



STUDIECENTRUM VOOR ECONOMISCH EN SOCIAAL ONDERZOEK

VAKGROEP PUBLIEKE ECONOMIE

COST-EFFECTIVENESS ANALYSIS OF PRENATAL  
SCREENING AND VACCINATION AGAINST  
HEPATITIS B VIRUS  
- THE CASE OF BELGIUM -

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report 90/243

April 1990

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D/1990/1169/02

ABSTRACT

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The study analyzes the cost-effectiveness of the screening of pregnant women on the Hepatitis B Virus (HBV). If they are found to be positive for the virus, their babies are vaccinated. The alternative considered is 'doing nothing'.

In the overall Belgian population, the prevalence of the HBV amounts to about 0.67 %. Provided that a pregnant woman is infected with the virus, there is a 30 % chance that she transmits the HBV to her baby. In his later life, this baby will be at risk for serious complications, such as active chronic hepatitis and cirrhosis of the liver.

The incremental cost-effectiveness ratio for the screening and vaccination strategy amounts to 1,477,896 BEF per year of life saved. To test the stability of the cost-effectiveness ratio, we performed a sensitivity analysis. The cost-effectiveness ratio is found to be quite sensitive to the prevalence of HBV, to the probability of transmission from mother to child, to the costs for screening and vaccination and to the discount rate. Varying the treatment costs for a HBV complication hardly changes the cost-effectiveness ratio.

## ACKNOWLEDGEMENTS

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The authors are grateful to Smith Kline Biologicals for their financial support. They also thank Prof. Dr. J. De Groote (Katholieke Universiteit Leuven), Dr. P. Van Reempts (Universitair Ziekenhuis Antwerpen) and a group of General Practitioners associated with the Department of General Medicine (University of Antwerp) for their advice.

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## 1. I N T R O D U C T I O N

Hepatitis B is one of the world's major health problems. It has been estimated that there are about 300 million chronic carriers in the world (WHO, 1988). Transmission of hepatitis B virus (HBV) from mother to infant during the perinatal period represents one of the most important modes of HBV infection and often leads to important and severe long-term complications (MMWR, 1988). Patients often deacease prematurely. Note that in hyperendemic areas, 30 to 50% of the carriers have acquired their infection during the perinatal period (Beasley RP, 1983).

In Belgium, one registers yearly about 790 births from pregnant women infected with the hepatitis B virus; approximately 145 of these neonates become chronic HBV carriers. Prenatal screening of all pregnant women would identify those who are infected and would allow preventive measures towards their newborns. Hepatitis B immunoglobulin (HBIG) and hepatitis B vaccine are known to be 85% to 95% effective in preventing the development of the HBV chronic carrier state (Stevens CE, 1985; Beasley RP, 1983; Wong VCW, 1984).

This study assesses the importance of HBV-infection among the pregnant population and provides some estimates about perinatal transmission and about the costs related to the screening, diagnosis, vaccination and treatment of the disease. Our main objective is to provide an answer to the question whether

screening of all pregnant women in Belgium and immunization babies at risk would be cost-effective, compared to the situation where no action is undertaken to prevent HBV infections. The methodology used to address this question is that of medical decision analysis.

In the following sections we first describe a HBV infection and its complication. Next, we present the decision tree we used to calculate the expected costs and benefits of a screening and vaccination campaign. Then the costs for screening & vaccination and for the treatment of HBV complications are analyzed. Finally, we calculate the cost-effectiveness ratio and draw some conclusions.

## 2. DESCRIPTION OF THE INFECTION AND COMPLICATIONS

### 2.1 HBV and its transmission

Several Hepatitis B Virus (HBV) particles have been observed, among which are the 'Hepatitis B surface Antigen' (HBsAg), the 'Hepatitis B core Antigen' (HBcAg) and 'Hepatitis B envelope Antigen' (HBeAg). They all can be found in the serum of infected persons. HBsAg is a part of the surface of the virus. The incubation period - the time between the moment of infection and the first signs or symptoms of illness - is 60 to 160 days. During this period the virus invades the liver and replicates in the liver cells. The HBsAg marker indicates that viral replication is still taking place in the liver. HBeAg belong to the inner structure (HBcAg) of the virus. They are associated with virus replicating activity and are correlated with very high infectivity.

The HBV is transmitted from one human being to another in several ways. Generally, HBV infections are transmitted by blood or blood products/body fluids from HBsAg carriers. Another important channel is the perinatal transmission from mother to child. In this study we focus exclusively on this type of vertical transmission. Neonatal infection seems to be passed on mainly (95%) during childbirth when it is difficult to avoid exposure to maternal blood. The most likely route of transmission is via a break in the maternal fetal circulation at the time of delivery. Note that the HBV prevalence rate

among pregnant women in Belgium is estimated to be 0.67 % (1). We mention especially that perinatal transmission rates are considerably higher for mothers who are positive for both the HBsAg and the HBeAg. In our analysis we use a transmission rate of 90 % if the mother is positive for the HBeAg and 15 % if she is negative for the HBeAg (Maazel, 1986).

## **2.2 Patterns of disease**

Hepatitis B varies widely in its manifestations and severity. We distinguish acute hepatitis, fulminant hepatitis, chronic persistent hepatitis, chronic active hepatitis and cirrhosis & primary hepatocellular cancer. The estimates presented for the occurrence of the various diseases are based on data from MAAZEL (1986).

### **(i) Acute hepatitis**

Acute hepatitis is a systemic infection affecting the liver predominantly. It is the usual complication of a HBV infection. The patient has HBsAg markers in his blood until the fifth month after the infection. By the time, the HBsAg disappear and are replaced by anti-HBsAg, which indicate that the individual is immune for infections with the HBV. It is important to note that the HBeAg will have disappeared after a period of four months. During this period the risk of HBV transmission to other persons is still quite considerable, however.

In our analysis we estimate that babies who are infected by a



HBeAg positive mother develop acute hepatitis in 2.8 % of the cases, 90.2% become chronic carriers and 7 % experience an asymptomatic infection. If the mother is negative for the HBeAg, 3.2 % develop acute hepatitis, 15.7 % become chronic carriers and 81.1 % show no symptoms.

(ii) Fulminant hepatitis

A much feared complication of hepatitis is fulminant hepatitis, implying massive liver cell damage and necrosis. We estimate that 25 % of the babies with acute hepatitis experience the disease in a fulminant way. Most patients (90%) die within 2 to 10 days after onset of the disease.

(iii) Chronic hepatitis

Some of the infected persons remain carriers of the virus, HBsAg remaining in their serum. These carriers are more likely to develop chronic hepatitis. 90 % of the chronic carriers are estimated to develop chronic hepatitis.

Two types of chronic hepatitis may occur after viral hepatitis: chronic persistent hepatitis and chronic active hepatitis (De Groote J, 1968).

Chronic persistent hepatitis

The clinical picture is characterized by some occasional episodes of fatigue, malaise and abdominal pain. The important distinction between persistent and active chronic hepatitis is that the former rarely (if ever) progresses to cirrhosis or portal hypertension. In addition, only some cases of chronic

persistent hepatitis show a modest excess mortality. We assume that 20 % of the carriers with chronic hepatitis develop persistent hepatitis and that these can expect to live until their 70th life-year.

#### Chronic active hepatitis

Chronic active hepatitis is a chronic progressive liver disorder, with an obvious degeneration and necrosis of liver cells. The clinical picture shows recurrent episodes of malaise, fatigue, abdominal pain, loss of appetite and possible jaundice. The course of chronic active hepatitis is variable. The infection may occasionally remit into a clinically inactive phase, alternating with continuing hepatocellular necrosis and progression to cirrhosis (Boyer JL, 1976). The case fatality rate, if untreated, may be high (50 to 75%), and those who survive inevitably develop cirrhosis (Brackenridge RCD, 1977). If treated, the 5-year survival would be 82% (Lo KJ, 1982). In the present study, it is estimated that patients with active chronic hepatitis die at the age of 65 and that 12.5 % develop cirrhosis or PHC.

#### (iv) Cirrhosis & Primary Hepatocellular Cancer

Cirrhosis may develop in a patient in whom the disease has progressed steadily from the acute stage through the chronic active hepatitis stage. Cirrhosis of the liver results from fibrosis of the liver, and is characterized by extensive loss of liver cells and further necrosis. We expect that babies who are infected by their mother and who develop cirrhosis,

die at the age of 45. The same assumption holds for patients developing primary hepatocellular cancer. Primary hepatocellular carcinoma (PHC) is one of the most lethal and most common cancers in the world (Blumberg BS, 1981). PHC accounts for 80 to 90% of liver carcinomas.

### **2.3 Prevention of the infection**

HBV is transmitted primarily at or near the time of delivery rather than in utero. This provides the opportunity for prevention through immunoprophylaxis (Stevens CE, 1975).

#### **Immunoglobulines**

Previous studies have demonstrated that passive prophylaxis of the newborn with a single dose of hepatitis B immune globulin (HBIG) at birth reduces the carrier rate to about 50% among infants whose mothers are HBeAg positive

#### **Hepatitis B vaccine**

Several studies (Lo KJ, 1985; Xu Z-Y, 1985) have demonstrated the safety and immunogenicity of both plasma derived and recombinant vaccines in newborns. HB vaccine given without HBIG prevents 70-81% of perinatal HBV infections .

#### **Combination HBV vaccine and HBIG**

The highest efficacy (81-95%) was demonstrated in studies with a combined HBIG and HBV vaccine prophylaxis, HBIG being administered within 2 to 12 hours after birth (Stevens 1985;

Beasley 1983; Wong 1984, Stevens 1987). The first vaccine dose can be given at birth, or 1 week or 1 month later, without important changes in efficacy. Concurrent use of vaccine and HBIg offered higher protection than did the vaccine alone.

### 3. PRESENTATION OF THE DECISION TREE

In Figure 1 we present the decision tree used to evaluate the strategy of screening and vaccination against HBV. This decision tree presents the various outcomes following upon HBV infection in a structured way. The first square at the left symbolizes a decision node. The decision to be taken here concerns the policy question : "Do we screen all pregnant women systematically or do we not ?". If the decision is taken to screen them, we follow the branch upwards from the decision node. In the absence of screening, the branch downwards from the decision node is selected. The difference between the screening and the non-screening branch is that decision nodes 3 and 11 of the screening branch do not appear in the non-screening branch. Note that we took account of a specificity and sensitivity rate of the screening procedures of 99 %. However, for the sake of saving space this assumption is not made explicit in Figure 1.

Figure 1

The decision tree to evaluate screening and vaccination against Hepatitis B

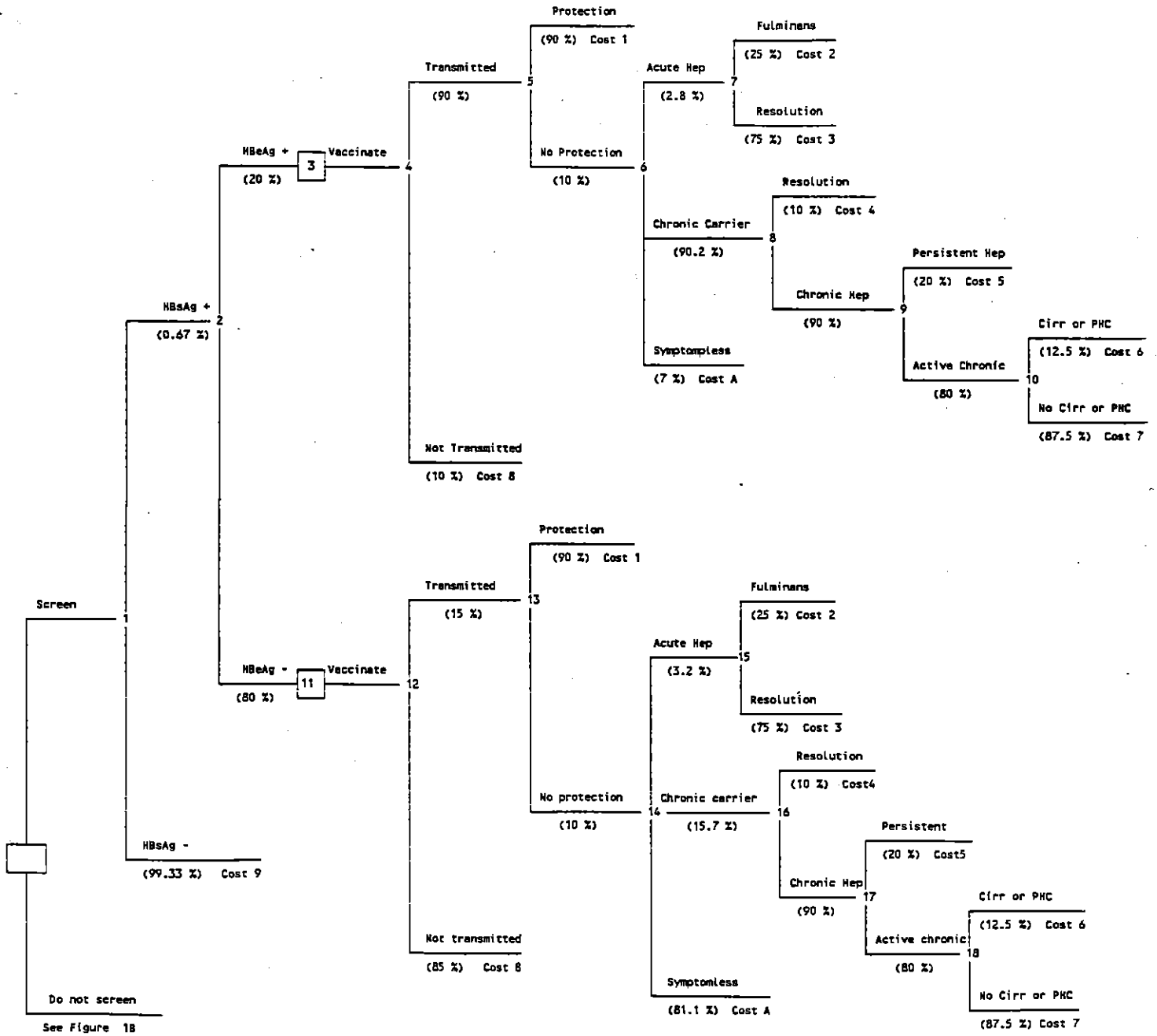
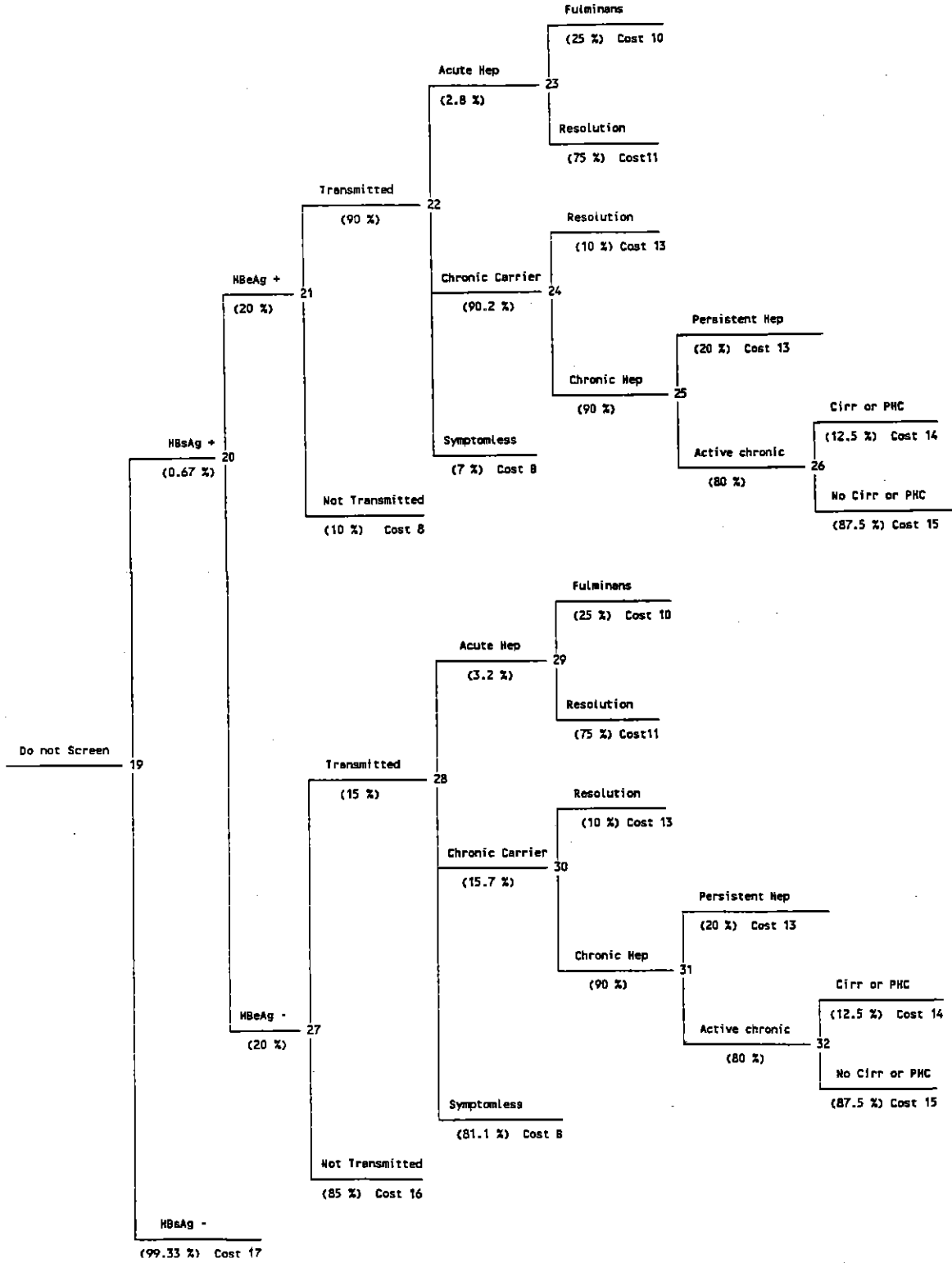


Figure 1 (Cont.)

The decision tree to evaluate screening and vaccination against Hepatitis B



## 4. COST DATA

### 4.1 Methodology

To measure the costs associated with a HBV infection, we need data for six basic components of health care costs, viz. those related to :

- 1) The screening of a pregnant woman
- 2) The vaccination of a neonate
- 3) Medical care for babies with acute hepatitis
- 4) Medical care for patients with persistent hepatitis
- 5) Medical care for patients with cirrhosis or PHC
- 6) Medical care for patients with active chronic hepatitis

In the event of HBV infection, medical care costs are further divided into hospital and ambulatory costs. In order to obtain an estimation of the cost for **ambulatory care**, a questionnaire was submitted to 15 general practitioners (GP). For each type of HBV infection and for their sequelae, we asked how many consultations and visits they would perform on a yearly basis. In addition, we asked how many times a standard set of lab-tests (<sup>2</sup>) would be prescribed yearly. We also gathered additional information about medication and absenteeism at work.

The estimation of the cost due to **hospital care** was much more



complex. First, we analyzed 20 records of hepatitis B patients in different hospitals, viz. Algemeen Kinderziekenhuis Antwerpen (AKA), A.Z. Stuivenberg (Antwerpen), U.Z Pel- lenberg (Leuven). Second, to correct for the limited sample size, we consulted a data set <sup>(3)</sup> provided by the 'Université Catholique de Louvain' (UCL), containing data about three university hospitals. We used cost data for the patients who were classified in the categories 5715, 5718, 5728 of the ICD <sup>(4)</sup> classification. Cost data were also available for patients in the DRGs (Diagnosis Related Groups) 202 and 203 <sup>(5)</sup>. A total of 272 patients with diseases linked to a Hepatitis B infection were hospitalized after April 1, 1985 and were discharged or died between July 1, 1985 and December 31, 1985.

The cost data from the data-set comprise all costs incurred during the stay in the hospital. Firstly, they include the costs of lab-tests, pharmaceuticals, blood transfusions, medical material, physician services in the field of radiology, surgery, anaesthesia, reanimation, etc. Secondly, costs related to 'nursing care' and 'hotel costs' (linen, administration etc.) are included.

In the following cost analysis we allow for different points of view : that of society as a whole, that of the Belgian national health insurance scheme, RIZIV <sup>(6)</sup>, and that of the patients. With respect to the hospital costs, there is a co-payment for the stay in the hospital itself (189 BEF per day),

for drugs (25 BEF per day) and minor lab-tests (25 % of the costs). Note that all future costs are discounted at a rate of 5 %.

#### **4.2 The cost of screening a pregnant woman**

To screen pregnant women for the HBV carriership, basically two tests are needed :

- a test for surface antigen (HBsAg)
- a test for core antibodies (HBcAb)

In Belgium, patients have to pay a (lump sum) supplement for the tests : 135 BEF; of which 93 BEF is reimbursed by the RIZIV. We also assume that 1 visit to a GP takes place preceding these tests. Given this information, the costs of the screening are calculated in Table 1.

Table 1

The costs for screening a pregnant woman (in BEF)

	Total costs	RIZIV costs	Patient costs
Test HBsAg	192	192	0
Test HBcAb	226	226	0
Supplement	135	42	93
GP visit	407	329	78
<b>TOTAL</b>	<b>960</b>	<b>789</b>	<b>171</b>

If the mother is found to be HBsAg positive, an additional test for the HBeAg is required; The latter costs 267 BEF, which is fully reimbursed by the RIZIV.

#### 4.3 The costs of vaccinating a neonate

We assume that, if a pregnant woman is found to be HBsAg positive, the following vaccination scheme is followed for the neonate : immediately after birth, then after the first and the second month. We further suppose that 4 ml immunoglobulines are administered immediately after birth and that a vaccine booster is given after the first year. This results in the cost computation of Table 2.

Table 2

The costs for vaccinating a neonate (in BEF)

	Total costs	RIZIV costs	Patient costs
Vaccination			
- month 0	1246	0	1246
- month 1	1246	0	1246
- month 2	1246	0	1246
- month 12	1246	0	1246
Immunoglobulines	470	0	470
GP visit(4x)	1628	1313	312
<b>TOTAL</b>	<b>7082</b>	<b>1316</b>	<b>5766</b>

4.4 Costs of treatment of neonates with acute hepatitis

HOSPITAL COSTS

Note that for this form of infection, no data were available in the UCL data-set. The examined records reveal that these patients require one hospital admission, with a mean stay of 13 days. On average the costs (hospital stay, clinical biology, pharmaceutical, etc.) amount to 7299 BEF per day. The total cost of one episode in hospital is therefore 94,894 BEF [RIZIV : 93,057 BEF]. Here we must add that the relevant information was obtained from a non-university hospital (AKA). Given that all other data are from university hospitals, we

decided to adjust the cost related to a stay in hospital : the fee of 6200 BEF per bed-day in a university hospital was used instead of 4159 BEF in AKA.

#### AMBULATORY COSTS

On average there are 7 consultations by a GP, 3 GP visits and 6 times the set of standard lab-tests. This results in a total cost of 16,028 BEF [RIZIV : 13,925 BEF].

#### 4.5 The costs for the treatment of persistent hepatitis

Epidemiological studies show that patients with persistent hepatitis have a shorter life expectancy. We assume they de cease at the age of 70.

#### HOSPITAL COSTS

Based upon the UCL data set and our own analysis of patient records we calculate that the mean hospital stay for persistent hepatitis is about 6 days, and that the average total cost amounts to 11,313 BEF. We assume that three hospital admissions are required later in the patient's life, viz. at the age of 40, 55 and 65 (<sup>7</sup>). The discounted hospital costs amount to 19,875 BEF [RIZIV : 17,399 BEF].

#### AMBULATORY COSTS

The GPs state that a patient with persistent hepatitis requires ambulatory care from the age of 40 until the age of 70.

Each year, there are 8 consultations, one GP visit and 6 lab-exams. The discounted sum of these ambulatory costs is 31,516 BEF [RIZIV : 27,678 BEF].

#### **4.6 Costs for the treatment of chronic active hepatitis**

Epidemiological studies show that patients with chronic active hepatitis have a lower life expectancy than a healthy person. We suppose they deacease at 55.

##### **HOSPITAL COSTS**

UCL data were not available for this category of illness. In the records we analyzed, we encountered only 1 patient with active chronic hepatitis. His hospital stay was 7.5 days, with a cost of 11,259 BEF per day. Referring to Arevalo et al. (1988), we assume that such a patient needs 3 hospitalizations during his life : at the age of 40, 45 and 55. After discounting the costs we obtain a total of 28,521 BEF [RIZIV : 27,979 BEF].

##### **AMBULATORY COSTS**

Our questionnaire gives the following results : 7 GP consultations, 8 GP visits and 6 lab-exams yearly, from the age of 40 until 55. The discounted sum gives 37,364 BEF [RIZIV : 31,593 BEF].

#### 4.7 Costs for the treatment of cirrhosis and PHC

We assume that a patient with cirrhosis or PHC dies on average at the age of 45 <sup>(8)</sup>.

##### HOSPITAL COSTS

Based upon Arevalo and Washington [1988], we make the assumption that a patient with cirrhosis or PHC needs 3 hospitalisations during his life time : at the age of 35, 40 and 45. The mean stay in hospital is 11.4 days, with an average cost of 12,136 BEF. The latter is an average based on our own analysis of patient records and on the UCL data-set. Discounting the total cost for hospitalization gives 62,611 BEF [RIZIV : 62,180 BEF].

##### AMBULATORY COSTS

The GPs that we interviewed stated that a patient with cirrhosis or PHC needs 14 consultations, and 13 visits, yearly. In addition, each year 7 lab-exams are required. At current prices this results in a cost of 25,529 BEF. We suppose that, on average, this cost is incurred annually from his 40th life year until his 45th. The sum of discounted costs gives 15,587 BEF [RIZIV : 12,959 BEF].

#### 4.8 Overview of the cost data and assumptions

Table 3

#### Hospital and ambulatory costs

	Acute Hepatitis	Persistent Hepatitis	Active chronic Hepatitis	Cirrhosis and PHC
<b>Hospital</b>				
- Number	1	3	3	3
- Mean stay	13 days	6 days	7.5 days	11.4 days
- Cost/day	7300	11313	11259	11139
- Discounted Total (BEF)	94,894	19,875	28,521	62,611
<b>Ambulatory</b>				
- GP visits	3	1*	7*	13**
- GP consul.	7	8*	8*	14**
- Lab exams	6	6*	6*	7**
- Discounted Total (BEF)	16,028	31,516	37,364	15,578
<b>TOTAL</b>	<b>110,922</b>	<b>51,391</b>	<b>65,886</b>	<b>78,199</b>

\* : Yearly from his 40th till his 70th life-year

\*\* : Yearly from his 40th till his 55th life-year



## 5. BASELINE COST-EFFECTIVENESS RESULTS

### 5.1 Cost comparison between screening-vaccination and 'do nothing'

By connecting the probabilities of the decision tree presented earlier in Figure 1 with the health care costs associated with HBV (screening, vaccination, complications), we obtain the expected costs for the screening cum vaccination strategy and for the case where no action is undertaken to prevent vertical transmission of the virus. Consequently, we are able to calculate whether the screening and vaccination strategy results in either net costs or net savings per patient vis-à-vis the decision to abstain from prevention strategy. The baseline results are given in Table 4.

In Table 4 one reads that on average the **net costs for society** of the screening and vaccination strategy, per pregnant woman, amount to 1,088 BEF. If a pregnant woman is not screened on the Hepatitis B virus, society pays 77 BEF for the treatment of diseases caused by the (expected) transmission of the Hepatitis B virus from mother to baby during birth. The additional, or incremental, costs incurred as a consequence of the screening and vaccination strategy are equal to 1011 BEF (=1088 - 77). As can be derived from the decision tree, the probability of avoiding HBV-infection in newborns by vaccination is high. However, the numbers of prevented infections are of insufficient magnitude to result in **overall** health care

Table 4

**Expected cost of Screening and Vaccination  
vs. Doing Nothing Strategy, in BEF  
(per pregnant woman)**

Costs for	Strategy		Net Costs
	Screening and Vaccination	Do Nothing	
RIZIV	821	70	751
Patient	267	7	260
Society	1088	77	1011

cost savings. Consequently, society will have to pay an additional cost if it wants to prevent morbidity and mortality following upon a HBV infection at birth.

Table 4 also shows how that burden is shared between the health insurance (RIZIV) and the individual patient. In the absence of a prevention strategy society spends 77 BEF per pregnant woman to treat HBV-morbidity, of which 70 BEF is borne by the health insurance and 7 BEF by the patient. Under the assumption that the screening and vaccination strategy is carried out, health insurance and the patient have to pay 821 BEF and 267 BEF, respectively. The expenses of the health insurance are determined to a large extent by the costs of the screening tests.

## 5.2 Life Years saved thanks to the screening and vaccination strategy

As we have shown earlier in this paper, HBV infection can cause rather serious complications. Premature deaths will occur as a consequence of these complications. Our assumptions concerning time of death due to a HBV-complication can be verified in section 2.4.

To evaluate the screening strategy properly we have to estimate the deaths it can prevent. By using the DEALE method (<sup>9</sup>), we compare the life span of patients suffering from HBV-complications to the life-time of healthy people.

Screening a cohort of 100,000 pregnant women on the presence of HBV and vaccinating babies at risk result in 127 years of life lost as a consequence of a HBV complication. Losses still occur, even under a screening strategy, in view of the assumption that the protection rate of the vaccine would be 90 % and that 1 % of the screening tests would be false-negative. If the same cohort of 100,000 pregnant women is not screened, we can expect to loose 1,092 years of life due to a HBV complication, however. The strategy of screening 100,000 pregnant women consequently saves 965 (undiscounted) life years.

### 5.3 Cost-effectiveness ratio : Costs per life year saved

In section 6.1 we demonstrated that the screening and vaccination strategy against Hepatitis B infection requires extra expenses from both the health insurance and the patients. However, it is obvious from the previous section that setting up such a strategy will result in beneficial effects. We can therefore consider the outlays for the strategy as investments that yield a return in terms of life years gained.

In this section we calculate the incremental costs required to save one year of life by a screening and vaccination strategy against hepatitis. The incremental or net costs consist of the costs for setting up the screening strategy minus the averted treatment costs for HBV-complications. Note that the saved life years as well as the costs are discounted by 5 %. After the discounting, the strategy against Hepatitis B Infection saves 68.39 life years compared to the 'doing nothing strategy' per 100,000 pregnant women. The net costs amount to 101.1 million BEF.

Dividing the net costs for the screening strategy by the life years gained thanks to the strategy, results in the cost-effectiveness ratio. For the base run it amounts to 1,477,896 BEF per discounted life year saved (<sup>10</sup>).

## 6. SENSITIVITY ANALYSES

To test the stability of the findings based on our baseline assumptions, we perform sensitivity analyses on the crucial parameters of the model. We assess the influence of variations in some parameters on the cost-effectiveness ratio. The results are presented in Table 5. We modify selected probabilities from our decision tree. This is a useful exercise, since there is still quite some uncertainty regarding the various probabilities due to lack of epidemiologic data. More particularly, we vary the rates of prevalence and protection of the vaccine, as well as different probabilities of perinatal transmission. We also reduce and augment the medical costs and the costs for screening and vaccination by 30 %. Results from this sensitivity analysis may contribute to policy discussions at government level concerning the price and reimbursement of the vaccine. Finally, the influence of the discount rate will be investigated.

In a first sensitivity analysis, we analyze the effect of changes in prevalence rates. It is obvious that focussing on ethnic groups with higher prevalence rates result in lower net costs for the screening and vaccination strategy. In addition more life years are gained and, consequently, cost-effectiveness ratios drop. In Belgium, prevalence rates are 6.25 % and 20.4 % among the African and Asian population, respectively<sup>(11)</sup>. The costs per life of year saved amount to 132,242 BEF and 20,169 BEF, respectively.

Secondly, the protection rate of the vaccine was varied from 75 % to 95 %. The cost-effectiveness ratio shows to be quite insensitive to these variations.

The third analysis tests for the sensitivity of cost-effectiveness ratios to alternative transmission rates. In the base run, we assumed that 90 % of the babies are infected provided their mother is positive for the HBeAg. If she is negative, transmission decreases to 15 %. In this sensitivity analysis we develop a low risk and a high risk scenario. In the low risk scenario, we assume transmission rates of 5 % (HBeAg -) and 85 % (HBeAg +), respectively. In the high risk scenario, these rates rise to 25 % (HBeAg -) and 95 % (HBeAg +), respectively. Under the low risk scenario, it costs about 1.82 million BEF to save one life year. If we consider the high risk scenario, costs rise to 1.24 million BEF.

Fourthly, it is immediately apparent that changes in the costs for **medical treatment** of complications following on a HBV infection are not apt to affect the net cost for the screening strategy significantly. However, in the fifth analysis, modifications in the costs of the **screening and vaccination** procedure have a major impact on net costs. In other words, any cost reductions in the screening and vaccination strategy prove to have an immediate downward effect on net costs : a

reduction in the screening and vaccination costs of 30 % results in a decrease in the net costs of 32.1 %. The reduction in the costs for the screening test are dominant.

In the sixth sensitivity analysis, we examine the effect of changing the discount rate from 5 % to 2 % and 7 %. The costs of the doing nothing strategy, given a discount rate of 2 %, are almost three times the costs for the same strategy given a 5 % discount rate. The variation of net costs and health effects due to a changing time preference or discount rate, results in a quite considerable fluctuation of the cost-effectiveness ratio. If we assume weak time preference (2 % discount rate), it costs about 410,000 BEF to save one year of life. Strengthening time preference by raising the discount rate to 7 %, implies a cost of more the 2.4 million BEF to save one life year.

Table 5

## Overview of the results of the sensitivity analyses

Sensitivity	Costs of strategies, in BEF		Cost-effectiveness ratio
	Screening and Vaccination	Do Nothing	
<b>BASELINE</b>	<b>1088</b>	<b>77</b>	<b>1,477,896</b>
<b>PREVALENCE OF HBV BY PREGNANT WOMEN</b>			
0.33 %	1059	38	3,030,794
0.77 %	1097	89	1,282,150
2.80 %	1270	323	331,325
6.25 %	1565	721	132,242
20.40 %	2773	2353	20,169
<b>PROTECTION RATE OF THE VACCINE</b>			
75 %	1100	77	1,797,722
85 %	1092	77	1,571,810
95 %	1084	77	1,477,896
<b>PERINATAL TRANSMISSION RATE</b>			
Low	1087	67	1,822,487
High	1089	88	1,239,184
<b>COSTS OF MEDICAL TREATMENT</b>			
- 30 %	1085	54	1 625 172
+ 30 %	1088	100	1 560 934
<b>COSTS OF SCREENING AND VACCINATION</b>			
- 30 %	764	77	1,004,570
+ 30 %	1412	77	1,951,222
<b>DISCOUNT RATE</b>			
2 %	1112	284	409,836
7 %	1083	36	2,396,008



## 7. CONCLUDING REMARKS

We have shown that, at a baseline prevalence of HBV in pregnant women of 0.67 %, a screening and vaccination strategy implies incremental costs vis-à-vis a 'doing nothing' policy. However, the former strategy would also save lives or life years. In the discussion about possible social security reimbursement of the cost of an HBV vaccine, it is up to governmental decision-makers to decide how worthwhile promoting the vaccine will be. A nationwide use will save additional patients' lives, of course. National health insurance will be confronted with extra financial outlays, however.

A number of final remarks ought to be made. **Firstly**, cost calculations are geared to treatment at university hospitals. To obtain a broader picture of treatment of HBV infection and its sequelae, one also needs data not least about treatment schedules at regional general hospitals. Medical costs implied by treatment patterns in different categories of hospitals could vary substantially. However, as shown by the relevant sensitivity analysis, the effect of a significant variation in costs is not likely to have a substantial impact on cost-effectiveness ratios. **Secondly**, when performing sensitivity analyses with HBV prevalence rates in non-European populations, no modifications were applied to transmission and/or mortality rates. Yet, as is also indicated by Arevalo and Washington [1988,p.369], the latter may well be population-specific. **Thirdly**, effectiveness was only measured by means of

life years saved; Substantial additional research would be needed to show effectiveness on quality of life. The latter would be fairly important in making comparisons with other life-saving interventions. Remark that life years saved by hepatitis-B vaccination are years spent in perfect health. However, life years in good health are far from being produced by interventions, say, in the fields of cardiology (e.g. bypass surgery) or oncology (e.g. chemo- or radiotherapy). It stands to reason, therefore, that comparisons between the cost per quality-of-life-year of different interventions could well reveal more favourable incremental cost-effectiveness ratios for the hepatitis B-vaccination strategy. **Fourthly**, we wish to emphasize the sensitivity of incremental cost-effectiveness ratios to changes in the cost of the screening and vaccination procedure. Decreases in the price of both screening and vaccination lead rapidly to more favourable cost-effectiveness ratios.

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## Notes

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1. This estimate is based on a HBV screening among 6000 pregnant women. We refer to : **ALGEMEEN KINDERZIEKENHUIS ANTWERPEN, HBV-prevalence rates among pregnant women of different ethnic origin, Antwerpen (Belgium), Unpublished statistics.**
2. This standard set of lab tests contains 22 tests which cost all together 1962 BEF. Only 186 BEF had to be paid by the patient, the rest is reimbursed by the national health insurance.
3. The data were prepared by M.-C. Closon. They contain costs related to HBV infection in three Belgian university hospitals.
4. The categories contain the following patients :
  - 1) 5715 : Cirrhosis of liver without mention of alcohol
  - 2) 5718 : Other chronic nonalcoholic liver disease
  - 3) 5728 : Other sequelae of chronic liver disease
5. The categories contain patients with the following illnesses :
  - 1) DRG 202 : Cirrhosis and alcoholic hepatitis
  - 2) DRG 203 : Malignancy of hepatobiliary pancreas
6. RIZIV is the acronym of 'Rijksinstituut voor de Ziekte en Invaliditeitsverzekering'. RIZIV is translated into French as INAMI (Institut National d'Assurance Maladie et Invalidité).
7. De Groote, J. (Personnel communication)
8. Arevalo et al. (1988)
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10. This amount is equal to the net costs per 100 000 pregnant women divided by the number of discounted life-years saved:  
 $1,477,896 \text{ BEF} = [(1088 \text{ BEF} - 77 \text{ BEF}) * 100000] / 68,4.$
11. AKA, Op. Cit.