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Impact and cost effectiveness of pneumococcal conjugate vaccine in India

Yuvaraj Krishnamoorthy [a], Salin K. Eliyas [a], Nayana P. Nair [b,*], Manikandanesan Sakthivel [a], Gokul Sarveswaran [a], Palanivel Chinnakali [a]

[a] Department of Preventive and Social Medicine, Jawaharlal Institute of Postgraduate Medical Education and Research (JIPMER), Puducherry 605008, India
[b] Wellcome Trust Research Laboratory, Christian Medical College, Vellore, India

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ABSTRACT

Background: World Health Organization has recommended the introduction of pneumococcal conjugate vaccine (PCV) in the childhood immunisation programme of all the countries in the world. In lieu of its introduction in India, there is a need to generate evidence on cost-effectiveness of this vaccine. The current study looks into the impact and cost-effectiveness of PCV vaccine in India.

Methods: We evaluated the cost effectiveness of implementation of PCV 13 vaccination program at national level by comparing with no vaccination program for a period of 10 birth cohorts from 2018 to 2027. UNIVAC, a deterministic static cohort model is developed by giving the conservative estimates of vaccine program related to mortality, disease event rates, vaccine efficacy and coverage projections, system and health care costs for the first five years of life. Cost effectiveness is reported as Incremental Cost Effectiveness Ratio (ICER). Further scenario and sensitivity analysis were done. Probability of PCV intervention to be cost effective at a willingness to pay (WTP) threshold equal to per capita gross domestic product (GDP) is calculated using the government perspective.

Results: We found that the introduction of PCV vaccination program can cost an additional $467 (INR 31,666) for averting per DALY which is less than one time GDP per capita of India. Even with the most unfavourable scenario for PCV vaccine, cost per DALY averted is found to be $2323 (INR 1,57,520) which is still a cost effective intervention in India. Probabilistic sensitivity analysis found the ICER for PCV to be $649 (INR 44,008) with 95% CI: $374-$1161.

Conclusion: This study shows that the PCV program is a highly cost effective intervention and justifies the introduction of PCV into routine immunisation schedule in some of the states and recommends introducing it throughout the country to reduce morbidity and mortality among the under-five children.

1. Introduction

Pneumococcal disease caused by *Streptococcus pneumoniae* (SP) is one of the major killers of under-five children worldwide with majority of the deaths occurring in Sub-Saharan Africa and Asia [1]. It causes variety of common conditions such as otitis media, pneumonia, sinusitis and meningitis. India is one of the high burden countries for pneumococcal disease accounting for approximately 20% of the pneumonia related deaths in the under-five age group globally. In 2010, pneumonia caused by SP accounted for about 16% of all the severe forms of pneumonia cases and 30% of all cause pneumonia related deaths in India [2].

World Health Organization has recommended the introduction of pneumococcal conjugate vaccine (PCV) in the childhood immunisation programme of all the countries in the world. It protects the children from severe forms of infections like pneumonia, septicaemia and meningitis as well as non-severe form of pneumonia, otitis media and non-pneumonia non-meningitis (NPNM) infections [3]. The vaccine introduction is expected to reduce the number of outpatient visits and hospitalization rates of under-five children leading to significant reduction in the economic burden of healthcare system of the country.

Various types of PCV vaccine are available for prevention of SP like PCV 7, PCV 10, PCV 13 and PPSV 23. In India, PCV 13 (Prenvar® manufactured by Pfizer) has been introduced into the universal immunization programme (UIP) under the childhood immunisation schedule in a phased manner from 2017 [2]. This vaccine is provided at 6 and 14 weeks followed by booster dose at 9 months.

* Corresponding author.
E-mail address: nayanapnair.chinnu@gmail.com (N.P. Nair).

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In the first phase, it was introduced in Himachal Pradesh and in some districts of Bihar and Uttar Pradesh. During second phase, it has been planned to scale up in the remaining districts of Bihar and Uttar Pradesh and in a few other states including Rajasthan and Madhya Pradesh [2]. With PCV 13 being the costliest vaccine provided under UIP, this decision by Government of India is expected to cause an additional economic burden on the country. Even though previous studies report the vaccine effectiveness in reducing mortality among under-five children, information on cost effectiveness of the vaccine in a low and middle income setting is limited [4–6].

Pfizer has decided to provide the vaccine at a subsidized rate of $7 per dose for low middle income countries like India till 2025 [7]. In addition, Government of India has partnership with Global Alliance for Vaccines and Immunizations (GAVI) for providing financial support in the implementation of PCV program till 2021. This further reduces the cost of vaccine to $3.30 per dose [8]. However, there is a need to generate evidence on the status of vaccination program in India without any external support as it may be the scenario in the future and see whether the intervention is still cost effective. We have adopted a decision support model called UNIVAC, developed by Pan American Health Organization, Provac Initiative and GAVI HiB initiative for economic evaluation of interventions especially for low and middle income countries [9]. Using this model, the current study assesses the impact and cost effectiveness of introduction of PCV vaccination program at national level by comparing with no vaccination program among under-five children.

2. Materials and methods

This study is done to assess the cost effectiveness of pneumococcal conjugate vaccine (PCV) which is being implemented throughout India in a phased manner into the Universal Immunization Programme. The vaccines provided under the universal immunisation programme in India are described in Table 1 [10]. PCV vaccine is provided at 6 weeks and 14 weeks (alongside pentavalent vaccine 1st and 3rd dose) followed by booster dose at 9 months (alongside measles vaccine) as per the manufacturer recommendation. We evaluated the cost effectiveness of implementation of PCV 13 vaccination program at national level by comparing with no vaccination program for a period of 10 birth cohorts from 2018 to 2027. Disease event rates and costs of treatment are estimated for the first five years of life. Future costs and health related benefits are discounted at an annual rate of 3%, as recommended by WHO [11]. Results are examined through government perspective only by including direct medical care costs like cost of vaccination programme, outpatient care and hospitalization costs. All the monetary units are adjusted to 2017 US dollars at the exchange rate of INR 67.809 using the Internal Revenue Service yearly average currency exchange rates [12].

Primary outcome of our study is the discounted cost required for averting one disability adjusted life year (DALY) as it represents the weighted combination of morbidity and mortality effects of the intervention. Other outcomes assessed are the incremental cost of the vaccine program, number of cases and deaths averted, outpatient visits and hospitalizations prevented, and the total cost of treatment reduced.

3. Decision support model

The UNIVAC (version 1.3.07) decision support model is used for evaluating the cost effectiveness of PCV vaccination program in India. It is a Microsoft Excel spreadsheet software developed by Pan American Health Organization (PAHO) Provac initiative, PATH and Centre for Disease Control and Prevention (CDC). This model was designed for low and middle income countries to calculate the Incremental Cost Effectiveness Ratio (ICER) and other relevant indicators for three vaccines, namely, Haemophilus Influenza B (HiB), Rotavirus vaccine (RVV) and PCV [9].

Fig. 1 describes the decision support model used in our paper for understanding the various associated health states and transitions while the assumptions and transition probabilities required in the model are listed in the Table 2. This is a deterministic static cohort model giving the conservative estimates of impact of the newer vaccines.

4. Disease burden (incidence, severity and mortality)

We obtained the burden of otitis media in India from a previously published systematic review conducted among 90 developing countries which provided country specific estimates including India. We found that 35% of the total otitis media infection is caused by *Streptococcus pneumoniae* giving final disease rate to be 3220 cases per 1,00,000 children in five year group per year [13]. With respect to streptococcus pneumonia, we obtained data based on systematic review by Rudan et al (2013) which provides global and country level estimates for non-severe, severe and deaths due to pneumonia for the year 2011–12 [14]. Burden of non-severe, severe and deaths due to streptococcus pneumonia was 1353 cases, 581·6 cases and 99.98 deaths per 1,00,000 under five children per year respectively [14].

Owing to the absence of national level estimates for streptococcal meningitis and NPNM, the systematic review by O'Brien et al. was used as reference [15]. Incidence of meningitis was reported to be 13 per 1,00,000 under five children per year with the case fatality rate of 57% providing the mortality estimate to be 7 per 1,00,000 under five children per year. Age specific rates per 1,00,000 under five children per year due to non-severe and severe form of Streptococcus NPNM was 67 cases and 6 cases respectively. Mortality due to severe NPNM was 3 deaths per 1,00,000 under five children per year. As per WHO position paper for PCV vaccine,

Table 1
Vaccines that are provided under the universal immunisation programme in India.

Type of vaccine	No of doses	Time of each dose from birth	Dosage (in ml)	Route of administration
Bacillus Calmette–Guérin (BCG)	1	At birth	0.1	Intradermal
Hepatitis B	1	At birth	0.5	Intramuscular
Oral Polio Vaccine (OPV)	4 primary + 1 booster	At birth, 6, 10 and 14 weeks + 16–24 months	2 drops	Oral
Pentavalent (Diphtheria + Pertussis + Tetanus + Hepatitis B + Haemophilus influenza B)	3 primary	At 6, 10 and 14 weeks	0.5	Intramuscular
DPT (Diphtheria Pertussis Tetanus)	1 booster	16–24 months	0.5	Intramuscular
Measles	1 primary + 1 booster	9 months + 16–24 months	0.5	Sub-cutaneous
Japanese encephalitis (JE) (in selected endemic districts only)	1 primary + 1 booster	9 months + 16–24 months	0.5	Sub-cutaneous
Rotavirus Vaccine (RVV) (in selected states only	3 primary	At 6, 10 and 14 weeks	5 drops	Oral

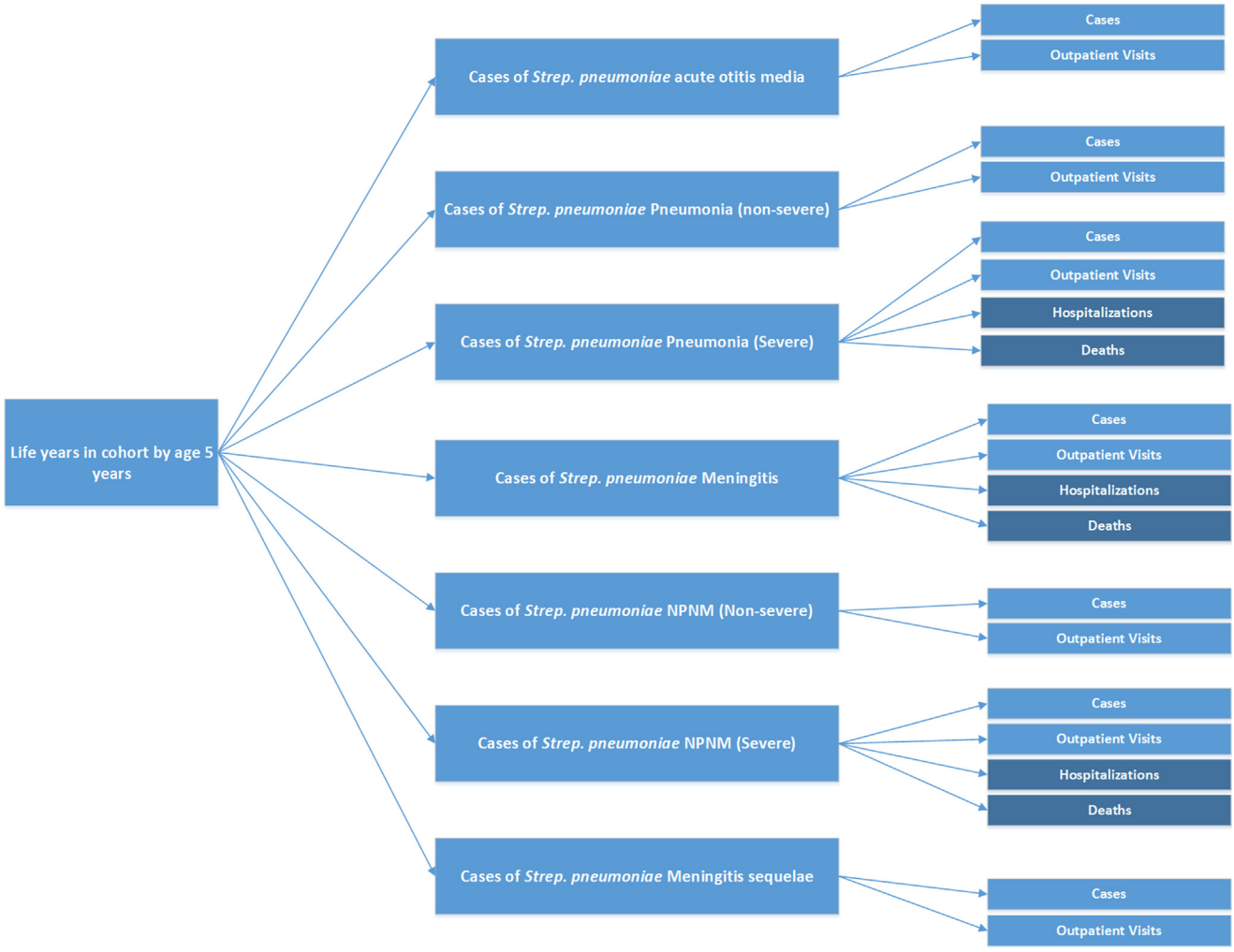

Fig. 1. Decision analysis model.

it was reported that 58% of surviving under-five children with meningitis will develop sequelae [16]. We used this to estimate the burden of meningitis related sequelae to be 2·1 cases per 1,00,000 under five children per year.

5. DALY estimates

Disability weights were provided for all the forms of diseases due to streptococcus pneumonia in a study done by Salomon et al (2015) on the disability weights for global burden of diseases [17]. Least disability weights were provided for otitis media (0·013) followed by non-severe form of NPNM (0·05) and non-severe form of pneumonia (0·051). Highest disability weights were provided for meningitis sequelae (0·26) followed by severe pneumonia (0·133), severe NPNM and meningitis (0·13).

6. Vaccination coverage and efficacy

Since the PCV vaccine is administered along with pentavalent vaccine 1st and 3rd dose and booster dose provided alongside measles vaccine, we have used the nationwide immunisation coverage data obtained from the WHO UNICEF estimates (2017) for India [18]. However, since there will be a transition phase initially for acceptability of newer vaccine, we have used the coverage estimate of inactivated polio vaccine (IPV) for PCV 1st dose during the initial years of its introduction and then transitioned to the current pentavalent vaccine coverage rate [18]. Similarly, for PCV 2nd dose, coverage estimate of pentavalent vaccine during the initial years of introduction followed by the current estimate was used [18]. Since there was similar coverage estimates provided for pentavalent 3rd dose and measles vaccine, same estimates were used for PCV 3rd dose. The coverage after transition (about 2 years) was reported as 91% for pentavalent 1st dose and 88% for both pentavalent 3rd dose and measles vaccine [18].

Vaccine efficacy for the first dose, second dose and booster dose was obtained from a systematic review on prevention of vaccine type pneumococcal disease by PCV conducted by Lucero MG et al (2009) [19]. Search strategy adopted in this systematic review was the inclusion of Randomized controlled trials comparing PCV with placebo or other vaccine in the databases such as Cochrane Central Register of Controlled Trials (CENTRAL), MEDLINE and EMBASE. Six trials with more than 1,00,000 participants were included in the review. The trials were conducted in both high and low income settings. The quality of evidence was reported to be high. Meta-analysis was performed and calculated the possible absolute effect in areas with low, medium or high baseline rates for the relevant outcomes. It has been reported that there was no potential bias in the review as per Cochrane risk of bias tool. The vaccine efficacy was reported to be 29% after first dose and 58% after second dose and booster dose. The duration of efficacy was assumed to be long lasting in the model.

Table 2
Base case parameters input in the model.

Input parameter	Value	Source
Incidence, Mortality and Health care utilization		
Streptococcus otitis media		
Incidence rate <5 years (per 1,00,000)	3220	Systematic review by DeAntonio et al
Outpatient visits <5 years (per 1,00,000)	2479	Assumption
Streptococcus pneumonia (non-severe form)		
Incidence rate <5 years (per 1,00,000)	1353	Systematic review by Rudan et al (2013)
Outpatient visits <5 years (per 1,00,000)	1042	WHO UHC service coverage index report for India
Streptococcus pneumonia (severe form)		
Incidence rate <5 years (per 1,00,000)	581·6	Systematic review by Rudan et al (2013)
Outpatient visits <5 years (per 1,00,000)	448	WHO UHC service coverage index report for India
Hospitalizations <5 years (per 1,00,000)	448	WHO UHC service coverage index report for India
Deaths <5 years (per 1,00,000)	99·98	Systematic review by Rudan et al (2013)
Streptococcus meningitis		
Incidence rate <5 years (per 1,00,000)	13	Systematic review by O'Brien et al
Outpatient visits <5 years (per 1,00,000)	13	Assumption
Hospitalizations <5 years (per 1,00,000)	13	Assumption
Deaths <5 years (per 1,00,000)	7	Systematic review by O'Brien et al
Sequelae cases <5 years (per 1,00,000)	2·1	WHO position paper for PCV vaccine
Streptococcus NPNM (Non-severe)		
Incidence rate <5 years (per 1,00,000)	67	Systematic review by O'Brien et al
Outpatient visits <5 years (per 1,00,000)	52	Assumption
Streptococcus NPNM (Severe)		
Incidence rate <5 years (per 1,00,000)	6	Systematic review by O'Brien et al
Outpatient visits <5 years (per 1,00,000)	6	Assumption
Hospitalizations <5 years (per 1,00,000)	6	Assumption
Deaths <5 years (per 1,00,000)	3	Systematic review by O'Brien et al
Disability weights		
Streptococcus acute otitis media	0·013	Disability weights for Global Burden of Diseases 2013 by Salmon et al
Streptococcus pneumonia (non-severe)	0·051	
Streptococcus pneumonia (severe)	0·133	
Streptococcus meningitis	0·133	
Streptococcus NPNM (non-severe)	0·051	
Streptococcus NPNM (severe form)	0·133	
Streptococcus meningitis sequelae	0·260	
Vaccine coverage and efficacy		
PCV 1st dose coverage (along with pentavalent-1) after transition phase	91%	WHO UNICEF estimates (2017) for India
PCV 2nd dose coverage (along with pentavalent-3) after transition phase	88%	WHO UNICEF estimates (2017) for India
PCV Booster dose coverage (along with measles vaccine) after transition phase	88%	WHO UNICEF estimates (2017) for India
PCV efficacy 1st dose	29%	Assumption (half of full efficacy)
PCV efficacy 2nd dose	58%	Systematic review by Lucero et al (2009)
PCV efficacy booster dose	58%	Systematic review by Lucero et al (2009)
Vaccine programme and health system costs incurred		
Vaccine price per dose (2018–2021)	$3·30	Multi-year strategic plan 2013–17 for Universal immunisation program
Vaccine price per dose (2022–2025)	$7·00	UNICEF Supply division Vaccine price data for PCV
Vaccine price per dose (after 2025)	$15·68	PAHO revolving fund, UNICEF supply division
Syringe price per dose	$0·03	Chatterjee et al (2016)
Vaccine and syringe wastage	5%	Assumption
Incremental health system costs per dose	$0·74	Multi-year strategic plan 2013–17 for Universal immunisation program
Health system costs incurred for outpatient visits for all the forms of diseases	$2	Prinja et al (2016)
Health system costs incurred for hospitalizations for all the forms of diseases	$10	Prinja et al (2016)

7. Vaccination programme costs

Data on vaccine price and delivery costs was obtained from Multi-year strategic plan 2013–17 for Universal immunisation program released by Ministry of Health and Family Welfare (MoHFW) [20]. The vaccine price per dose was $3·30 till 2021 and $7·00 till 2025 and $15·68 after the end of partnership with GAVI and subsidization by Pfizer. We found the syringe price per dose to be $0·03 and percentage wastage for both PCV vaccine and syringes to be 5% [21]. Incremental health system costs per dose based on personnel, transportation, cold chain equipment, maintenance, training, social mobilization, advocacy, communication activities, disease surveillance and program management activities for introduction of PCV vaccine into the routine immunisation programme was also estimated and found to be $0·74 per dose and fixed at the same rate for the 10 year cohort [20]. The time horizon was set at 10 years because we expect the vaccine to be implemented completely throughout the nation.

8. Healthcare utilization

Care seeking behaviour (outpatient visits) for suspected pneumonia was obtained from the universal health coverage (UHC) service index indicators reported by WHO for India [22]. It was found that 77% of under-five children with suspected pneumonia have been brought to any health care facility. We used the same proportion for outpatient visits of otitis media and non-severe form of NPNM while all the cases of meningitis and severe form of pneumonia and NPNM were assumed to be hospitalized.

9. Costs of outpatient visits and hospitalization

Cost of outpatient visits at primary health care level and hospitalization at secondary health care level from government perspective was obtained from an economic study conducted by Prinja et al (2016) which reported the costs incurred by government at different levels of health care [23]. The costs incurred for outpatient visit was reported to be $2·00 and hospitalization to be $10·00. We assumed the same cost irrespective of the type of illness due to *Streptococcus pneumoniae*.

10. Uncertainty analysis

10.1. Scenario analysis and probabilistic sensitivity analysis

After running the model for best case estimates for each of the inputs, we ran an additional uncertainty analysis to account for the uncertainty in the model inputs and assumptions. Parameters in which uncertainty considered were mortality, disease event rates, vaccine efficacy and coverage projections, system and health care costs. Plausible range of uncertainty provided in the model is ±10% of the base case estimates for most of the parameters. Analysis is run with the most and least conservative estimates. In addition to the scenario analysis, Probabilistic Sensitivity Analysis (PSA) is done. It is a technique used to quantify the level of confidence in the output captured in the analysis, in relation to the uncertainty level in model inputs. This provides more reliable estimates and act as a powerful tool for policy decisions and discussions.

Probability of PCV intervention to be cost effective at a willingness to pay (WTP) threshold equal to per capita gross domestic product (GDP) is calculated using the government perspective. We simulated the parameters using Monte Carlo model for 1000 iterations. All the parameters in the model are assumed to have beta distribution except for the cost which is assumed to have gamma distribution. Median is computed along with the 2·5th and 97·5th percentile to estimate 95% CI.

11. Results

11.1. Base case scenario

We are presenting the cost effectiveness results of PCV vaccination program through discounted ICER. Calculation of outcome is done by dividing the net cost required for introduction of PCV vaccine program by incremental health benefits obtained through the implementation of program. We found that the discounted cost required for averting one DALY to be $467 (INR 31,666) from the government perspective. This makes the vaccination program highly cost effective intervention in India relative to the per capita gross domestic product (GDP) threshold of $1939·6 (INR 1,31,522) [24]. Table 3 shows the vaccine impact and cost effectiveness discounted at 3% for the 10 year cohort (2018–2027).

Table 3
PCV vaccine impact and cost-effectiveness aggregate estimates over the period of 2018–2027.

Parameters	Results
Vaccine impact, undiscounted	
Total cases averted	2,51,34,220
Total visits averted	1,93,73,106
Total hospitalizations averted	22,38,862
Total lives saved	4,07,708
Cost effectiveness, discounted at 3%	
Vaccine programme costs	$4,79,13,39,140
Health care costs averted	$5,16,83,454
DALYs averted	$1,01,59,402
Incremental cost effectiveness ratio (ICER)	$467

11.2. PCV vaccine impact

PCV vaccine has nearly 40% impact on reduction of disease burden, outpatient visits, hospitalization and mortality. Between 2018 and 2027, introduction of PCV vaccination program in India is estimated to reduce more than 25 million cases, 19 million outpatient visits, 2·2 million hospitalizations, prevention of more than 10·1 million DALYs and averts about 4·07 lakh deaths. Annual reduction in cases and deaths due to pneumococcal infection is found to be 2·9 million and more than 40,000 following full implementation of PCV vaccine in the country. Annual reduction in undiscounted DALYs after introduction of PCV vaccine is found to be 2·8 million DALYs and discounted DALYs averted is 9·2 lakhs.

11.3. PCV vaccine program costs

After discounting at 3% per year, the estimated vaccination programme costs for the period of 2018–2017 is approximately around $4791 million. The incremental health system cost required for introduction of PCV vaccine would be approximately $46 million per year. After discounting at 3% per year, incremental health system cost would be $35 million for implementation of program.

11.4. Healthcare costs averted by PCV vaccine

The total healthcare cost averted over the period of 2018–2027 would be $51·6 million from the government perspective after discounting at a rate of 3% per year. Costs averted for outpatient visits during the period of program would be $32·7 million while costs averted for hospitalization would be around $18·9 million.

11.5. Uncertainty analysis

Table 4 shows the results obtained through scenario analysis and probabilistic sensitivity analysis to account for the uncertainties in the estimates.

11.5.1. Scenario analysis

We conducted scenario analysis by keeping the scenarios favourable and unfavourable to the vaccine program with respect to disease events, vaccination and costs. A change of 10% in each parameter is assumed for most of the variables, while predetermined confidence interval for some of the model parameters is used for scenario analysis. For vaccine price in unfavourable scenario, we assumed the cost of PCV per dose without partnership of GAVI and subsidization by Pfizer as the cost for full 10-year cohort. We found that the discounted final cost required in averting per DALY for scenario favourable to vaccine to be $238 (INR

Table 4
Scenario and probabilistic sensitivity analysis outputs.

Parameter	Results
Scenario analysis	
Base case scenario	$467 (INR 31,666)
Unfavourable to vaccine	$2323 (INR 1,57,520)
Favourable to vaccine	$238 (INR 16,138)
Probabilistic sensitivity analysis	
Median ICER	$649 (INR 44,008)
Lower 95%	$374 (INR 25,360)
Upper 95%	$1161 (INR 78,726)

16,138) and unfavourable to vaccine to be $2323 (INR 1,57,520). This shows that the cost obtained for averting one DALY even for scenario unfavourable to the vaccine is cost effective when compared to three times GDP per capita for India.

11.5.2. Probabilistic sensitivity analysis

We conducted probabilistic sensitivity analysis and ran 1000 iterations using the Monte Carlo model. Parameters such as vaccine coverage, efficacy, disease burden and costs were included in the PSA to account for uncertainties. All the parameters in the model are assumed to have beta distribution except for the cost which is assumed to have gamma distribution. Fig. 2 shows the simulations done for probabilistic sensitivity analysis. The points in the scatter plot shows that after consideration of all the uncertainties in analysis, major concentration of simulated results lie within the first quadrant of cost-effectiveness plane. This implies that PCV intervention has additional health benefits at an additional cost. The results of probabilistic sensitivity analysis used for plotting the cost effectiveness acceptability curve are shown in Fig. 3. The median ICER is found to be $649 (INR 44,008) with 95% CI: $374-$1161. Thus, by accounting for all kinds of uncertainties in the analysis, PCV intervention is found to be highly cost effective even with 100th percentile of ICER $1694 (INR 1,14,868) at WTP threshold of GDP per capita of India $1939·6 (INR 1,31,522) in 2017.

12. Discussion

We undertook this economic evaluation to study the costs and consequences of implementation of PCV program when compared to status quo. This study provides a unique platform using available data to estimate cost effectiveness of a vaccine and can be adapted for newer vaccine introductions. We used UNIVAC model to explore the implications of various plausible scenarios in the implementation of PCV vaccination program. We reported the findings from only government perspective.

Introduction of PCV vaccination program in India is estimated to reduce more than 25 million cases, 19 million outpatient visits, 2·2 million hospitalizations, prevention of more than 10·1 million DALYs and averts about 4·07 lakh deaths. The per capita GDP threshold of India used in our study was $1939·6 (INR 1,31,522) in 2017 [24]. We found that the introduction of PCV vaccination program can cost an additional $467 (INR 31,666) for averting per DALY. WHO commission for macroeconomics on health has recommended that an intervention can be considered cost effective if the cost required per DALY is less than three times the country's per capita GDP and highly cost effective if it is less than one per capita GDP [25,26]. As per this recommendation, introduction of PCV will be a highly cost effective intervention for India.

In spite of ample clinical evidence, there will be some amount of unavoidable and inherent uncertainty in a diverse population like India. We conducted uncertainty analysis by scenario and probabilistic sensitivity analysis to account for this diversity. In scenario analysis, we explored the effect of adding wide range of unfavourable and favourable assumptions in the input parameters of the model. Even with the most unfavourable scenario for PCV vaccine in terms of disease rates, vaccine properties and health system costs, cost per DALY averted was found to be $2323 (INR 1,57,520) which is still a cost effective intervention in India. Even though the WHO thresholds have been debated widely, the fact that the most unfavourable scenario is well within the range of three times GDP per capita suggests that the PCV vaccine would be of greater value for the Indian Government. Probabilistic sensitivity analysis found the ICER for PCV to be $649 (INR 44,008) with 95% CI: $374-$1161.

Recently published work by Megiddo et al (2018) has also found similar major results that the PCV13 is a cost-effective intervention with recommendation for inclusion in India's Universal Immunization Programme. Healthcare cost averted $48.7 million and number of deaths averted 34,800 per year was also found to be similar to the current study finding. However, previous work also captured the serotype diversity using Simpson Index which was not done in the current study [27].

Estimates were also available for number of individual child health interventions in India. On comparison with the cost effectiveness of other individual vaccine interventions in India, PCV

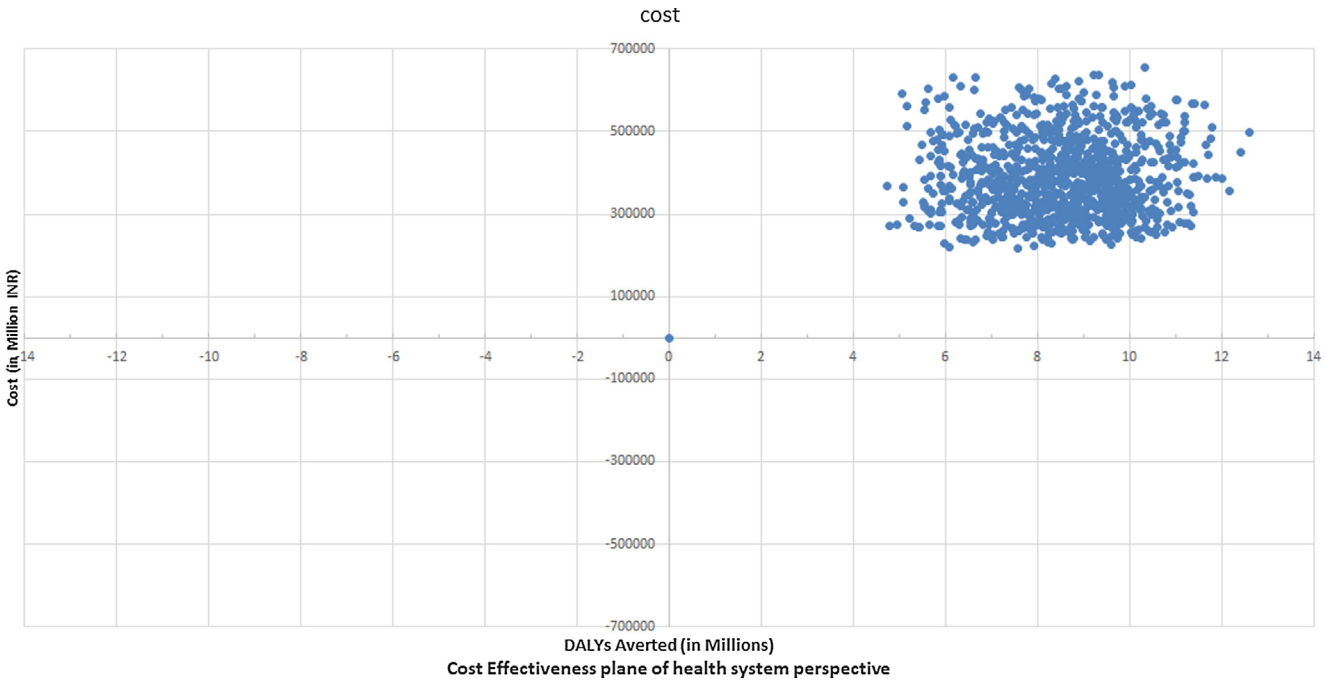

Fig. 2. Cost effectiveness plane of health system perspective.

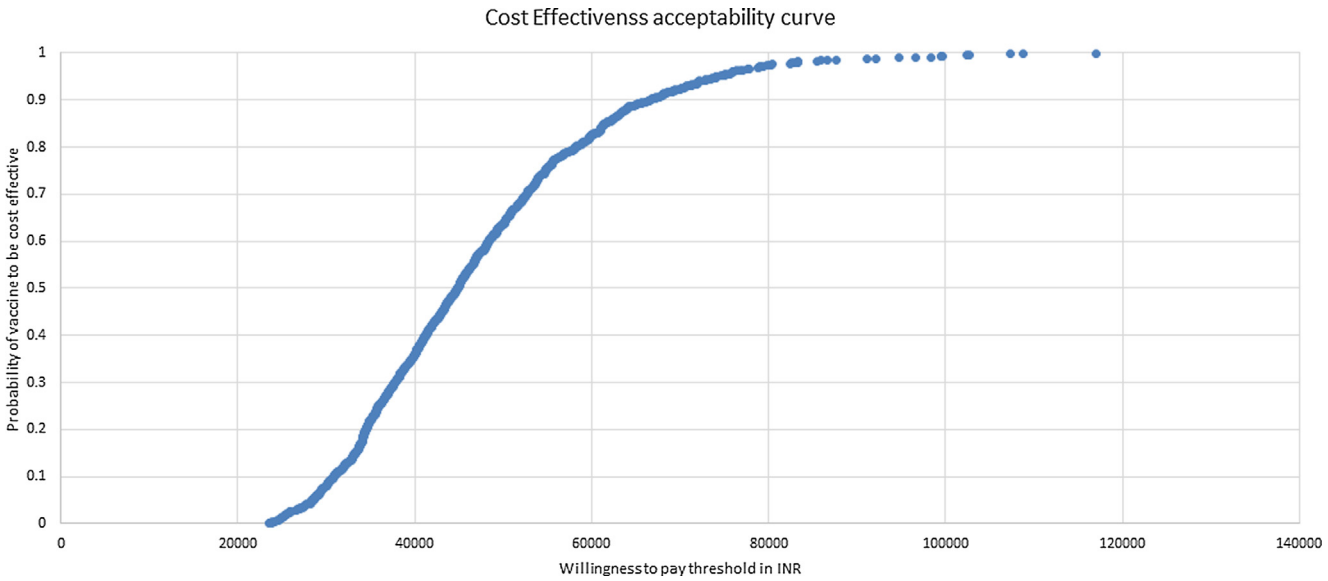

Fig. 3. Cost effectiveness acceptability curve.

($229) is less cost effective when compared to HPV vaccination ($1·1), measles ($13·8), Hepatitis B ($31), rotavirus vaccination ($139), typhoid vaccine ($227–621) and haemophilus influenza B ($363) but more cost effective than cholera vaccine ($595–1310) [28–31].

Total vaccination programme cost for the Government of India in introduction of PCV program nationwide would be approximately around $4791 million for a period of 10 years (2018–2027). However, current spending on vaccines by the government is far less accounting for only 2% of national health budget [32]. After the end of partnership with GAVI and subsidization of rate by Pfizer, the amount need to be spent on vaccines will be manifold compared to the current expenditure. Hence, Government of India need to increase the level of expenditure on vaccination programmes as any interruption in PCV programme after full scale implementation can cause public outcry.

We have attempted to study the impact and cost effectiveness of nationwide implementation of PCV program in India using a unique model called UNIVAC. Use of this model for conducting the analysis will help to increase the transparency of the procedure and make the policymakers understand the economic evaluation process better when compared to other "black box" models which are difficult to understand. Analysis was also done to account for the uncertainty involved in the estimates by doing comprehensive scenario and probabilistic sensitivity analysis. This makes the results obtained in our study more reliable and provides robust estimates which will contribute towards evidence based decision making for the MoHFW.

Our study has certain limitations. Since, the model used in our study is a static cohort model, the indirect effects among unvaccinated children like herd immunity or serotype replacement cannot be taken into account. There was lack of nationally representative Indian data for some of the input parameters. Hence, some of our estimates in the model are uncertain. We have tried to overcome this limitation by using certain internationally validated estimates in the model which were also tested by doing uncertainty analysis. Our model cannot capture the wide heterogeneity that exists in the large population of India.

Available evidences have indicated that the common risk factors of pneumonia to be low birth weight, malnutrition, non-exclusive breast feeding for the first six months, overcrowding and indoor air pollution. Interventions targeting most of these risk factors can be effective only if it is provided long term as they are related to socioeconomic factors like poverty and social-cultural factors.

Thus, currently PCV seems to be the only public health tool that has the capacity to reduce the burden of pneumococcal related diseases in developing countries including India at a cost that easily satisfies the cost effectiveness criteria and justifies its inclusion in the National Immunization Program. Nonetheless, it is important to continue the surveillance activities studying the impact of PCV vaccine as the introduction is being scaled up. Further analyses need to be done to compare vaccination with other less expensive interventions to make certain that the most cost effective solutions do not go unexplored.

13. Conclusion

This study shows that the PCV program is a highly cost effective intervention and justifies the introduction of PCV into routine immunisation schedule in some of the states and recommends introducing it throughout the country to reduce morbidity and mortality among the under-five children. This study is the first step towards finding the cost effectiveness of PCV and further primary data should be collected and analysed to provide conclusive evidence on its impact.

Conflict of interest

None declared.

Funding

Nil.

Ethical approval

Not required.

Appendix A. Supplementary material

Supplementary data to this article can be found online at https://doi.org/10.1016/j.vaccine.2018.12.004.

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