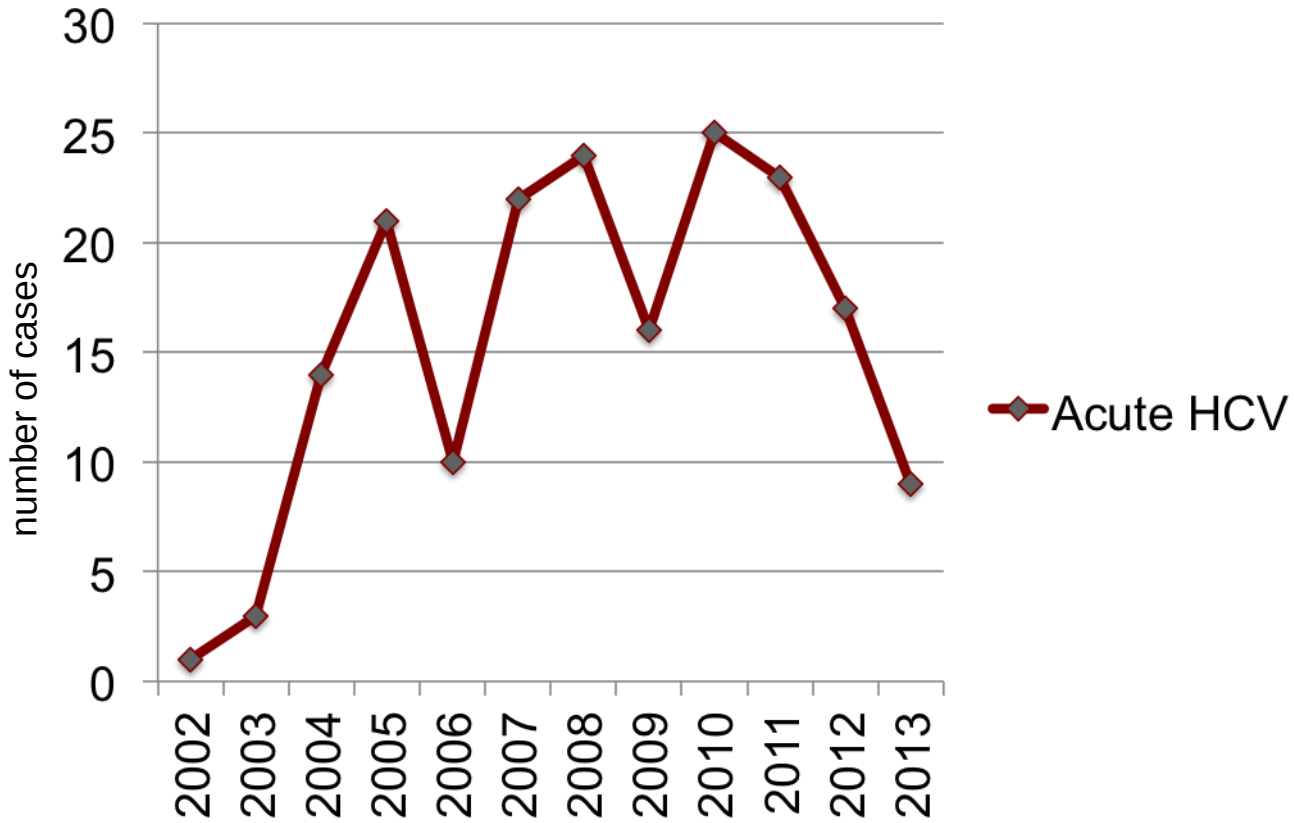

Browne et al. *Sex. Transm. Inf*. 2004; 80: 326-327

# Continous increase in new infections in HIV+ MSM: Berlin data



Outpatient Clinic in Berlin Center; ~1500 HIV+, 185 cases of acute HCV since 2002 up to 5/2013

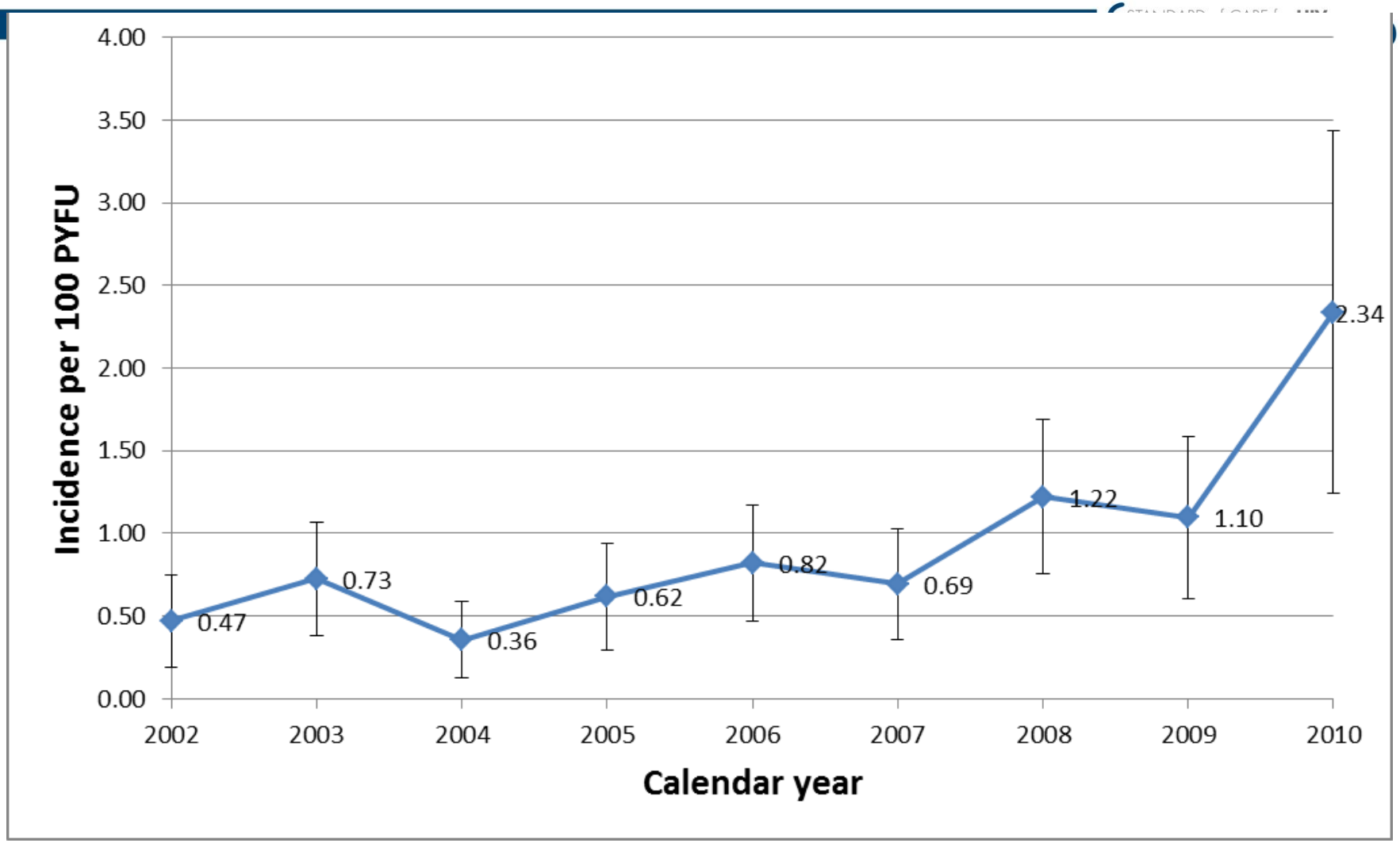
2 cases in HIV- MSM, 2 IVDU, 1 female




**Ingiliiz P personal communication**

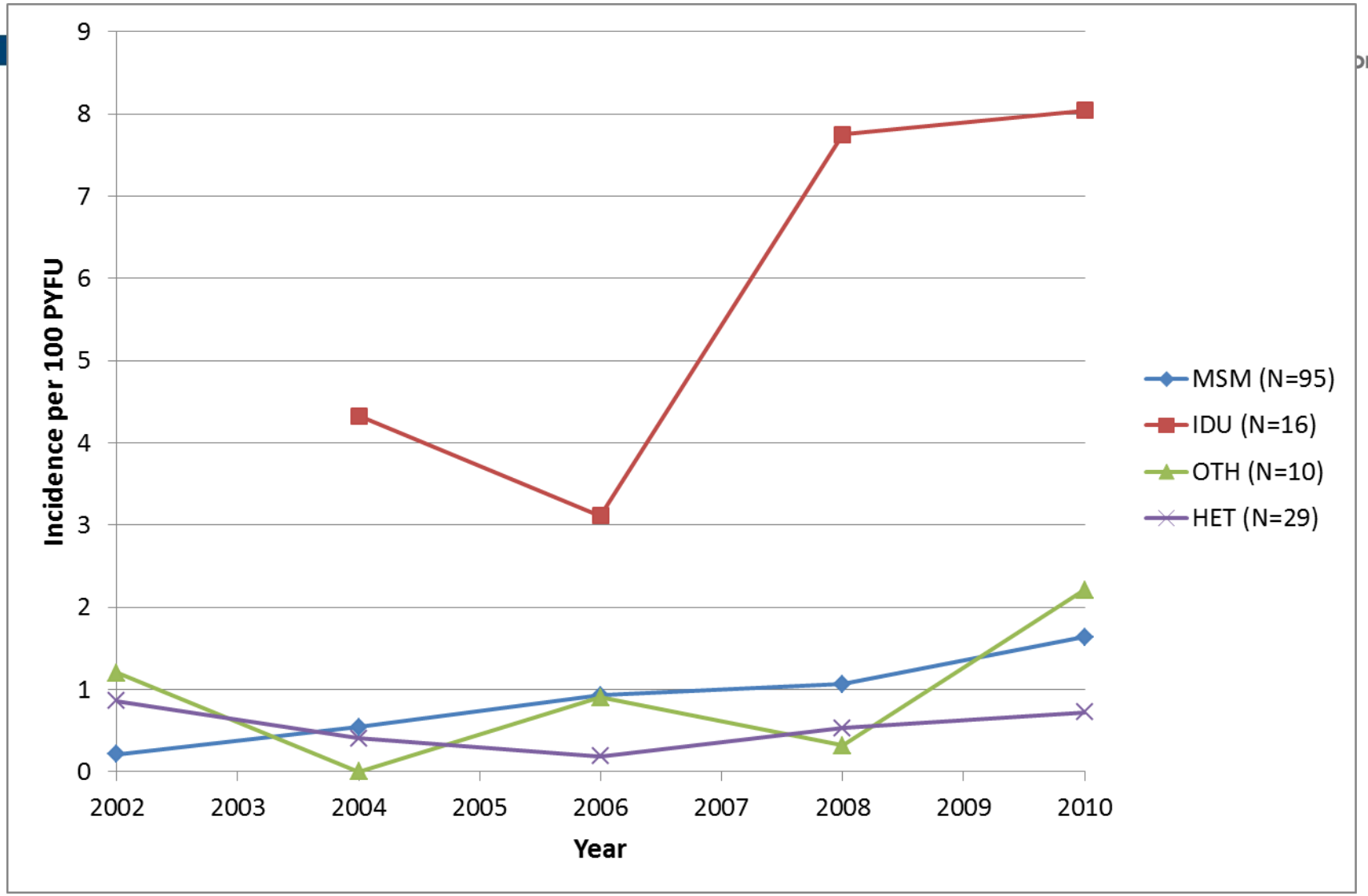
Own data, MIB

# Incidence of Acute HCV within EuroSIDA by Calendar Year



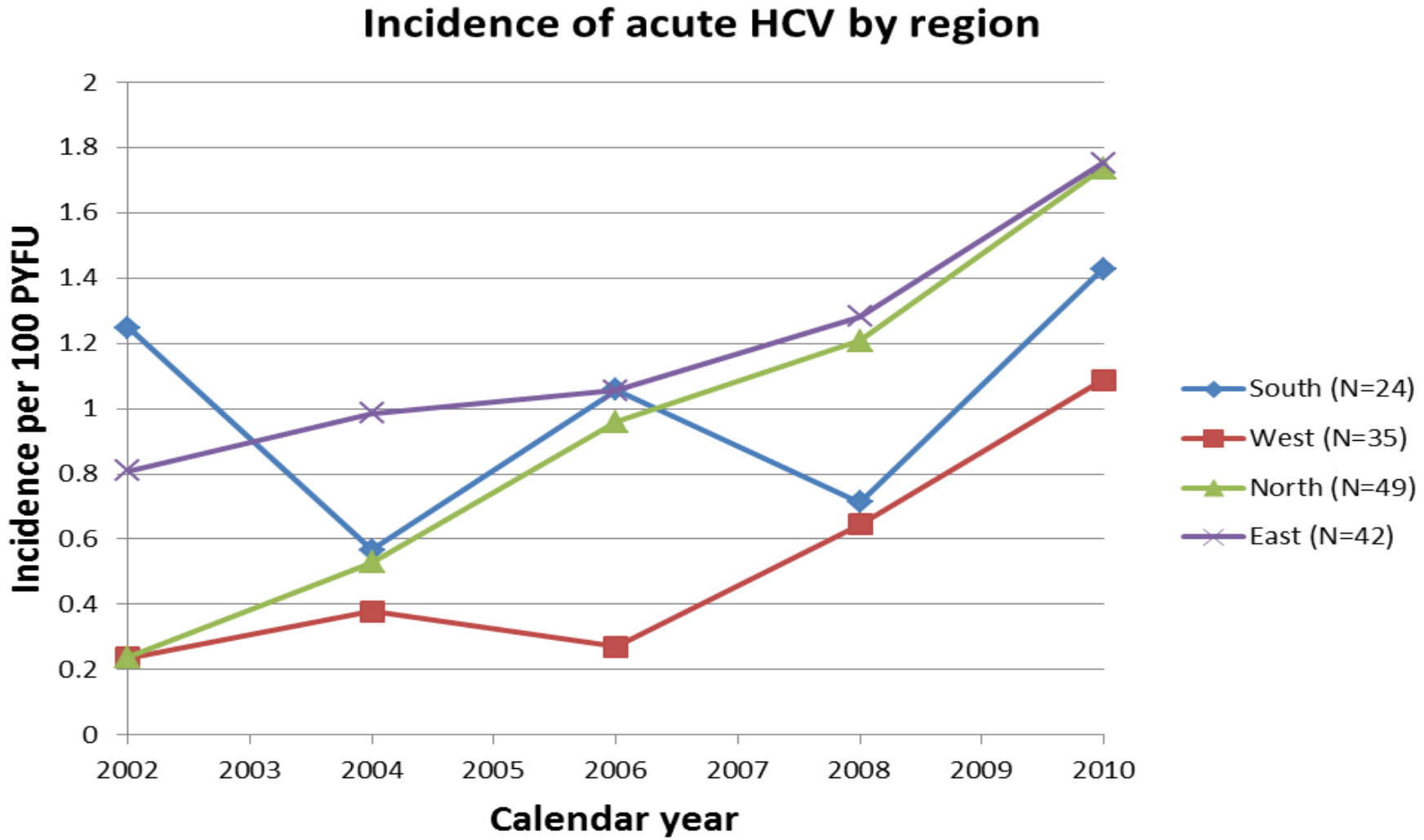

Rockstroh/Kirk, Glasgow 2012

# Incidence of Acute HCV by Risk Group




Rockstroh/Kirk, Glasgow 2012

# Incidence of Acute HCV by regions of EuroSIDA by Calendar Year




Rockstroh/Kirk, Glasgow 2012

# Patient access to screening is variable across Europe

- HIV infection is the main driver of testing for HCV co-infection
- HCV screening guidelines most likely to be applied in large HIV centres
- Screening for HIV is advocated for all HCV-infected individuals
  - But may be limited/absent for HCV patients treated by Gastroenterology and/or Hepatology specialists
- Co-infection has a large impact on the management of both diseases
  - Missed diagnosis of HIV may lead to poorly informed treatment decisions and poor outcomes

Taylor LE. et al. Clin Infect Dis 2012:55(S1):S33–4

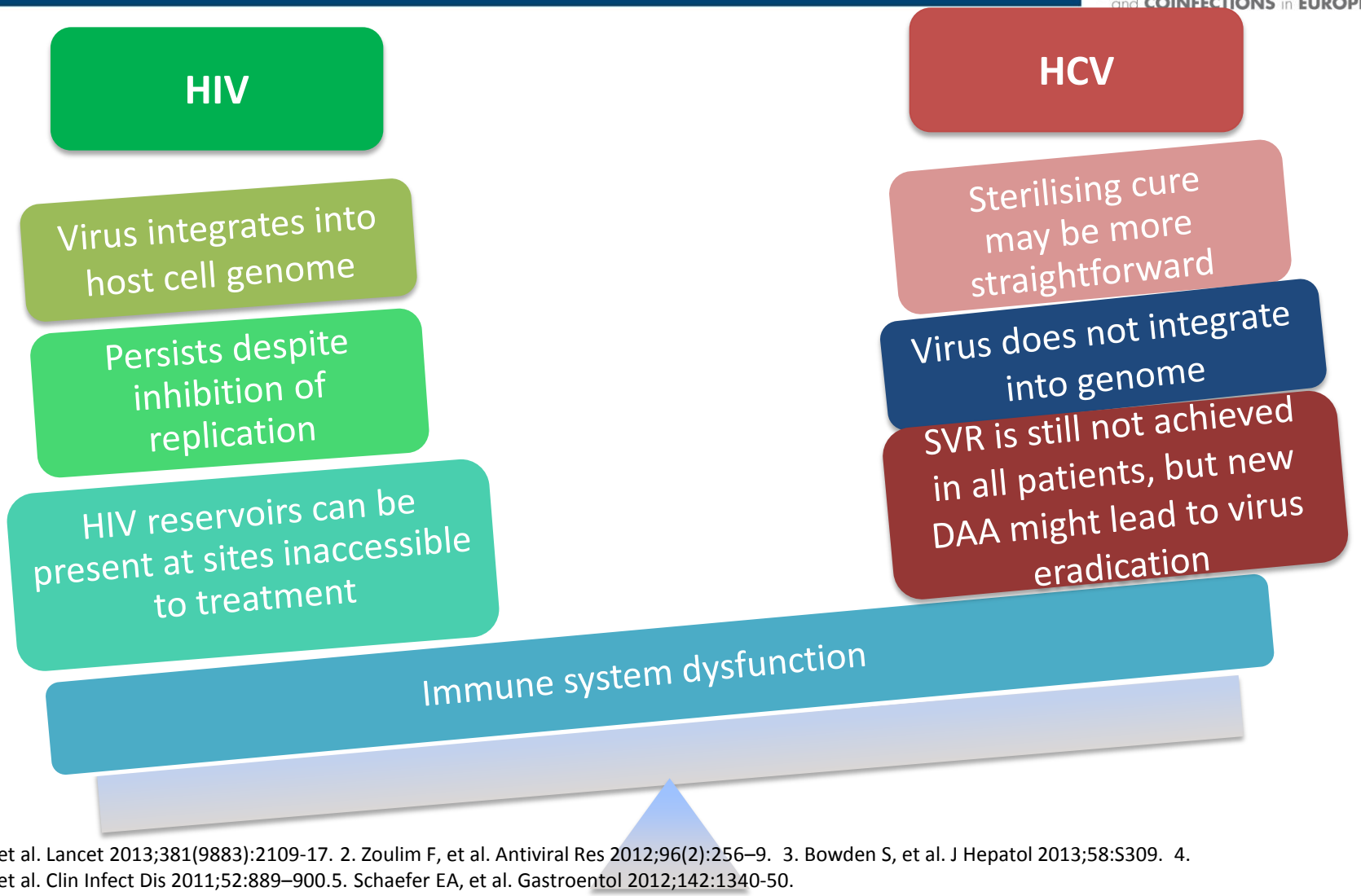
# Guidelines – screening and monitoring

- EACS guidelines recommend HCV screening (and genotyping if positive) in all HIV-infected patients[1]
  - Endorsed by various national guidelines[2,3]
- Guidelines also emphasise the value of additional HCV testing:
  - HCV RNA and antibody tests for HIV+ patients with recent risk or unexplained hepatic transaminase elevations[1]
  - MSM should be informed about transmission risks and tested annually for HCV if they have HIV[1]

1. European AIDS Clinical Society (EACS). Guidelines Version 7.0. EACS, 2013. http://www.eacsociety.org/Portals/0/Guidelines_Online_131014.pdf. 2. British HIV Association (BHIVA). HIV Medicine 2013;14(S4):1–71; 3. Ministère des Affaires sociales et de la Santé. Rapport 2013 sur la prise en charge médicale des personnes vivant avec le VIH. Direction de l'information légale et administrative 2013; Paris, France. http://www.sante.gouv.fr/rapport-2013-sur-la-prise-en-charge-medicale-des-personnes-vivant-avec-le-vih.html

# Challenges to cure






1. Katlama C, et al. Lancet 2013;381(9883):2109-17. 2. Zoulim F, et al. Antiviral Res 2012;96(2):256–9. 3. Bowden S, et al. J Hepatol 2013;58:S309. 4. Pearlman BL, et al. Clin Infect Dis 2011;52:889–900.5. Schaefer EA, et al. Gastroentol 2012;142:1340-50.

# HIV/HCV in Europe: conclusions



- ✓ Data mainly from cohorts, few Country reports
- ✓ Different prevalences of HIV/HCV coinfection across Europe, highest in Eastern and Southern Europe
- ✓ HCV-HIV epidemic mainly driven by IDU
- ✓ New HIV cases with chronic HCV infection are decreasing, according to changing HIV epidemiology
- ✓ Acute HCV increasing mainly driven by MSM
- ✓ Importance of HCV testing to prevent liver disease and to eradicate HCV infection

# HIV/HCV in Europe: conclusions



Special thanks to:

- ✓ Jurgen Rockstroh
- ✓ Cristiana Oprea
- ✓ Eurosida cohort
- ✓ Icona cohort