Results of the PanEuropean Hepatitis C Project

Presentation at the

China HCV Management Forum

Beijing, 16 November 2007

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The Project

- **Funding:** In part funded by an unrestricted educational grant from pharmaceutical industry
- **Intention:** To have a third party policy institute examine the issues associated with the treatment of Hepatitis C in Europe both from a medical and economic perspective.
- **Target audience:** Decision makers, physicians, patients
- **Geographical focus:** 22 countries of the WHO-European region, including 18 EU countries (if possible, all countries of the WHO European region)

Parts and Research Questions of the Project

1. HCV-related burden of disease in Europe ➔ Size of the problem?

2. Market uptake of state-of-the-art antiviral drugs (Peginterferons) ➔ Inequality of health care services?

3. Long-term effectiveness and cost-effectiveness of antiviral therapy ➔ Should we treat?

4. Long-term effectiveness and cost -effectiveness of screening ➔ Should we screen?

Background: Hepatitis C

- Caused by hepatitis C virus (HCV) discovered in 1989
- Leading cause of chronic liver disease with life threatening sequelae such as end-stage liver cirrhosis and liver cancer
- 15-25% of HCV infections progress to severe liver disease. Progression is slow and may take more than 30 years.
- Because progression often is silent, many cases are diagnosed at a late stage, when therapeutic options are already limited. ➔ **“Silent killer”**
- In late stages liver transplantation is the only therapeutic option. However, if detected in time, progression to severe disease can be prevented by antiviral treatment in about 60% of the patients.
- Transmission is via blood to blood contact. New infections decreased substantially with the introduction of routine blood screening in 1991. However, many patients infected prior to the 1990s via contaminated blood products are still at risk to progress to severe liver disease. ➔ **“Awakening giant”**

Part 1:

HCV-related burden of disease in Europe

Objectives

- To summarise presently available burden of disease data.
- To calculate burden of disease estimates, where HCV specific data are missing.
- To identify areas, where better data are needed.

Investigated Burden of Disease Indicators

- Incidence
- Prevalence
- Mortality
- DALYs (Disability adjusted live-years)
- Liver transplants

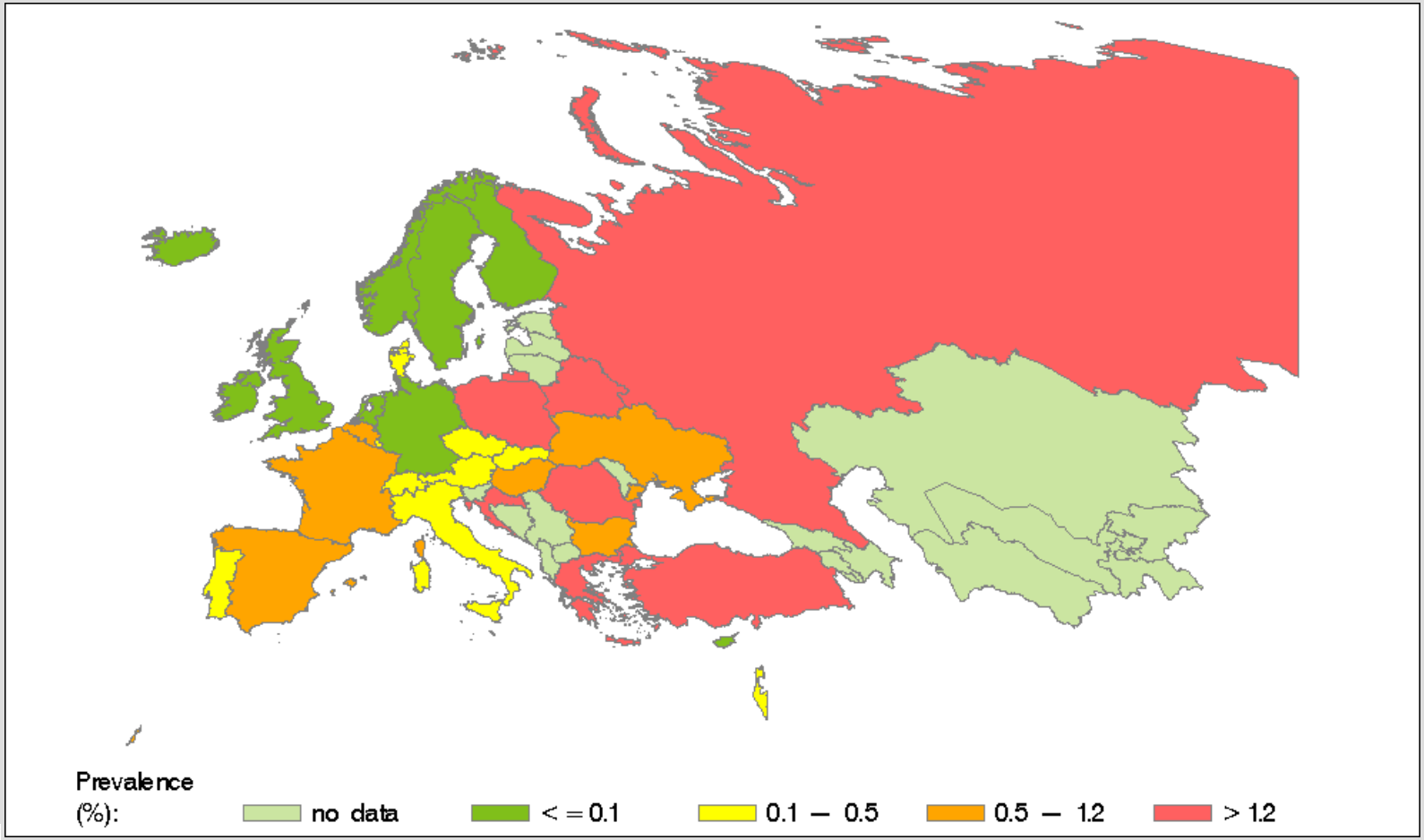
Key Findings: Incidence

- Quantifies new infections
- Assessed by national surveillance (notifiable disease)
- At present, no uniform hepatitis C surveillance exists at the European level.
- National surveillance data are not fully comparable due to differences in surveillance.
- Further efforts are needed to increase the sensitivity of HCV surveillance and to standardise surveillance data.
- Incidence does not appropriately reflect the size of the hepatitis C problem, since many infections were acquired in the past.

Key Findings: Prevalence

- Quantifies disease frequency in pop. → key measure to quantify the size of the hepatitis C problem.
- Most complete HCV prevalence data for Europe are available from WHO. However, it is widely accepted that these do not necessarily represent true prevalence and need to be updated.
- Estimates communicated by national authorities tend to be higher but are less frequently available.
- Based on available data, 1.1–1.3% of the population in our 22 focus countries are infected (7.3–8.8 million).
- In the EU, based on conservative WHO data, 0.7% (3.5 million) are infected.

Prevalence
(WHO 1999)



Source: WHO 1999
Data extracted from published studies and/or submitted to WHO by countries/areas

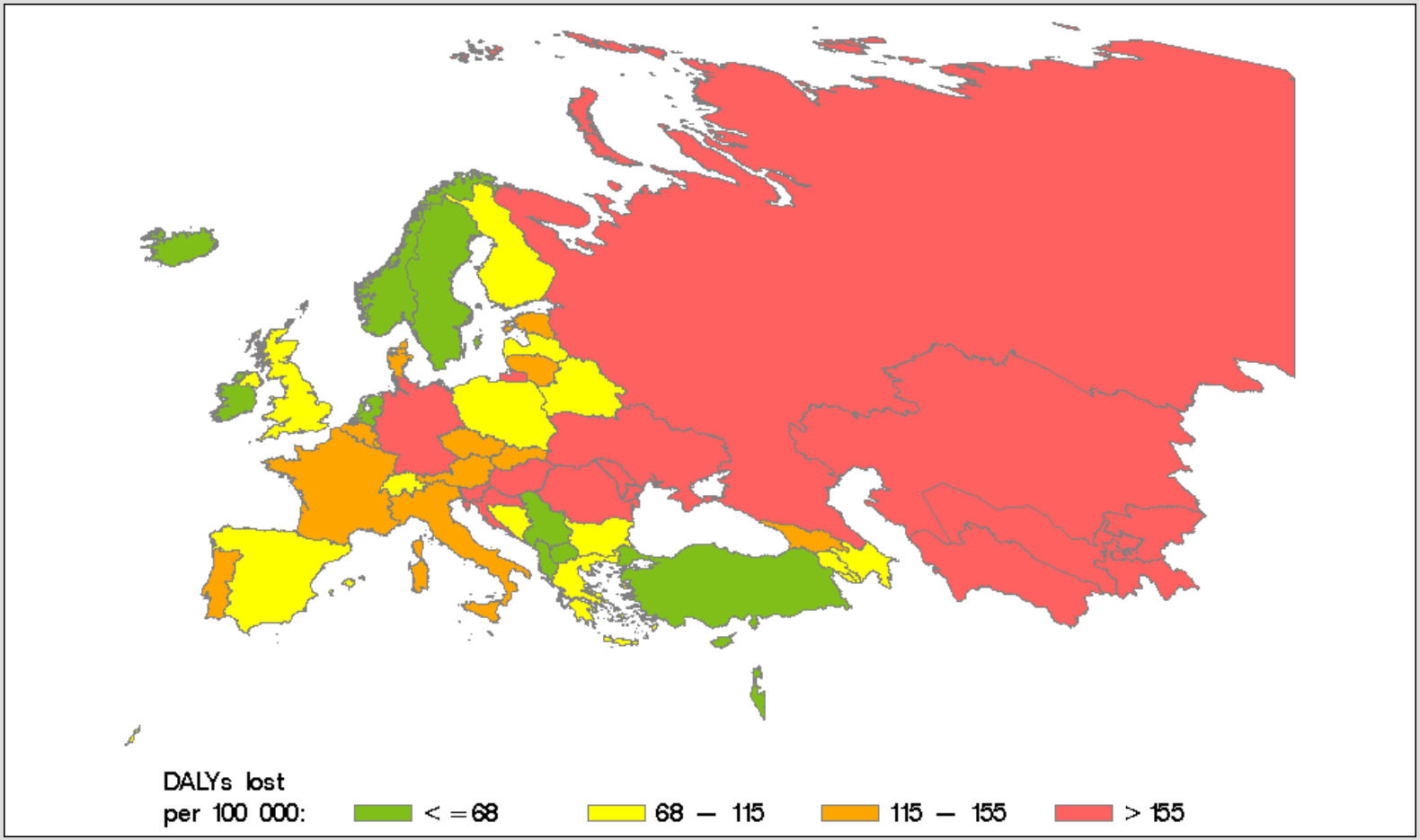
Key Findings: Mortality

- Main causes of death associated with HCV infection are end-stage liver cirrhosis and liver cancer.
- However, HCV-specific mortality data accounting for these conditions are currently not available.
- Therefore, HCV-related mortality was estimated from data of the WHO Global Burden of Disease study (GBD) via HCV attributable fractions.
- HCV-related deaths per year:
  WHO Europ. Reg.: 86,000 (HIV/AIDS ~ 40,000)
  EU: 55,000 (HIV/AIDS ~ 7,000)
- Death rates for HCV-related cirrhosis and liver cancer show opposite east-west gradients.

Key Findings: DALYs

- Quantify years of 'healthy' life lost
  (Years of life lost from premature death + years of healthy life lost due to disability)
- DALYs for HCV-related cirrhosis and liver cancer are currently unavailable. → Calculated from data of the WHO Global Burden of Disease study (GBD) via HCV attributable fractions.
- HCV-related DALYs lost per year:
  WHO Europ. Reg.: 1.2 million (HIV/AIDS ~ 1.4 million)
  EU: 0.6 million (HIV/AIDS ~ 0.3 million)
- 95% of the DALYS are accumulated by patients in advanced disease stages (cirrhosis or liver cancer). → potential benefit of antiviral treatment.

DALYS
(2002)



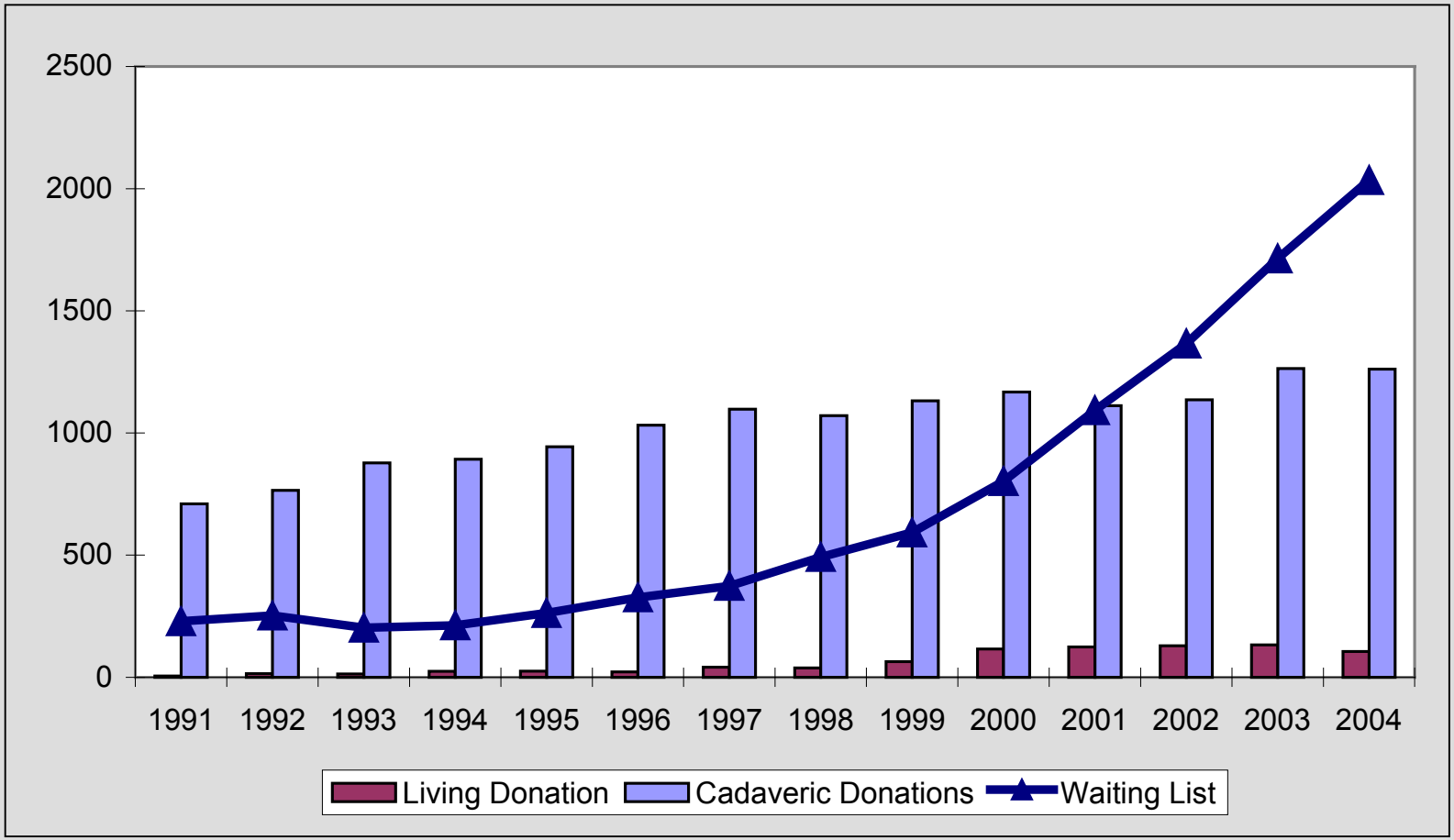
Source: Calculated from WHO GBD data 2002

Key Findings: Liver Transplant

- Europe-wide HCV-specific transplant data are currently unavailable. → Calculated from various data sources via HCV attributable fractions.
- HCV accounts for about 1/4 of the liver transplants in Europe, and therewith is a major cause for the already existent shortage of donor organs.
- The variation of HCV-related transplantation rates suggests inequality of health care service across Europe.

Shortage of Donor Organs

(Liver transplants and waiting list 1991 to 2004)



Source: Eurotransplant

Conclusions Part 1

- Hepatitis C is a major public health problem in the WHO European region, costing twice as many lives and about as many 'healthy' live years as HIV/AIDS.
- Burden of disease caused by advanced disease highlights the potential benefit of antiviral treatment.
- Varying mortality and transplantation rates suggest inequality of health care services across Europe.
- The lack of data indicates that hepatitis C still is a neglected disease.
- What is needed are **PUBLIC AWARENESS**, coordinated action plans, more and better data.

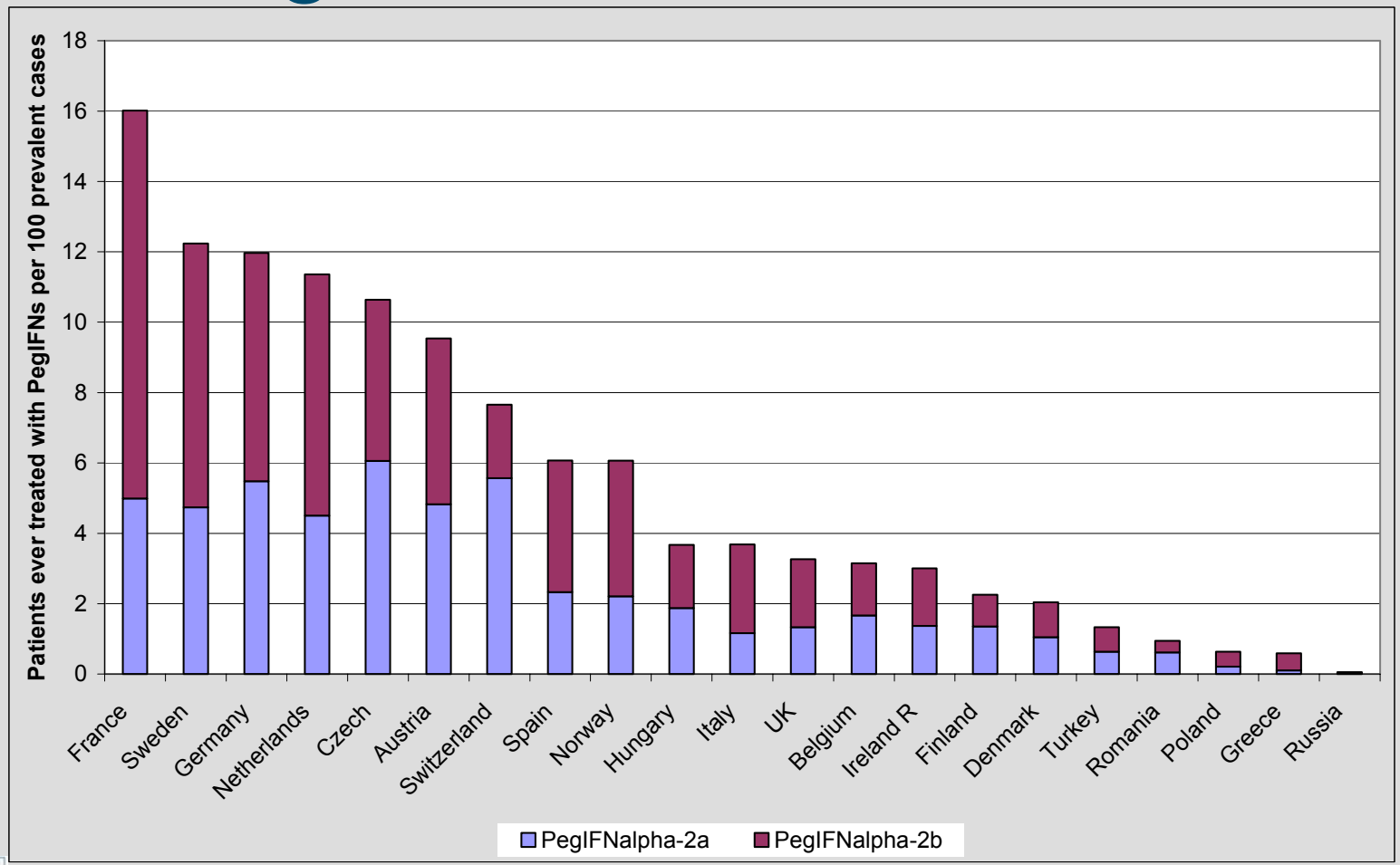
Part 2:

Market uptake of state-of-the-art antiviral drugs (Peginterferons)

Objectives

- To assess the market uptake of peginterferons in 21 countries of the WHO European region up to 2006.
- To convert peginterferon sales data into numbers of patients treated and compare prevalence-adjusted treatment rates across countries.
- To find out whether there is unequal access to optimised therapy.

Prevalence-adjusted Cumulative PegINF Treatment Rates



Source: Calculated from IMS Health data and HCV prevalence rates derived from national sources

Conclusions Part 2

- Peginterferon market uptake and treatment rates differed considerably across countries.
- Results indicate unequal access to optimised therapy across Europe.
- Reasons for unequal access are budget restrictions, and differences in surveillance and treatment policies.

Part 3:

Long-term effectiveness and cost-effectiveness of antiviral therapy

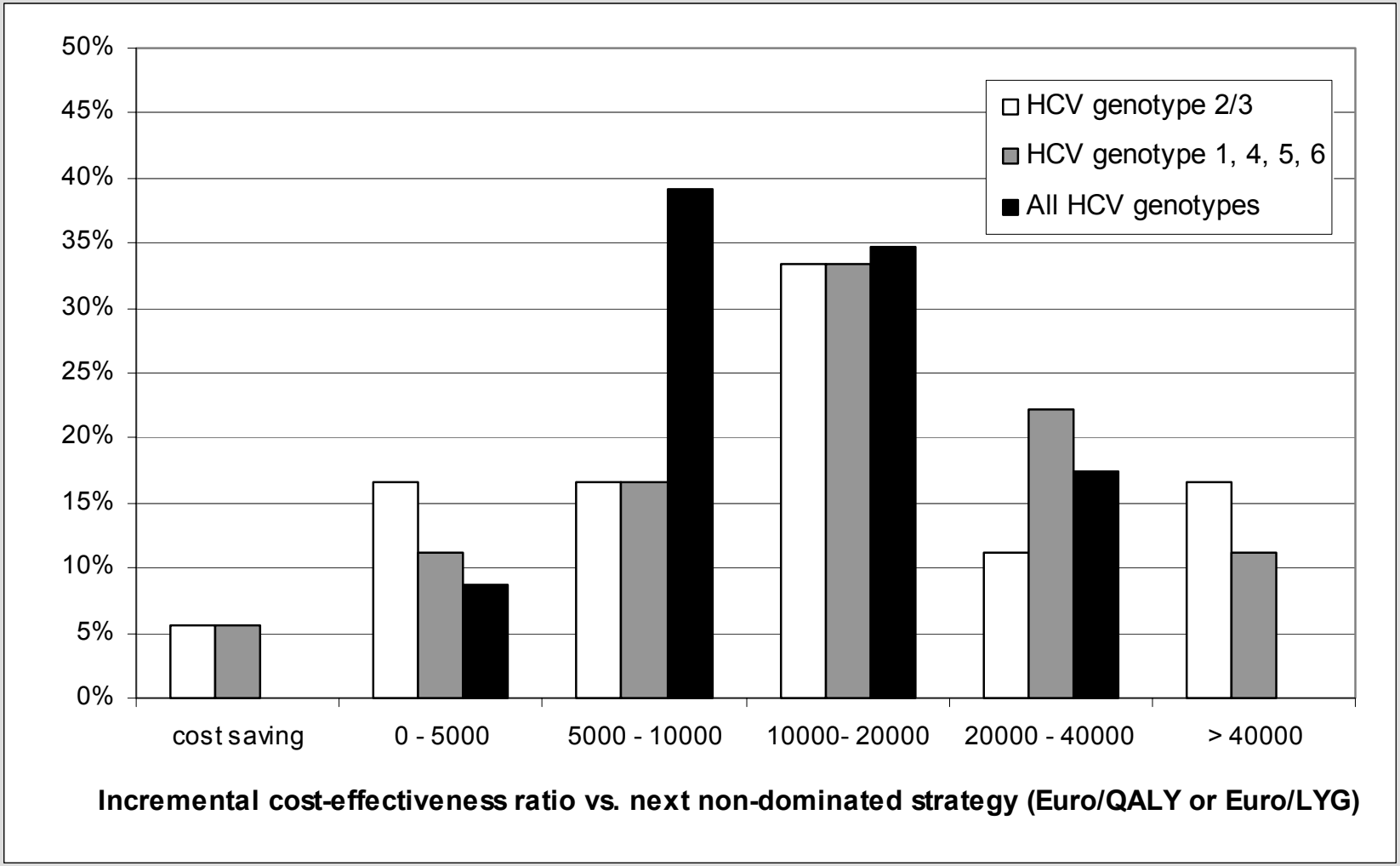
Objectives

- To systematically review the evidence for long-term effectiveness and cost-effectiveness of antiviral treatment (AVT) in patients with chronic hepatitis C.
- Emphasis was placed on the comparison of peginterferon/ribavirin treatment with interferon/ribavirin treatment, which was the previous standard of care.

Key Findings: CE of AVT

- 49 studies evaluating the cost-effectiveness of AVT were reviewed. Of those, 21 evaluated combination therapy with peginterferon/ribavirin (16 in treatment-naïve patients, 5 in other patient groups).
- In treatment-naïve patients peginterferon/ribavirin therapy compared to interferon/ribavirin gained 0.6-1.8 life years or 0.5-1.9 quality-adjusted life years (QALYs).
- Costs per QALY gained ranged from <0 to 84,700 EUR/QALY (discounted incremental cost-utility ratio).
- Results varied with length of treatment, genotype, liver histology, population characteristics and discount rate.

Distribution of PegINF+Riba ICERs



Summary of 16 studies comparing PegINF+Riba vs. INF+Riba in treatment-naïve patients with chronic hepatitis C, ICER: incremental cost-effectiveness ratio, PegIFN: peginterferon, Riba: ribavirin

Conclusions Part 3

- Our review proves that peginterferon/ribavirin therapy of treatment-naïve patients with chronic hepatitis C without doubt is cost-effective (i.e. gains additional life-years and quality of life at acceptable cost).

- Evidence is only weak for special patient groups (e.g., co-infection with HIV or HBV, haemophilia, intravenous drug users, mild hepatitis, persistently normal ALT levels)

Part 4:

Long-term effectiveness and cost -effectiveness of screening

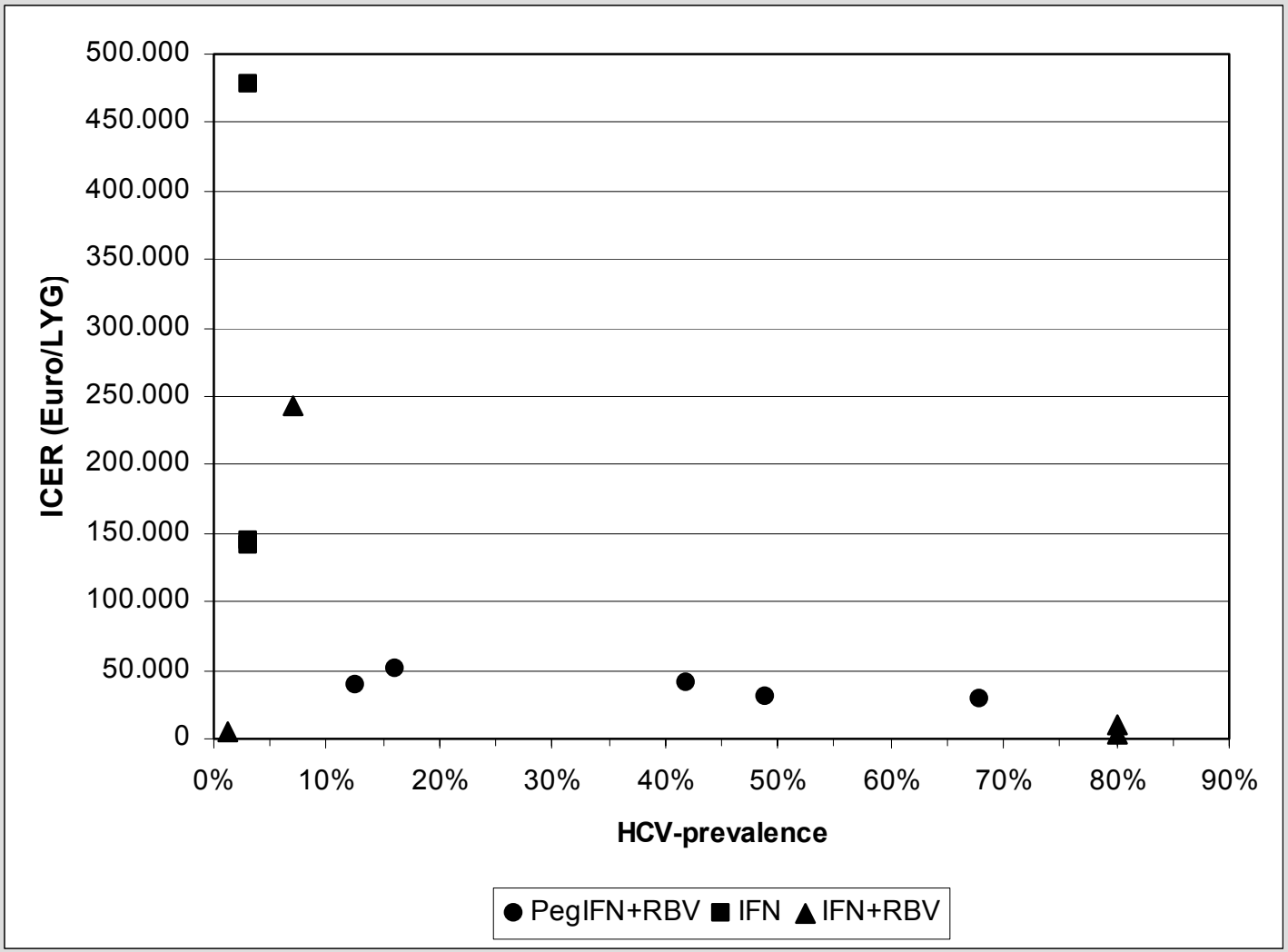
Objectives

- To systematically review the evidence for long-term effectiveness and cost-effectiveness of screening for hepatitis C.
- Emphasis was placed on the influence of HCV-prevalence on the cost-effectiveness of screening.

Key Findings: CE of Screening

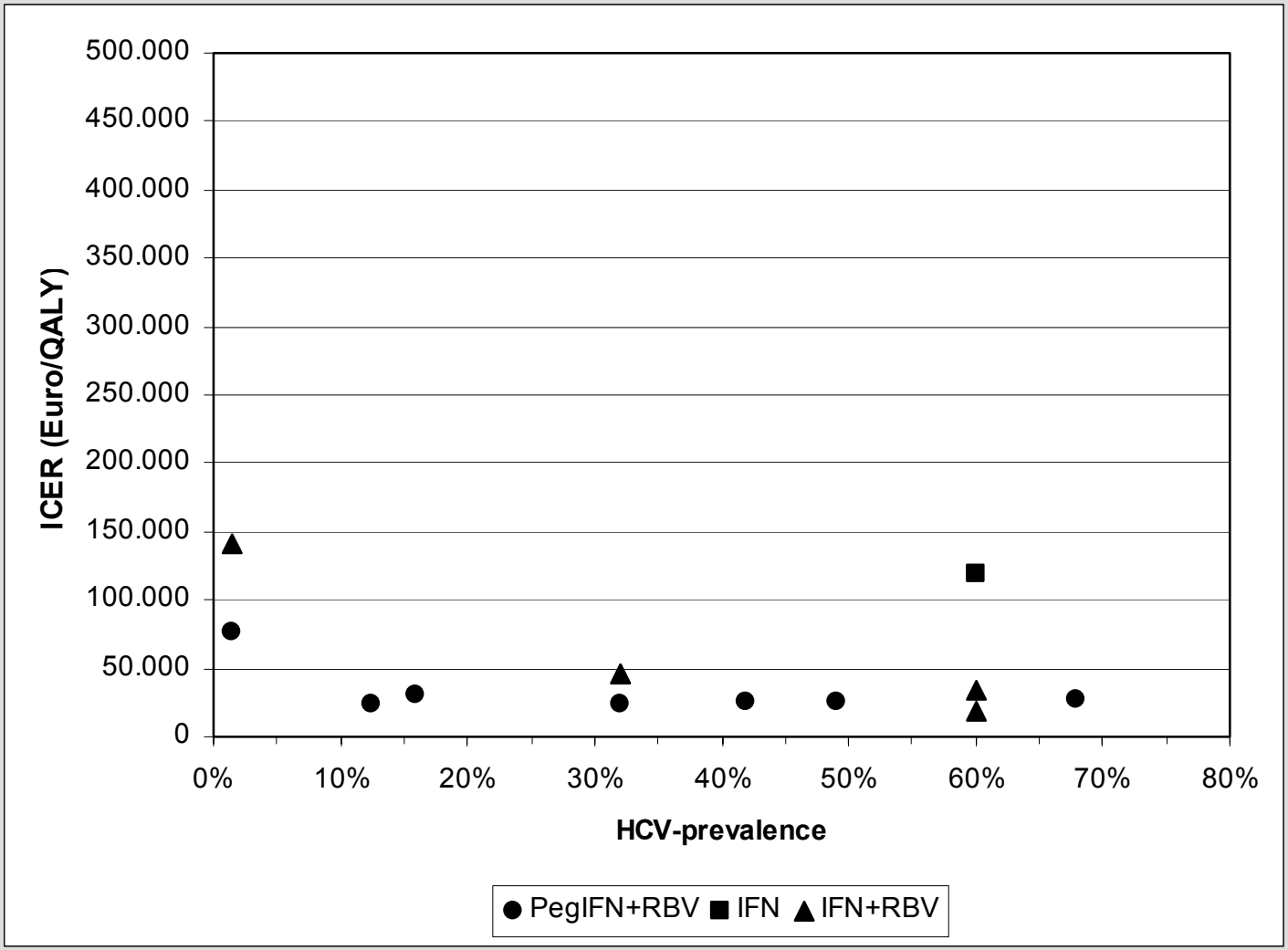
- 10 studies evaluating the cost-effectiveness of hepatitis C screening were reviewed.
- Studies varied regarding target population, HCV prevalence, study perspective, discount rate, mode of screening and antiviral treatment.
- Compared to no screening and standard care, HCV screening and early treatment gained 0.0004-0.066 life years (0.15-24 days) or 0.0001-0.072 QALYs.
- Costs per QALY gained ranged from 18,300 to 1,151,000 EUR/QALY (if screening was not domimated)
- Specifically, in target groups with ‘low’ HCV prevalence costs per QALY gained were high.

ICER of Screening by Prevalence



ICER: incremental cost-effectiveness ratio, HCV: hepatitis C virus, IFN: interferon, RBV: ribavirin, PegIFN: peginterferon.

ICUR of Screening by Prevalence



ICER: incremental cost-utility ratio, HCV: hepatitis C virus, IFN: interferon, RBV: ribavirin, PegIFN: peginterferon. §One point out of range: 1,150976 Euro/QALY with 1% HCV prevalence, PegIFN+RBV.

Conclusions Part 4

- Our review indicates that screening is cost-effective only in target groups with elevated HCV prevalence.
- If cost-effectiveness is chosen as a decision criterion, high prevalence target groups should be tailored based on risk factor profiles (e.g., history of blood transfusion, elevated ALT, IVDU, age, visit in hepatology wards)
- However, cost-effectiveness is not the only decision criterion. Considering the multitude of iatrogenic infections, other ethical aspects like fairness should be considered as well.
- Currently, many European countries plan to introduce national screening programs, but the question is whom to screen and how to screen.