

Late presentation for care: the burden of disease in mono- and co-infected patients and who are the late presenters

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HIV, HBV and HCV

- All 3 are life-threatening blood-borne viruses that affect hundreds of millions of people worldwide.
- All can remain asymptomatic for many years
- Ignorance about all of the major forms of viral hepatitis, reminds many people of the early years of the AIDS epidemic, when a combination of misinformation and unwillingness to candidly address stigmatised behaviours and social inequalities led to a widespread failure to formulate a cohesive public health response.
- Agreement on a definition of late presenters in HIV has been an important tool incorporated into surveillance structures to understand to what extent a large undiagnosed population remains a problem and to impact the public health response.

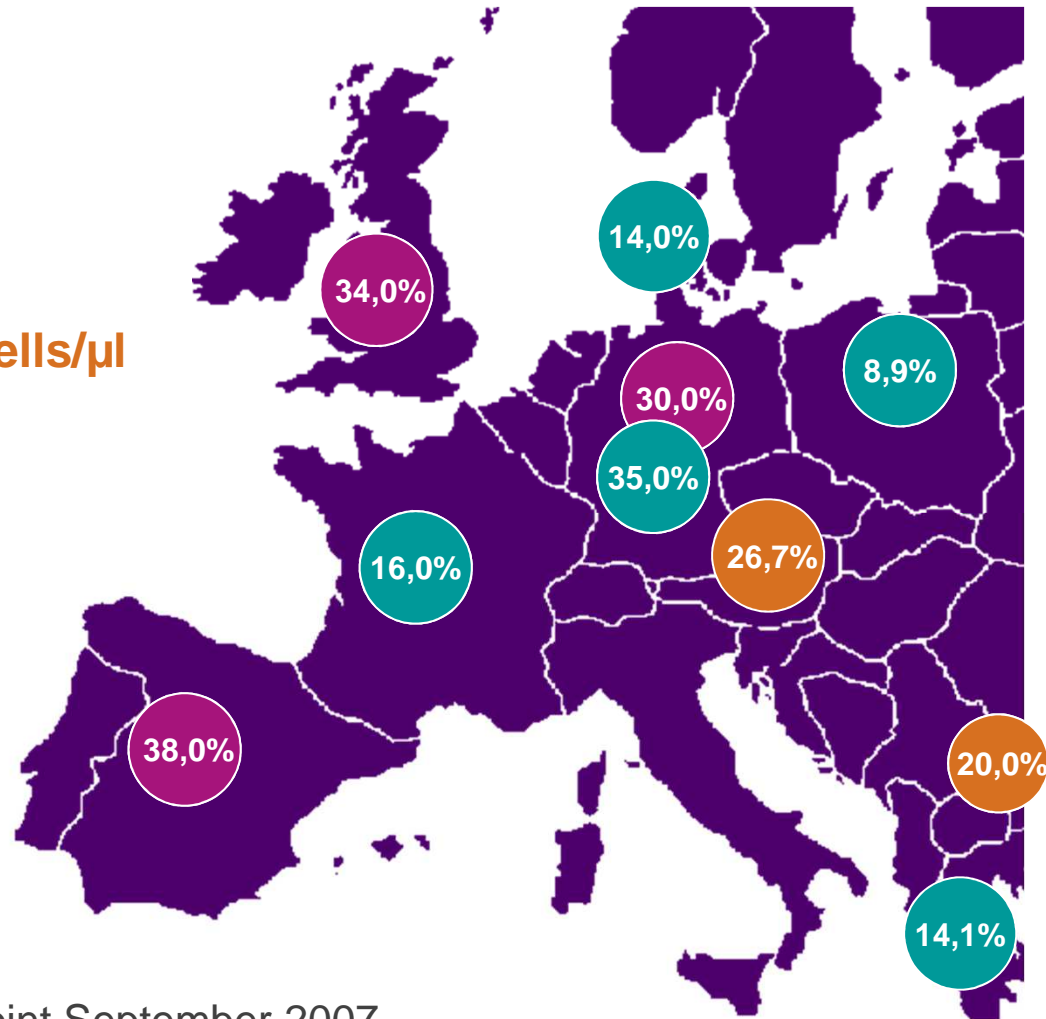
Background

- **Of the estimated 2.3 million PLHIV in the European Region, 1 in 3 remain undiagnosed; only between 10% and 40% of people with HCV in Europe are aware of their infection**
- **Undiagnosed HIV, HBV and/or HCV is harmful to the person infected as appropriate health interventions are delayed**
- **Also detrimental to society, as persons unaware of their viral infection may transmit to others more frequently than those aware of their viral infection**
- **Late presentation associated with higher medical costs**
- **Need for innovative approaches to better target testing for those at risk of being infected**

Variation in Prevalence depending on the underlying definition of *Late Presenter*

Definition based on:

- AIDS
- CD4 < 200 cells/ μ l
- AIDS and CD4 < cells cells/ μ l



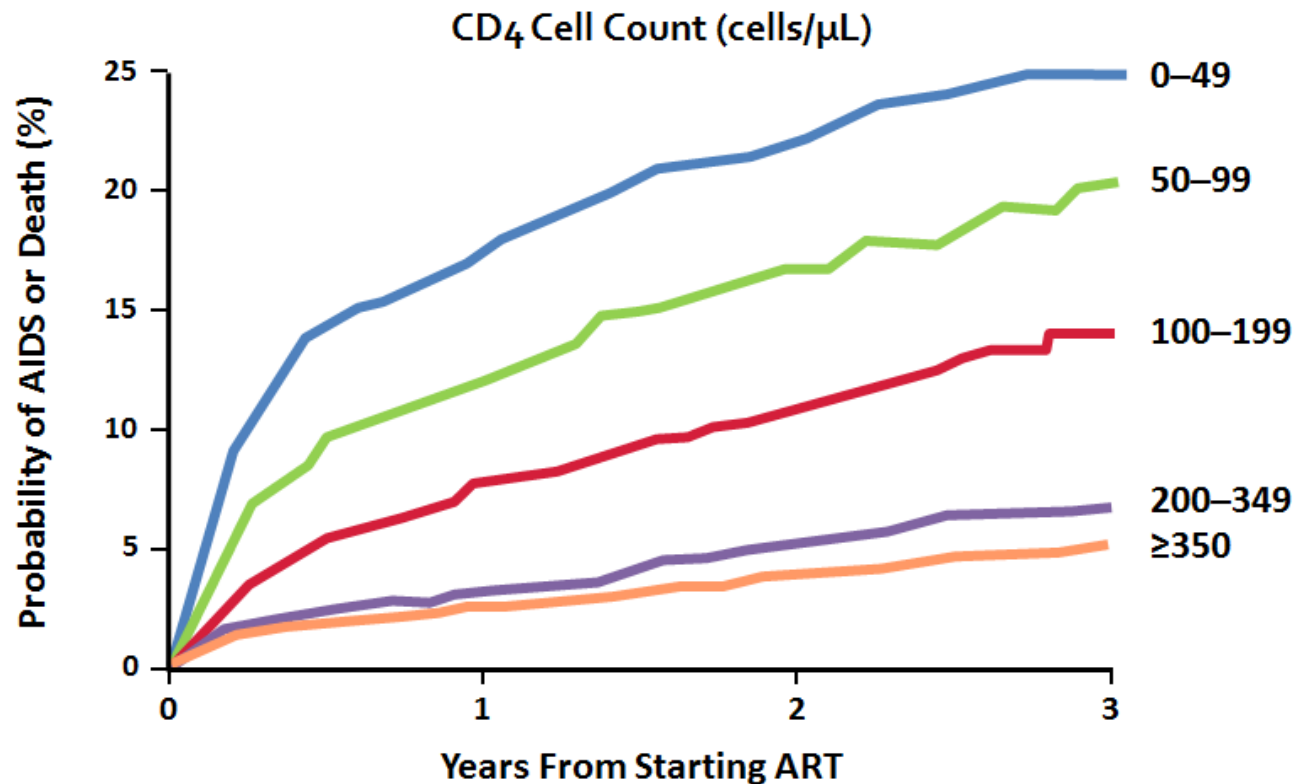
Late Presenter (%), survey timepoint September 2007

The consensus definition of late presentation for HIV care

- Late presentation: Persons presenting for care with a CD4 count below 350 cells/mL or presenting with an AIDS-defining event, regardless of the CD4 cell count.
- Presentation with advanced HIV disease: Persons presenting for care with a CD4 count below 200 cells/mL or presenting with an AIDS-defining event, regardless of the CD4 cell count.

Prognosis from starting ART according to pre-therapy CD4 cell counts and HIV-RNA levels

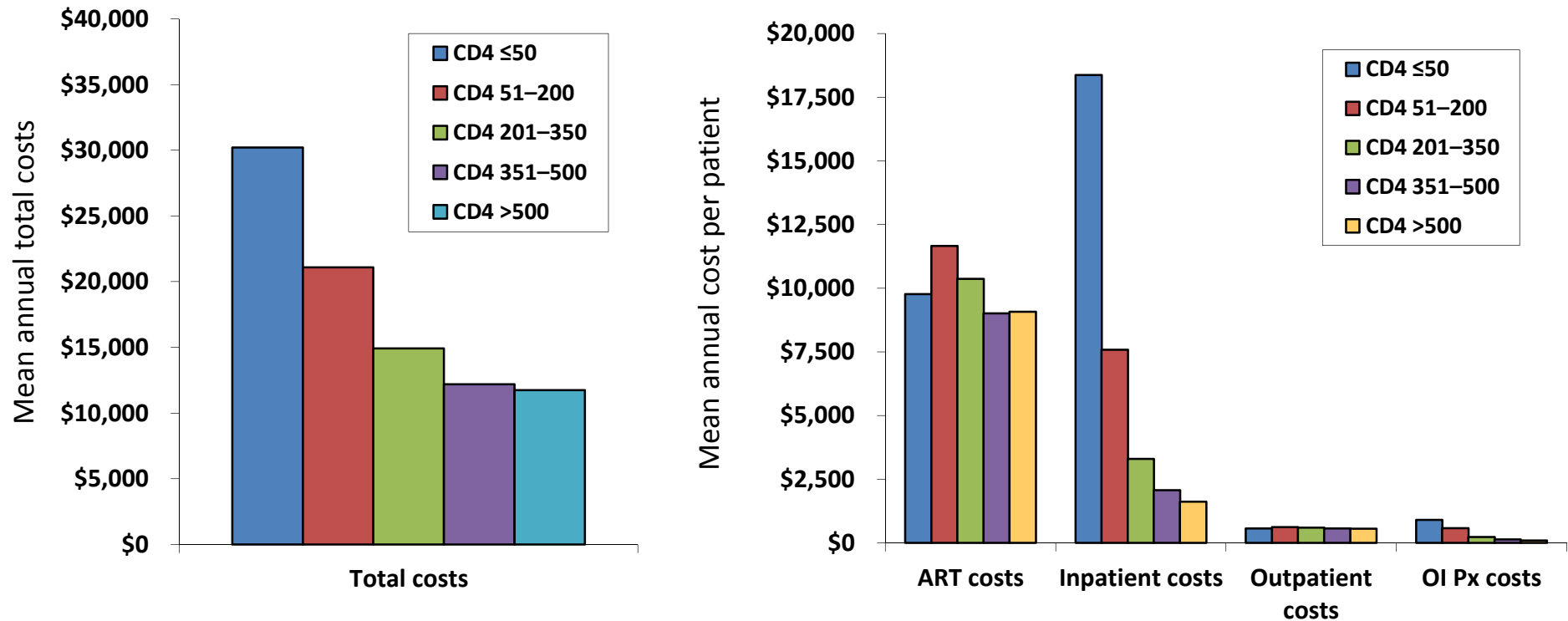
ART Cohort Collaboration, 13 cohort studies from Europe and North America. Analysis of adult patients starting HAART with a combination of at least three drugs (N=12,574)



- CD4 cell count at commencement of HAART was the most strongly prognostic factor

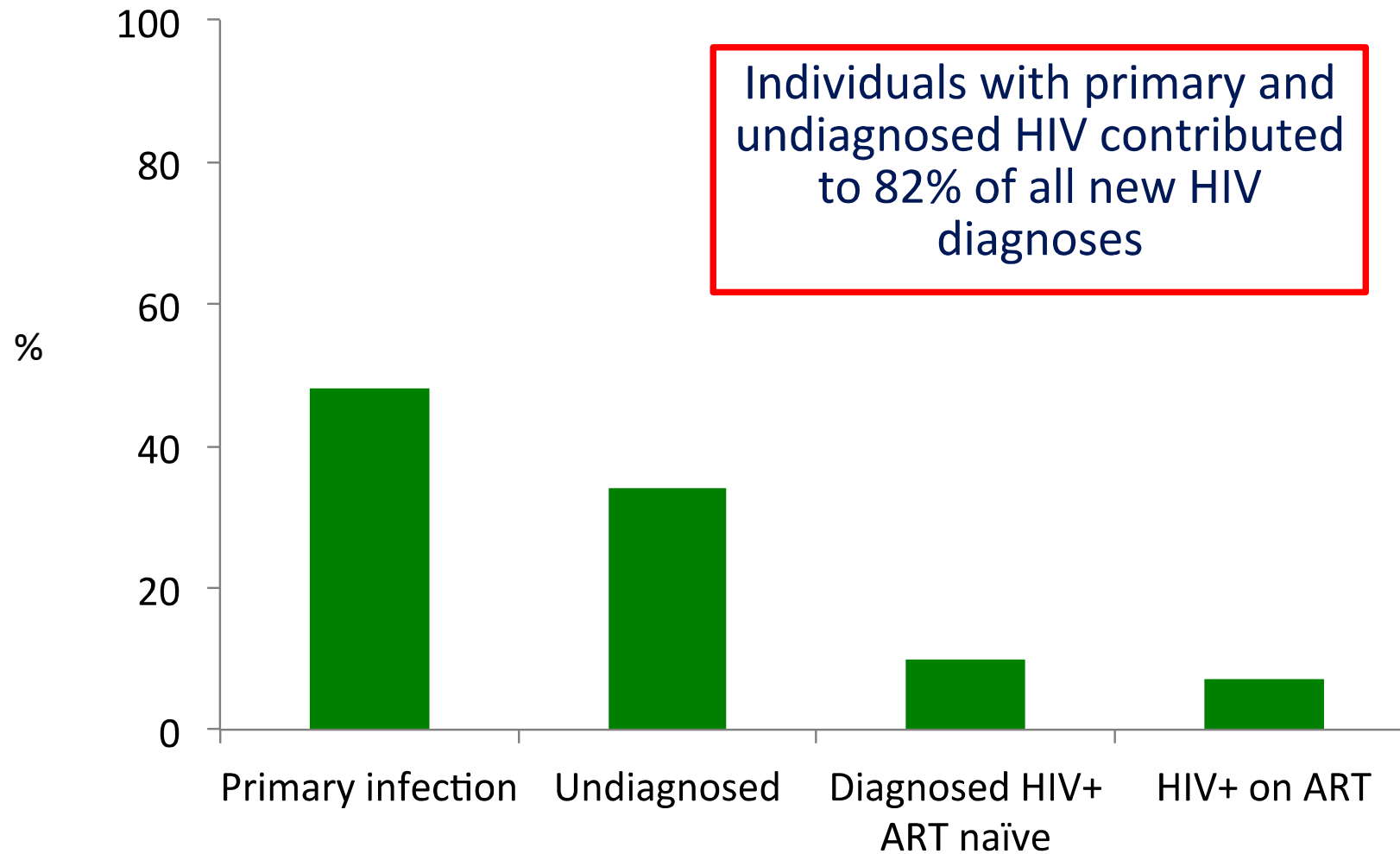
Higher cost of medical care for late presenters

Data for 10,433 patients from 7 primary HIV care sites



- Annual total cost of late care is ~2.5 times the cost of care for early therapy (CD4 >500)
- Inpatient costs attributed the most to the total cost in late presenters

The UK epidemic & limitations of TasP



What are the consequences of starting late?

Short Term

Higher risk of mortality in the 1st year
ART CC and ART LINC, Lancet 2006; 367: 817–24

Reduced chance of viral suppression
Waters L, HIV Med 2011 12(5), 289–298.

Increased risk of hospitalization
Sabin CA, AIDS 2004; 18:2145–2151

More potential drug-drug interaction
Rockstroh JK, Antivir. Ther 2010.15 (S1), 25-30

More likely to have IRIS
Barber D, Nature Rev 2011 vol 10: 150

Long Term

Increased risk of non-AIDS events
Reekie, AIDS. 2011;25(18):2259-68

Increased risk of neurocognitive impairment
Ellis RJ, AIDS 2011;25(14):1747-51

Potentially increased risk of HIV transmission
Cohen MS, N Engl J Med. 2011;365(6):493-505

Higher direct cost of care
RY Chen, et al; Clin Infect Dis 2006

**How frequent is late presentation?
Who is the late presenter and how
have numbers evolved over time?**

Who is presenting late?

- **Objective and Methods:**

- To explore the impact of late presentation (LP) on AIDS and mortality. 84,524 individuals from 23 cohorts in 35 countries contributed data.

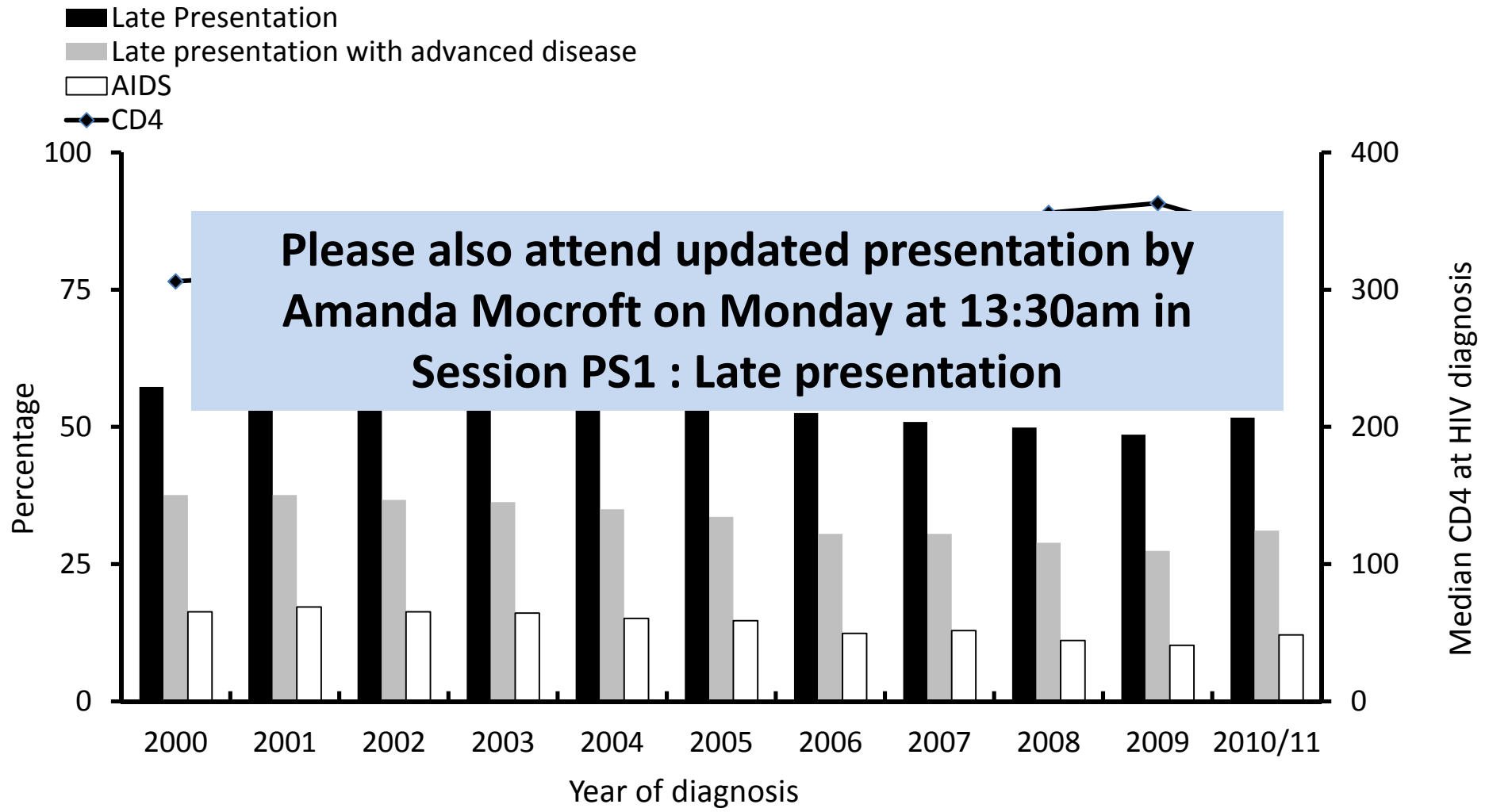
- **Results:**

- 45,488 were LP (53.8%).
- LP was highest in heterosexual males (66.1%) Southern European countries
- **Please also attend updated presentation by Amanda Mocroft on Monday at 13:30am in Session PS1 : Late presentation**
- Late presentation (LP) increased in male IDUs and female heterosexuals from Southern Europe and IDUs in Eastern Europe.
- LP was associated with an increased rate of AIDS/deaths, particularly in the first year after HIV diagnosis, with significant variation across Europe.

- **Conclusions:**

- Earlier and more widespread testing, timely referrals after testing positive, and improved retention in care strategies are required to further reduce the incidence of LP.

Changes over time in late presentation and CD4 count at HIV-diagnosis : COHERE 2000-2011



N 7367 7404 8046 7756 8591 8663 8251 8618 9057 7548 3223

Late presentation: diagnosed with HIV with a CD4 count below 350/mm³ or an AIDS defining event regardless of the CD4 count, in the 6 months following HIV diagnosis. Late presentation with advanced disease: diagnosed with HIV with a CD4 count below 200/mm³ or an AIDS defining event, regardless of CD4 cell count, in the 6 months following HIV diagnosis. Mocroft A. PLOS Medicine 2013

Who is presenting late?

- **Methods:**

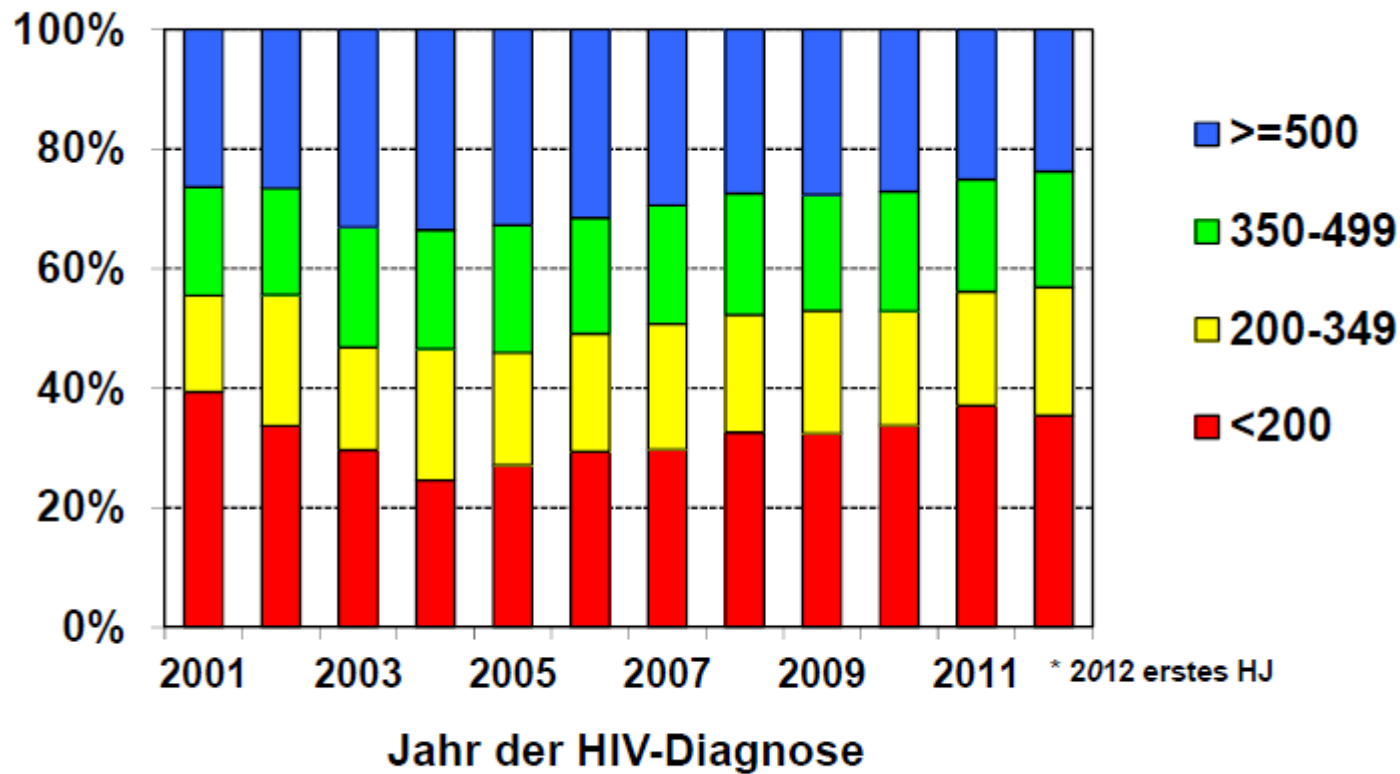
- Case surveillance data for all individuals newly diagnosed with HIV infection in Germany in the years 2001–2010 and data for the years 1999–2010 from the German Clinical Surveillance of HIV Disease (ClinSurv) cohort study, a large multicentre observational study, were analysed.

- **Results:**

- Among 6897 treatment-naïve patients in the ClinSurv cohort, 58.1% were late presenters for care.
- Late presenters for care were older (median 42 vs. 39 years for early presenters), more often heterosexuals from low-prevalence countries (18.1% vs. 15.5%, respectively) and more often migrants (18.2% vs. 9.7%, respectively; all $P < 0.005$).
- The probability of late presentation was >65% throughout the observation period in migrants.
- The probability of late presentation for care clearly decreased in men who have sex with men (MSM) from 60% in 1999 to 45% in 2010.

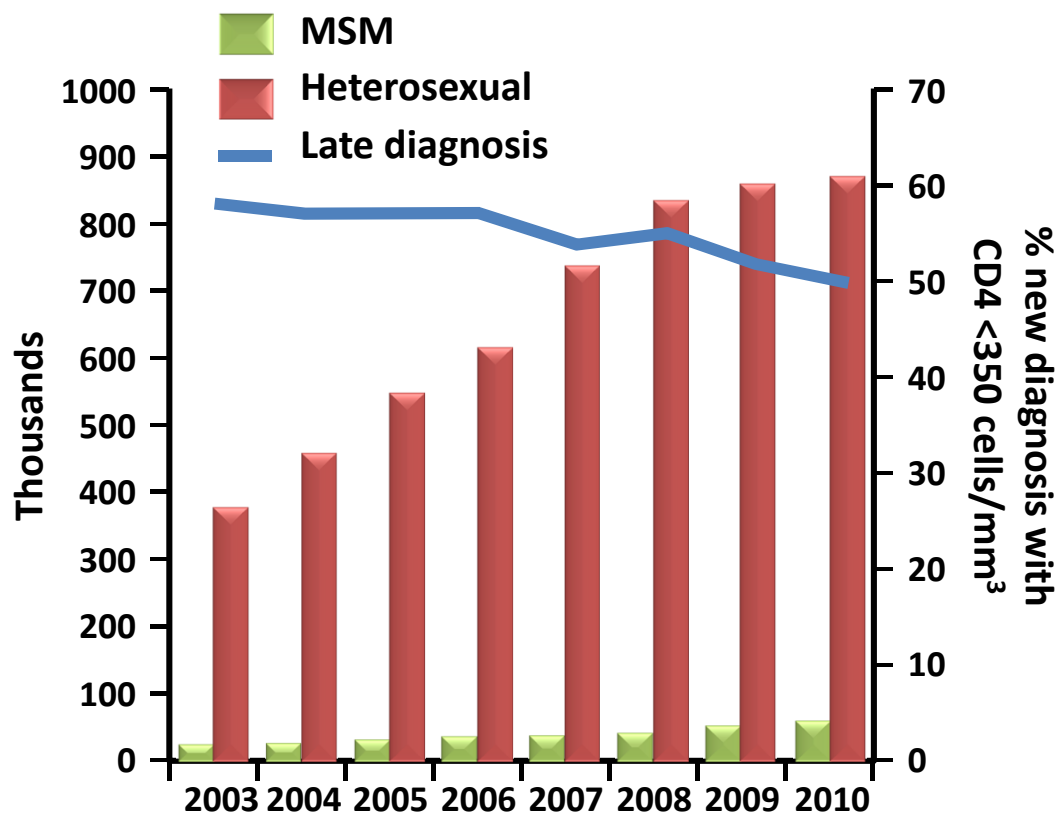
HIV in Germany (08/2012)

CD4-cell count/ μl at HIV diagnosis



Increased HIV testing correlates with a reduction in late diagnosis of HIV

HIV tests among English STI clinic attendees vs overall UK late HIV diagnosis, 2003–2010



Late diagnosis: CD4+ count <350 cells/mm³

“The proportion diagnosed late (CD4 count <350 cells/mm³) remained high (50%) despite a slow and significant decline over the last decade”

Why need a definition for late presentation for viral hepatitis?

- Effective treatments for HBV and HCV are in recent developments with great impact on the possibility to treat
- A late presentation by Maria Buti on: Late presentation of viral hepatitis for medical care: a consensus definition on Tuesday at 08:30am-10:30
- Consequently, a large (but as yet undetermined) section of the chronically infected population enters care once they have developed clinical symptoms.
- Use of a common definition allows to compare surveillance data on many levels

How many patients with viral hepatitis B or C present late?

HepHIV 2014
5-7 OCTOBER BARCELONA

Loko et al. *BMC Infectious Diseases* 2010, **10**:303
<http://www.biomedcentral.com/1471-2334/10/303>



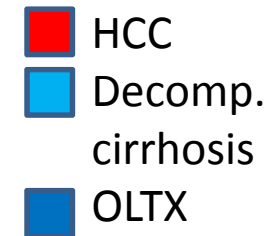
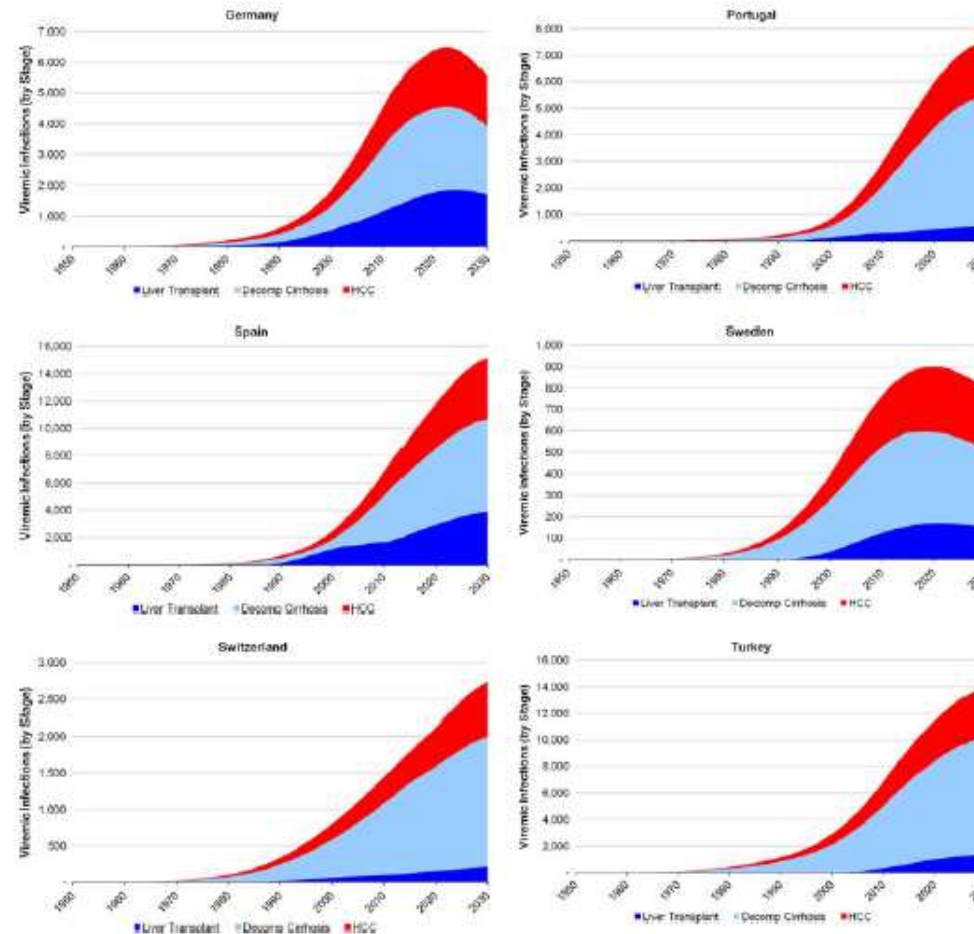
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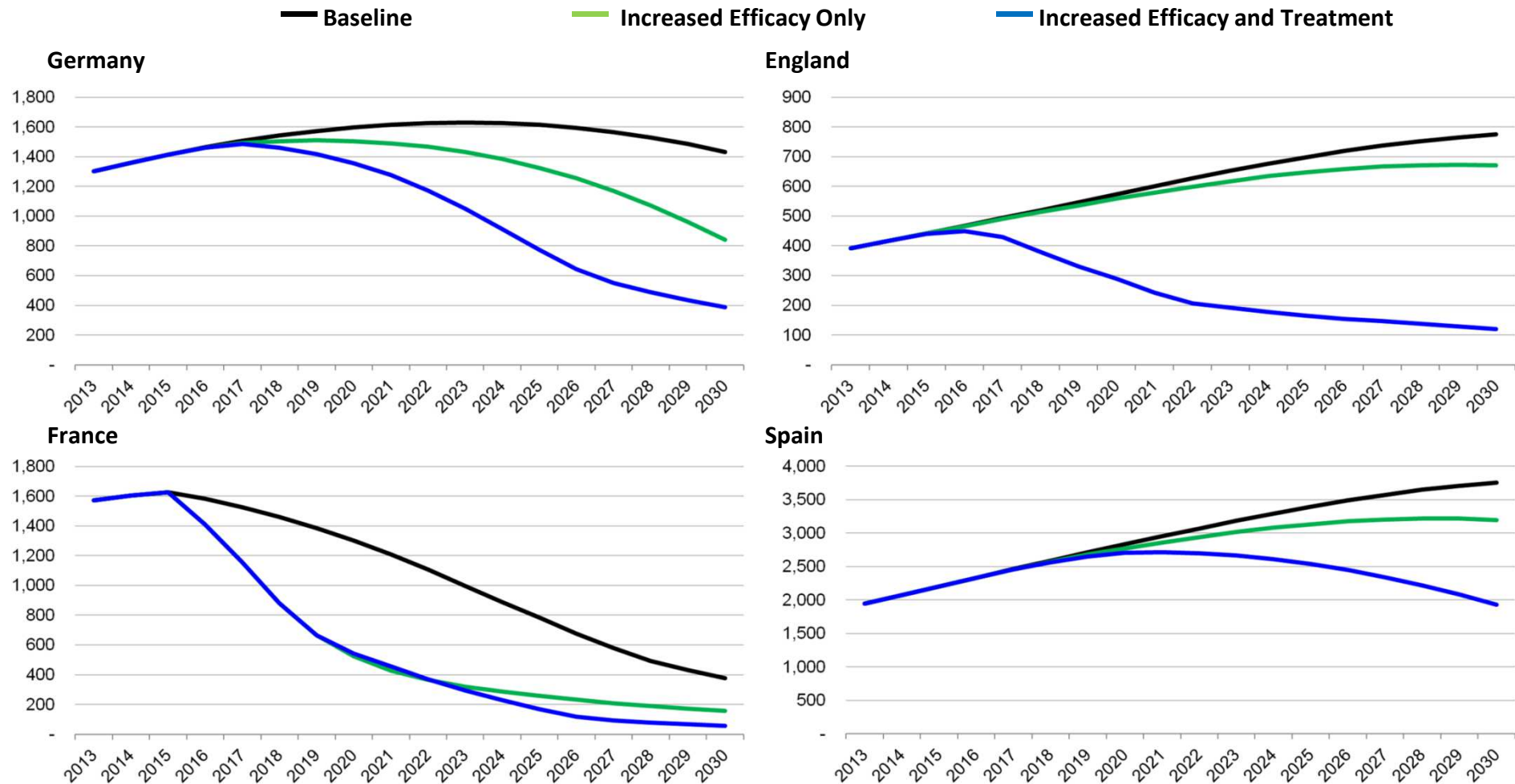
The French national prospective cohort of patients co-infected with HIV and HCV (ANRS CO13 HEPAVIH): Early findings, 2006-2010

- **Results:**
 - A total of 1,175 patients were included from January 2006 to December 2008. Their median age at enrolment was 45 years and 70.2% were male. The median CD4 cell count was 442 (IQR: 304-633) cells/ μ l and HIV RNA plasma viral load was undetectable in 68.8%. Most participants (71.6%) were on HAART.
 - Among the 1,048 HIV-HCV chronically co-infected patients, HCV genotype 1 was predominant (56%) and cirrhosis was present in 25%.

Change in the number of liver transplants, decompensated cirrhosis cases and HCC cases over time.

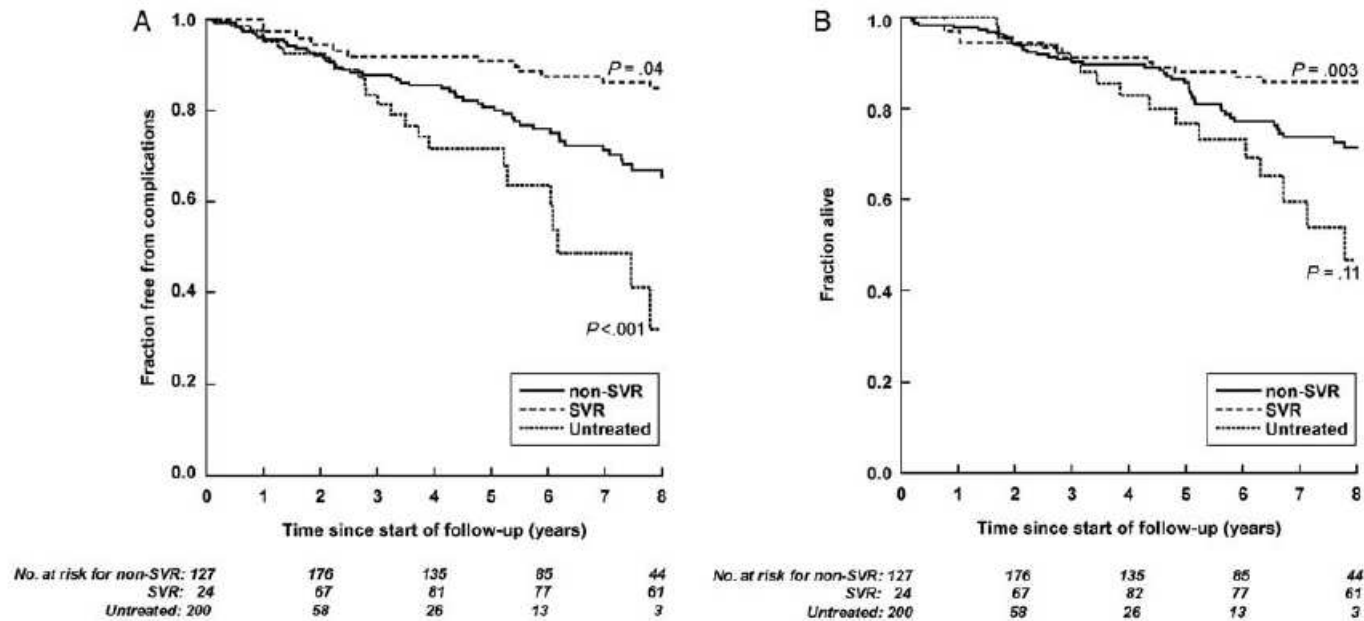


Liver-related deaths, 2013–2030: Germany, England, France and Spain



Is cure (SVR) of HCV in cirrhotic patients enough?

351 compensated cirrhotics followed up to 8 years



HCC incidence: SVR=1.0 vs; non-SVR=2.3 per 100 PY

➔ But risk of HCC still present: regular liver assessment +++

¹Aleman. Clin Infect Dis 2013

Summary

- Late presentation remains a challenge for HIV as well as HBV and HCV
- Establishment of common definitions is helpful and can contribute to shape the public health response
- It will be part of the surveillance that each country undertakes as part of the governmental response to addressing HIV and viral hepatitis.
- Broad introduction of non-invasive fibrosis stage assessment will help to better characterize the hepatitis epidemic