Comparative Cost-efficacy of Hepatitis-B-Vaccination in Indian Infants

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Background: Universal Hepatitis B Vaccination of newborns in India is being launched at the recommendation of Indian Academy of Pediatrics, without estimating in any detail the morbidity and mortality due to sequelae of Hepatitis B infection, leave aside estimating the cost-efficacy of the Hep-B vaccine compared to other vaccines being used in the Universal Immunization Programme in India.

Objective: To estimate the cost-efficacy of measles and hepatitis B vaccination amongst Indian infants.

Methods: Based on available data on prevalence of HBsAg positivity rates amongst Indian children, and data from international literature, Quality Adjusted Life Year (QALYs) and lives lost due to the five morbid sequelae of Hep-B infection (acute hepatitis, chronic persistent hepatitis, chronic active hepatitis, cirrhosis, hepatocellular carcinoma) were estimated in a hypothetical cohort of 1 million Indian infants. Based on this, cost-efficacy of Hep-B vaccine and life time risk of dying due to Hep. B infection in infants was estimated. A similar exercise was done for measles vaccination.

Results: The cost-efficacy of Hep-B and measles vaccination was respectively Rs. 705 and Rs. 21 per QALY saved. Average lifetime risk of dying due to the sequelae of Hep. B-infection amongst the normal population and Hep-B-carriers was found to be very low, 0.13% and 5.6% respectively, compared to the oft quoted figure of 25%.

Conclusion: Compared to the QALYs gained, the cost of Hep-B vaccination in India is too high compared to that of the measles vaccination and the lifetime risk of dying due to the sequelae of Hep. B-infection is too low. Hence the introduction of Hep-B vaccine in the Universal Immunization Programme in India needs to be reconsidered.

Key-Words: Cost–efficacy, QALYs, life-time-risk, universal hepatitis-B vaccination, measles vaccination.

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Introduction

Many experts in India, mainly from the Indian Academy of Pediatrics, have been advocating inclusion of the hepatitis-B vaccine in the Universal Immunization Programme (UIP) in India. [(1)] This programme would cost Rs. 1000 million annually for the vaccine alone, even at a very reduced cost of Rs. 40 per newborn for three doses, for the 25 million annual births in India. Before recommending such a major policy involving annual expenses of tens of millions, it is necessary to estimate the cost-efficacy (cost per Quality Adjusted Life Year -QALY- saved) of this Hep-B vaccination and to compare it with that of other UIP vaccines. We have not come across any such exercise by the IAP. Though Aggarwal, Ghoshal and Naik have estimated the cost-efficacy of Hep-B vaccination by using the Markov-model[(2)] they have not compared it with that of any of the current (UIP)vaccines. In this paper, we have attempted to fill these lacunae. Such comparative cost-efficacy exercise should become the norm; as newer, safe and effective vaccines are becoming available in India (Hib, chicken-pox, rubella) inclusion of any of these vaccines in the UIP should be based on health-care priorities in India and the comparative cost-efficacy of these new vaccines.

Methods –

We used a hypothetical life time cohort of 1 million Indian infants to estimate the Quality Adjusted Life Years (QALYs) lost due to morbidity and mortality due to the five diseases caused by Hep-B-infection: acute hepatitis, chronic persistent hepatitis, chronic active hepatitis, cirrhosis, and hepato-cellular carcinoma. Assuming the protective efficacy of Hep-B vaccine to be 100%, the vaccine cost for a million infants divided by total QALYs saved due to Hep-B vaccine gave us the cost efficacy of the Hep-B vaccine. We carried out this exercise by employing the following steps –

1) Estimation of prevalence of hepatitis-B carrier rate amongst Indian infants-

For this we used the available published data about Hep-B positivity rate. Hep-B positivity rate found in screening testing for Hep-B infection, multiplied by the Positive Predictive Value (PPV) of this testing gives the point prevalence rate of Hep-B infection. (PPV = number of true positives/number of true positives + number of false positives.) Assuming the sensitivity and specificity of the Hep-B screening test (HBsAg) to be 100% and 99% respectively, the PPV of HBsAg testing for a prevalence rate of 3% works out to be 75%. (In India, the overall Hep-B positivity rate is about 3%. Hence we have used the PPV for 3% positivity rate.). The positivity rate in infants multiplied by the PPV gave us the point prevalence of Hep-B infection.

We then estimated the Hep-B chronic carrier rate by multiplying the point prevalence of Hep-B infection by 0.8 because it has been found that Hep-B chronic carrier rate is 80% of the Hep-B point prevalence rate. [(3)]

2) Estimation of number of long-term carriers in this life-time cohort of 1 million infants-

Except in the case of acute hepatitis, it is essential to arrive at the number of Hep-B infected infants who in their lifetime would develop chronic liver disease due to chronic Hep-B infection. To estimate this number we first posited the category of 'long-term' and not just 'chronic carriers'. This is because it is long-term Hep-B infection which causes chronic liver disease and not just the status of being a chronic carrier. (A chronic carrier is defined as one who harbours Hep-B infection for 6 months onwards.) Chronic carriers eliminate the Hep-B -virus at the rate of 0.3% to 2% per year [(4)]. Those who would still harbour the virus after 'n' number of years would be given by the formula: $(1-r)^n$ where r is the annual virus clearance rate. Based on relevant literature, (quoted in the footnotes of our tables) we assumed the virus annual clearance rate to be 1%, and calculated the average number of 'long-term chronic carriers' during the remaining life years of this birth cohort.

3) Estimation of number of persons suffering from the chronic sequelae of Hep-B infection during the life time of the cohort -

To estimate the prevalence of the five pathological sequelae of Hep-B-infection, since appropriate Indian data are not available, we used data from mostly international literature by relying heavily on the thorough literature review by Lodha Rakesh, Jain Yogesh, *et al* [(5)]. We first estimated the number of long term chronic hep-B carriers who have normal liver function tests (LFTs) and those who have abnormal LFTs. This break up is necessary because amongst long term chronic carriers, 1% later develop Chronic Active Hepatitis if the LFTs are normal and 15% if LFTs are abnormal. [(6)] (This break up is not necessary in the case of Chronic Persistent Hepatitis (CPH) as CPH is a relatively non-progressive, benign condition.)

4) ***Estimation of QALYs lost on account of morbidity and mortality due to the five morbid sequelae of Hep-B infection***

For this we first estimated the number of clinical cases and deaths amongst the long term chronic carriers. This was estimated with the help of the literature review by Lodha Rakesh, Jain Yogesh, *et al* (ibid) who systematically reviewed studies of long term follow up of chronic long term Hep-B carriers. These studies have shown that a certain proportion of these cases develop Chronic Persistent Hepatitis, Chronic Active Hepatitis, Cirrhosis and

Hepato Cellular Carcinoma. We then estimated QALYs lost on account of morbidity and mortality due to the five morbid sequelae of Hep-B-infection by using the 'Catalogue of Preference Scores' [7] to take into account the extent of functional disability caused by these five conditions. We estimated the total number of QALYs lost by adding up the QALYs lost due to all the five clinical sequelae of hepatitis-B infection, including acute hepatitis.

5) Estimation of cost-efficacy of Hep-B vaccine –

As mentioned above, we assumed the Hep-B vaccine to have a protective efficacy of 100%. Hence the QALYs gained due to this vaccine are equal to the QALYs lost as estimated in step 4. The cost for 1 million children to receive 3 doses of the Hep-B vaccine divided by total number of QALYs gained due to vaccination gave cost-efficacy in terms of rupees per QALY saved. The Hep-B vaccine is available in the retail market at the rate of Rs. 180 per 0.5 ml ampoule. However, special discount price of Hep-B vaccine for doctors is Rs. 130 per vial of 5ml. The cost of vaccine per child was thus about Rs. 40 (3 doses of 0.5 ml each). We used this discounted price of the vaccine in our estimation. In the estimation of cost of hep-B vaccination, we have not taken into account the cost of administering the vaccine. This underestimation of the cost of Hep-B vaccination, however, strengthens our case that the cost of universal Hep-B vaccination of infants is too high compared to that of the established vaccine like the measles vaccine.

Some specific assumptions, based on the literature, made in preparing respective tables for these five conditions, have been given in the respective table footnotes.

6) Estimation of Cost-efficacy of measles vaccine-

A similar exercise of estimating the cost-efficacy of the measles vaccine was done by estimating QALYs lost in a hypothetical cohort of 1 million infants. In this exercise, based on literature (quoted in the footnotes to the table no. VIII) it was assumed that -

1. In absence of vaccination 100% of infants would get measles.
2. 1% of them would develop measles encephalitis and that a certain proportion of these cases of measles encephalitis would suffer from varying degrees of disability for varying periods.
3. Uncomplicated measles would affect 49.9% of infants and would lead to 10 days' of illness in each of these infants.
4. The rest (i.e. 50%) of the infants would develop one of the five complications: diarrhoea, pneumonia/LRTI, exacerbation of TB, nutritional deterioration, and other complications.

Finally, cost-efficacy of measles vaccine was estimated by assuming 85% protective efficacy but by ignoring the cost of administering the vaccine as in the case of Hep-B vaccine.

Results:

The results are seen in tables I to IX.

Tables I to V present detailed estimation of QALYs lost in the life time of the cohort due to acute hepatitis, chronic persistent hepatitis, chronic active hepatitis, cirrhosis, hepatocellular carcinoma respectively.

Table VI presents a summary of the estimated QALYs lost due to these five morbid conditions **and the cost-efficacy of Hep-B vaccine (**Rs. 705 per QALY saved).

Table VIIa a presents the estimated **QALYs lost due to uncomplicated cases of measles and due to measles encephalitis,** which together account for about 50% of the measles cases in a birth cohort of one million. Table **VIIb** presents estimated **QALYs lost due to other complications of measles, which account for the rest 50 % cases of measles** in this same birth-cohort.

Table VIII presents the **cost-efficacy of the measles vaccine** in infants (Rs.21/- per QALY saved).

Table IX summarises the estimated **number of deaths due to these five conditions** in this birth cohort and **the life-time risk of dying due to Hep-B infection** in the general population. which was estimated to be 0.13% amongst general population of infants and 5.6% amongst Hep-B carriers.

Discussion:

This comparative cost-efficacy exercise is necessary to assess the scientificity and appropriateness of recommending universal hepatitis-B vaccination of the newborns in India and ours is the first attempt to do this comparative exercise. By using the Markov-model, Aggarwal *et al*. have estimated the marginal cost-efficacy of Hep-B vaccine to be US $16.27 per life year gained. Their estimation is comparable to our above estimate. However their exercise is not for infants and they have not compared it with that of measles or any other vaccine in the Universal Immunization Programme, but with the per capita GNP![2] They have recommended Universal Hep-B vaccination of infants because its cost per QALY saved is less than per capita GNP. We argue that comparing cost-efficacy of vaccination with per capita GNP is not the appropriate method as it does not lead us to make any worthwhile decision about the affordability of a vaccination programme. No standards are available as regards the affordability level of expenditure on the vaccination programme in relation to per capita GNP. Would we recommend addition of a new vaccine if the cost per QALY saved is less than per capita GNP but is say four times the cost of the current vaccines in the UPI? (In case of Hep-B vaccine, the cost per QALY saved is almost 35 times that of the measles vaccine!) Comparison with the cost-efficacy of vaccines already in use in Universal Immunization Programme offers a much better parameter to use.

We have used the available Indian data on prevalence of HBsAg positivity. But as stated earlier, there are no appropriate Indian data about chronic sequelae of Hep-B infection. We have therefore used the data from the extensive Western research on this subject. Lack of Indian data is a limitation of our exercise. But it is necessary to make some approximate estimation based on the Western data that are available. Otherwise policy on this issue would become just a matter of entirely subjective opinions. Secondly those who recommend universal Hep-B vaccination also inevitably use Western literature to point out to the dangerous sequelae of Hep-B infection.

To estimate the QALYs lost due to acute hepatitis B, we needed *incidence rates* for Hep-B infection. In absence of these data, we used the *prevalence data*. This has meant overestimation of the QALYs lost. But this has strengthened rather than weakened our argument that compared to the QALYs saved, the cost of Hep B vaccination is very high.

In our tables, we have made some specific assumptions, based on available data about the sequelae of Hep-B infection. Though our assumptions and extrapolations are reasonable, there could be differences of opinion on some of the assumptions. However, our experience in preparing various drafts of these tables indicates that some modifications in our assumptions would not materially affect the picture that emerges from these tables: that the life-time mortality due to Hep-B disease in normal and Hep-B carrier population is around 0.1 % and 5 % respectively even though we have not conducted rigorous sensitivity analysis of our exercise.

The results of our exercise seriously question the view that 25% of Hep-B-carriers would subsequently die of liver diseases. It has been claimed that “Infants who are chronically infected have 25% life time risk of cirrhosis in comparison to 15% seen in adults”. [(8)] This statement is claimed to be based on the results of the seminal work by Beasely. But in fact there is no such evidence in the famous paper which has been quoted and re-quoted by different authors! [(9)] In his seminal paper ‘Hepatitis B Virus - The Major Etiology of Hepato Cellular Carcinoma’, Beasley studied hepatocellular carcinoma and incidentally found that 23 of 3007 (0.76%) HBsAg positive male Taiwanese civil servants aged mostly over 40 who did not have cirrhosis or a history of hepatitis at baseline died of cirrhosis during a mean of 8.9 years follow up.[(10)] He did not report data on the development of non-fatal cirrhosis so his data cannot be extrapolated to make an overall estimation of the lifetime risk due to Hep-B infection. Our own estimation of risk of dying due to the sequelae of Hep. B-infection amongst the normal population and Hep-B-carriers of 0.13% and 5.6%, respectively, also does not support this oft quoted claim by some Indian authors.

Conclusion:

Compared to the QALYs saved, the cost of Hep B vaccination is very high compared to that of the measles vaccination. The life-time risk of dying due to sequelae of Hep-B infection in India is very low. Hence the introduction of the Hep-B vaccine in the Universal Immunization Programme in India needs to be reconsidered.

We are grateful to friends in the Medico Friend Circle, who gave suggestions and encouraged us to pursue our rather unconventional arguments, analysis about Hep-B vaccination programme when we first presented it many years back. We are grateful to Peter Mansfield for his help in detailed editing and in reworking of the measles cost-efficacy estimation and to Kerry Scot for last-minute copy-editing. The usual disclaimer remains.

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Annexure

Table - I			
Estimated QALYs Lost Due to **Acute Hepatitis-B** in a Cohort of 1 Million Infants in India.			
Sr.No.			
1	Average age of the cohort (years)	0.5	
2	HBsAg positivity rate	3.3%	(a)
3	Positive Predictive Value (b)	75%	
4	Prevalence of HBV infection (row2 x row3)	2.47%	
5	No. of persons harbouring HBV (Row 4 x 1 million)	24675	
6	Clinical hepatitis as proportion of HBV infected persons (c)	5%	
7	Number of patients of acute hepatitis-B	1233.75	
8	Duration of illness per patient in days (d)	30	
9	Mortality rate (e)	0.1%	
10	No. of deaths in the cohort (Row 7 x Row 9)	1	
11	Age at death	0.5	
12	QALYs lost from illness Row7xRow 8 x 0.9(f)/365	91	
13	QALYs lost due to deaths (Life expectancy of 65years(g) - age at death) x no. of deaths	65	
14	Total QALYs lost (row 12 + row 13)	156	
Explanatory notes & references			
a -	Average from **A1)** Kant Lalit & Hall Andrew, Epidemiology of childhood Hepatitis-B in India - Vaccination Related Issues, Indian J. Pediatric 1995; 62:0635 row 1 of Table 5 and Table 8. **A 2)** in Tandon B.N., Irshad M et al. Prevalence of HBsAg & anti-HBs in children & strategy suggested for immunization in India, IJMR; Nov. 1991 [A] 93, 1st Row from table 1. **A 3)** A Chakravarti et al. A study on the perinatal transmission of the Hepatitis B virus. Indian Journal of Microbiology, (2005), 23 (2): 128-130. Separate data for 0-1 age-group are not available. We have assumed this rate to be half the rate for older children.		
b -	We assume the sensitivity and specificity of HBsAg screening test to be 100% and 99% respectively. It's positive predictive value for a prevalence of 3% works out to be 75%.		
c -	Diseases of the liver and biliary system. Sheila Sherlock and James Doolley, 9th edition, Chapter 16, Page: 272.		
d -	Harrison's Principles Of Internal Medicine, 14th edition, page:1689.		
e -	Harrison, op. cit. p. 1689		
f-	(1 - Preference score for acute hepatitis); preference score denotes the degreee of functionality during this period. Preference scores for acute hepatitis - 0.90. - Catalogue of Preference Scores. Tufts-New England Medical Center http://www.tufts-nemc.org/cearegistry/data/phaseIpreferenceweights.pdf, page 29		
g -	Draft National Health Policy, Govt. of India, 2001.		

Table - II		
	Estimated QALYs Lost Due to **Chronic Persistent Hepatitis** Due to Chronic hepatitis-B Infection in a Cohort of 1 Million Infants in India.	
Sr.No.		**Age group**
1	Average Age of Cohort (years)	0.5
2	Prevalence of HBV infection (row 4, table I)	2.47%
3	Carrier rate - row 2 x 0.8 [(a)]	1.98%
4	No. of carriers in the cohort (Row 3 x 1 million)	19760
5	No. of long-term carriers in the cohort [(b)]	16825
6	Rate of CPH amongst carriers [(c)]	14%
7	No. of CPH patients (row 5 x row 6)	2356
8	Death rate in CPH (d)	0
9	QALYs lost due to illness (Life expectancy of 65 years -age of cohort) x row 7 x 0.1 [(e)]	15193

Explanatory notes & References

a -	Elavia A.J, Banker D.D. Prevalence of hepatitis B surface antigen & its sub types in high risk group subjects & voluntary blood donors in Bombay. IJMR (A) 93, Sept. 1991, table II. This and other studies found that carriers rate is 80% of prevalence rate.
b -	Many carrierns clear the virus and escape serious chronic liver diseases like cirrhosis and hepatoma. The virus clearance rate is 0.3 to 2% per year [Infectious Diseases, Mendel et al, editors, 3rd edition, 1990 Part -III, page 1211, 1215. Lodha Rakesh, Jain Yogesh et al, Hepatitis B in India, A Review of Disease Epidemiology. Indian Pediatrics, 2001, 38:349-371. page, 356.] Hence only those who harbour the virus much longer than 6 months, i.e. the long term carriers should be considered for estimating the long term cosequences of hep. B infection.
	Those who would still harbour the virus after n number of years would be given by the formula - (1-r)n; where r is the annual virus clearance rate. We have assumed the virus annual clearance rate to be 1%, and have calculated the average number of carriers during the remaining life years of each of the cohort.
c -	Lodha Rakesh, Jain Yogesh, et al, op.cit, (Reference 8) table III. We have taken a weighted average of the three studies quoted by Lodha-Jain et al.
d -	We assume that no body dies die due to CPH as such and that all deaths due to CPH are due to cirrhosis and Hepato Cellular Carcinoma. Such deaths would be covered in table no. IV and V
e -	(1 - Preference score for chronic hepatitis) ; Preference score for chronic hepatitis - 0.90. Catalogue of Preference Score, op. cit. p. 29

Table - III		
Estimated QALYs Lost Due to **Chronic Active Hepatitis** Due to Chronic Hepatitis-B Infection in a Cohort of One Million Infants in India.		
Sr.No.		
1	Average age of cohort	1
2	long-term carriers amongst the Cohort - Row 5 from table II	16825
3	Long-term carries who have normal Liver Function Tests, (75% of the carriers) [(a)] - row2 x 75%	12619
4	Rate of CAH in long - term carriers who have normal LFT [(b)]	1%
5	Number of persons amongst the carriers with normal LFT who would develop CAH -row 3 x row 4	126
6	Long-term carries with deranged LFT - 25% of row 2	4206
7	CAH amongst carriers with deranged LFT - 15% of row 6 [(c)]	631
8	Total number of CAH in the cohort - row5+row7	757
9	Number of CAH patients who would not suffer from cirrhosis - 80% of row 8 [(e)]	606
10	Death rate due to CAH [(d)]	0
11	QALYs lost due to illness = (life expectancy of 65 years - age of cohort) x row 9x 0.1 [(f)]	3876
References & explanatory notes		
a -	Lodha Rakesh, Jain Yogesh et al, op. cit, page 357, section 2.4.1	
b -	Lodha Rakesh, Jain Yogesh et al, op. cit, table III. CAH was seen in only 1-5% of these individuals. We have made assumptions within this range.	
c -	Lodha Rakesh, Jain Yogesh et al, op. cit, section 2.4.4, page 357.	
d -	All deaths due to CAH are due to cirrhosis and HCC. They are covered in table IV and V.	
e -	Lodha Rakesh, Jain Yogesh, et al. op. cit, section 2.4.4, page 358. The remaining 20% of CAH patients would be covered in table IV.	
f -	For those CAH patients who do not develop cirrhosis or HCC, the level of dysfunctionality would be (1 - Preference score for chronic hepatitis) ; Preference score for chronic hepatitis - 0.90. Catalogue of Preference Score, op. cit. p. 29	

Table -IV		
	Estimated QALYs Lost Due to **Cirrhosis** Due to Chronic Hepatitis-B Infection in a Cohort of 1 Million infants in India.	
Sr.No.		**Age group**
1	Average age of cohort	0.5
2	No of CAH patients in the cohort (Row 8 from table III)	757
3	No. Of CAH patients developing cirrhosis (20% of row 2) [(a)]	151
4	No of CPH patients in the cohort (Row 7 from table II)	2356
5	No of CPH patients developing cirrhosis [(b)]	94
6	Total no of cirrhotic patients in the cohort (row no 3+ row no 5)	245
7	Deaths due to cirrhosis (row3 + row5) [(c)]	245
8	Age at death due to cirrhosis [(d)]	8
9	QALYs lost due to deaths due to cirrhosis [(e)]	13979
10	QALYs lost due to cirrhotic illness of 7.5 years. row 6 x 7.5 years x 0.5.(f)	920
11	Total QALYs lost due to cirrhosis (row 9 + row 10)	14898

a -	About 20% of CAH patients develop cirrhosis. Lodha Rakesh, Jain Yogesh, et al op. Cit, Section 2.4.4, page. 358.
b -	Generally CPH runs a benign course and only 3% die in 5 years. Weissberg et. al as quoted by Lodha & Jain et al op. cit section C. Hence we have assumed that only 5% will develop cirrlosis and would die of cirrhosis. - row 4 x 5%.
c -	Lodha Rakesh & Jain Yogesh et al. Section 2.4.4, page 358. Weissberg et al (85), found that the estimated 5 years survival rates for patients with CAH and Cirrhosis was 55%. We assume 100% mortality in 10 years.
d -	Avg. age of cohort plus 7.5 years of illness, on an average, as 50 to 100% die in 5 to 10 years, with an average illness period of 7.5 years before death.
e-	(row 6 x (Life expectancy 65 yrs - row 8).
f -	(1 - Preference score for cirrhosis); Preference score for cirrhosis - 0.50. Catalogue of Preference Score, op. cit. p. 30

Table V		
Estimsted QALYs Lost Due to **Hepato Cellular Carcinoma** Due to Due to Chronic Hepatitis-B Infection in Cohorts of 1 Million Infants in India.		
Sr. No.		
1	Average age of the cohort	0.5
2	No. of long term carriers in the cohort (Row 5 from table II)	16825
3	Annual incidence HCC in carriers after average latency of 40 yrs. (b)	0.25% (a)
4	Age of onset of HCC (average age of cohort + 40 years)	40.5
5	Cumulative incidence of HCC in Carriers (c)	6.13%
6	No. of chronic carriers who would develop HCC (row 2 x row 5)	1031
7	Age at death (five years after onset of cirrhosis - row 1 + 40)	45.5
8	No. of QALYs lost per HCC patient due to death (Life - expectancy 65 years- row 7)	19.5
9	Life years lost by the cohort due to HCC deaths (row 6x row 8)	20095
10	No. of QALYs lost due to illness of HCC - row 6 x .5 x 5 (d)	2576
11	Total no. of QALYs lost due to morbidity and mortality due to HCC (row 9+row10)	22672
Explanatory Notes, references:		
a -	The annual incidence of H.C.C. amongst adult chronic carrier has varied from 0-0.5% in different studies. Quoted by Lodha - Jain et.al; Section - H. We have taken an average - 0.25%.	
b -	The data suggest that after perinatal acquisition of HBV infection, HCC appears after a latency of 30-50 years. Lodha - Jain et.al; op. cit. Section -H. We have taken an average of this range - 40 years of latency	
c -	After the onset of H.C.C., the Cohort will generate new cases of H.C.C. every year at the rate of 0.25% per year, for the remaining part of the life of the cohort - population. Hence cumulative incidence would be (Life expectancy 65 years - age of onset of H.C.C.) x 0.25%.	
c -	Adrion M, Bisceglie DI et al, Hepatocellular Carrinoma, NIH Conference, Annals of Internal Medicine, 1988: 108: p 397. Mean 5 year survival after resection of HCC was 20 to 30%. Taking into account more severe inoperable cases, we have assumed overall 5 year mortality due to HCC to be 100%.	
d -	As per Catalogue of Preference Score, op. cit. p. 30. Preference score for 'liver cancer' is - 0.90. However we assume that the patient with H.C.C. would have only 50% functionality during the last five years of this terminal illness.	

Table VI		
Cost per QALYs saved, due to Hep-B vaccination in a Cohort of One Million Infants in India.		
Sr.No.		
1	Average age of cohort	0.5
2	Acute hepatitis (last row, table I)	69
3	Chronic Persistent hepatitis (last row, table II)	15193
4	Chronic Active Hepatits (last row, table III)	3876
5	Cirrhosis (last row, table IV)	14898
6	Hepato-Cellular Carroinoma (last row, table V)	22672
7	Total QALYs lost due to HBV diseases (add row 2 to 6)	56708
8	Total QALYs gained due to Hep B vaccination	56708
9	Vaccination Cost (Rs. 40/- per child for 3 doses*) in Rs. Million	40
10	Cost per QALYs saved, due to Hep-B vaccination, in Rs. (row 9/row8)	705
	* The the hep. B vaccine is available in the retail market at the rate of Rs. 180 per 0 .5 ml ampoule. However, special discount price of Hep. B vaccine for doctors is Rs.130 per vial of 5ml. The cost of vaccine per child is thus about Rs. 40 (3 doses). We chose this discounted price of the vaccine in our estimation.	

	Table VII-a							
	Estimated QALYs Lost due to Measles in a Cohort of 1 million Infants							
Sr. No.	**1,000,000**	**Uncomplicated Measles with full recovery**	**Measles Encephalitis**	**Measles Encephalitis with full recovery**	**Fatal Measle Encephalitis**	**Encephalitis with mild perminant disablity (33.33% x 20%)**	**Encephalitis with moderate perminant disablity (33.33% x 60%)**	**Encephalitis with severe perminant disablity (33.33% x 20%)**
A	Incidence rate of each major diagnosis(1,2)	49.90%	0.10%					
B	Incience of each subgroup diagnosis within the main diagnoses(3)	100.00%		33.33%	33.33%	6.67%	20%	6.67%
C	Incidence for each subdiagnosis = A x B	49.9%		0.0333%	0.0333%	0.0067%	0.0200%	0.0067%
D	Number of affected children = C x 1,000,000	499000		333	333	67	200	67
	Duration of illness in days (4)	10		28	14			
E	Duration of illness in years	0.027		0.077	0.038	65	55	4
F	Utility score for illness (5)	0.848		0.1	0.1	0.9	0.4	0.1
G	Utility lost from illness = 1 - F	0.152		0.90	0.9	0.1	0.6	0.9
H	QALY lost per person from illness = E x G	0.004		0.069	0.035	6.5	33	3.6
I	Total QALY lost in the cohort from illness = D x H	2078		23	12	433	6600	240

J	Years lost per person from premature death(2)	0		0	65	0	10	61	
K	Utility score for death	0		0	0	0	0	0	
L	Utility lost from death = 1 - K	1		1	1	1	1	1	
M	QALY lost per person from death = J x L	0.000		0.00	65.00	0.00	10	61	
N	Total QALY lost in the cohort from death = D x M	0		0	21665	0	2000	4067	Grand Total
O	**Total QALY lost in the cohort from illness and death = I + N**	2078		23	21676	433	8600	4307	**37117**
1	Ghai , Essential Pediatrics - 5th ed; 2002, page 180								
2	Zwanziger J, Szilagyi PG, Kaul P. Evaluating the benefits of increasing measles immunization rates. Health Serv Res. 2001 Oct;36(5):885-909.								
3	Chand P, Rai RN, Chawla U, Tripathi KC, Datta KK. Epidemiology of measles--a thirteen years prospective study in a village.J Commun Dis. 1989 Sep;21(3):190-9.								
4	Harrison, op. cit. - p 1123 14th ed 1998								
5	Stein CE, Birmingham M, Kurian M, Duclos P, Strebel P. The global burden of measles in the year 2000--a model that uses country-specific indicators. J Infect Dis. 2003 May 15;187 Suppl 1:S8-14								
i	It is assumed that the cost of measles vaccination per child in a mass vaccination programme would be half the current market price of Rs. 30/- per child.								

Table VII b							
Estimated QALYs Lost due to Measles in a Cohort of One Million Infants in India							
Sr.No.	**1,000,000**	***Other Measles Complications***	**Diarrhoea**	**Pnemonia/LRTI**	**Exacerbation of TB**	**Nutritional deterioration**	**Other Measles Complications fatal**
A	Incidence rate of each major diagnosis(1,2)	50.00%					
B	Incience of each subgroup diagnosis within the main diagnoses(3)		27.50%	40%	10.00%	20.00%	2.50%
C	Incidence for each subdiagnosis = A x B		13.7500%	20%	5%	10%	1.25%
D	Number of affected children = C x 1,000,000		137500	200000	50000	100000	12500
	Duration of illness in days (4)		14	14	28	56	10
E	Duration of illness in years		0.0384	0.0384	0.0767	0.1534	0.0274
F	Utility score for illness (5)		0.8	0.8	0.8	0.8	0.8
G	Utility lost from illness = 1 - F		0.2	0.200	0.2	0.2	0.2
H	QALY lost per person from illness = E x G		0.008	0.008	0.015	0.031	0.005
I	Total QALY lost in the cohort from illness = D x H		1055	1534	767	3068	68
J	Years lost per person from premature death(2)		0	0	0	0	65
K	Utility score for death		0	0	0	0	0
L	Utility lost from death = 1 - K		1	1	1	1	1
M	QALY lost per person from death = J x L		0	0	0	0	65

N	Total QALY lost in the cohort from death = D x M		0	0	0	0	812500
O	Total QALY lost in the cohort from illness and death = I + N		1055	1534	767	3068	812568
	Grand Total QALY lost in the cohort from illness and death due to all "Other Complications" (total of row O)						818993
P	Grand Total QALY lost in the cohort from illness and death due to all complications of measles- total of rows O of table VII a and VII b						856110
1	Ghai , Essential Pediatrics - 5th ed; 2002, page 180						
2	Zwanziger J, Szilagyi PG, Kaul P. Evaluating the benefits of increasing measles immunization rates. Health Serv Res. 2001 Oct;36(5):885-909.						
3	Chand P, Rai RN, Chawla U, Tripathi KC, Datta KK. Epidemiology of measles--a thirteen years prospective study in a village.J Commun Dis. 1989 Sep;21(3):190-9.						
4	Harrison, op. cit. - p 1123 14th ed 1998						
5	Stein CE, Birmingham M, Kurian M, Duclos P, Strebel P. The global burden of measles in the year 2000--a model that uses country-specific indicators. J Infect Dis. 2003 May 15;187 Suppl 1:S8-14						
i	It is assumed that the cost of measles vaccination per child in a mass vaccination programme would be half the current market price of Rs. 30/- per child.						

Table VIII		
Cost per QALYs saved by Measles Vaccination in a Cohort of One Million Infants in India.		
Sr.No.		
A	Grand Total QALYs lost in the cohort from illness and death due to measles. (sum of row no.'O' in VII-a and VIIb)	856110
B	Percentage protected by vaccination	85%
C	QALYs gained from vaccination = O x P	727694
E	Cost of the vaccine @ of rate Rs. 15 per child (i) for 1 million children (in Rs.)	15000000
F	Cost in Rupees per QALY saved = S/R	20.61

Table IX		
No of Deaths Due to HBV-infection in a Cohort of 1 Million infants		
Sr.No.		**Age group**
	Average age of the cohort	0.5
1	Number of deaths due to Acute hepatitis (row 6, table I)	1
2	Number of deaths due to Chronic Persistent hepatitis	0
3	Number of deaths due to Chronic Active Hepatits	0
4	Number of deaths due to Cirrhosis (row 7, table IV)	245
5	Number of deaths due to Hepato-Cellular Carcinoma (row 6 table V)	1031
6	Total no. of deaths due to HBV diseases (total of row 1 to 5)	1277
7	Number of deaths as % of the cohort (row6/ 1 million x 100)	0.13%
8	Proportion of population in India belonging to this age group	2.50%
11	Number of carriers in the cohort (row 4, table II)	22800
12	Number of deaths as proportion of carriers (row 6/row 9 X 100)	5.60
	* Estimated from Health Information of India, 1997-98, VBHI Government of India, 2000	