

## **Evidence for the cost-effectiveness of screening for chronic hepatitis B and C among migrant populations: results from a review of the literature**

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This paper is an update of data described in a previous publication:

Hahné SJ, Veldhuijzen IK, Wiessing L, Lim TA, Salminen M, van de Laar MJ. Infection with hepatitis B and C virus in Europe: a systematic review of prevalence and cost-effectiveness of screening. *BMC Infect Dis.* 2013;13:181.

### **Background**

Screening for chronic hepatitis B or C and subsequent treatment of patients can decrease morbidity and mortality as a cause of these chronic infections. Migrants born in endemic countries are an important risk group for chronic viral hepatitis infection. Treatment for chronic hepatitis B virus (HBV) and hepatitis C virus (HCV) infection is improving but not benefiting individuals unaware to be infected. Chronic viral hepatitis related morbidity and mortality are associated with a significant economic burden. To inform screening policies we assessed the cost-effectiveness of screening migrant populations for chronic HBV and HCV infection.

In a cost effectiveness analysis the costs and health benefits of different intervention scenarios are quantified and compared against the baseline situation.<sup>1</sup> The intervention we are focussing on is screening for chronic hepatitis B or C infection.

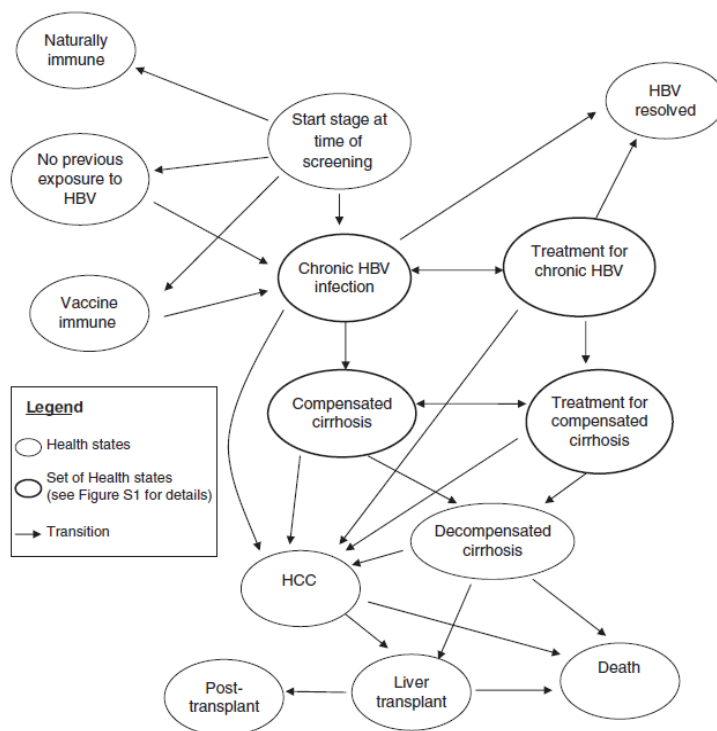
### *Health benefits*

To quantify the impact on health mathematical models are used that describe the course of the disease for a hypothetical cohort of patients. These models describe the different health

states in the natural history of chronic viral hepatitis. The figure below shows an example of a hepatitis B model. Typically the following health states are included:

- Chronic infection without cirrhosis
- Compensated cirrhosis
- Decompensated cirrhosis
- Hepatocellular carcinoma
- Liver transplant
- Death

Based on the disease progression observed in clinical studies yearly progression rates are assigned to each health state. For example, a HBeAg negative patient with active chronic hepatitis B and compensated cirrhosis has a chance of about 3% annually to develop decompensated cirrhosis. Each health state is also assigned a quality of life value, the so called utility. A utility can vary between 0 and 1 where 1 refers to perfect health and 0 to death. The health gain is expressed in QALYS (Quality adjusted life years).



Example of a Markov model of HBV infection and progression from Wong et al. Liver Int 2011.

### Costs

To evaluate the cost effectiveness the costs related to the screening programme need to be included, as well as the costs of medical care. When the cost effectiveness of screening for chronic hepatitis B or C is assessed typically the following costs are considered:

- Costs of organising the screening
- Costs of diagnostic tests
- Costs related to clinical follow up

- Costs of antiviral treatment of patients eligible for treatment
- Costs of medical care for different stages of disease (e.g. liver transplant for decompensated cirrhosis)

### *Cost effectiveness of screening*

Cost effectiveness studies often only look at the cost effectiveness of treatment. But as patients are usually asymptomatic, they need to be identified first and that is where you would need a screening programme. Screening can be organised at the primary care level, with subsequent referral to specialist care if needed. Patients need to be evaluated by the specialist and if they qualify for treatment, start treatment. Another important assumption that needs to be made regards the prevalence in the target population. When studying the cost effectiveness of a screening programme, estimates for the following factors need to be taken into account:

- Prevalence of chronic infection
- Participation in screening
- Referral to specialist care
- Start antiviral treatment

In a mathematical model different scenarios are simulated for a cohort of patients. This can be no screening versus screening and treatment. The health gain is expressed in QALYS (Quality adjusted life years) and the cost effectiveness is expressed as costs per QALY gained.

### **Methods**

Peer-reviewed literature was systematically searched for data on cost-effectiveness of screening of migrants for the period 2000-2012, and updated with studies published in 2013 and 2014. The costs per quality-adjusted life year (QALY) were converted to 2010 Euros (including purchasing power parity conversion factor) for comparison. The results of the sensitivity analyses of the individual studies were summarized. See the publication in BMC Public Health for more details including the search strategy.<sup>2</sup>

### **Results**

The initial systematic review of papers published between 2000 and 2012 identified 29 papers on cost effectiveness of screening of which 4 on migrant screening (all HBV). In 2013-2014 another three papers were identified. In total seven papers on the cost-effectiveness of migrant screening were included, 5 on HBV and 2 on HCV.

### *HBV*

Five economic analyses of screening migrants for chronic hepatitis B virus infection were found. One of these compared 4 community outreach screening programs for Asian Americans by assessing cost per person screened and cost per HBsAg positive individuals identified, concluding that screening in outpatient settings was the most cost-effective but

reached the lowest number of participants.<sup>3</sup> The four other studies assessing cost per QALY all concluded migrant screening was cost-effective, with ICERs ranging from €8.694<sup>4</sup> to €46.260<sup>5</sup>.

Author	Country	Indicator	Result (€ 2010)	Cost effective
Hutton, 2007 <sup>6</sup>	USA	Cost per QALY	€ 31.692	Yes
Veldhuijzen, 2010 <sup>4</sup>	NL	Cost per QALY	€ 8.694	Yes
Rein, 2011 <sup>3</sup>	USA	Cost per case detected	€ 499 - € 3.818	Yes
Wong, 2011 <sup>5</sup>	CA	Cost per QALY	€ 46.260	Yes, moderately
Rossi, 2013 <sup>7</sup>	CA	Cost per QALY	€ 29.638*	Yes, reasonably

\*costs converted without PPP (Purchasing Power Parities) correction

The studies that looked at including vaccination after screening for HBV concluded this is not cost-effective. This can be explained as vaccination is costly but only has a small effect on morbidity and mortality for susceptible adults and has no effect on morbidity and mortality among those already chronically infected.

#### HCV

Two studies assessing the cost effectiveness of screening migrants for HCV were found. The study from the UK found that screening of South Asians in primary care could be cost effective with an ICER of € 27.144.<sup>8</sup> In the Netherlands adding HCV screening to the antenatal screening for women born in endemic countries was considered moderately cost-effective.<sup>9</sup> One other economic analysis of HCV screening of migrants was found.<sup>10</sup> In this study, the target group for screening included migrants from countries with a HCV prevalence >10%, as well as from other population subgroups. Separate estimates of cost-effectiveness of screening migrants were, however, not presented.

Author	Country	Indicator	Result (€ 2010)	Cost effective
Miners, 2013 <sup>8</sup>	UK	Cost per QALY	€ 27.144*	Could be
Urbanus, 2013 <sup>9</sup>	NL	Cost per QALY	€ 47.113*	Yes, modest

\*costs converted without PPP (Purchasing Power Parities) correction

#### Sensitivity analysis

All six cost effectiveness studies reported the results of sensitivity analyses, so which factors have most influence on the ICER. the factors mentioned in the different studies are summarized below, with the number of studies mentioning the factor in brackets. The arrow indicates if an increase in the factor has a positive or negative on the cost effectiveness. For example, a higher prevalence has a positive influence on the cost effectiveness (i.e. the ICER

lowers which is more favourable). An increase in the cost of antiviral treatment has a negative influence on the cost effectiveness.

Reported factors influencing the cost effectiveness results in sensitivity analysis:

- Prevalence ↑ (4)
- Disease progression rates ↑ (4)
- Cost of antiviral treatment ↓ (3)
- Effectiveness of treatment ↑ (3)
- % visiting specialist / accepting treatment ↑ (3)
- Participation ↑ (2)
- Screening age ↓ (2)
- Probability of leaving the country ↓ (1)

### **Discussion and conclusion**

There is evidence that screening of migrants for chronic viral hepatitis could be cost-effective. The five publications examining HBsAg screening of migrants born in endemic countries (HBsAg prevalence  $\geq 2\%$ ) suggest this is cost-effective. The two publications on screening and treatment of migrants for chronic hepatitis C indicate this could be modestly cost-effective.

The cost-effectiveness of screening migrants for chronic HBV and HCV infection varies between studies and is most influenced by the assumptions related to the prevalence of infection, disease progression rates with and without treatment, costs of treatment and the proportion of patients visiting the specialist and of treatment uptake of eligible patients. Further research should focus on these areas of uncertainty. For example on what the lower threshold prevalence is for screening to be cost effective, and to assess the impact of the new antiviral treatment for HCV which has a higher cure rate but is more costly. Furthermore, the effect of antiviral treatment on preventing further transmission could be taken into account when dynamic models are used. Another issue that should be addressed is what is the most effective approach to screening by comparing the cost effectiveness of outreach, opportunistic and systematic screening. how to optimize participation in screening and referral pathways.

Given that HBV and HCV could be tested using the same blood sample and that migrants generally have a higher prevalence of both chronic HBV and HCV, an economic assessment of combined HBV/HCV screening for migrants is a priority. Taking this even further it would also be interesting to assess the cost effectiveness of integrated strategies where chronic viral hepatitis screening is combined with HIV and/or TB screening.

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## Disclaimer

Responsibility for the information and views set out in this paper lie entirely with the authors. The European Commission is not responsible for any use that may be made of the information contained herein.



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