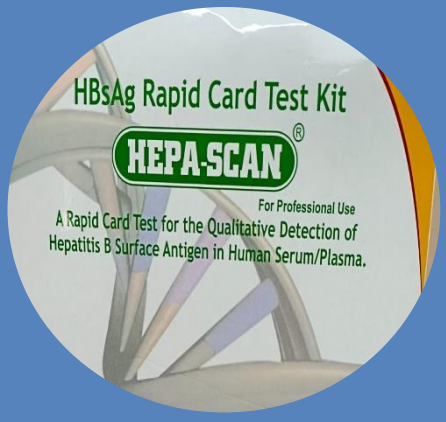
Health Technology Assessment for screening of Hepatitis B and C at Primary Health Centers in Tamil Nadu

2020



Conducted by

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INDIA

Health Technology Assessment for screening of Hepatitis B and C at Primary Health centers in Tamil Nadu

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Resource Centre for

Health Technology Assessment in India (HTAIn)

ICMR – National Institute for Research in Tuberculosis

Chennai

India

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Abbreviation

CoCoPop	Condition Context Population
ELISA	Enzyme Linked Immunosorbent Assay
HBsAg	Surface Antigen
HBV	Hepatitis B Virus
HCV	Hepatitis C Virus
HCC	Hepatocellular Carcinoma
HIV	Human Immunodeficiency Virus
ICER	Incremental Cost Effectiveness Ratio
IDSP	Integrated Disease Surveillance Program
MoHFW	Ministry of Health and Family Welfare
NVHCP	National Viral Hepatitis Control Program
PHC	Primary Health Care
PSA	Probabilistic Sensitivity Analysis
QALY	Quality Adjusted Life Year
MSM	Men having Sex with Men

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Summary

Background: Hepatitis B viral infection (HBV) affects nearly 50 million people in India with an average prevalence of 4%. Hepatitis C virus infection (HCV) prevalence in the general population is estimated to be between 0.09-1.5% and it is reported that there are 6-12 million people with HCV in India. Prevalence of HBV and HVC was higher than average in key population like persons with sexual risk behavior, blood donors, individual with STD, people living with HIV and mem having sex with mem (MSM), chronic kidney disease, on dialysis, with thalassemia, haemophilia, leukaemias, those receiving immunosuppressives and cancer chemotherapy.

Methods: Decision tree cum Markov model was developed to estimate the cost effectiveness of strategies to screen and treat HBV and HCV or prevent HBV in population with various prevalence. The cost effective analysis was performed for the following strategies: (Strategy-1) screen for HBV infection and provide early treatment for positives and provide vaccination for negatives (proposed) (Strategy-2) screen for HCV infection and provide early treatment (proposed). The outcomes of the proposed strategy were expressed in incremental cost effectiveness ratios (ICERs) per quality adjusted life years (QALY) and life years (LY) gained and death averted as compared to current strategy. Discount rate of 3% was applied for cost and QALY.

Findings: The strategy-1 had ICER of ₹ -1,80,749 per QALY gained and strategy-2 had ICER of ₹ -1,14,571 per QALY gained as compared with current strategy. Strategy-1 resulted in 505 discounted QALYs gained and Strategy-2 resulted 38 discounted QALYs gained. In terms of death averted, 293 and 4 from strategy-1 and strategy-2 respectively. The other finding in the present study was shown in the OWSA, the quality of life score holds much influence on the ICER for HBV and HCV intervention. The proposed intervention will incur an additional budget of ₹ 142 crores for HBV and ₹ 57 crores for HCV implementation. It will vary depending on the proportion required for intensive care treatment for liver disorders. It was also estimated that the proposed intervention reduced out of pocket expenditure significantly to the patient.

Interpretation: The current results confirmed that the proposed interventions were dominant compared with current practice. It also indicates that the proposed intervention is worthwhile as result showed the screening key population for HBV and HCV at PHC level was more cost saving with negative ICER value per QALY gained.

Keywords. hepatitis B; hepatitis C; cost effectiveness; treatment; screening; vaccination.

1. INTRODUCTION

Viral hepatitis is a most important and growing public health problem of India. The burden of hepatitis is very high and its health related impacts are comparable to that of HIV, tuberculosis and malaria.[1] The health system burden associated with treating the terminally ill viral hepatitis infection and associated liver carcinoma could greatly constrain the health system resources of India.[2] At present the burden of viral hepatitis in India remains much underestimated and majority of the population are not covered by the present screening and diagnostic services. Controlling hepatitis epidemic has gained importance under the ambit of universal health coverage of India.

1.1 National Viral Hepatitis Control Program (NVHCP)

Population and health facility based surveillance of viral hepatitis is mandated under the Integrated Disease Surveillance Program (IDSP). The Ministry of Health and Family Welfare (MoHFW), Government of India, launched the National Viral Hepatitis Control Program (NVHCP) in July 2018.[3] The key components of the program are awareness creation, prevention, diagnostic and treatment services for viral hepatitis B (HBV) and Hepatitis C (HCV) . The national hepatitis program is in the process of establishing laboratory networks for undertaking laboratory based surveillance and prevalence of different types of viral hepatitis in different geographical locations of India. In this background the Government of Tamil Nadu had initiated the implementation of hepatitis diagnosis program and had expanded the hepatitis screening among different key populations (who are at increased risk at primary health care center (PHC) level.

The HBV and HCV screening in Tamil Nadu has so far been implemented at the diagnostic facilities present at the secondary health care level for individuals with abnormal liver functions. In addition to this sub populations s like blood donors and organ donors are also screened for HBV and HCV infections at the tertiary health care centers. As a part of the national hepatitis program, Government of Tamil Nadu has initiated HBV and HCV screening program at the primary health care centres to screen the key population in the states. The present study aims

to comparatively assess the screening strategy for HBV and HCV with specific focus on selected key populations at different health facility levels (tertiary, secondary vs primary health care) in Tamil Nadu. The study estimated the cost effectiveness of scaling-up the existing screening (rapid finger prick test) and diagnostic (ELISA) services for the key populations at the primary health care level in Tamil Nadu.

1.2 Basics of Hepatitis Viral Infection

Viral hepatitis is a major public health problem globally. Among the five types of hepatitis viruses, HBV and HCV predominantly lead to the development of liver diseases. HBV is transmitted vertically through mother to child transmission and horizontally through transfusion of infected blood or blood products, intravenous drug use, unsafe therapeutic injections, occupational injuries, nosocomial transmission during surgery, haemodialysis and organ transplantation. A narrative review reported that HBV affects nearly 50 million people in India with an average prevalence of 4%.[4] HBV surface antigen (HBsAg) positivity in the general population ranges from 1.1% to 12.2%, with an average prevalence of 3-4%. The prevalence of HBV was found to be endemic among tribal population of Nicobarese with 23% and among Jara population with 66% prevalence.[5] Chronic HBV infection accounts for 10 - 20% of cirrhosis and 40 - 50% hepatocellular carcinoma (HCC) in India.[6] Recently it has been estimated that viral hepatitis contributes to 2.85% of all deaths in India.[7]

HCV antibody prevalence in the general population is estimated to be between 0.09-15% and it is reported that there are 6-12 million people with HCV in India (NCDC 2016). Chronic HCV infection accounts for 12-32% of HCC and 10-20% of cirrhosis.[8] A population based cross sectional study in Punjab estimated HCV prevalence of 3.6% and chronic infection of 2.6%. HCV infection was associated with male gender, rural residence, low educational status, 40–49 years of age and blood transfusion status.[9] A systematic review and meta-analysis conducted by Goel et al, estimated HCV prevalence 0.44% and 0.88% among blood donors and pregnant women respectively. This study also identified other populations at risk for HCV including dialysis patients, injecting drug users, sexually transmitted disease infected individuals, multi transfused persons and people with high risk sex behavior.[10] HCV mediated chronic liver disease is the major cause for 39.1% of liver transplant in India.[11] It was reported that among

HCV infected patients 52% had history of dental treatment[12] and 45% had therapeutic injections with reusable syringes.[13]

A community based prevalence study conducted in Tamil Nadu reported that the prevalence of HBV was 1.63% and HCV was 0.3%. The study reported that among detected HBV and HCV more than 70% were males and prevalence was highest (5%) among slum population, followed by 203/8047 (2.52%) in rural population and 156/10542 (1.47%) in urban areas. HBV and HCV infection was prevalent among all patients who underwent dialysis.[14]

1.3 Economics burden

It was reported that cost for liver related hospitalization charges was $1,175 and $675 for HBV and HCV respectively. It was associated with a cost equivalent to 1.5 times GDP per capita. The total annual cost per chronic HBV patient was $3094. Overall economic burden of chronic HBV infection and its related diseases was estimated to be $657 million and $608 thousand dollars.[15] In addition, out-of-pocket (OOP) cost of all HBV related diseases except acute HBV exceeded 40% of the patient's household income, making it a catastrophic expenditure for the household.[16]

1.4 Cost and Cost effectiveness of screening HBV and HCV infection

Cost effectiveness of HBV and HCV screening programs is mainly determined by the prevalence of HBV or HCV in a particular population. It is shown that screening key population with the prevalence of > 30% was cost effective whereas screening of HBV and HCV in certain populations with 1.5% to 16% prevalence was found to be not cost effective which is even dominated by no-screening scenario.[17] There are very less or no evidences available for the cost effective analysis of HBV and HCV screening in India. Screening of HCV infection in key population was more cost-effective, which was calculated as $848 to $4,825 per QALY gained, than general population screening ($749 to $2,297 per QALY) in Japan.[18] In Gambia, a community based HBV screening of adults followed by treatment achieved an incremental cost of $566 per disability adjusted life years (DALYs) averted. The ICER per DALY averted was found to be two time less than the GDP per capita threshold.[19] However, in Korea screening followed by treatment in adult population gained incremental cost effectiveness ratio (ICER) of $5,714 to $8,889 per QALY gained which was considered as cost effective.[20]

1.5 Diagnosis of HBV and HCV

The diagnosis of HBV or HCV requires specific hepatitis virus blood tests which could detect specific markers of hepatitis virus. Markers found in the blood can confirm hepatitis B or C infection. Both acute and chronic infections can be diagnosed with blood tests. Hepatitis viral antigens or antibodies developed in the blood indicates the presence of hepatitis viral infection. HBV infection is diagnosed by the surface antigen (HBsAg) and HCV infection is detected by anti HCV in the blood. Literature review on the sensitivity and specificity of the diagnostic tests published from India are provided in the Table-1. Diagnosis of HBV and HCV by rapid diagnostic test (RDT) kits represents better sensitivity and specificity similar to Enzyme Linked Immunosorbent Assay (ELISA) tests.

1.6 Hepatitis B vaccination

Hepatitis B vaccination was introduced as part of the universal immunization program in ten states of India during 2007-08. A study conducted among HBV vaccinated and unvaccinated children found anti-HBs prevalence among 53% of vaccinated and 18% of unvaccinated children. The frequency of chronic infection in terms of carrier state with HBsAg was equal among both unvaccinated and vaccinated (0.17% vs 0.15%).[21] In countries which have implemented universal childhood HBV immunization, HBV carrier rates have declined markedly and incidence rates of long term consequences have decreased.[22] A review of available studies on economic analysis of HBV vaccine in India shows that this vaccine is highly cost effective in terms of cost per life year gained and cost per QALY gained. A cost benefit analysis showed that the cost of HBV immunization program would be offset by savings in treatment costs of long term sequelae of chronic HBV infection.[23]

2. RESEARCH QUESTION

To identify the cost effective screening strategy for HBV and HCV among different key population at primary health care level in Tamil Nadu.

3. OBJECTIVES

- To estimate life years gained, QALYs gained and deaths averted by annual screening of HBV and HCV at primary health care facilities as compared to current scenario.
- To estimate incremental cost of annual screening for HBV and HCV at primary healthcare facilities as compared to current scenario.
- To estimate incremental cost effectiveness ratio (ICER) of annual screening for HBV and HCV at primary healthcare facilities as compared to current scenario.
- To estimate effect on out of pocket expenditure by annual screening of HBV and HCV at primary care healthcare facilities.

4. METHODOLOGY

This study was model based estimation of incremental costs and QALYs gained by introduction of screening of HBV and HCV. ICER was estimated through decision tree integrated with Markov model.

4.1 Data collection

Parameters required for the model were synthesized from published literature, medical procurement records and expert opinions. The parameters pertaining to HBV and HCV prevalence, diagnostic accuracy of point of care test, natural history of HBV and HCV infection, transition probabilities, health system cost and out-of-pocket expenditure for the management of HBV and HCV were included in the model. Quality of life (QoL) for each health state were obtained from literature review. QALY gained along with deaths averted due to early diagnosis of HBV and HCV infection were estimated through modeling. Systematic review was conducted to ascertain the prevalence of HBV and HCV in selected key population such as individuals with sexual risk behaviour, blood donor, antenatal women, individuals with STDs, people living with HIV and men who have sex with mem (MSM) as shown in Table-2.

Cost involved in diagnosis and management of HBV and HCV infections were collected from the national costing data bases, literature and hospital record. The cost for screening of HBV and HCV infection in various key population through rapid diagnostic test followed by conformation with ELISA test at tertiary hospital was collected through hospital record. Further the overall cost incurred for the management of liver diseases at tertiary hospital was also collected from a published literature. The mean out of pocket expenditures for treatment of liver diseases at tertiary hospital was also obtained from the literature.

4.2 Systematic review

A systematic review was conducted to identify the prevalence of HBV and HCV infections in selected key populations in Tamil Nadu and India. The CoCoPop (Condition, Context, Population) framework was used for the systematic review.[24] All the studies that reported on epidemiology of HBV and HCV infection, key population of HBV and HCV infection were considered. Detailed methodology and results of the systematic review are given in Annexure-1.

4.3 Economic model overview

A combination of decision tree (Figure-1 and Figure-6) and Markov model (Figure-2 and Figure-7) was developed to estimate cost effectiveness of screening HBV and HCV infection in key population compared with current practice. Two separate models were adopted for two proposed strategies (Strategy-1) screen for HBV infection and provide early treatment for positives and provide vaccination for negatives (proposed) and (Strategy-2) screen for HCV infection and provide early treatment (proposed). The two strategies were compared with current strategy (Table-3).

Start age of cohort in the model was 35 years, which was based on the mean age of HBV and HCV positive patients during the time of screening. The transition probabilities of HBV and HCV positive between different health states (acute HBV and HCV infection, chronic HBV and HCV infection, compensated cirrhosis, decompensated cirrhosis and hepatocellular carcinoma) were based on the natural clinical history published in the literature. Health state transition of cohort population was simulated in the Markov model for both comparator and intervention.

The parameters are diagnostic accuracy of screening tests, demographic details, transition probabilities between health states during natural history and treatment, treatment efficacy and vaccine efficacy. The parameters required for the model are collected from the published literature, secondary source and experts' opinion. All the parameters used in the model and its respective source are given in the Table-4 and Table-6. A lifetime horizon was considered to model the costs and consequences.

4.4 Estimation of ICER

Utility, life years and cost are calculated based on the proportion of cohort in each respective health state. QALY of the intervention strategies and comparator were from the utility and life years. Incremental cost and incremental QALY is calculated from the difference between the cost and QALY of intervention scenarios and comparator. ICER is the ratio of incremental cost and incremental QALY which represents the cost-effectiveness of the intervention to gain one QALY. Discount of 3% was incorporated in the total cost and QALY and discounted ICER was also calculated.

4.5 Sensitivity Analysis

The sources of uncertainty especially patient heterogeneity, methodological structural model and parameter uncertainties which would influence over cost-effectiveness outcome has been evaluated by one-way sensitivity analysis (OWSA). The robustness of the model was further evaluated by probabilistic sensitivity analysis (PSA). Monte Carlo method was used for simulating the results over 999 times.

4.6 Budget Impact Analysis

The budget impact for the state of Tamil Nadu in implementing the one time screening of key population for HBV and HCV at primary health care level was estimated. The fiscal requirement for the implementation of screening strategies was calculated and the expected outcomes in terms of life years saved, deaths averted and QALYs gained were assessed. Based on estimated total number of key adult population, estimated number of HBV and HCV cases, proportion accessing PHC the proposed budget was calculated.

5. RESULTS

5.1 Cost-effectiveness of HBV screening, early treatment and vaccination for negatives

Base case results

Considering overall cost for HBV including diagnosis and treatment costs for inactive chronic infection, out of pocket expenditure and vaccination for HBV negatives were estimated 505 QALYs gained for a cohort of 1000 population with an incremental cost saving of ₹180749. Based on model estimates the screening followed by early treatment and vaccination for negatives of HBV at PHC level was cost saving compared to the current scenario (Table-5). The negative ICER of the proposed intervention indicates that the screening followed by treatment and vaccination for negative was less expensive and more effective compared with current scenario (Figure-3). In terms of death averted the proposed intervention could avert 294 deaths. In terms of life years gained the proposed intervention could gain 293 life years. The proposed strategy resulted in the reduction of out of pocket expenditure of ₹ 3274 per person for HBV management during his life time.

Sensitivity analysis

The sensitivity analysis was performed to find out the variation in ICER due to changes in individual parameters. Parameters pertaining to quality of life, discount rate, diagnostic cost, treatment cost and transition to differ health states were used. One way univariate analysis found that ICER was most impacted by quality of life score of chronic and asymptomatic (Figure-4). The ICER range estimated for parameter changes in quality of life of chronic HBV was -256986 to -96986, and ICER range estimated for parameter changes in quality of life of asymptomatic was -215572 to -155612. Probability sensitivity analysis was conducted to find out the impact of joint uncertainty in parameter values. It was found that 100% probability of being a dominant as proposed strategy as compared to current strategy (Figure-5).

Budget impact

The implementation of screening, treating and vaccinating HBV negative individual of selected key population would require additional budget of ₹141,86,89,188 for government of Tamil

Nadu (Table-8). Budget for current strategy was ₹ 77,10,78,920 and proposed strategy was ₹ 218,97,68,107. This was calculated based on the assumption of 30% of population accessing PHCs. Estimated target population was 34,14,638 and estimated HBV cases for current strategy and proposed strategy was 92,939 and 41,822 cases respectively. The unit cost for screening and HBV treatment was ₹ 32,522, unit cost for rapid test was ₹ 85 and unit cost for vaccination ₹ 56. The estimated budget will vary depending on the proportion required for intensive care treatment for liver disorders.

5.2 Cost-effectiveness of HCV screening and early treatment

Base case results

Considering overall cost for HCV including diagnosis and treatment costs for inactive chronic infection, out of pocket expenditure we estimated 38 QALYs gained for a cohort of 1000 population with an incremental cost saving of ₹114571. Based on model estimates the screening followed by early treatment of HCV at PHC level was cost saving compared to the current scenario (Table-6). The negative ICER of the proposed intervention indicates that the screening followed by treatment was less expensive and more effective compared with current scenario (Figure-8). In terms of death averted the proposed intervention could avert four deaths. In terms of life years gained the proposed intervention could gain four life years. The proposed strategy resulted in the reduction of out of pocket expenditure of ₹ 65497 per person for HCV management during his life time.

Sensitivity analysis

The sensitivity analysis was performed to find out the variation costs by individual parameters on the ICER. Parameters pertaining to quality of life, discount rate, diagnostic cost, treatment cost and transition to differ health states were used. One way univariate analysis found that ICER was most impacted by quality of life score of asymptomatic, transition probability of chronic to compensated cirrhosis and quality of life score of compensated cirrhosis (Figure-9). The ICER range estimated for parameter change in quality of life of chronic HCV was -309906 to -71953, for change in transition probability of chronic to compensated cirrhosis -274561 to -72281 and for parameter change in quality of life of compensated cirrhosis was -82907 to -197508.

Probability sensitivity analysis was conducted to find out the impact of joint uncertainty in parameter values. It was found that 100% probability of being a dominant as proposed strategy as compared to current strategy (Figure-10)

Budget impact

The implementation of screening and treating for HCV among selected key population would require additional budget of ₹ 57,35,87,287 for Government of Tamil Nadu (Table-9). This was calculated based on the assumption of 30% of key population accessing PHCs. Estimated target population was 48,21,286 and estimated HCV cases for current strategy and proposed strategy was 69,914 and 70,907 cases respectively. The unit cost for HCV screening and treatment was ₹ 19,395 and unit cost for rapid test ₹ 115. The estimated budget will vary depending on the proportion required for intensive care treatment for liver disorders.

6. DISCUSSION

National Viral Hepatitis Control Program (NVHCP) has been launched in India since July 2018.[3] Awareness, prevention, diagnosis and treatment are key components of NVHCP. Phase wise implementation of NVHCP has been initiated by Government of Tamil Nadu. At present the health care workers are being screened for HBV and treated or vaccinated in case of positive and negative diagnosis respectively. All jaundice patients attending the health care facilities are also tested for HBV infection and associated disorders. Similarly, all the health care workers and jaundice patients are tested and treated for HCV. Currently ELISA test is being employed for diagnosing the HBV and HCV infection at tertiary health care facilities.

The present HTA study conducted a cost effectiveness modeling for a screening intervention to diagnose HBV and HCV at the primary health care centre. The proposed intervention included a rapid diagnostic test based screening at primary health care facilities which would be followed by confirmatory ELISA test at tertiary level. The early diagnosis of HBV was followed with early treatment and vaccination for HBV negatives. For HCV early diagnosis using rapid diagnostic test followed with early treatment. Screening of HBV and HCV infection involved rapid test at PHC followed by confirmation with ELISA at tertiary. The

markers used for the screening and diagnosis of HBV and HCV were HBsAg and Anti HCV in the blood. This study provided estimates of early diagnosis using rapid diagnostic test followed with early treatment for HBV and HCV in the cost effectiveness using decision tree and Markov model. The proposed model assessed the intervention among selected key population for HBV and HCV infection. The cost effectiveness analysis found that the HBV screening and early treatment strategy, HBV screening and vaccination for HBV negatives, and HCV screening and early treatment was cost saving to the government. The current results confirmed that the proposed interventions were dominant compared with current practice. The cost saving of proposed intervention could be due to the higher prevalence of HBV (pooled estimate of 3%) and HCV (pooled estimate of 1%) infection among key population in Tamil Nadu and disease progression rate from asymptomatic to chronic HBV and HCV.

While our model considered optimal access of HBV and HCV diagnosis by the key population, still the real world access might not be the same. Hence the implementation of this intervention would require increased coverage of key population. Our study finding corroborate with the recent evidences from HBV high prevalence and resource poor settings which showed that universal screening for HBV to be cost effective.[25] The prevalence of HBV in our study setting among key population was also higher and thus our findings could be comparable. Our study had found that the proposed screening intervention as cost saving since the population screened is less in numbers and diagnostic and treatment benefits are higher. It is also important that the implementation of this intervention at PHC level which is first point of care has been found to be cost saving. A systematic review on the economic evaluations of HBV screening and vaccination interventions among younger adults in low and middle income countries had highlighted the cost benefits in LMICs.[26]

A similar cost effectiveness study on HBV and HCV screening among migrant populations in a low endemic country was found to be cost effective. It was also recommended that implementation of targeted HBV and HCV screening programmes to increase early diagnosis and treatment was important to reduce the burden of chronic hepatitis B and C among migrant population.[27] An economic evaluation for birth dose HBV vaccination conducted in Thailand, showed the incremental cost comparing HBsAg screening followed by HBeAg was

20,000 baht. However this study concluded that the universal vaccination of neonates without screening was cost effective with the ICER of 151.05 baht over no vaccination.[28] For adult vaccination, Anti HBc marker is used to identify the true HBV negative population for adult vaccination.[29]

The cost of downstream diagnosis and antiviral therapy represent larger proportion in the screening and early treatment than the current scenario. This could be attributed to early treatment strategy which prevented end stage liver diseases which would be much costlier to treat. Therefore, apart from the diagnosis and antiviral therapy cost, the screening and early treatment of HBV and HCV incurred lower cost for management of liver diseases. In Gambia, community based screening showed ICER of $540 per DALY averted, $645 per life year saved and $511 per QALY gained. It was recommended by the study that the higher cost effectiveness might be achievable with targeted facility based screening, price reductions of drugs and diagnostics.[30]

The present model showed that the adult vaccination in key population was effective and cost saving. Earlier literature from India suggest that the cost of preventing one HBV carrier under universal vaccination was nearly one fourth of that with selective immunization. Further, it was noted that the selective immunization of neonates born to HBsAg mother will have very minimal effect on the HBV carrier rate.[31] Even in South Africa, the prevention of a single case of neonatal HBV infection by routine screening of pregnant women was costly.[32] The cost effectiveness of screening pregnant women for HBV followed by targeted HBV vaccination is due to the low rate of vertical HBV transmission. Contrastingly, for adult vaccination, the screening followed by vaccination yields more benefit than the vaccination without screening. There was an evidence from China that immunization after screening strategy provided greater value than the non-screening strategy. The benefit cost ratio of immunization for adults with the screening based vaccination strategy (1.42) was higher than the vaccination with out screening strategy (1.06).[27]

Our sensitivity analysis highlights that the quality of life score holds much influence on the ICER for HBV and HCV screening intervention. It could be explained that since chronic

HBV and HCV infections are mostly asymptomatic, screening intervention would increase early diagnosis and thus impact on quality of life status.[33,34,35]

Both chronic HBV and HCV infections are generally asymptomatic and may remain undetected or diagnosed at a late stage thus potentially increasing the health care expenditure to patient and their family. In this context our findings highlights that the proposed screening intervention educes out of pocket expenditure significantly to the patients and their family. This could specifically attributed to the PHC level implementation of screening would reduce time and resources spent for visiting tertiary health care facility.

7. Limitations of the study

This model was constructed using information available in India. We didn't get the more information to synthesis evidence or perform meta-analysis. This model is now representative of Tamil Nadu state alone and it requires modifications for other states with different scenarios.

8. CONCLUSIONS

Based on the present model the interventions such as HBV screening and early treatment, HBV screening and vaccination for HBV negatives and HCV screening and early treatment of key population in Tamil Nadu is cost saving. The model findings confirmed that the proposed interventions were dominant compared with current practice. It also indicates that the proposed intervention would be more cost saving with negative ICER value per QALY gained for key population. The implementation of HBV and HCV intervention may reduce the burden of HBV and HCV infection and its related liver disorders in Tamil Nadu. This will require additional budget for the Government of Tamil Nadu around ₹ 63,04,31,436 for implementing screening, early treatment and vaccinating HBV negatives and ₹ 55,67,16,635 for implementing screening, early treatment for HCV. The estimated budget will vary depending on the proportion required for intensive care treatment for liver disorders.

Recommendations

- The prevalence of HBV was 1.63% and HCV was 0.30% in Tamil Nadu. Three-fourths of HBV and HCV infected people were males. Prevalence of HBV and HCV was higher in rural areas. The pooled estimate of HBV and HCV prevalence among selected key population was 3% and 1% respectively. Overall burden of HBV and HCV was considerably higher in Tamil Nadu.
- Majority of people with hepatitis are unaware of their infection due to a lack of knowledge and availability of testing services. The new action plan of Government of Tamil Nadu had initiated HBV and HCV screening at PHC level will provide a major opportunity to improve identification and treatment of persons with chronic hepatitis, and help country efforts to achieve the targets outlined.
- Active screening and diagnosis of HBV and HCV infection among key population at PHC level is the gateway for access to both prevention as well as care and treatment services.
- Early identification of persons with chronic HBV or HCV infection enables them to receive the necessary care and treatment to prevent or delay progression of liver disease.
- Early screening and hepatitis B vaccination will provide an opportunity to link to interventions to reduce transmission and cost to the patients and their family members
- HBV infection rates can be reduced by active screening of key population and increasing HBV vaccination rate and linking patients with the care cascade.
- Hepatitis B vaccination and screening are cost saving to government of Tamil Nadu and this effective intervention will help to reduce the burden of HBV and HCV.
- Vaccination coverage and increasing access to PHC among key population is essential
- Implementation of this intervention pose practical challenges to policy makers, where there is currently very limited access to HBV and HCV diagnostic and treatment services due to lack of awareness and other barriers.
- The recommended intervention will help Global Health Sector Strategy (GHSS) on viral Hepatitis targets on testing (i.e. to identify 30% of persons living with HBV and HCV infection by 2020 and 90% by 2030.) and treatment. This in turn will improve clinical outcomes, save lives, reduce HBV and HCV transmission and prevent new infections.

Tables

Table 1: Sensitivity and specificity of tests for HBV and HCV diagnosis

Author	Year	HBsAg/Anti-HCV	Diagnostic Tests	Sensitivity (%)	Specificity (%)
Kaur H etal[36]	2000	HBsAg	Rapid Test	100	93
		Anti-HCV	Rapid Test	100	87
Abraham P etal[37]	1998	HBsAg	RAPID - Quickchaser assays	77	99
			RAPID - Virucheck assays	79	97
Maity S et al[38]	2012	HBsAg	ELISA 1	100	100
			ELISA 2	100	98
			ELISA 3	100	100
		HBsAg	RAPID 1	100	100
			RAPID 2	100	100
			RAPID 3	100	100
		Anti-HCV	ELISA 1	100	88
			ELISA 2	100	94
			ELISA 3	100	100
		Anti-HCV	RAPID 1	95	100
			RAPID 2	100	100
			RAPID 3	100	100
Raj AA et al[39]	2001	HBsAg	RAPID – Hepacard	79	99
S Raghuraman et al[40]	1999	Anti-HCV	RAPID (100 Sera samples)	100	100
			RAPID (186 Sera Samples)	95	100
Garg G et al[41]	2016	HBV	RT-multiplex PCR	89	100
		HCV		87	100

Table 2. Pooled prevalence of HBV and HCV among key populations in Tamil Nadu

Risk Populations in Tamil Nadu	Pooled Prevalence	
	HBV %	HCV %
Sexual risk behaviour	2.3	0.9
Blood donor	3.0	1.0
Antenatal women	3.0	NA
Individuals with STDs	NA	2
People living with HIV	7	2
MSM	2.00	NA
All pooled estimate	3 (2-4)	1(0-3)

Table 3. Proposed strategies for HBV

Strategies	Diagnostic facility	Diagnostic tool	Population	Frequency
HBV				
Proposed strategy	PHC	Rapid test followed by ELISA and vaccination for negatives	Key population	Annual
Comparator	Tertiary	ELISA	Opportunistic Screening	-
HCV				
Proposed strategy	PHC	Rapid test followed by ELISA	Key population	Annual
Comparator	Tertiary	ELISA	Opportunistic Screening	-

Table 4. Input parameters used for model based cost-effectiveness analysis of HBV screening through rapid test followed by ELISA and vaccination for negatives

	Parameters	To Model	Lower	Upper	Reference
Demographic values	Average Age of HBV infection	35	28.00	42.00	42
	Cohort population	1000	800	1200	Assumption
	Life expectancy at age 35	43.6	34.88	52.32	43
Mortality	All cause mortality	0.063	0.0076	0.0114	44
	Mortality due to asymptomatic	0	0.01	0.01	3
	Mortality due to chronic	0	0.01	0.01	3
	Mortality due to compensated cirrhosis	0.01	0.01	0.01	3
	Mortality due to decompensated cirrhosis	0.206	0.16	0.25	3
	Mortality due to hepatocellular carcinoma	0.468	0.38	0.56	3
Prevalence	Prevalence of HBV	0.04	0.03	0.04	Estimated
Diagnostic accuracy	Sensitivity of ELISA	1.00	0.80	1.20	4
	Specificity of ELISA	0.978	0.80	1.20	41
	Sensitivity of rapid diagnosis test	0.79	0.80	1.20	5
	Specificity of rapid diagnosis test	0.980	0.80	1.20	42
Probability of disease progression	Normal to asymptomatic carrier	0.0604	0.0483	0.1087	Calculated
	Asymptomatic carrier to chronic HBV	0.40	0.32	0.48	3

	Parameters	To Model	Lower	Upper	Reference
	Asymptomatic carrier to cure (Normal)	0.00425	0.0034	0.0077	45
	Chronic HBV to compensated cirrhosis	0.016	0.01	0.02	3
	Chronic HBV to hepatocellular carcinoma	0.001	0.008	0.018	3
	Chronic to asymptomatic	0.3	0.24	0.54	6
	Chronic to cure (Normal)	0.008	0.536	0.804	6
	Compensated cirrhosis decompensated cirrhosis	0.05	0.04	0.06	`3
	Compensated HCC	0.002	0.016	0.036	3
	Compensated cirrhosis to asymptomatic	0.165	0.132	0.297	6
	Decompensated cirrhosis to hepatocellular carcinoma	0.03	0.02	0.04	3
Quality of life	Normal	1.00	0.80	1.20	3
	Asymptomatic HBV	0.73	0.58	0.88	3
	Chronic HBV	0.68	0.54	0.82	3
	Compensated cirrhosis	0.69	0.55	0.83	3
	Decompensated cirrhosis	0.35	0.28	0.42	3
	Hepatocellular carcinoma	0.38	0.30	0.46	3
Discount rate	QALY	0.03	0.02	0.04	3
	Cost	0.03	0.02	0.04	3
Diagnostic	Screening cost of rapid test	85.00	68.00	102.00	Hospital Procurement Record
	Screening cost of ELISA	1157.00	925.60	1388.40	Hospital Procurement Record
	Diagnostic cost pre-treatment RNA, LFT, Fibro-Scan	8000	6400.00	9600.00	46
	Diagnostic cost post treatment	6000	4800.00	7200.00	7
Treatment	Treatment cost inactive chronic infection	17280.16	13824.13	20736.19	47
	Treatment cost intensive care treatment liver disorders	73228.00	58582.40	87873.60	48, 10
	Out of pocket (OOP) Cost	64321.00	51456.80	77185.20	49, 50
	Drug cost	900	720	1080	Expert Opinion
Vaccine	Vaccine efficacy	0.80	0.64	0.96	3
	Vaccine cost	56	44.80	67.20	3
Stage-wise	Delayed clearance/Normal	0.55	0.50	0.75	3

	Parameters	To Model	Lower	Upper	Reference
distribution of HBV patients	Chronic hepatitis	0.195	0.16	0.23	[3]
	Compensated cirrhosis	0.14	0.09	0.13	[3]
	Decompensated cirrhosis	0.045	0.00	0.00	[3]
	Hepatocellular carcinoma	0.07	0.06	0.08	[3]

Table 5. Cost-effectiveness of active screening and vaccination for HBV

Life time outcomes	**Strategy**
	Screening, early treatment & vaccination for negatives
Quality Adjusted Life Years (QALYs)	
QALYs Gained (Undiscounted)	904
QALYs Gained (Discounted)	505
Life years gained	
Undiscounted	293
Discounted	132
Mortality	
Deaths averted	294
OOP reduction	₹ 3274
Incremental cost effectiveness ratio	
Incremental cost/QALY (Discounted)	-1,80,749
Budget impact (INR)	
Budget required for one time Screening followed by early treatment or vaccination	₹ 63,04,31,436

Table 6. Input parameters used for model based cost-effectiveness analysis of HCV screening through rapid test followed by ELISA

	Parameter	Default	Lower	Upper	Reference
Demographic	Average age of HCV infection	35	28	42	[51]
	Cohort population	1000	750	1250	Assumption
	Life expectancy	44	35	53	[43]
Mortality	All cause mortality (%)	0.00951	0.007133	0.011888	[43]
	Mortality due to decompensated cirrhosis	0.13	0.0975	0.1625	[52]
	Mortality due to hepatocellular carcinoma	0.43	0.3225	0.5375	[52]
Prevalence	Prevalence of HCV	0.035	0.028	0.042	Estimated
	Incidence of HCV	0.0002	0.00016	0.00024	[53]
	Transmission rate	0.01399	0.0105	0.0175	Calculated
Diagnostic	Sensitivity of ELIZA	1	0.75	1.25	[41]

	Parameter	Default	Lower	Upper	Reference
accuracy	Specificity of ELIZA	1	0.75	1.25	[54]
	Sensitivity of rapid diagnosis test	0.985	0.73875	1.23125	[54]
	Specificity of rapid diagnosis test	1	0.75	1.25	[54]
Probability of disease progression	Asymptomatic carrier to chronic HCV	0.79	0.632	0.948	[54]
	Asymptomatic to normal	0.25	0.1875	0.3125	[55]
	Chronic HCV to compensated cirrhosis	0.13	0.104	0.156	[55]
	Chronic HCV to hepatocellular carcinoma	0.00067	0.000503	0.000838	[44]
	Compensated cirrhosis to decompensated cirrhosis	0.03	0.0225	0.0375	[55]
	Decompensated cirrhosis to hepatocellular carcinoma	0.03	0.0225	0.0375	[55]
Relative Risk (RR)	Asymptomatic carrier to chronic HCV	1	0.75	1.25	Calculated
	Asymptomatic to normal	1	0.75	1.25	Calculated
	Chronic HCV to compensated cirrhosis	1	0.75	1.25	Calculated
	Chronic HCV to hepatocellular carcinoma	1	0.75	1.25	Calculated
	Compensated cirrhosis to decompensated cirrhosis	1	0.75	1.25	Calculated
	Decompensated cirrhosis to hepatocellular carcinoma	1	0.75	1.25	Calculated
	Mortality due to compensated cirrhosis	1	0.75	1.25	Calculated
	Mortality due to decompensated cirrhosis	1	0.75	1.25	Calculated
	Mortality due to hepatocellular carcinoma	1	0.75	1.25	Calculated
Quality of life	Normal	1	0.75	1.25	[55]
	Asymptomatic HCV	0.9	0.675	1.125	[55]
	Chronic HCV	0.7	0.525	0.875	[55]
	Compensated cirrhosis	0.55	0.4125	0.6875	[55]
	Decompensated cirrhosis	0.49	0.3675	0.6125	[55]
	Hepatocellular carcinoma	0.58	0.435	0.725	[55]
Discount rate	QALY	0.03	0.0225	0.0375	[55]
	Cost	0.03	0.0225	0.0375	[47]
Diagnostic	Screening cost of rapid test	115	86.25	143.75	Hospital Procurement Record
	Screening cost of ELISA	2000	1500	2500	Hospital Procurement Record
	Diagnostic cost pre-treatment RNA, LFT, Fibro-Scan	8000	6000	10000	[48]
	Diagnostic cost Post Treatment	6000	4500	7500	[48]
Treatment cost	Treatment cost inactive chronic infection	17280.16	12960.12	21600.2	[48]
	Treatment cost intensive care treatment liver disorders	112658	84493.5	140822.5	[49,50]
	Drug cost	21283	17026.4	25539.6	[53]
	DAA efficacy	90	72	108	[53]
	OOP cost (total cost)	98956	74217	123695	[49,50]

	Parameter	Default	Lower	Upper	Reference
Stage-wise distribution of HCV patients	Delay clearance/normal	0.014	0.01	0.02	[44]
	Chronic hepatitis	0.79	0.63	0.95	[56]
	Compensated cirrhosis	0.13	0.10	0.15	[56]
	Decompensated cirrhosis	0	0	0	[56]
	Hepatocellular carcinoma	0.07	0.06	0.08	[56]

Table 7. Cost-effectiveness of active screening and treatment for HCV

Quality Adjusted Life Years (QALYs)	
QALYs Gained (undiscounted)	57
QALYs Gained (Discounted)	38
Life Years gained	
Undiscounted	4
Discounted	2
Mortality	
Deaths averted	4
Incremental cost effectiveness ratio	
Incremental cost/QALY	-1,14,571
Budget required for one time screening followed by early treatment	₹ 55,67,16,635

Table 8. Estimated required budget for proposed and current strategy for HBV screening and treatment

Target population	Estimated population	Estimated Cases	Estimated Non-cases	Estimated budget proposed strategy			Current strategy	
				Screening & Treatment	Screening & vaccination	Total cost	Estimated Cases	Screening & Treatment
Sexual risk behavior	2127852	48,941	20,78,911	₹ 90,64,77,719	₹29,31,26,508	₹1,19,96,04,227	22,023	₹40,60,42,996
Blood donor	211227	6,337	2,04,890	₹11,73,70,395	₹2,88,89,517	₹14,62,59,912	2,852	₹ 5,25,74,295
Antenatal women	900000	27,000	8,73,000	₹50,00,94,000	₹12,30,93,000	₹62,31,87,000	12,150	₹22,40,09,550
People living with HIV	143000	10,010	1,32,990	₹18,54,05,220	₹1,87,51,590	₹20,41,56,810	4,505	₹ 8,30,49,467
MSM	32559	651	31,908	₹ 1,20,61,156	₹44,99,003	₹1,65,60,159	293	₹ 54,02,613
Total	3414638	92,939	33,21,699	₹1,72,14,08,490	₹46,83,59,617	₹2,18,97,68,107	41,822	₹77,10,78,920
Addition budget required						₹1,41,86,89,188		

Note: The estimated budget will vary depending on the proportion required for intensive care treatment for liver disorders

Table 9. Estimated required budget for proposed and current strategy for HCV screening and treatment

		Proposed		Current	
Target population	Population	Cases	Estimated budget	Cases	Estimated budget
Sexual risk behaviour	21,27,852	19,151	₹61,39,30,923	18,883	₹36,40,58,752
Blood donor	2,11,227	2,112	₹ 6,50,16,009	2,083	₹ 4,01,54,755
Individual with STD	23,39,207	46,784	₹1,17,10,14,510	46,129	₹88,93,77,625
People living with HIV	1,43,000	2,860	₹ 7,15,86,258	2,820	₹ 5,43,69,280
Total	48,21,286	70,907	₹1,92,15,47,699	69,914	₹1,34,79,60,412
Addition budget required				₹ 57,35,87,287	

Note: The estimated budget will vary depending on the proportion required for intensive care treatment for liver disorders

Figures

Figure 1. Decision tree to active screening and vaccination for HBV

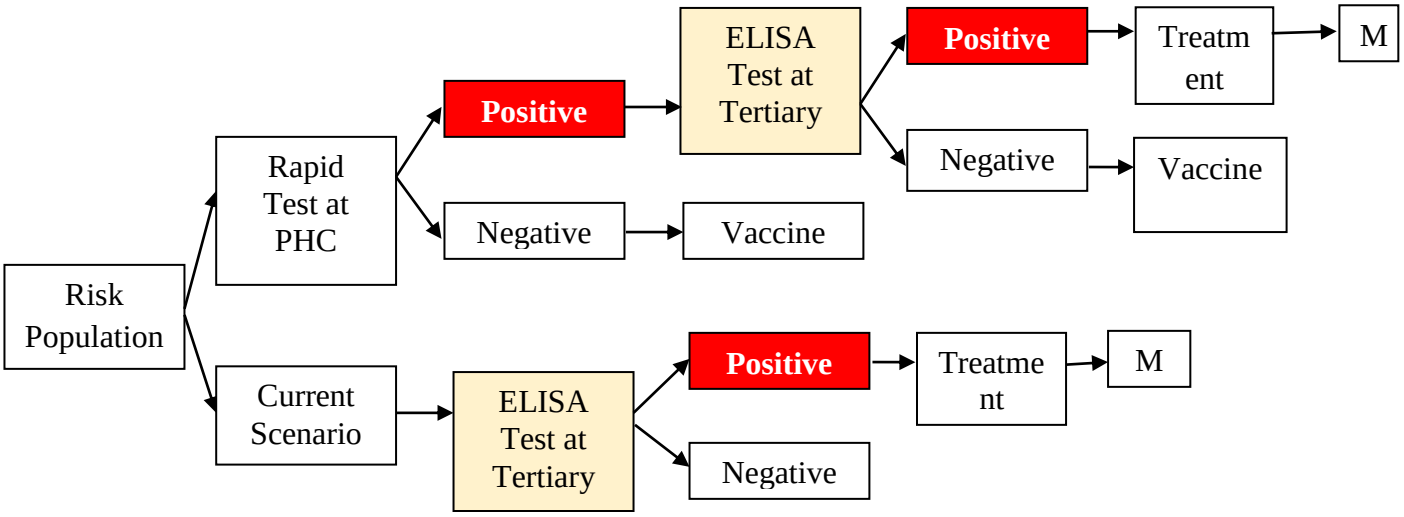


Figure 2: Hepatitis B infection Markov model pathway HBV

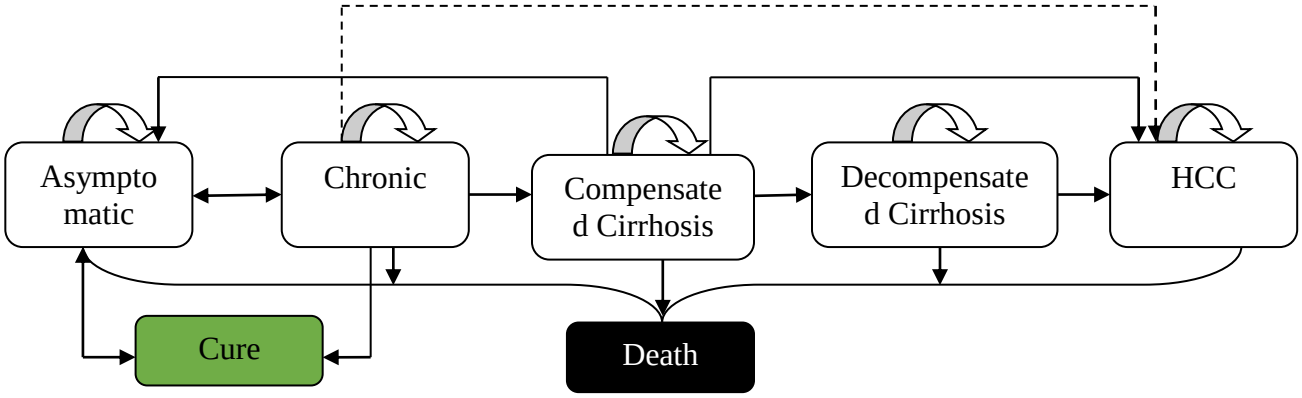


Figure 3. Cost Effectiveness Plane for strategy-1 HBV

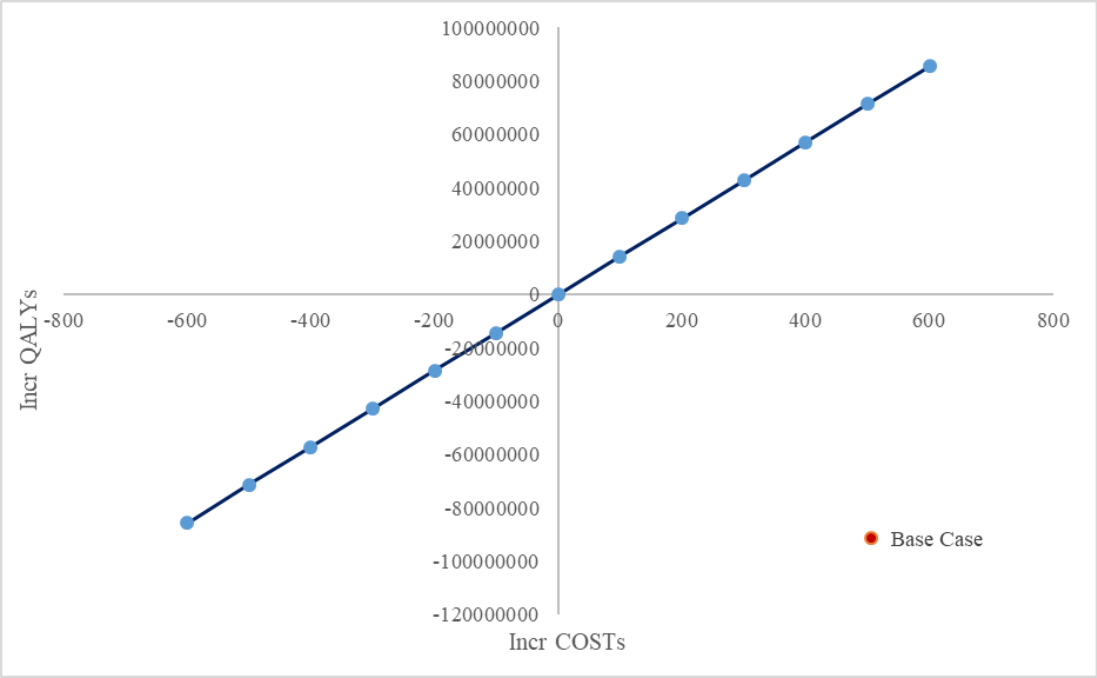


Figure 4. One-way sensitivity analysis to see impact of variation in input parameters on ICER (stratwegy-1) HBV

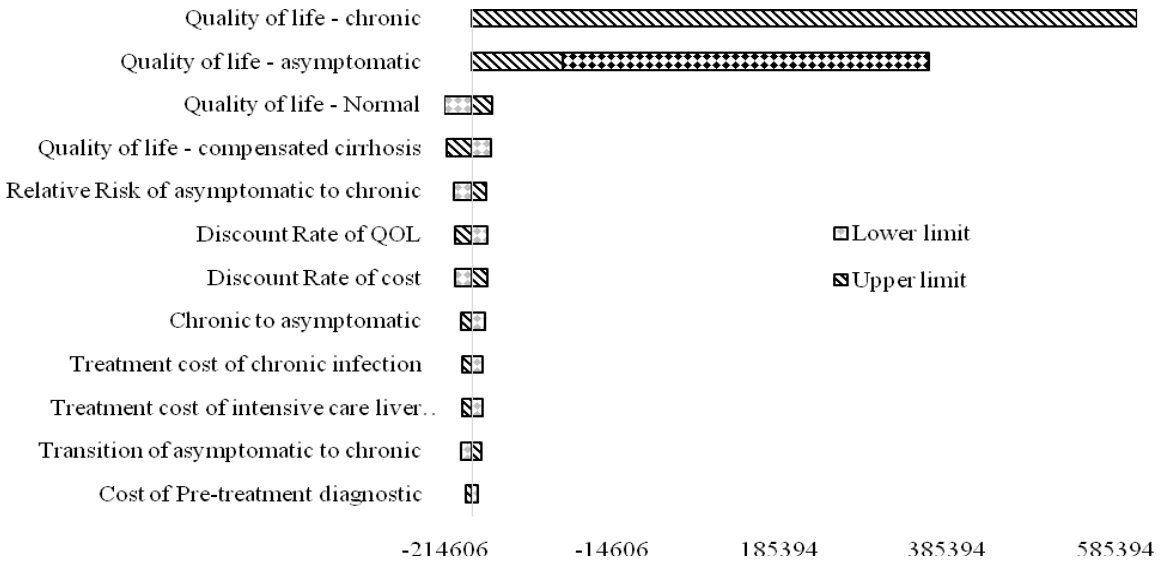


Figure 5. Probability sensitivity analysis for strategy-1 HBV

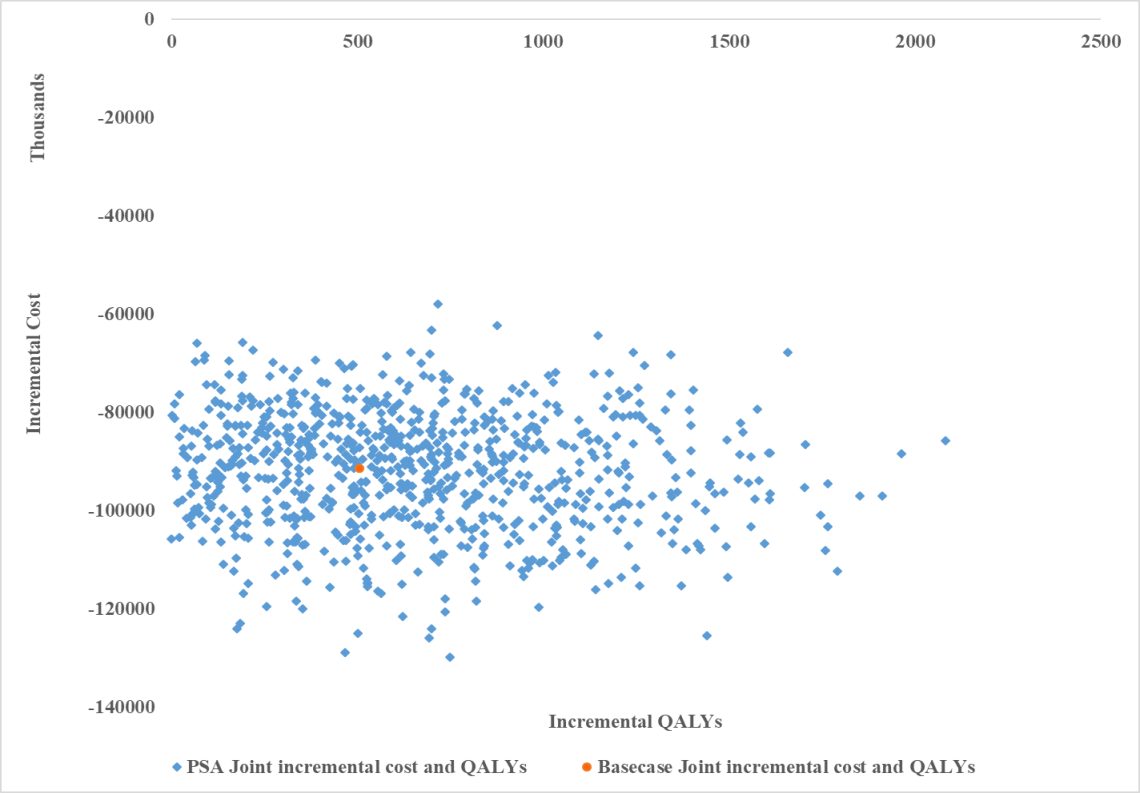


Figure 6. Decision tree to active screening and vaccination for HCV

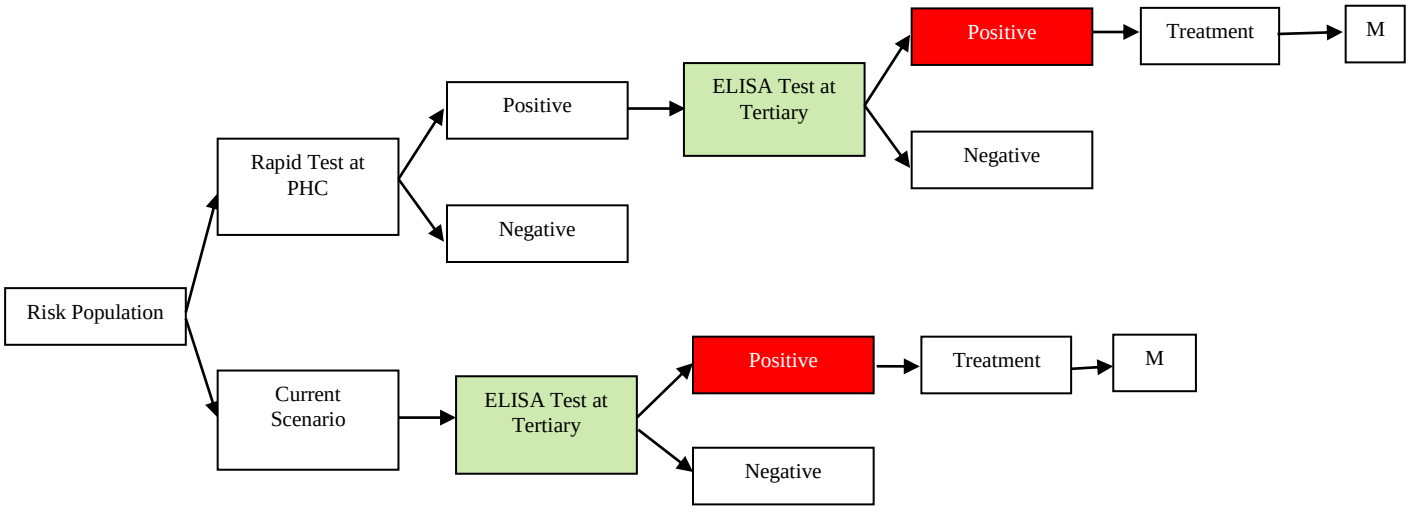


Figure 7: Hepatitis C infection Markov model pathway HCV

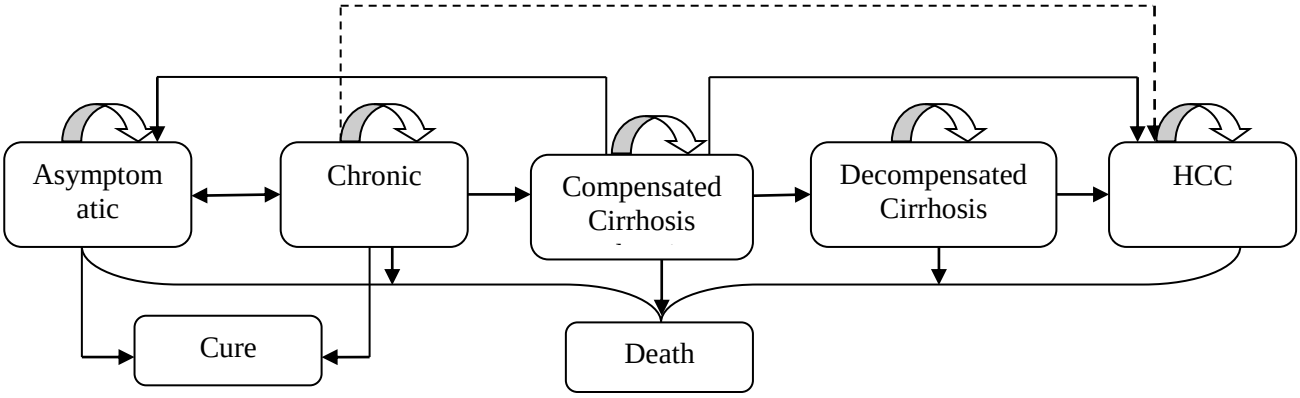


Figure 8. Cost Effectiveness Plane for screening HCV at PHC level

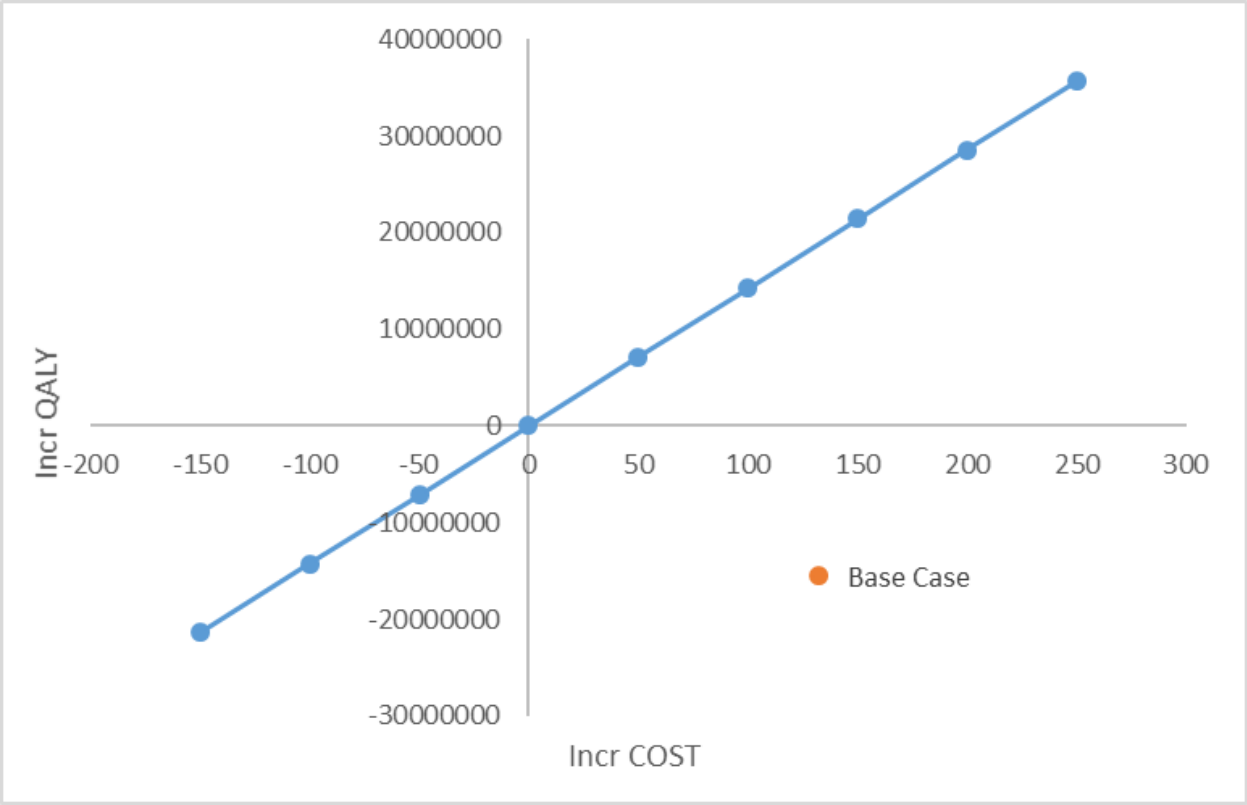


Figure 9. One-way sensitivity analysis to see impact of variation in input parameters on ICER for screening HCV at PHC level

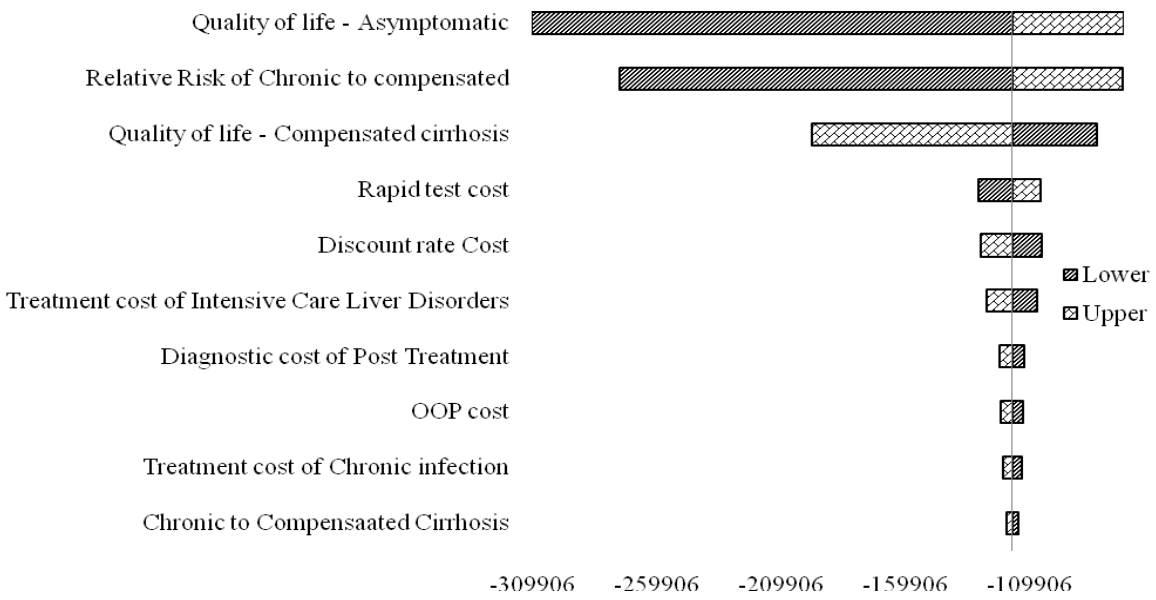


Figure 10. Probability sensitivity analysis for screening HCV at PHC level

Annexures I

Systematic Review

Systematic review on prevalence of HBV and HCV infection in various key populations in India

INTRODUCTION

Viral hepatitis is a key public health issue in India which has high impacts similar to other infectious diseases like tuberculosis. Among the five types of hepatitis viruses, Hepatitis B (HBV) and Hepatitis C (HCV) viruses predominantly lead to the development of liver diseases. Both HBV and HCV could be transmitted through vertical transmission and horizontal transmission. The prevalence of HBV and HCV in India remains underestimated due to asymptomatic nature of the disease and gaps in diagnosis of the disease. Under the National Viral Hepatitis Control Program (NVHCP) hepatitis laboratory networks to undertake surveillance and prevalence of different types of viral hepatitis has been initiated. The objective of the present systematic review is to estimate the prevalence of HBV and HCV in various key population in India.

METHODOLOGY

The systematic review protocol has been registered at the PROSPERO registry (Registration No. 134164). The present systematic review was conducted following the PRISMA guidelines.[57] The condition, context and population (CoCoPop) used for the review has been provided in Table-A1. All the studies published in English language till June 2019 on prevalence and incidence of HBV and HCV were included in the review. Pubmed, and Cochrane databases were searched using search strategies given in Table-A2.

Data Extraction and Synthesis

The retrieved literature from the tow data bases were imported in the EndNote software to identify the duplicates and further exported to Rayyan software for review.[58] Two independent reviewers screened the abstract and title of the literature and finalized the relevant literatures based on the study inclusion and exclusion criteria using Rayyan software. Discrepancy arising in this process was resolved in consultation with the third reviewer.

The data extraction was done using data extraction sheet which included study characteristics, study area, study population, study sample size, prevalence and incidence. Pooled prevalence of HBV and HCV in various key population was calculated using R software.

Quality check of selected literatures

The risk of bias in the studies reporting prevalence data was assessed using Joanna Briggs Institute (JBI) appraisal checklist.[59]

RESULTS

The step by step process of literature collection screening and selection from data bases has been indicated as a PRISMA flow chart (Figure-A1). The literatures search from three different data bases yielded 1223 studies in which 4 were removed from duplicates. All other studies titles were screened for relevant and 544 studies were retained from abstract level screening based on inclusion and exclusion criteria. A total of 453 studies met inclusion criteria and was reviewed with the full text which yielded 127 studies. Of this 61 were excluded based on data relevance criteria and 66 was included for data synthesis.

General population prevalence of HBV and HCV infection in Tamil Nadu was estimated as 2.7% and 0.3% respectively. The prevalence of HBV and HCV positivity among blood donor was 3.4% and 0.73% respectively. The of HBV and HCV for various key population in Tamil Nadu is provided in Table-A3 and India Table-A4.

The pooled HBV and HCV prevalence among key population are given in Table-A5. The pooled prevalence of HBV and HCV prevalence among key population was 3% (2-4) and 1 (0-3) respectively (Figure-A8 and Figure-A9). The parlance of HBV among this key population was ranged from 2% among MSM and 7% among people living with HIV (Figure-A2 to Figure-A7). The parlance of HCV among this key population was ranged from 1% among Blood donors and 2% among people living with HIV and individuals with STDs.

Annexure Tables

Table A1. Framework for Systematic Review

Co	**Condition**	HBV or HCV infection
Co	**Context**	India
Pop	**Population**	Population with prevalence above the current general population prevalence of HBV or HCV in India

Table A2. Searched Strategies used the systematic review

Databases	**Search Strategies Hepatitis**	
Pubmed	I A) "hepatitis B" [MeSH Terms] OR "hepatitis C" [MeSH Terms] OR "Hepatitis B virus" [Mesh] OR "Hepatitis C virus" [Mesh] OR "hepacivirus" [Mesh] (Selected) OR "hepatitis B surface antigens" [MeSH Terms] OR "Hepatitis C antibodies" [MeSH Terms] OR "Hepatitis C Antigens" [Mesh] OR "Hepatitis B Antibodies" [Mesh] OR "Hepatitis B Antigens" [Mesh]	130022
	OR	
	B) ("Australia Antigen") OR "hepatitis B") OR "hepatitis C") OR "hepacivir*") OR "HBV") OR "HCV") OR "HBsAg") OR "core HCV antigen") OR "HCVcAg") OR "HCV RNA" OR HBV DNA (All field search)	171061
	1 A OR I B	171333
	AND	

Databases	Search Strategies Hepatitis	
	II Prevalence [TIAB]; Population Surveillance [TIAB]; Seroepidemiologic Studies [TIAB]; prevalence*[TIAB]; seroprevalence [TIAB]; epidemiolo*[TIAB]; incidence; seroepidemiolo*[TIAB]; AND III "India" OR "india*" OR "south* india*" OR "north* india*" OR "east* india*" OR "west* india*" OR andhrapradesh OR aruna AND "India" OR "Andhra Pradesh" OR "Arunachal Pradesh" OR "Assam" OR "Bihar" OR "Chhattisgarh" OR "Goa" OR "Gujarat" OR "Haryana" OR "Himachal" OR "Pradesh" OR "Jammu" OR "Kashmir" OR "Jharkhand" OR "Karnataka" OR "Kerala" OR "Madhya" OR "Pradesh" OR "Maharashtra" OR "Manipur" OR "Meghalaya" OR "Mizoram" OR "Nagaland" OR "Odisha" OR "Punjab" OR "Rajasthan" OR "Sikkim" OR "Tamilnadu" OR "Tamil" OR "nadu" OR "Telangana" OR "Tripura" OR "UttarPradesh" OR "Uttar Pradesh" OR "Uttarakhand" OR "West Bengal" OR "Westbengal" OR andaman OR nicobar OR "Andaman and Nicobar" OR "Chandigarh" OR dadras OR nagar OR haveli OR "Dadra and Nagar Haveli" OR daman OR Diu OR "Daman and Diu" OR "Lakshadweep" OR "Delhi" OR "Newdelhi" OR "New Delhi" OR "Puducherry" (All field search) I A OR I B AND II AND III	1505466 533178 1158
Cochrane	#1 MeSH descriptor: [Hepatitis B Antigens] explode all trees #2 MeSH descriptor: [Hepatitis B Antibodies] explode all trees #3 MeSH descriptor: [Hepatitis C Antigens] explode all trees #4 MeSH descriptor: [Hepatitis C Antibodies] explode all trees #5 MeSH descriptor: [Hepatitis B Surface Antigens] explode all trees #6 MeSH descriptor: [Hepacivirus] explode all trees #7 MeSH descriptor: [Hepacivirus] explode all trees #8 MeSH descriptor: [Hepatitis B virus] explode all trees #9 MeSH descriptor: [Hepatitis C] explode all trees #10 MeSH descriptor: [Hepatitis B] explode all trees #11 #1 OR #2 OR #3 OR #4 OR #5 OR #6 OR #7 OR #8 OR #9 OR	1036 598 14 111 594 1229 1229 738 2989 2438

Databases	Search Strategies Hepatitis	
	#10	5646
	#12 ("Australia Antigen"):ti,ab,kw	6
	#13 ("hepatitis b"):ti,ab,kw	8333
	#14 ("hepatitis c"):ti,ab,kw	8202
	#15 ("hepacivir$"):ti,ab,kw	0
	#16 ("hbv"):ti,ab,kw	4034
	#17 ("hcv"):ti,ab,kw	6162
	#18 (HBsAg):ti,ab,kw	1786
	#19 ("core HCV antigen"):ti,ab,kw	0
	#20 (HCVcAg):ti,ab,kw	2
	#21 ("HCV RNA"):ti,ab,kw	2543
	#22 ("HBV DNA"):ti,ab,kw	2041
	#23 #12 OR #13 OR #14 OR #15 OR #16 OR #17 OR #18 OR #19 OR #20 OR #21 OR #22	17370
	#24 ("India" OR "india*" OR "south* india*" OR "north* india*" OR "east* india*" OR "west* india*" OR andhrapradesh OR aruna AND "India" OR "Andhra Pradesh" OR "Arunachal Pradesh" OR "Assam" OR "Bihar" OR "Chhattisgarh" OR "Goa" OR "Gujarat" OR "Haryana" OR "Himachal" OR "Pradesh" OR "Jammu" OR "Kashmir" OR "Jharkhand" OR "Karnataka" OR "Kerala" OR "Madhya" OR "Pradesh" OR "Maharashtra" OR "Manipur" OR "Meghalaya" OR "Mizoram" OR "Nagaland" OR "Odisha" OR "Punjab" OR "Rajasthan" OR "Sikkim" OR "Tamilnadu" OR "Tamil" OR "nadu" OR "Telangana" OR "Tripura" OR "UttarPradesh" OR "Uttar Pradesh" OR "Uttarakhand" OR "West Bengal" OR "Westbengal" OR andaman OR nicobar OR "Andaman and Nicobar" OR "Chandigarh" OR dadras OR nagar OR haveli OR "Dadra and Nagar Haveli" OR daman OR Diu OR "Daman and Diu" OR "Lakshadweep" OR "Delhi" OR "Newdelhi" OR "New Delhi" OR "Puducherry")	22901
	#25 (Prevalence):ti,ab,kw	
	#26 (Population Surveillance):ti,ab,kw	
	#27 (Seroepidemiologic):ti,ab,kw	33617
	#28 (prevalence*):ti,ab,kw	1946
	#29 (seroprevalence):ti,ab,kw	107
	#30 (epidemiolo*):ti,ab,kw	33776
	#31 (incidence):ti,ab,kw	344
	#32 (seroepidemiolo*):ti,ab,kw	58119
	#33 #25 OR #26 OR #27 OR #28 OR #29 OR #30 OR #31 OR #32	104565 138
	#34 #23 AND #24 AND #33	170371 65
	Total Literatures Collected	**1223**

Table A3. Prevalence of HBV and HCV among key population in Tamil Nadu

Ref	Study Populations	Year	Place	Sample	HBV Positive	HCV Positive	Prevalence	
							HBV (%)	HCV (%)
60	Heterosexual risk behavior	2018	Chennai	428/618	10	4	2.3	0.9
4	Hospital Staff	2000	Madurai	75	4	0	5.3	0
61		2015	Chennai	50	1	-	2	-
62	Blood Donors	2018	Puducherry	1102	156	-	4.7	-
63		2000	Madurai	1819/3574	75/1819	27/3574	4.1	0.8
64		2000	Tamil Nadu	22245	-	172	-	0.8
62		2018	Puducherry	1102	156		4.71	
63		2000	Tamil Nadu	22245		172	0.77	
62		2018	Puducherry	1102	52		4.71	
65		2015	Salem	3680		29		0.78
66		2012	Vellore					
66		2012	Vellore	1565		2		0.13
67		2012	Chennai	9100	199	-	2.2	
68		2019	Chennai	7136	78	37	1.1	0.5
69	Antenatal women	2013	Vellore	12,037	190	-	1.58	-
70		2015	Vellore	510	30	-	5.9	-
1	Injecting drug users	2018	Chennai	1184	121	614	10.2	51.9
71		2010	Chennai	1158	-	631	-	55

Ref	Study Populations	Year	Place	Sample	HBV	HCV	Prevalence	
54		2016	Chennai	1042	371	-	35.6	-
72		2008	Chennai	912	101	566	11.1	62.1
73		2017	Chennai	14450	-	6575	-	45.5
74	Individuals with STDs	2003	Pondicherry	100	-	6	-	6
11		2012	Vellore	310	-	1	-	0.3
24	Heamodialysis Patients	2018	Tamil Nadu	23	4	19	17.4	82.6
75	General Population	2003	Pondicherry	661	-	4.8	-	0.7
76		2009	Vellore	6233	106	-	1.7	-
77		2005	General population	1981	113	-	5.70	-
78		2018	General population	18589	-	56	-	0.3
79		2015	General population	2291	-	5	-	0.2
80		2017	Chennai	751	-	4	-	0.5
81		2013	General population	978	-	2	-	0.2
82	Men Sex with Men (MSM)	2010	Chennai	721	15		2	
83	Tribal Population	2018	Irula tribes	372	-	19	-	5.1
84		2013	Irula tribes	72	8	-	11.11	-
85	People living with HIV	2007	HIV positive patients	500	45	11	9	2.2
86		2013	HIV positive patients	120	5	3	4.2	2.5

Table A4. Prevalence of HBV and HCV in various key populations in India

Ref	Study Population	Year	Study Area	Sample Size	HBV Positive	HCV Positive	Prevalence	
							HBV (%)	HCV (%)
87	Hemodialysis Patients	2016	Mumbai	225		38		16.8
88		2009	New Delhi	119		33	27.7	
89		1999	New Delhi	208				61.2
90	Blood Donors	2014	Punjab	995	888			
91		2010	Southern Haryana	5849			1.7	1.0
92		2007	Patiala	5000				0.88
93		2015	Arunachal Pradesh & Manipur	24223	206	133	0.85	0.55
94		2008	Kanpur	20,000	450		2.25	
95		2007	West Bengal	113051 (2004) 106695 (2005)	1448 vs 1768 (2004 vs 2005)	314 vs 372 (2004 vs 2005)		
96		2014	Tripura	177302	2136	195	1.2	0.109
97		2008	West Bengal	6751	67	13	0.99	0.19
98		2001	Rajasthan	46,957			3.44	0.285
99		2008	Chandigarh	1700			8.4	
100		2013	Eastern India	2195			24.25	
101		1997	Delhi				32.8	31.3
102		2010	Southern Haryana	5849	99	61	1.7	1
92		2007	Patiala	5000		44		0.88
103	General Population	2018	Uttar Pradesh	3750			3.9	1.76
104		2013	New Delhi	73,898	779	186	1.05	0.25
105		2003	West Bengal	2,973		26	0.87	
106		1999	West Bengal	960			5.3	

Ref	Study	Year	Study Area	Sample Size	HBV Positive	HCV Positive	Prevalence	
[107]		2014	Punjab	995		888		82.81
103		2018	Utter Pradesh	3750	147	66	3.9	1.76
104		2013	Delhi	73,898	779	186	1.05	0.25
[108]		2014	Kerala	818	52	7	6.35	0.85
[109]		2009	Central India	852			2.9	4.6
93		2015	Northeast India	24223	116	133	0.85	0.55
[110]	Injecting Drug Users	2004	Manipur	250	11	90		
[111]		2007	Nagaland	221		30		
[112]		1997	Kolkata	76		17		
[113]		2003	Kolkata	140 (2002) 102 (2003)	18; 18	66;80		
[114]		2004	Kolkata	205		43		
[115]		2006	Darjeeling	228		48		
[116]		2003	Delhi	246	40	37		
[117]		2013	Northern India	472		124		8.1
109	Sexually Transmitted Infections	2009	Central India	852			3.4	3.9
[118]	Clinically Diagnosed	2005	Haryana	70		3		4.28
[119]	Pregnancy	2003	North India	97			7.2	

Table A5: Pooled prevalence of HBV and HCV among key populations in Tamil Nadu

Risk Populations in Tamil Nadu	Pooled Prevalence		
	HBV %	HCV %	
Sexual risk behaviour	2.3	0.9	Only one study
Blood donor	3.0	1.0	
Antenatal women	3.0	NA	
Individuals with STDs	NA	2	
People living with HIV	7	2	
MSM	2.00	NA	Only one study
All pooled estimate	3 (2-4)	1(0-3)	

Annexure Figures

Figure A1: PRISMA Flow diagram indicating the process of the study selection

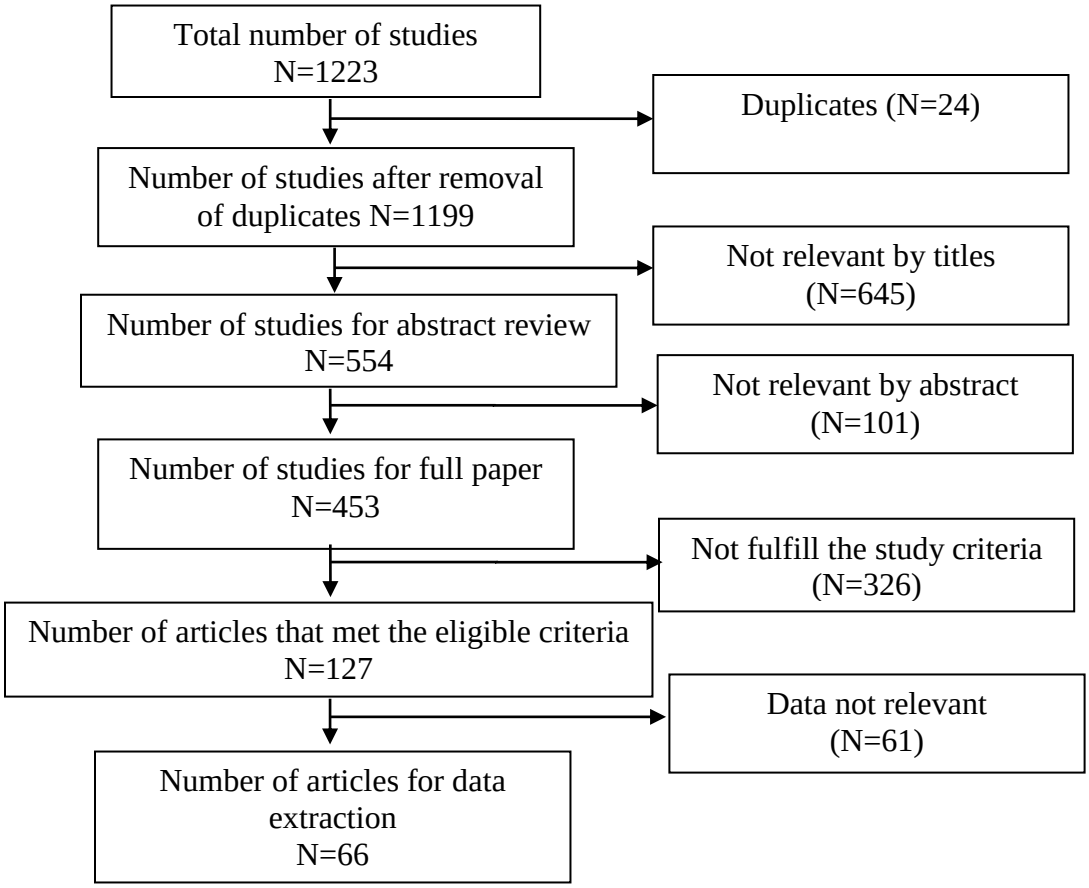


Figure A2. Pooled estimate on prevalence of HBV among blood donor

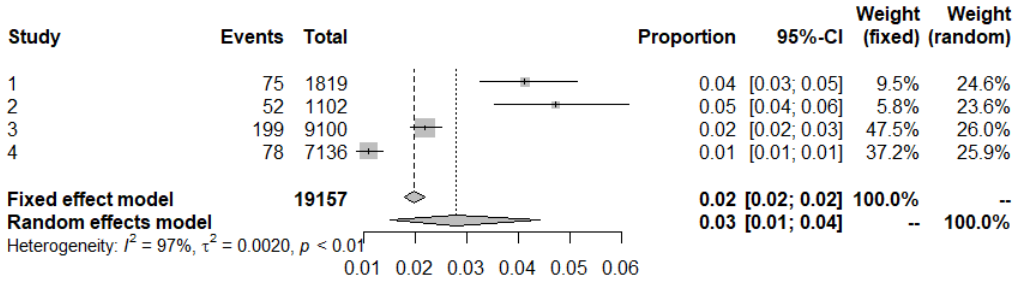


Figure A3. Pooled estimate on prevalence of HCV among blood donor

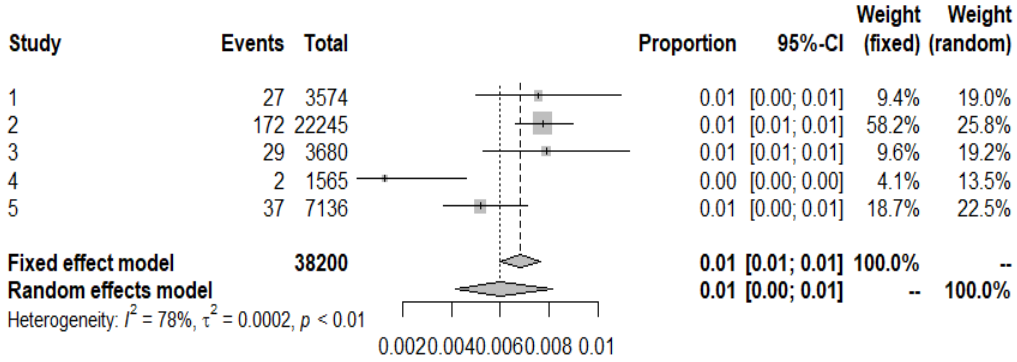


Figure A4. Pooled estimate on prevalence of HBV among Antenatal women

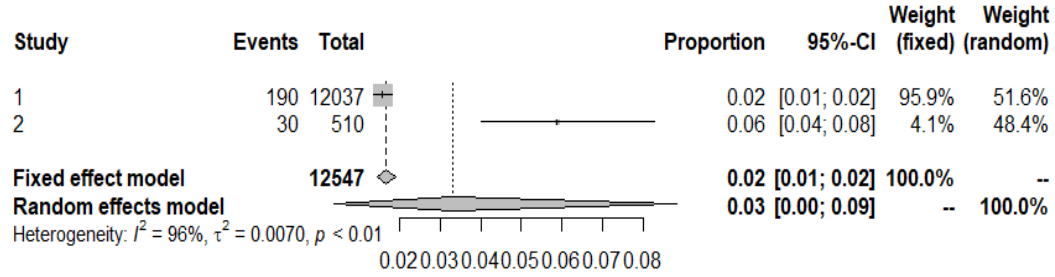


Figure A5. Pooled estimate on prevalence of HCV among Individuals with STDs

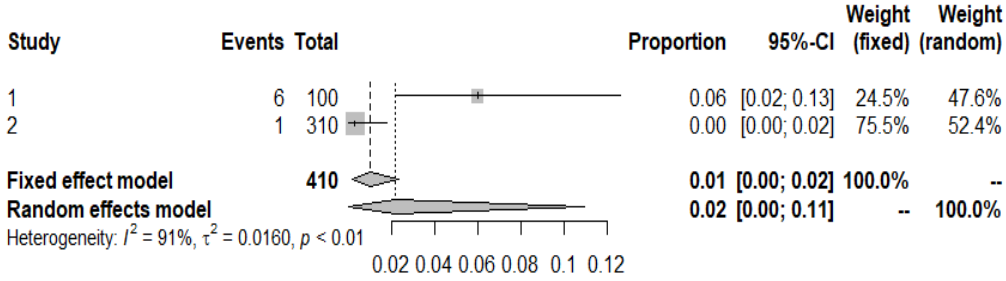


Figure A6. Pooled estimate on prevalence of HBV among people living with HIV

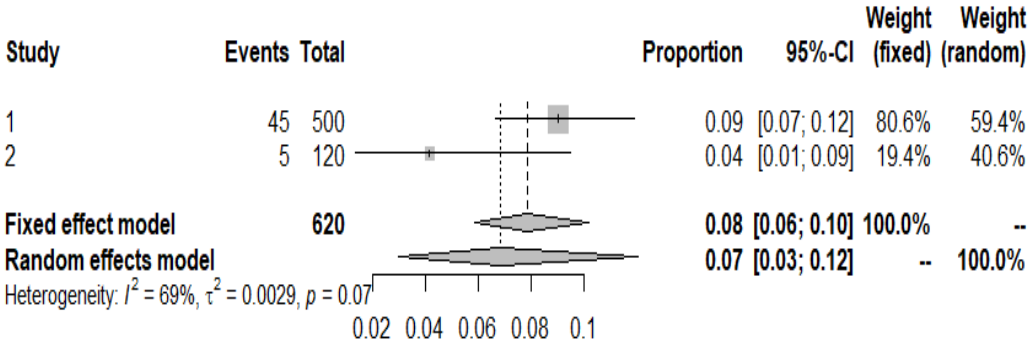


Figure A7. Pooled estimate on prevalence of HCV among people living with HIV

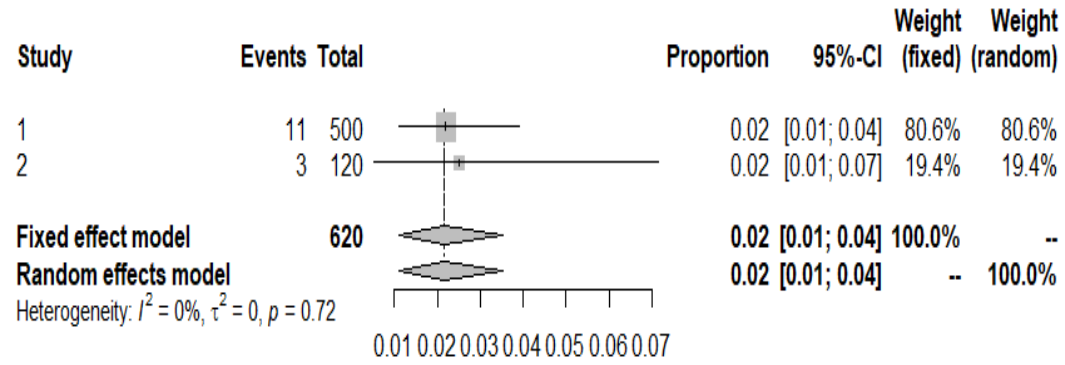


Figure A8. Pooled estimate on prevalence of HBV among key population (Sexual risk behaviour, Blood donor, Antenatal women, Individuals with STDs, People living with HIV, MSM)

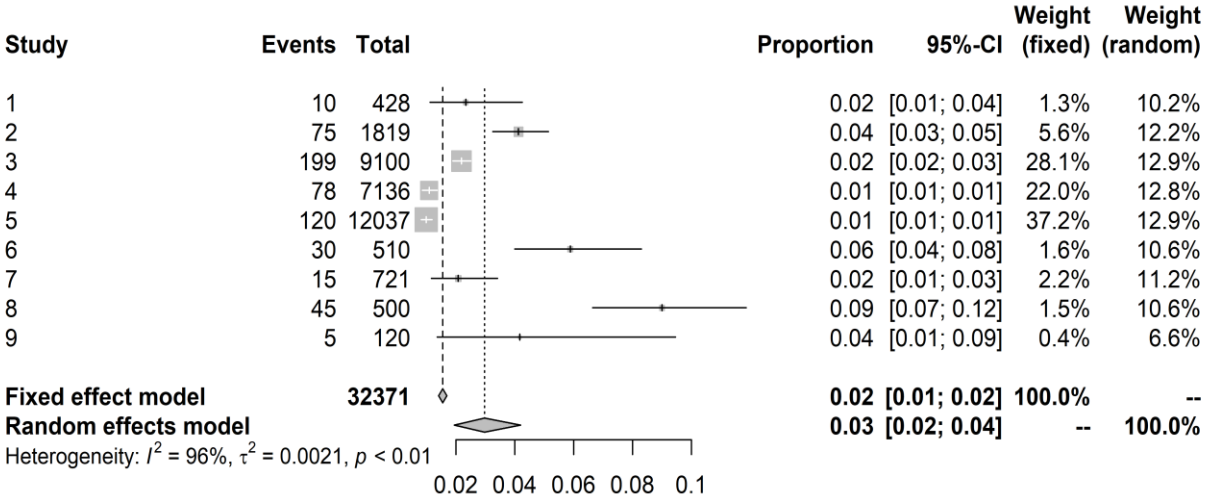
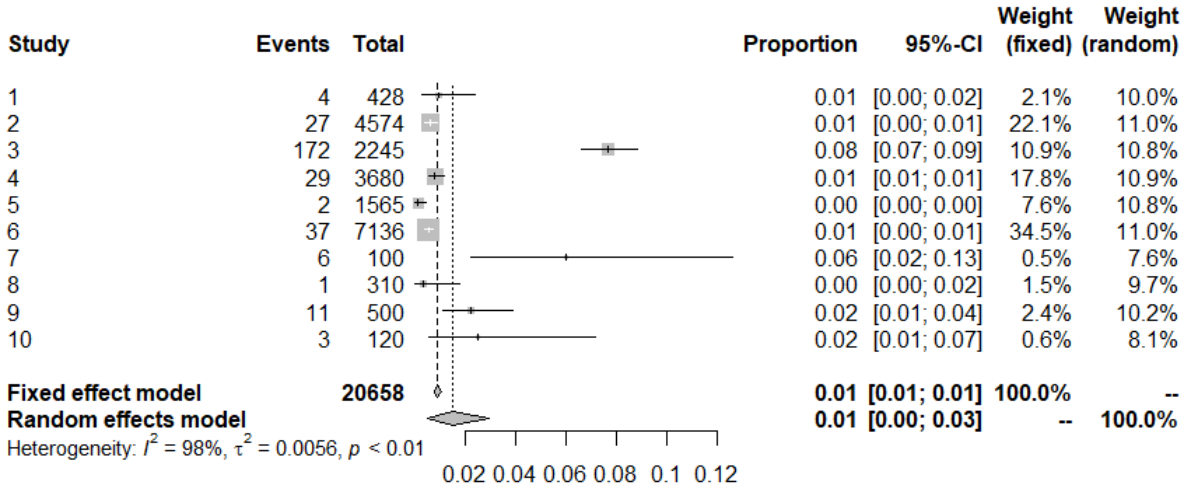


Figure A9. Pooled estimate on prevalence of HCV among key population (Sexual risk behaviour, Blood donor, Individuals with STDs, People living with HIV)



Data Extraction Sheet

Reviewer ID: _____

Date of form completion: _____

S. No.	**Variables**	**Data**
1	Author	
2	Year	
3	Country in which the study conducted	
4	Economic level of the country in which the study conducted (e.g. low income, lower-middle income or upper-middle income	
5	Type of study	
6	Population description	
7	Age group	
8	Setting of the population	
9	Method/s of recruitment of participants	
10	Total number of participants/Sample size	
11	Study design	
12	Sampling technique (e.g. random or convenience)	
13	Diseases condition	
14	Risk factors	
15	Types of outcome measures	
	Prevalence (Age/sex/population wise prevalence)	
	Incidence	
16	Type of measurement (Percentage/Odds ratio/Risk ratio)	
17	Confidence Interval	

JBI Critical Appraisal Checklist for Studies Reporting Prevalence Data

Reviewer _____ Date_____

Author _____ Year _____ Record Number _____

	Yes	No	Unclear	Not applicable
1. Was the sample frame appropriate to address the target population?	□	□	□	□
2. Were study participants sampled in an appropriate way?	□	□	□	□
3. Was the sample size adequate?	□	□	□	□
4. Were the study subjects and the setting described in detail?	□	□	□	□
5. Was the data analysis conducted with sufficient coverage of the identified sample?	□	□	□	□
6. Were valid methods used for the identification of the condition?	□	□	□	□
7. Was the condition measured in a standard, reliable way for all participants?	□	□	□	□
8. Was there appropriate statistical analysis?	□	□	□	□
9. Was the response rate adequate, and if not, was the low response rate managed appropriately?	□	□	□	□

Overall appraisal: Include □ Exclude □ Seek further info □

Comments (Including reason for exclusion)

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