Long-term Effectiveness and Cost-effectiveness of Screening for Hepatitis C Virus Infection

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WHO Principles of Screening

1. The condition should be an important health problem.
2. There should be a treatment for the condition.
3. Facilities for diagnosis and treatment should be available.
4. There should be a latent stage of the disease.
5. There should be a test or examination for the condition.
6. The test should be acceptable to the population.
7. The natural history of the disease should be adequately understood.
8. There should be an agreed policy on who to treat.
9. The total cost of finding a case should be economically balanced in relation to medical expenditure as a whole.
10. Case-finding should be a continuous process, not just a "once and for all" project.

WHO 1986

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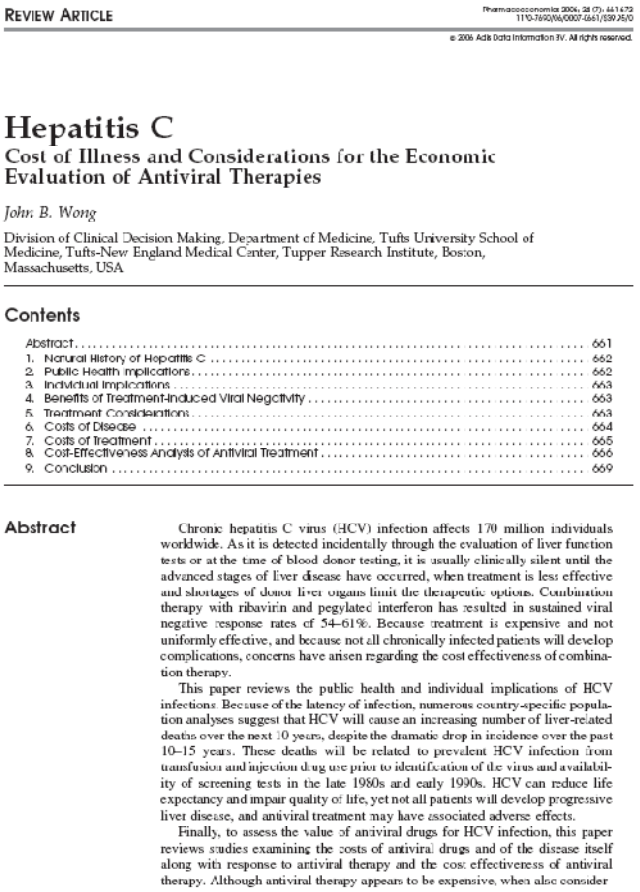
WHO 1968

Is Treatment Cost-Effective?



REVIEW ARTICLE

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Hepatitis C

Cost of Illness and Considerations for the Economic Evaluation of Antiviral Therapies

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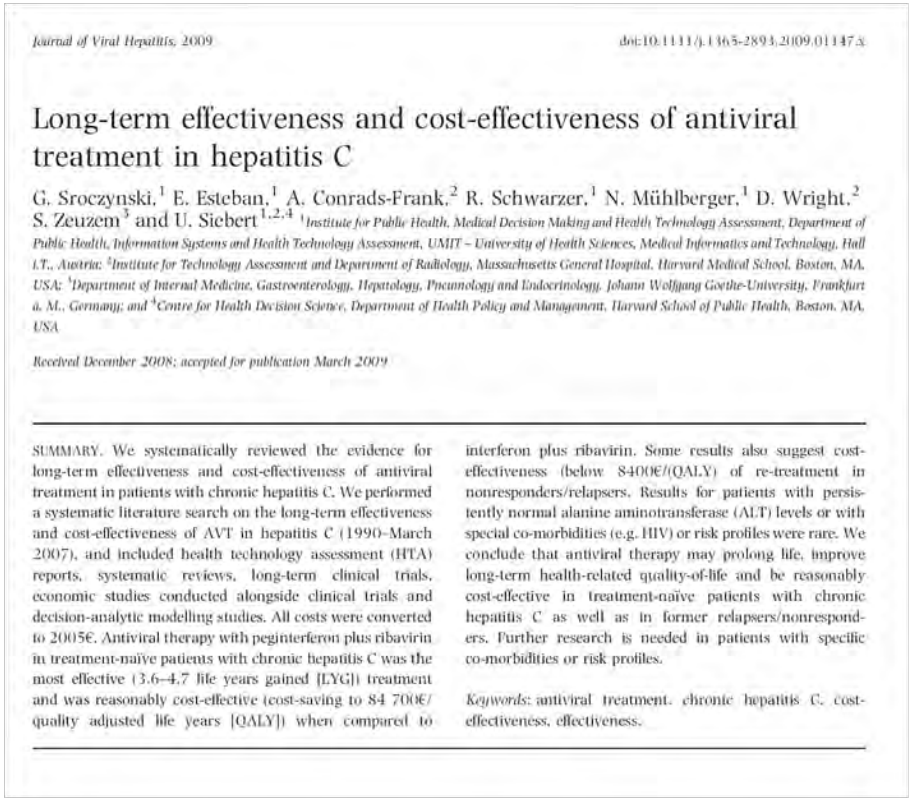
Contents

Abstract

Chronic hepatitis C virus (HCV) infection affects 170 million individuals worldwide. As it is detected incidentally through the evaluation of liver function tests or at the time of blood donor testing, it is usually clinically silent until the advanced stages of liver disease have occurred, when treatment is less effective and shortages of donor liver organs limit the therapeutic options. Combination therapy with ribavirin and pegylated interferon has resulted in sustained viral negative response rates of 54–61%. Because treatment is expensive and not uniformly effective, and because not all chronically infected patients will develop complications, concerns have arisen regarding the cost effectiveness of combination therapy.

This paper reviews the public health and individual implications of HCV infections. Because of the latency of infection, numerous country-specific population analyses suggest that HCV will cause an increasing number of liver-related deaths over the next 10 years, despite the dramatic drop in incidence over the past 10–15 years. These deaths will be related to prevalent HCV infection from transfusion and injection drug use prior to identification of the virus and availability of screening tests in the late 1980s and early 1990s. HCV can reduce life expectancy and impair quality of life, yet not all patients will develop progressive liver disease, and antiviral treatment may have associated adverse effects.

Finally, to assess the value of antiviral drugs for HCV infection, this paper reviews studies examining the costs of antiviral drugs and of the disease itself along with response to antiviral therapy and the cost effectiveness of antiviral therapy. Although antiviral therapy appears to be expensive, when also consider



Journal of Viral Hepatitis, 2009 doi:10.1111/j.1365-2893.2009.01147.x

Long-term effectiveness and cost-effectiveness of antiviral treatment in hepatitis C

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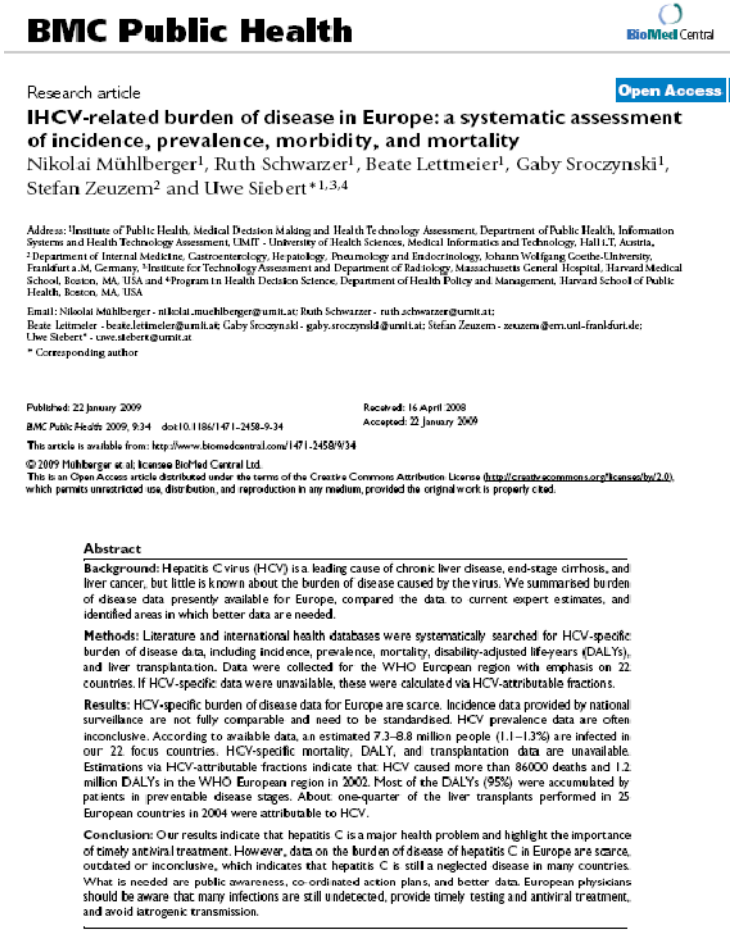
SUMMARY. We systematically reviewed the evidence for long-term effectiveness and cost-effectiveness of antiviral treatment in patients with chronic hepatitis C. We performed a systematic literature search on the long-term effectiveness and cost-effectiveness of AVT in hepatitis C (1990–March 2007), and included health technology assessment (HTA) reports, systematic reviews, long-term clinical trials, economic studies conducted alongside clinical trials and decision-analytic modelling studies. All costs were converted to 2005€. Antiviral therapy with peginterferon plus ribavirin in treatment-naïve patients with chronic hepatitis C was the most effective (3.6–4.7 life years gained [LYG]) treatment and was reasonably cost-effective (cost-saving to 84 700€/quality adjusted life years [QALY]) when compared to interferon plus ribavirin. Some results also suggest cost-effectiveness (below 84000€/(QALY) of re-treatment in nonresponders/relapsers. Results for patients with persistently normal alanine aminotransferase (ALT) levels or with special co-morbidities (e.g. HIV) or risk profiles were rare. We conclude that antiviral therapy may prolong life, improve long-term health-related quality-of-life and be reasonably cost-effective in treatment-naïve patients with chronic hepatitis C as well as in former relapsers/nonresponders. Further research is needed in patients with specific co-morbidities or risk profiles.

Keywords: antiviral treatment, chronic hepatitis C, cost-effectiveness, effectiveness.

Wong, Pharmacoeconomics (2006), 24 (7): 661-672

Sroczynski et al., Journal of Viral Hepatitis (2009), 17(1):34-50

Burden of Disease and Market Access



BMC Public Health

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IHCV-related burden of disease in Europe: a systematic assessment of incidence, prevalence, morbidity, and mortality

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Abstract

Background: Hepatitis C virus (HCV) is a leading cause of chronic liver disease, end-stage cirrhosis, and liver cancer, but little is known about the burden of disease caused by the virus. We summarised burden of disease data presently available for Europe, compared the data to current expert estimates, and identified areas in which better data are needed.

Methods: Literature and international health databases were systematically searched for HCV-specific burden of disease data, including incidence, prevalence, mortality, disability-adjusted life-years (DALYs), and liver transplantation. Data were collected for the WHO European region with emphasis on 22 countries. If HCV-specific data were unavailable, these were calculated via HCV-attributable fractions.

Results: HCV-specific burden of disease data for Europe are scarce. Incidence data provided by national surveillance are not fully comparable and need to be standardised. HCV prevalence data are often inconclusive. According to available data, an estimated 7.3–8.8 million people (1.1–1.3%) are infected in our 22 focus countries. HCV-specific mortality, DALY, and transplantation data are unavailable. Estimations via HCV-attributable fractions indicate that HCV caused more than 86000 deaths and 1.2 million DALYs in the WHO European region in 2002. Most of the DALYs (95%) were accumulated by patients in preventable disease stages. About one-quarter of the liver transplants performed in 25 European countries in 2004 were attributable to HCV.

Conclusion: Our results indicate that hepatitis C is a major health problem and highlight the importance of timely antiviral treatment. However, data on the burden of disease of hepatitis C in Europe are scarce, outdated or inconclusive, which indicates that hepatitis C is still a neglected disease in many countries. What is needed are public awareness, co-ordinated action plans, and better data. European physicians should be aware that many infections are still undetected, provide timely testing and antiviral treatment, and avoid iatrogenic transmission.

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Market uptake of new antiviral drugs for the treatment of hepatitis C☆

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See Editorial, pages 491–493

Background/Aims: Peginterferon plus ribavirin is the state-of-the-art antiviral therapy for prevention of serious complications of hepatitis C. Our aim was to compare market uptake of and access to these drugs across Europe.

Methods: We collected launch and sales data for peginterferons for 21 countries in the WHO European region and compared country-specific sales rates. Additionally, we converted sales figures into patient numbers and related those to country-specific hepatitis C prevalence, taking into account genotype distribution, patient characteristics and practice patterns.

Results: Peginterferon sales rates differed considerably across countries. The earliest, most rapid and highest adoption rates were in EU founder states, followed by EU members that joined after foundation, and EU non-member states. Most new member states showed a marked increase in sales. By the end of 2005, approximately 308,000 patients had been treated with peginterferons in the 21 countries evaluated. The number of patients ever treated ranged from 16% of prevalent cases in France to less than 1% of cases in Romania, Poland, Greece and Russia.

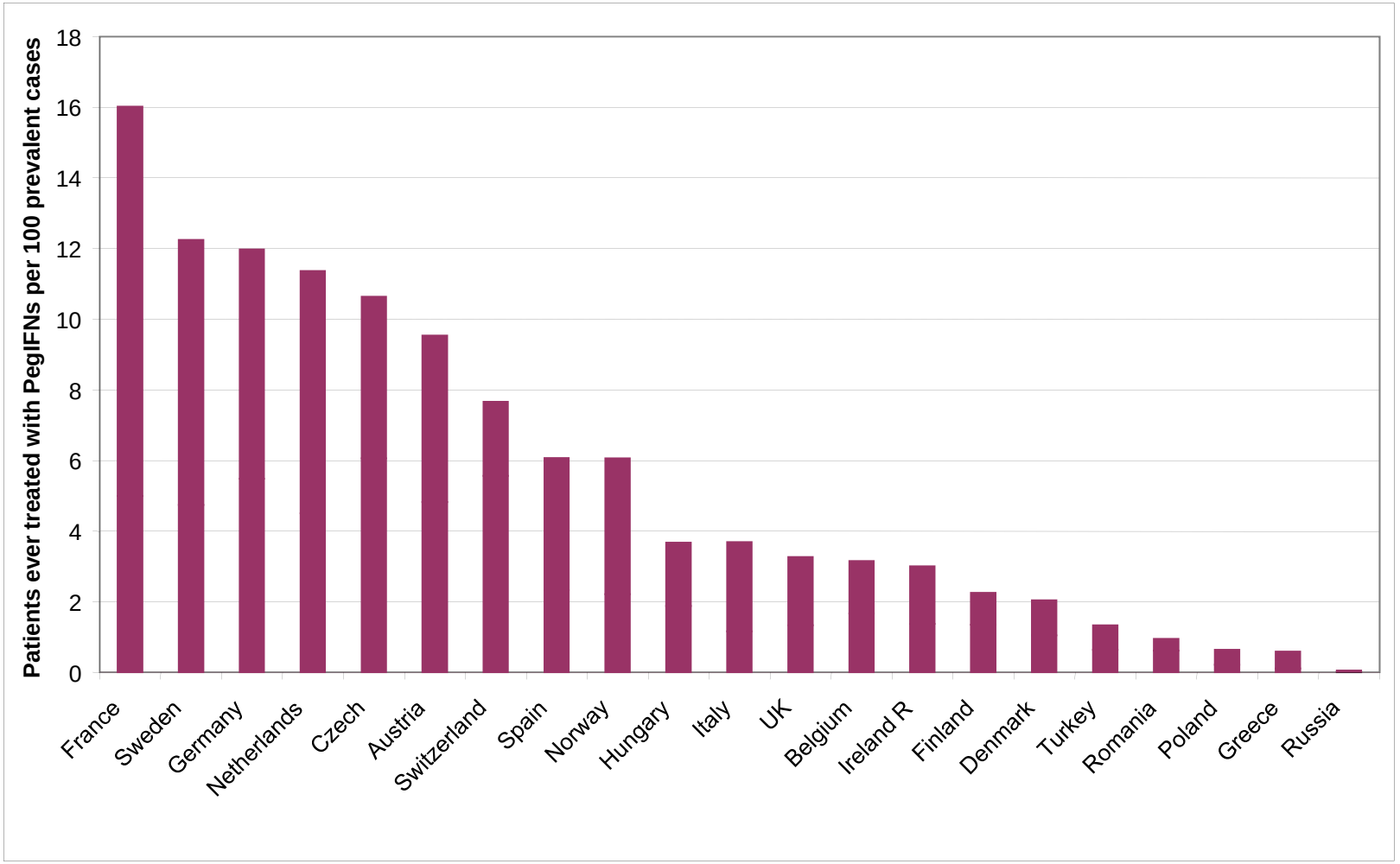
Conclusions: Peginterferon market uptake and access differed considerably across Europe, suggesting unequal access to optimised therapy. Besides budget restrictions, national surveillance and treatment policies should be considered as reasons for market access variation.

Keywords: Hepatitis C; Peginterferon; Market uptake; Market access

Mühlberger et al., BMC Public Health (2009), 9-34.

Lettmeier et al., Journal of Hepatology (2008) 49: 528-536.

Prevalence-adjusted Cumulative PegIFN Treatment Rates



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

Conclusions

- Market uptake of state-of-the art treatment (peginterferon) and relative treatment rates differed considerably across countries.
- Results indicate unequal access to optimised therapy across Europe.
- Reasons for unequal access are budget restrictions, and differences treatment policies, but also differences regarding policies for case finding and screening across these countries.

Systematic Review on Screening

Objectives:

- To systematically review the 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.

Methods

- Systematic literature search (March 2007) on the long-term health and economic effects of HCV screening.
- Inclusion: HTA reports, systematic reviews, long-term clinical trials, full health economic studies and decision-analytic modeling studies assessing the impact of HCV screening with a sufficiently long time horizon and a patient-relevant long-term outcome (LYG or QALY).
- Economic results were converted to 2005 Euros using GDP PPP and CPI.

Results - Studies

- 10 studies including 2 HTA met inclusion criteria. After removing duplicates, 7 studies were included.
- In the absence of original studies evaluating the long-term effectiveness of HCV screening we based our results on decision-analytic modeling studies.
- Studies varied regarding target population, HCV prevalence, study perspective, discount rate, mode of screening and antiviral treatment regimens and algorithms (e. g. treat all HCV-positives or only those with severe liver histology).
- Only three studies evaluated screening followed by peginterferon plus ribavirin (state-of-the-art therapy).

Results - Effectiveness

- 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.

- Screening in populations with higher HCV prevalence (32%-68%) compared to screening in populations with low/average prevalence (1%-16%) was more effective (0.036-0.066 LYG vs. 0.0004-0.013 LYG).

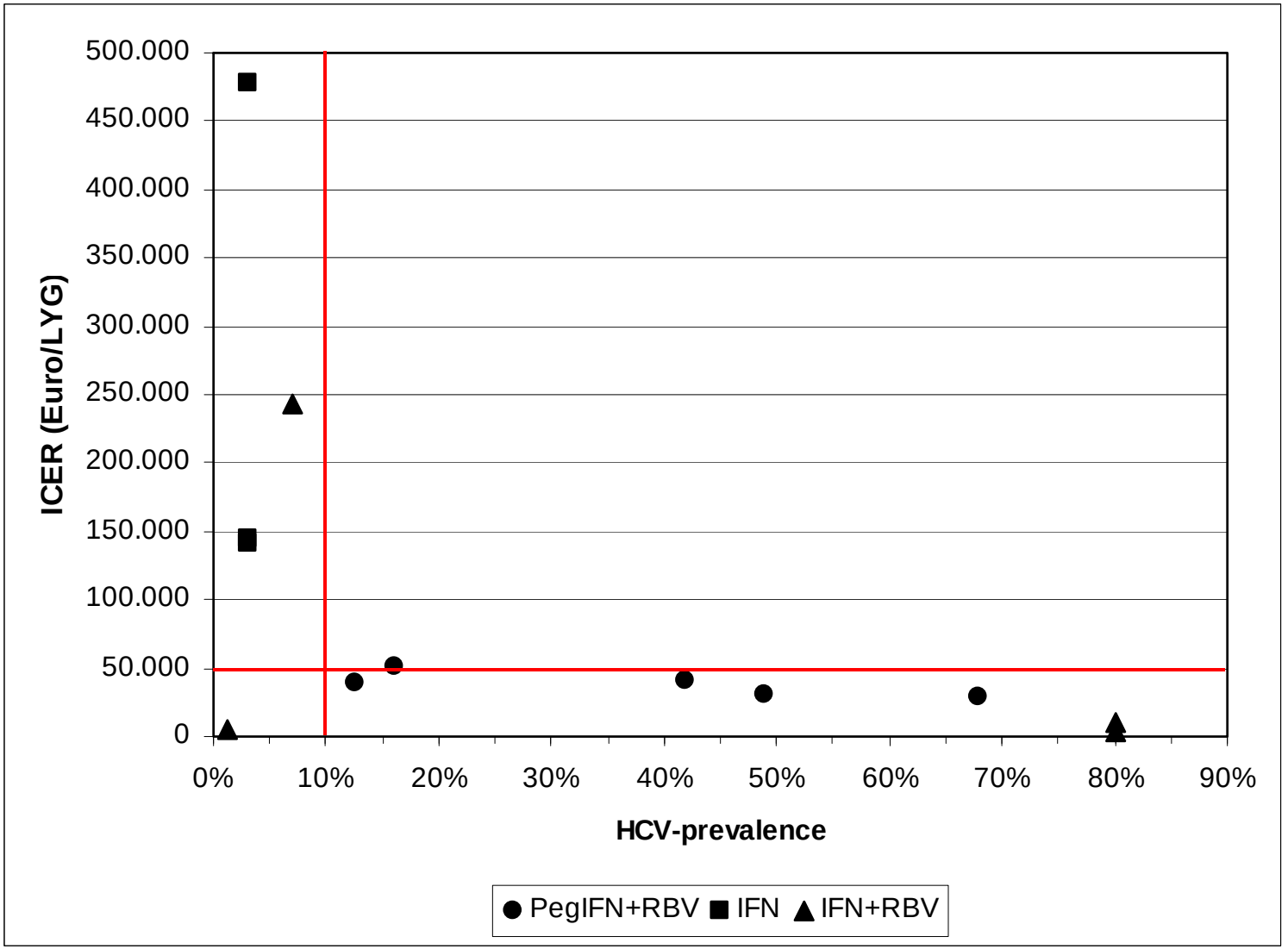
Results – Cost-Effectiveness

- Costs per QALY gained ranged from 18,300 to 1,151,000 EUR/QALY (if screening was not dominated)

- For target groups with HCV prevalence >10% most studies reported ICER/ICUR < 50 000 EUR/LYG or QALY.

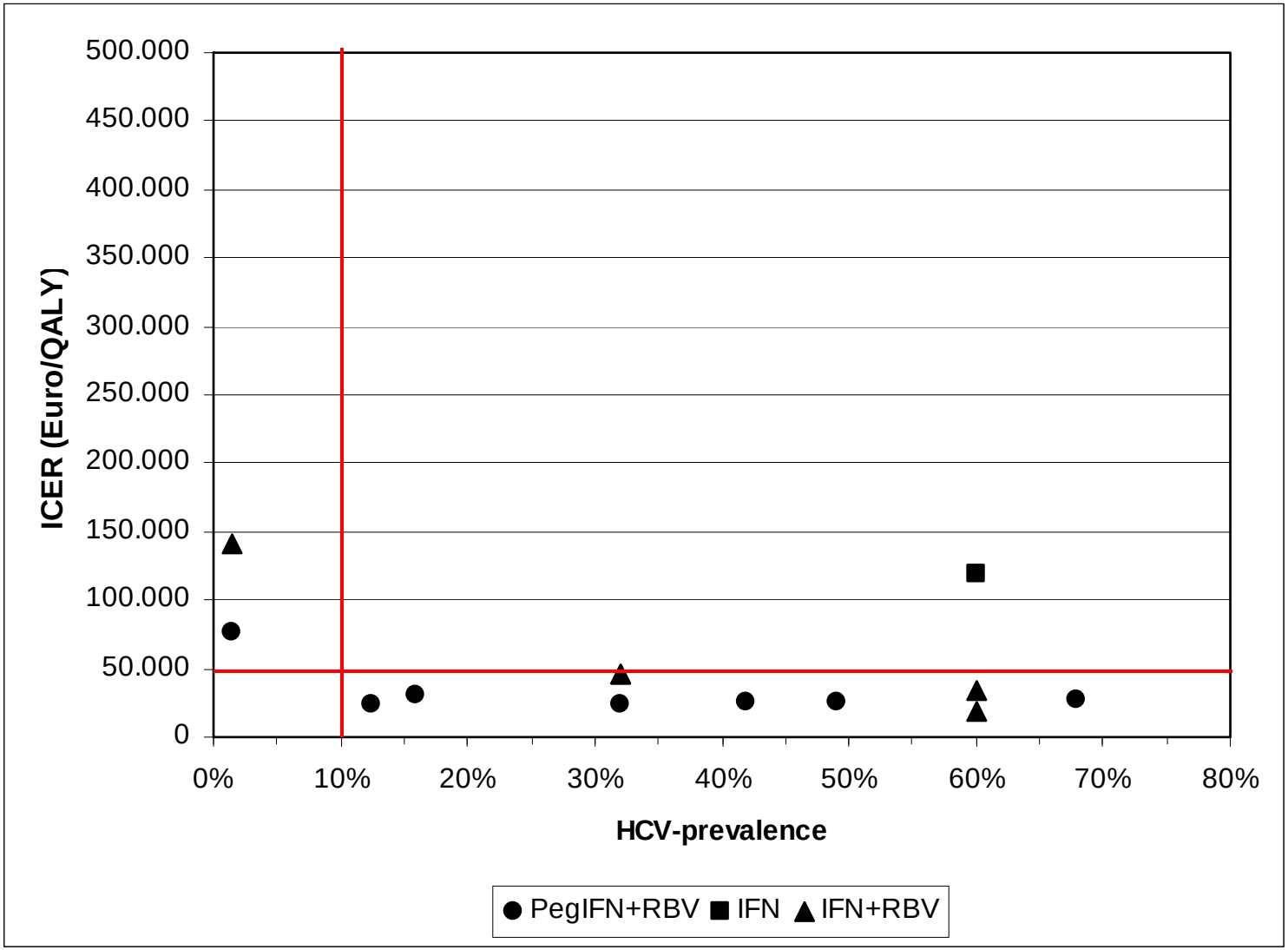
- With lower prevalence, ICER/ICUR were much higher.

ICER of Screening by Prevalence



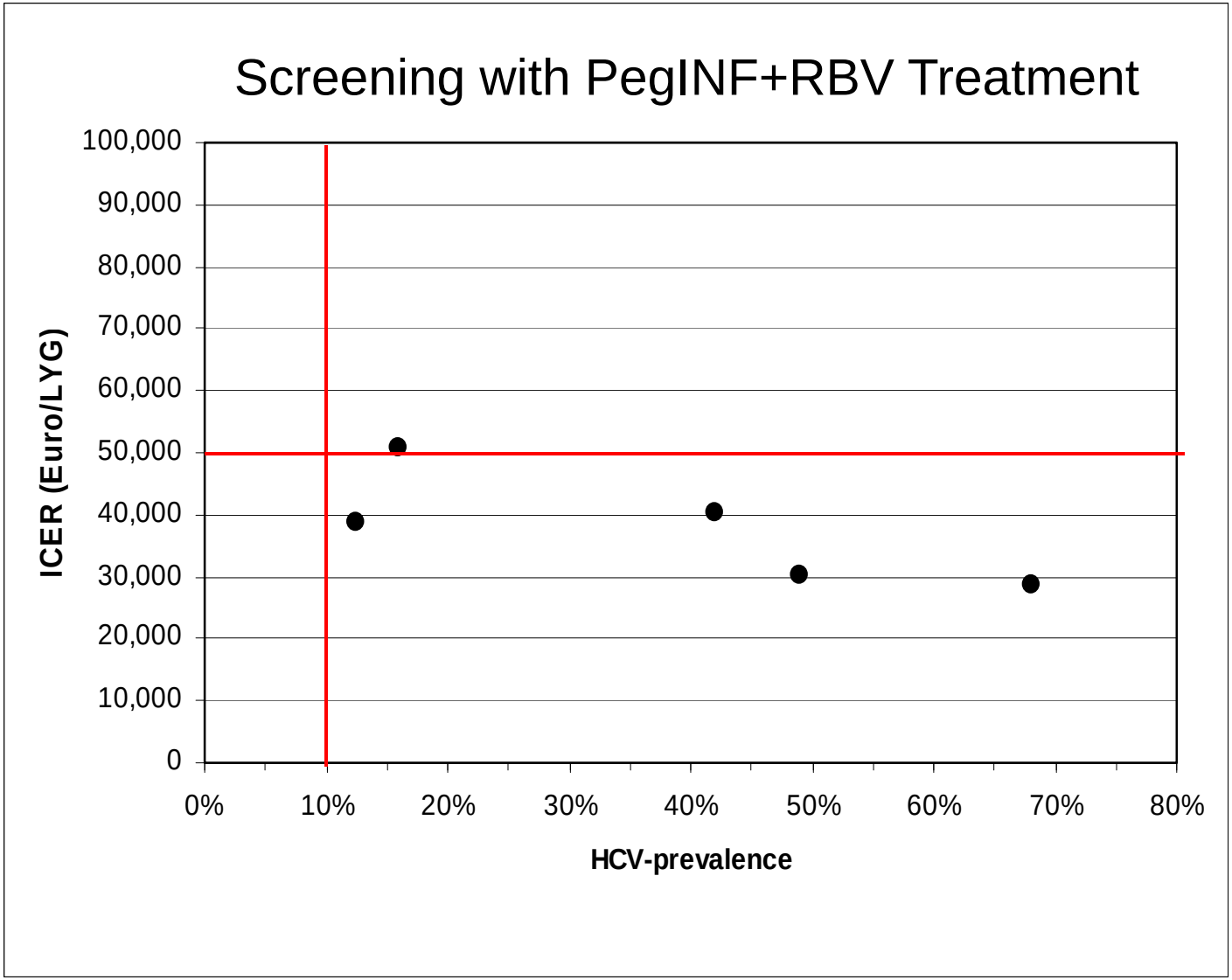
ICER: incremental cost-effectiveness ratio, HCV: hepatitis C virus, IFN: interferon, RBV: ribavirin, PegIFN: peginterferon.

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.

ICER of Screening by Prevalence



ICER: incremental cost-effectiveness ratio, HCV: hepatitis C virus

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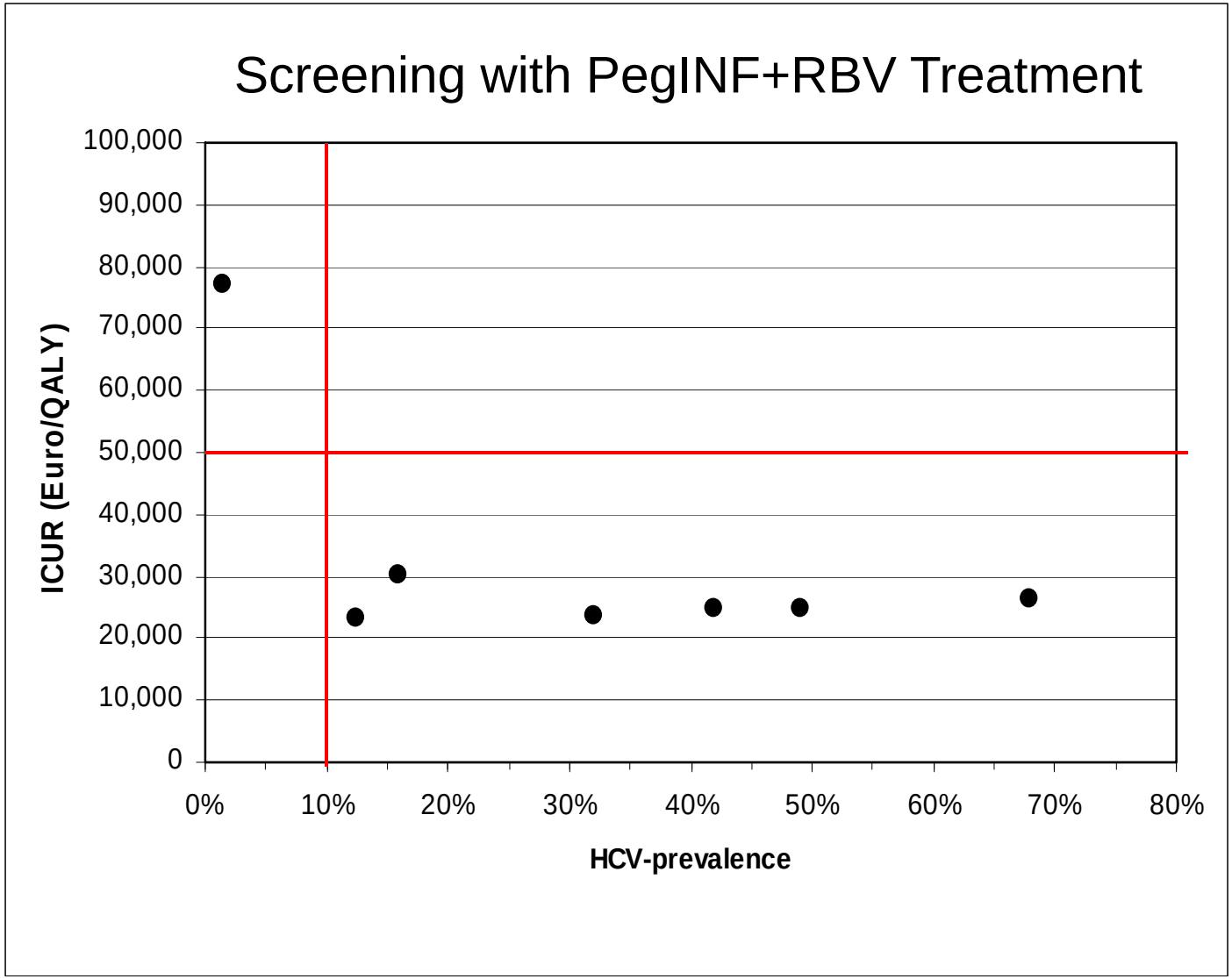

ICER: incremental cost-effectiveness ratio, HCV: hepatitis C virus

Conclusions

- HCV screening and early treatment has the potential to improve average life-expectancy, but should focus on populations with elevated HCV prevalence in order to be cost-effective.
- High prevalence target groups could be selected based on risk factor profiles (e.g., history of blood transfusion, elevated ALT, IVDU, age, visit in hepatology wards/ emergency departments etc.)
- Cost-effectiveness may not be the only decision criterion for the implementation of HCV screening. In view of the multitude of iatrogenic infections, aspects like fairness might 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.

Further Research

- Investigation of the long-term health-economic impact of HCV screening, when combined with appropriate monitoring and treatment strategies in different European health care systems.
- CE-studies in population with low or average HCV prevalence evaluating HCV screening with different strategies of monitoring and AVT of HCV-positives according to current treatment standard.
- Determining optimal target groups and settings for cost-effective HCV screening strategies.
- Pan-European HCV screening model, which can be adapted to the context of the different health care systems and countries within Europe.

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Background: Hepatitis C virus (HCV) infection is an emerging problem in public health. In most countries, the majority of HCV infected people are yet undiagnosed. Early detection and treatment may result in better health outcomes and save costs by preventing future advanced liver disease. The evidence for long-term effectiveness and cost-effectiveness of HCV screening was systematically reviewed. **Methods:** We performed a systematic literature search on long-term health-economic effects of HCV screening and included Health Technology Assessment (HTA) reports, systematic reviews, long-term clinical trials, full health economic and decision-analytic modelling studies with a sufficiently long time horizon and patient-relevant long-term outcomes such as life-years gained (LYG) or quality-adjusted life years (QALY) gained. Economic results were converted to 2005 Euros. **Results:** Seven studies were included. Target population, HCV prevalence, study perspective, discount rate, screening and antiviral treatment mode varied. The incremental effectiveness of HCV screening and early treatment compared to no screening and standard care varied from 0.0004 to 0.066 LYG, and from 0.0001 to 0.072 QALY. Incremental cost-effectiveness and cost-utility ratios of HCV screening vs. no screening were 3900–243 700 €/LYG and 18 300–1 151 000 €/QALY. HCV screening seems to be cost-effective in populations with high HCV prevalence, but not in low HCV prevalence populations. **Conclusions:** HCV screening and early treatment have the potential to improve average life-expectancy, but should focus on populations with elevated HCV prevalence to be cost-effective. Further research on the long-term health-economic impact of HCV screening when combined with appropriate monitoring strategies in different European health care systems is needed.

Keywords: chronic hepatitis C, cost effectiveness, screening.

Introduction

Chronic Hepatitis C (CHC) is an emerging problem in public health. In Europe, the Hepatitis C virus (HCV) infection affects > 1% of the population with a HCV-incidence of 8.6/100 000.[1,2] HCV prevalence differs considerably across countries and risk groups.[3] The highest HCV prevalence (36–81%) is currently found in intravenous drug users (IDUs).[1]

The majority of HCV-infected people progress to chronic disease.[4] Approximately 15–20% of CHC cases develop cirrhosis within 20–30 years,[5–12] which is associated with a high risk for advanced liver disease, quality of life impairment, reduced life expectancy and high treatment costs. CHC is considered to be the leading cause of liver cancer and liver transplantation in Europe.[13]

Screening for CHC clearly fulfils the general criteria for population screening[14,15] and may help to identify HCV-infected patients in an early stage of the disease (e.g. mild chronic hepatitis without fibrosis), so that they can be adequately monitored and treated. Moreover, it has been reported that it may be cost-effective to treat patients diagnosed with mild disease.[16,17] Furthermore, for the majority of acute HCV cases, which present no symptoms, early treatment and for symptomatic acute HCV cases watchful waiting may be currently the most effective and cost-effective strategies.[18] Thus, early detection and early treatment may have the potential to result in better health outcomes and to save costs by preventing future advanced liver disease. Another important reason to identify unaware HCV-infected persons is to prevent further HCV-transmission using appropriate interventions to change behaviour leading to HCV transmission (e.g. needle sharing).

However, currently most European countries lack specific policies for HCV screening. Only few European countries perform HCV screening in special subpopulations with elevated HCV prevalence. But even in these cases, the recommendations and medical practices are heterogeneous.[19–21] In March 2007, the European Parliament called for EU-wide action on Hepatitis C by formally adopting the Written Declaration on Hepatitis C.[22] Specifically, the European Parliament calls for a council recommendation on Hepatitis C screening to ensure early diagnosis and wider access to treatment and care within the member states. Furthermore, the European Liver Patients Association (ELPA) strongly suggests that the European Union should encourage tailored screening campaigns that target people in at-risk groups.[23]

Despite all potential benefits, HCV screening may have substantial health-economic consequences and it is not clear whether it leads to improved long-term health outcomes, because not all CHC patients will develop progressive liver disease in their lifetime, and not all CHC patients benefit from antiviral treatment.[16,24,25] Furthermore, current antiviral

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