

Ante-natal screening for hepatitis B surface antigen: an appraisal of its value in a low prevalence area

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SUMMARY

The costs and projected benefits of universal screening for hepatitis B virus (HBV) infection in pregnant women in East Anglia are calculated and compared with current practice. By adjusting data from West Midlands region for ethnicity, the prevalence of maternal hepatitis B surface-antigen (HBsAg) positivity in East Anglia is predicted to be 0·083% (1 in 1200). Published data on health risks of perinatal HBV infection and on immunisation efficacy are used to derive benefits of screening. The marginal direct cost of screening is identified from regional sources. Current clinical practice in East Anglia identifies 7 surface-antigen positive mothers per year, whereas 22 are expected. Routine antenatal screening in East Anglia would prevent 2·6 additional childhood carriers per year (compared with current practice), resulting in the prevention of 0·7 deaths per year occurring 40–50 years in the future. The direct cost per (undiscounted) life-year saved would be £2437, not including savings on treatment for chronic hepatitis B infection. Routine prenatal screening for maternal HBsAg should be introduced without delay and continue even if HBV vaccination is introduced into the UK childhood immunisation schedule.

INTRODUCTION

Hepatitis B virus (HBV) causes acute infection with a wide range of severity from asymptomatic infection to fatal, fulminant hepatic failure [1–3]. It is estimated that 300 million people world-wide are chronic carriers of the virus [4]. Chronic HBV reduces life expectancy as a result of primary liver cancer. It is estimated that at least 80% of primary liver cancer in the world is caused by chronic HBV infection [4].

Without preventive treatment, 88% of babies born to HBsAg carrier mothers in the UK that are also HBeAg positive are expected to become chronic carriers [5–7]. It is estimated that 25% of these chronic carriers will ultimately die of the compli-

cations of chronic liver disease with median survival into their fifth decade of life [8–10].

The 1992 edition of the UK Department of Health publication 'Immunisation against Infectious Disease' recommends that all antenatal clinics should consider the introduction of universal screening of their mothers for HBsAg in order to detect all carriers and hence all neonates requiring prophylaxis [3]. At present, however, only 27% of pregnancies in England and Wales are covered by such a service [11]. Many regions, including East Anglia, screen only those women with an obvious risk factor (mainly maternal ethnic origin) for HBV infection – targeted screening. We were concerned that many carrier women might be slipping through the net and we felt that widening screening to all pregnant women in East Anglia might prove to be a cost effective as well as beneficial service.

We estimate the potential for health gain then

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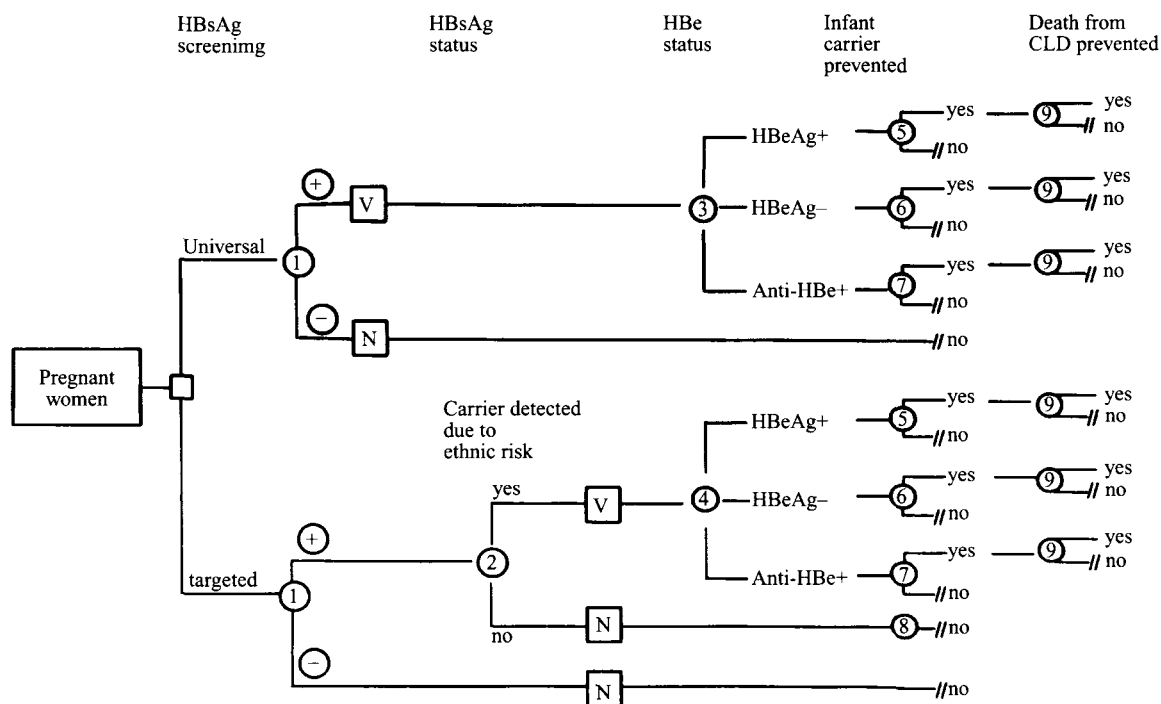


Fig. 1. Decision tree for predicting outcomes for universal or targeted hepatitis B surface antigen screening. Squares, decision nodes; circles, chance nodes; CLD, chronic liver disease; N, not vaccinated; V, vaccinated. The tree assumes 100% sensitivity for HBsAg test.

Table 1. Estimation of maternal HBsAg/HBeAg prevalence in East Anglia

	West Midlands region	Oxford region	East Anglia region
Ethnic proportions of female population (1991 census) [33]			
Asian (%)	5.22	2.52	0.64
Black (%)	1.97	1.29	0.63
Oriental (%)	0.85	1.16	0.74
White (%)	91.97	95.03	97.99
Ethnic proportions of HBsAg +ve mothers [19, 23]			
Asian	64.2		20.9
Black	7.7		6.5
Oriental	13.3		30.7
White	14.8		41.8
Actual HBsAg prevalence (%)	0.22	0.15	
Predicted HBsAg prevalence (%)		0.153*	0.083*

* Predicted using:

$$\text{prevalence}_{\text{target region (E. Anglia/Oxford)}} = \text{prevalence}_{\text{W. Midlands}} \times \left\{ \Pr \left(\frac{\text{race}}{\text{HBsAg}^+} \right) \times \left(\frac{\text{proportion}(\text{race})_{\text{target region}}}{\text{proportion}(\text{race})_{\text{W. Midlands}}} \right) \right\}$$

Table 2. Summary of assumptions used in the analysis

Variable	Symbol	Low	Base	High	Reference
Prevalence of HBsAg (%)	P	0.06	0.083	0.1	Calculated
Pregnant women who are HBsAg + ve					
Proportion HBeAg + ve	$f(\text{HBe}^+)$	0.1	0.22		Calculated
Proportion anti-HBe + ve	$f(\text{anti-HBe}^+)$		0.71		Calculated
Proportion HBeAg + ve (high-risk)	$fR(\text{HBe}^+)$	0.1	0.27		Calculated
Proportion anti-HBe + ve (high-risk)	$fR(\text{anti-HBe}^+)$		0.64		Calculated
Probability of neonatal carrier					
Mother HBeAg + ve	$I(\text{HBe}^+)$		0.88		5, 6, 7
Mother HBeAg - ve	$I(\text{HBe}^-)$		0.3		15
Mother anti-HBe + ve	$I(\text{anti-HBe}^+)$		0.01	0.05	Estim, 16, 17
Probability of no infection					
Mother HBeAg + ve	$o(\text{HBe}^+)$		0.1		Estimate
Mother HBeAg - ve	$o(\text{HBe}^-)$		0.5		Estimate
Mother anti-HBe + ve	$o(\text{anti-HBe}^+)$		0.85		Estimate
Protective efficacy					
Mother HBeAg + ve, vaccine + HBIg	$e(\text{HBe}^+)\text{vaccine} + \text{HBIg}$		0.94		12, 13, 17, 20
Mother HBeAg - ve, vaccine + HBIg	$e(\text{HBe}^-)\text{vaccine} + \text{HBIg}$		0.95		12, 13, 17, 20
Mother anti-HBe + ve, vaccine only	$e(\text{anti-HBe}^+)\text{vaccine}$		0.9		12, 13, 17, 20
Prevention of childhood infection			0.95		12, 13, 17, 20
Screening test characteristics					
Sensitivity (%)	Se	98	100		Estimated
Specificity (%), before confirmatory tests		98	99.5		
Proportion of re-tests (%)	r	0	40		
Secondary benefits					
Pr(secondary carrier)		0	0.1		Estimate
Pr(later carrier mother HBsAg + ve)		0	0.2	0.12	Estim, 25
Natural history of hepatitis B					
Pr(death childhood carrier)		0.125	0.25		10, 23, 24
Median age of death			45		10, 23, 24
Costs					
Screening test (£)			0.75	2.00	Estimated
Screening overheads (£'000)			15		Estimated
Dose of HBIg (£)			40		Estimated
Course of vaccination (£)			30		Estimated
Confirmatory blood tests			10		Estimated
Other					
Annual pregnancies (000s)	N	20	26.6		Estimated
Number of HBsAg+tests 'ad-hoc'	z		7		Estimated
Uptake or compliance	U	80	95		Estimated

consider the cost-effectiveness and feasibility of ante-natal screening to prevent neonatal hepatitis B (HBV) infection. The study concentrates on the principal direct costs, the immediate costs to the health service.

The outcome measures chosen are intended to be useful from the point of view of purchasers of health care. In the UK this means the management of the National Health Service, and therefore ultimately the taxpayer. The main outcomes are: (1) The number of chronic HBV carriers, caused by perinatal transmission, which may be prevented; (2) the direct cost of screening and subsequent treatment; (3) a 'cost-

effectiveness' measure to facilitate comparison with other forms of health care – direct cost per life-year saved.

METHOD

Decision analysis model

Decision analysis uses a method of comparing various alternative strategies to a particular clinical problem by weighing outcomes. We constructed a decision tree (Fig. 1) to compare two alternative strategies: to screen all pregnant women in East Anglia for the

presence of HBV infection (universal screening), or alternatively to screen only women of non-white ethnic status (targeted screening).

Baseline probabilities used in our model were calculated or estimated by ourselves or were taken from published data.

Target population and prevalence (node 1)

Detailed knowledge of HBsAg prevalence in pregnant women is only available in those places where screening already takes place or a prevalence survey has been performed. Nationally, the figure is estimated to be 0.1–0.2% [4], though the prevalence has been found to be 1% or more in inner-city antenatal clinics [5].

Prenatal screening for HBsAg has been routine in West Midlands region since 1974, 80000 pregnant women are screened annually and the prevalence of HBsAg is found to be 0.22% [12]. The racial composition of the carriers detected is: 64.2% Asian (i.e. from Pakistan, Bangladesh or India), 14.8% Caucasian, 13.3% Oriental and 7.7% African/West Indian. The proportion of carrier-mothers who are also HBeAg-positive in West Midlands is *c.* 16% (but varies between different ethnic groups), most of the remainder are anti-HBe positive [12, 13].

The maternal HBsAg prevalence (and HBeAg/anti-HBe status) in East Anglia was estimated by using published information from antenatal screening in West Midlands region (during 1983–7) [12, 13]. The ethnic proportions within the female populations of East Anglian and West Midlands regions (obtained from the 1991 census [14]) were used to adjust for differences in ethnic composition. To simplify analysis, it was assumed that the maternal prevalence of HBsAg (and HBeAg/anti-HBe status) within a given ethnic group is the same in each region. Effects arising from secular trends in HBsAg prevalence and 'e'-marker status were ignored. Data listed in Table 1 were the basis for calculations of HBsAg prevalence in East Anglia (and in Oxford) by the formula

$$\text{prevalence}_{\text{target region (E. Anglia/Oxford)}} = \text{prevalence}_{\text{W. Midlands}} \times \sum \left\{ \Pr \left(\frac{\text{race}}{\text{HBsAg}^+} \right) \times \left(\frac{\text{proportion}(\text{race})_{\text{target region}}}{\text{proportion}(\text{race})_{\text{W. Midlands}}} \right) \right\}.$$

Burden of disease (nodes 2–4)

Infectivity of HBsAg carriers correlates well with the presence of hepatitis B virus surface antigen (HBsAg)

in the serum. At present it is practical to use 'e'-antigen (HBeAg) as a marker for those HBsAg carriers who are highly infective [4]. The presence of antibody to HBeAg (anti-HBe) usually indicates a state of very low infectivity. The probability of chronic carrier status occurring in an infant born to a carrier mother, is therefore dependent on the 'e'-marker status of the mother. Three clinically important states exist: (1) HBeAg-positive, when the probability is 0.88 [6–8]; (2) negative for both HBeAg and anti-HBe, the probability is about 0.3 [15]; (3) anti-HBe positive, the probability is very low and is difficult to ascertain accurately due to the small numbers involved. Transient HBV infection occurs with a probability of up to 0.1 [16]. Chronic carriage is rare and not well quantified in the literature [17]. We have used a figure of 0.01 as our base assumption.

It has been noted that whereas the presence of maternal anti-HBe makes acquisition of carrier state in the neonate unlikely, there is an increased risk of serious acute hepatitis (fulminant infection) which may prove fatal [12, 17–19]. This risk is still small (between 1 in 1000 and 1 in 5000) so that overwhelmingly, the health gain from prevention of neonatal infection is from prevention of the chronic carrier state.

Nine-tenths of hepatitis B infections in the newborn can be prevented by a combination of active and passive immunization [20–22]. The neonate is started on a course of vaccine (active immunization) as soon as possible following delivery. Passive immunization with hyperimmune globulin (HBIg) should also be given within 48 h of delivery unless the mother carries antibody to 'e'-antigen (which indicates a low state of infectivity) [3].

The number of neonatal carriers expected to arise annually in the absence of any preventive treatment will be affected by random fluctuation and will obey a Poisson distribution (assuming detection of maternal carriers to be independent random events). The number expected to arise in an average year, *n*, is given by:

$$n = N \times P \times (I(\text{HBe}^+) \times f(\text{HBe}^+) + I(\text{HBe}^-) \times f(\text{HBe}^-) + I(\text{anti-HBe}^+) \times f(\text{anti-HBe}^+)).$$

The symbols for this and other formulae, are defined in Table 2, as are the values ascribed to these variables (taken from published data, or estimated by ourselves).

Antenatal screening permits HBsAg positive mo-

thers to be identified. Combined active and passive immunization of the infant or infants at risk can then be instituted as recommended [3].

Potential health gain (nodes 5–9)

The number of neonatal carriers that would be prevented by this intervention annually, Δn , is given by:

$$\begin{aligned} \Delta n &= N \times P \times U \times Se \times \Sigma(I \times f \times e_{\text{vaccine/HBIg}}) \\ &= N \times P \times U \times Se \\ &\times (I_{(\text{HBe}^+)} \times f_{(\text{HBe}^+)} \times e_{(\text{HBe}^+)\text{vaccine+HBIg}} + I_{(\text{HBe}^-)} \times f_{(\text{HBe}^-)} \\ &\times e_{(\text{HBe}^-)\text{vaccine+HBIg}} \\ &+ I_{(\text{anti-HBe}^+)} \times f_{(\text{anti-HBe}^+)} \times e_{(\text{anti-HBe}^+)\text{vaccine}}). \end{aligned}$$

The uptake, U , is an aggregate term expressing the degradation in performance which may occur as a result of some neonates missing some, or all, of the vaccine doses.

The number of neonatal carriers prevented by the current practice of screening targeted at women thought to be at high risk, Δn_0 , was estimated by:

$$\Delta n_0 = z \times \Sigma I \times f^R \times e_{\text{vaccine/HBIg}}$$

The number of carriers prevented in addition to current practice was estimated by

$$\Delta n - \Delta n_0.$$

It was assumed that 25% of childhood chronic carriers of HBsAg ultimately die from the complications of chronic liver disease with median survival to age 45 [10, 23, 24]. The (undiscounted) loss of life years (assuming a normal lifespan of 72 years) is therefore:

$$(72 - 45) \times 0.25 = 6.75 \text{ life-years per carrier.}$$

Secondary health gains

Modelling the secondary benefits obtained from prevention of neonatal hepatitis B infection is limited by lack of accurate knowledge of the rates of horizontal transmission of the virus. In this analysis, some allowance for secondary benefits has been made by assuming ‘reasonable’ values for unknown rates.

Pregnant women who are anti-HBe positive, indicating low infectivity, often have other children who are HBV carriers. These may have been born when their mother was HBeAg-positive earlier during her

illness, i.e. when she was more highly infective [17]. These children present a risk of post-natal HBV infection to children born to HBsAg carrier mothers who escape infection at birth.

By vaccinating infants born to HBsAg-positive mothers, perinatal transmission is prevented but subsequent infection during childhood is also prevented for the duration of efficacy of the vaccine, in excess of 5 years [22]. The number of subsequent childhood carriers prevented in this way, $\Delta s^{(+)}$, is formed by the product of the number of infants vaccinated (born to HBsAg-positive mothers), the probability of avoiding perinatal infection (which, it is assumed would give rise either to chronic carrier status or immunity), the protective efficacy of the vaccine, e , and $\text{Pr}(\text{later carrier}|\text{mothers HBsAg}^+)$ which is the probability that a child (of a carrier-mother) who has avoided perinatal infection will acquire carrier status during the period for which the vaccine would have been protective:

$$\begin{aligned} \Delta s^{(+)} &= N \times P \times U \times Se \times \Sigma o \times f \\ &\times e \times \text{Pr}(\text{carrier}|\text{mother HBsAg}^+). \end{aligned}$$

The value of $\text{Pr}(\text{carrier}|\text{mother HBsAg}^+)$ is not known. Margolis and others estimated the risk at 0.12 [25]. Studies in areas of high endemicity have shown postnatal infectivity can be high [26, 27]. One study found that 38.1% of children, negative for hepatitis B markers at age 12 months, subsequently were infected within 3 years [26]. We allowed for the reduced probability of chronic carrier status in children compared with neonates [28]. A value of 0.02 was used as the base assumption for this study. The figure of 0.12 suggested by Margolis and colleagues was used in our sensitivity analysis.

By preventing childhood carriers, a number of secondary cases are also prevented, as given by:

$$\Delta s^{(2)} = (\Delta n + \Delta s^{(+)}) \times \text{Pr}(\text{secondary carrier}),$$

where $\text{Pr}(\text{secondary carrier})$ is the probability that a secondary carrier will arise from an index carrier. A value of 0.1 was estimated in the analysis.

It was assumed, to simplify analysis, that the health gain from avoidance of childhood carrier status was equal to that obtained from avoidance of neonatal carrier status so that health gain is reflected by the total numbers of childhood carriers prevented (including neonatal carriers), Δc , given by:

$$\Delta c = \Delta n + \Delta s^{(+)} + \Delta s^{(2)}.$$

Direct costs and cost-effectiveness

The cost to the National Health Service in East Anglia of providing routine antenatal screening for HBsAg can be minimized if the existing pattern of collection, transportation and testing of blood samples is utilized. Blood samples are taken from all women attending for antenatal care for blood grouping, rubella screening, syphilis serology and other routine tests. These same samples can be additionally tested for HBsAg so that the cost of providing screening consists of the 'test-kit' for each test, and the overheads of additional staff to process the extra volume of tests. These costs were estimated by two local laboratories.

The principal direct costs of the strategy were identified and quantified:

(1) *Screening.* The main additional cost is that of the 'kit' used to perform each test. The proportion of tests inadvertently repeated, r , must also be considered. Overheads are incurred in processing the extra volume of tests and in quality control.

(2) *Treatment.* Responding to a positive screening test involves confirmatory tests (improving specificity from 99.48% to virtually 100%), tests to establish HBeAg and anti-HBe status, three doses of vaccine and HBIg in those cases where the mother is anti-HBe negative.

Having arrived at estimates for the direct costs, the following cost-effectiveness measures were calculated:

(1) direct cost/carrier prevented (allowing for secondary benefits); (2) direct cost/life-year saved (undiscounted).

RESULTS

Population characteristics

By adjusting data from West Midlands for ethnicity, the predicted prevalence of HBsAg in East Anglia pregnant women is found to be 0.083%. The same method applied to Oxford region, where routine screening is conducted, produced a result very close to the 0.15% prevalence actually observed there (see Table 1).

Given that maternal HBsAg prevalence in East Anglia is 0.083%, 22 HBsAg-positive mothers would be expected from 26 500 pregnancies, annually (see Table 3).

Whereas in West Midlands 85% of HBsAg-positive mothers are non-white (and therefore identifiable by ethnic status alone), in East Anglia the comparable figures in only 59% (Table 1). These figures are the

Table 3. Predictions of health outcome in East Anglia

Predictions – East Anglia	
HBsAg + ve mothers – actual (C)	22.1
HBsAg + ve mothers – positive screen	22.1
Neonates vaccinated	21.0
Neonatal carriers expected (no treatment) (n)	4.9
Neonatal carriers prevented (screening) (Δn)	4.4
Neonatal carriers prevented ('ad-hoc') (Δn_0)	1.8
Death rate due to perinatal HBV transmission (deaths/100000 yr)	4.6
Improvement (compared to current practice)	
Neonatal carriers prevented, annual ($\Delta n - \Delta n_0$)	2.6
Childhood carriers prevented, annual	3.1
Death rate (deaths/100000 yr)	2.9
Deaths due to chronic HBV, annual	0.8
Life-years saved, annual	21.2
Annual direct costs (£)	
Screening test 'kits'	33250
Overheads	15000
Confirmatory tests	2437
Vaccine, 3 doses	629
HBIg	243
Total	51560
Cost-effectiveness	
Direct-cost per childhood carrier prevented (£)	16450
Direct-cost per life-year saved (£)	2437

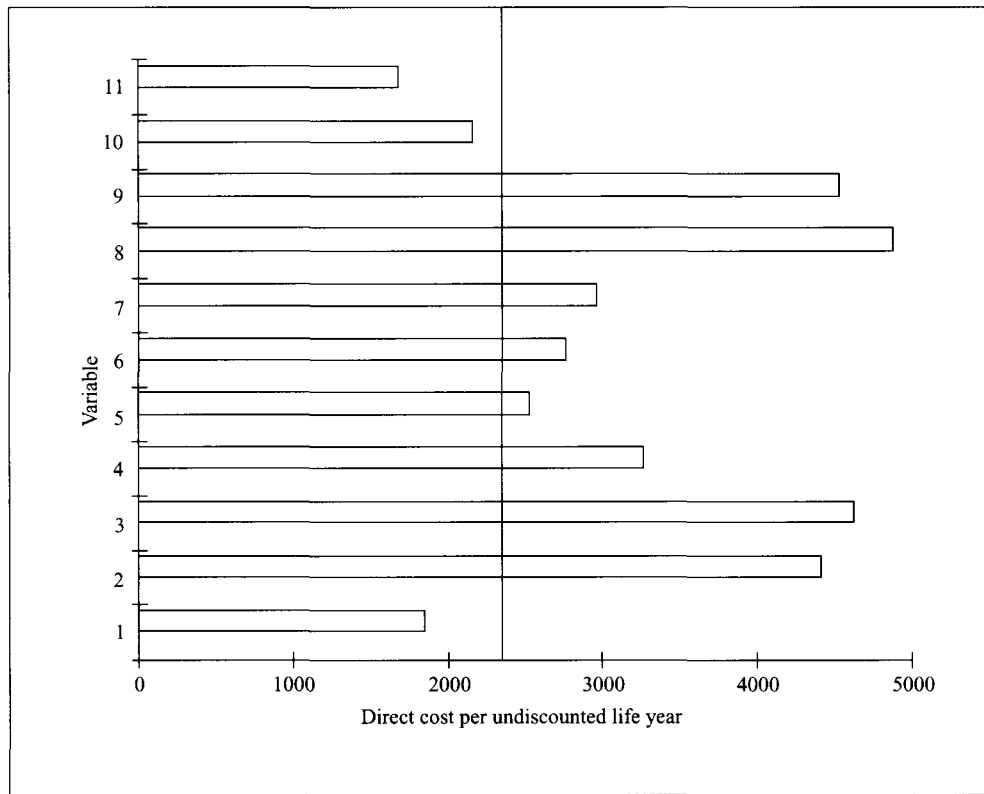
best attainable 'sensitivities' if ethnic status alone were to be used as the sole criterion for inclusion within the HBsAg screened group in targeted strategies in these regions.

The larger contribution from Orientals in East Anglia causes the expected proportion of HBeAg-positive carriers, and hence overall infectivity, to be higher (22%) than in West Midlands (17%).

Over the past 6 years, Cambridge Public Health Laboratory reported a total of 41 HBsAg-positive pregnant women (of which 28 were anti-HBe positive). The total applies to all of East Anglia as Cambridge Public Health Laboratory perform all the HBeAg/anti-HBe tests for the region. This suggests that annually, only about 7 (i.e. 32% of the predicted 22) HBsAg-positive pregnant women are identified by current clinical practice.

Estimation of costs

The target population for the analysis will conform to one of two patterns:



Variable	Description of change to variable	New value ascribed to symbol in Table 2
1	Higher maternal HBsAg prevalence	$P = 0.1\%$
2	Maternal HBsAg prevalence 0.06	$P = 0.06\%$
3	% maternal HBsAg carriers positive for HBeAg	$f(\text{HBe}+) = 0.1\%$
4	Uptake or compliance	$U = 80\%$
5	Sensitivity of laboratory tests for HBsAg test	$Se = 98\%$
6	Specificity of laboratory tests for HBsAg	98%
7	Zero secondary benefits	$\text{Pr}(\text{secondary carrier}) = 0$ $\text{Pr}(\text{later carrier}/\text{mother HBsAg}^+) = 0$
8	Better prognosis for infant carriers of HBV	$\text{Pr}(\text{death}/\text{carrier}) = 0.125$
9	Increased screening costs	$N = 20000$ $r = 0$ screening test = £2
10	Risk of infant carrier per anti-HBe+mother	$I(\text{anti-HBe}+) = 0.05$
11	Increase in secondary benefits	$\text{Pr}(\text{secondary carrier}) = 0.1$ $\text{Pr}(\text{later carrier}/\text{mother HBsAg}^+) = 0.12$

Fig. 2. Sensitivity analysis. Note that the vertical line denotes direct cost using base assumptions.

(1) The Regional Blood Transfusion Service receives samples from the whole of East Anglia except King's Lynn, and a small number from outside the region – Leicester. Approximately 40000 samples are processed annually but a proportion, r , of these are repeats ($c. 40\%$) so that $c. 26\,500$ separate pregnancies, N , are tested annually. Test kits for HBsAg are already used in large quantity for screening of donated blood. Because of this they can be obtained very cheaply (£0.50–£1.00), a price of £0.75 was used in the analysis.

(2) Clinical Microbiology and Public Health Lab-

oratory (Cambridge Public Health Laboratory) at Addenbrooke's propose a service involving 20000 tests per year. The precise geographical distribution is not yet defined. Test-kits for HBsAg would be more expensive (£2) but it will be assumed that arrangements will be made to avoid duplication of blood samples. This higher cost (with $r = 0$ and $N = 20000$) was employed in the sensitivity analysis.

In practice, given the existence of the internal market, the provision of a screening service might be put out to tender giving private laboratories the opportunity to compete. The contracting process

would, however, need to take into account any additional costs incurred in the separation and transportation of samples.

Estimation of health outcome in East Anglia

Antenatal screening should succeed in preventing 2.6 children per year from becoming carriers of HBV (in addition to current practice) (Table 3). This should prevent 0.8 deaths per year later in life (median age 45), and result in the saving of 21 life-years. Since morbidity is also prevented, more than 21 Quality Adjusted Life Years (QALYs) would be gained.

The annual direct cost of screening and preventive treatment is £51 560. This is comprised of £33 250 for test-kits, £15 000 overheads, £2437 for confirmatory tests, £629 for vaccine and £243 for immunoglobulin.

The direct cost (not allowing for future treatment savings) per undiscounted life-year saved is £2437.

Sensitivity analysis

The extent to which the above 'cost-effectiveness' measure is sensitive to variation of key variables is demonstrated in Figure 2. It is most sensitive to prevalence of HBsAg, screening-test cost, assumptions about the prognosis for chronic carriers, and the proportion of pregnant HBsAg carriers that are also HBeAg positive. It is relatively insensitive to: variations in the risk of infant carriers from anti-HBe positive pregnant HBsAg carriers, secondary benefits and variations in sensitivity, specificity or uptake of HBsAg screening tests.

DISCUSSION

Our prediction of maternal HBsAg prevalence is an important step in our analysis. Our method for prediction of HBsAg prevalence assumes equal HBsAg and HBeAg prevalence in equivalent ethnic groups in East Anglia and West Midlands but it does not make an assumptions of equal rates of births per female in different ethnic groups. Our method assumes universal coverage for HBsAg screening in the West Midlands antenatal population during the period of data collection: coverage was believed to be very close to 100% (estimated in excess of 99%, E Boxall, personal communication). The accuracy of our method is demonstrated for Oxford region where observed and predicted prevalences are similar (0.15 and 0.153%, respectively). We infer that our method

for calculation of the proportion of pregnant carriers that are also HBeAg positive is also robust. This is reassuring in view of the relatively high sensitivity of these variables in our sensitivity analysis.

The projected death rate from the complications of chronic hepatitis B caused by perinatal infection is 3.9/100 000 per year. To put this into perspective, this value is comparable with some of the reductions in mortality, aimed for in *Health of the Nation* [29], due to: (1) stroke in all persons under 65; (2) lung cancer in females under 75; (3) suicide and undetermined injury, all persons; (4) accidents, all persons under 15 and all persons aged 15–24.

At £2846 per life-year saved, antenatal screening for HBsAg compares very favourably with estimates for other forms of health care delivery, such as those listed in Table 4 [30–37], provided that the 'discount' rate for non-financial benefits (such as pain, suffering and human life) is taken to be zero. The role of discounting, which is a technique employed by health economists to compare costs and benefits distributed over time, for non-financial items is controversial. We agree with those that argue [38–40] that such discounting, which favours immediate benefits (e.g. from acute medical care) over delayed ones (e.g. from preventive measures) leads to myopic decisions, and that people do not wish collective decisions to be made this way even though their individual behaviour exhibits 'time-preference'.

Our calculated probability of perinatal transmission is much lower than that of US investigators [41]. This reflects the different ethnic mix in East Anglia and the consequently lower proportion of pregnant HBsAg carriers expected to be HBeAg positive. In addition the prevalence of HBsAg in pregnant women is much lower in East Anglia than in the USA. Both these differences will reduce the value of universal screening in East Anglia compared with the USA. It is therefore startling that our principle conclusions remain identical to the conclusions of this highly influential US study: targeted antenatal HBV screening performs poorly and universal screening is economically justifiable [42].

Since the direct cost per life-year saved of routine ante natal screening for HBsAg is inversely proportional to maternal HBsAg prevalence, it follows that if it is worth doing in a low prevalence area such as East Anglia, the case is even stronger elsewhere in the UK where the prevalence is higher.

Targeted screening in East Anglia using maternal ethnic status alone could not be expected to detect

Table 4. *Cost-effectiveness estimates of health care interventions*

Health care intervention	Cost/life-year (1991 £)
Intensive care for patients with multiple trauma	9977
Home dialysis for chronic renal failure	34000
Heart transplantation	29700
Liver transplantation for chronic active hepatitis	177000
Kidney transplantation	7460
Low osmolar contrast media in imaging processes	900400
CABG, males aged 55 with severe angina, 3 vessel disease and good left-ventricular function	8060

CABG, Coronary artery bypass graft.

more than 59% of maternal carriers. Our figures show that in practice only 32% (7 of 22) maternal carriers are detected annually. The shortfall represent women that have fallen through the net as a result of patchy implementation of the targeted screening as described by other workers [43]. This is consistent with the view that targeting screening performs poorly, failing even to detect established risk factors with reliability [44–47].

Cost-effectiveness is sensitive to variations in the prognosis for carriers. Prognosis was estimated from Taiwanese figures [10, 23, 24]. These are the best estimates available but their applicability to a largely European group is uncertain. Our calculations of secondary benefits from universal screening and vaccination of at risk infants uses estimated rather than observed figures for the relevant variables (Table 2). We note, however, that sensitivity analysis (Figure 1) shows the cost-effectiveness of universal screening to be relatively insensitive to changes in secondary benefits.

We did not attempt to calculate cost savings to the National Health Service in reducing the incidence of liver disease, nor did we estimate societal costs, such as loss of earnings. These calculations have been attempted by workers in the US [25, 41]. Although this would increase the attractiveness of universal screening we agree with the views of Mangtani and colleagues [48] who noted that these savings in the National Health Service will be offset by the cost of services for people who liver longer. The net effect is not easily calculable.

In 1991 the Global Advisory Group of the Expanded Programme on Immunisation (EPI) set targets for introduction of HBV vaccine into the EPI. It called for countries with a carrier prevalence of 8% or more to have national vaccination (of new-born)

programmes in place by 1995, and for all other countries to have programmes in place by 1997 [49].

If vaccination against hepatitis B becomes routine for all infants then it is possible that the first dose would be delivered at the age of *c.* 8 weeks with other routine vaccinations. Alternatively the UK may opt for adolescent vaccination as practised in British Columbia, Canada [50, 51]. In either event, the protection conferred against perinatal transmission would be poor or nil. The case for antenatal screening (and treatment soon after delivery for infants of HBsAg positive mothers) would be unaffected as would the cost-effectiveness of the intervention.

Introduction of screening would be straightforward from the logistic point of view since existing arrangement for the collection, transportation and processing of blood samples can be used.

Given the fore-going and the existence already of guidelines recommending prenatal screening for hepatitis B [3, 52], the exposure to risk of litigation in the distant future cannot be ignored [8].

Routine prenatal screening for maternal HBsAg conforms well to the criteria for a good screening test and is justifiable on medical, economic, medico-legal and logistical grounds. It should be introduced without delay and continue even if vaccine costs become low enough to permit routine vaccination.

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