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Original Research Article

A health benefit and cost-effectiveness analysis of pneumococcal conjugate vaccination program in Nigeria

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ABSTRACT

Background: Nigeria ranks third just behind India and China in the global disease burden of pneumococcal disease. The current sustainability approach for an affordable pneumococcal conjugate vaccine (PCV) for the national immunization program from 2014 till 2025 involves a cost sharing plan funded with a 75% financial support from GAVI and a subsidy from Pfizer pharmaceuticals. There is a strong need to generate evidence on the cost-effectiveness of the national PCV program in Nigeria from 2014-2025 and beyond 2025.
Methods: The following parameters (demography, disease burden, health services utilization and costs, vaccination coverage, vaccine efficacy, and vaccination costs) were used in a static cohort model to estimate the total cost, health and economic benefit, and cost-effectiveness of the implementation of PCV vaccination program, compared with no PCV vaccination among under-five children in Nigeria from 2014-2025 and from 2026-2033. A sensitivity analysis was conducted to evaluate the robustness of the data used.
Results: The national PCV vaccination program would have an approximated 31.4% and 30% reduction of the total burden of pneumococcal diseases over the period of 2014-2025 and 2026-2033 respectively. One-way sensitivity analysis reveals vaccine efficacy as most sensitive parameter followed by disease incidence rate and treatment cost. Removal and addition of DTP3 and 3+1 (measles vaccine) dose respectively resulted to a similar ICER from both.
Conclusions: The estimated ICER suggests that the national PCV program in Nigeria will be cost-effective post 2025 era. In addition, it is recommended for policy-makers adoption considering the budget and equity impact of the intervention in Nigeria.

Keywords: Cost-effectiveness analysis, Economic evaluation, Health benefit, Pneumococcal conjugate vaccine, Nigeria

INTRODUCTION

More than 60% of pneumonia deaths in Sub-Saharan Africa occur in children under five years, while about 86% of pneumonia deaths in the high-income region are among adults aged over 70 years.[1] Nigeria remains top, followed by the Democratic Republic of Congo, Ethiopia, Tanzania, South Africa and Kenya.[2] Pneumococcal diseases remain a public health concern in Nigeria. Nigeria accounts for the highest pneumonia disease

mortality in Sub-Saharan Africa (SSA) followed by the DR Congo, Ethiopia, Tanzania, South Africa and Kenya. More than 60% of pneumonia deaths in Sub-Saharan Africa occur in children under five years, while about 86% of pneumonia deaths in the high-income region are among adults aged over 70 years.[1] According to studies conducted in Nigeria, Kano state accounts for 60%, Enugu state accounts for 54.5% and Zaria state accounts for 50% of pneumococcal infections among all community-acquired pneumonia (CAP).[2,3] In Kano state, Nigeria pneumococcal account for 46.4% of CAP, meningitis, and bacteremia.[4] The emergence of antimicrobial resistance (AMR) have further contributed to the pneumococcal diseases burden.[5] Universal provision of antibiotics to children under-5 years could prevent an estimated mean of 445 000 deaths per year caused by CAP as antibiotics is effective for treatments.[6] However, inappropriate use of antibiotics can lead to the emergence and progression of antibiotic resistance, another serious public health threat.[7]

Mass vaccination is cost effective compared to antibiotics and indirectly decrease the AMR trend in the country. In Thailand's healthcare system, about $1.5 billion was estimated as the incremental medical cost due to antimicrobial resistance in the year 2010.[8] Whilst pneumococcal conjugate vaccines (PCVs) have evidently decreased the disease burden of *Streptococcus pneumonia*, PCV remains an unaffordable vaccine among LMICs. This negates the sustainability of the national PCV immunization programs. The PCV-13 introduction is proven to be cost-effective in the six regions of the United Nations.[9] The 71 GAVI-supported nations including Nigeria, India etc. account for 83% of PCV13-preventable deaths but has only 18% of the global vaccination costs.[9]

In 2014, the Nigerian government incorporated PCV into its National immunization schedule with support from Pfizer (worth of $7 per vaccine dose) and a 75% financial support on the total vaccination program cost from GAVI during a period of 2014-2025.[10-13] This further reduces the cost of vaccine to $3.30 per dose.[11] There is therefore a strong need to generate evidence on the cost-effectiveness of the national PCV program in Nigeria beyond 2025 (when rates are higher as a result of no subsidy from Pfizer) This paper is aimed to estimate the health benefits, budget impact, cost-effectiveness (ICER) of PCV vaccination comparing with no vaccination among under-five children in Nigeria from 2014-2025 and from 2026 to 2033.

METHODS

Description of analysis and model used

For the purpose of this paper, the UNIVAC (version 1.4, developed by a group of infectious disease modelers at the London School of Hygiene and Tropical Medicine) model was used to evaluate the cost effectiveness of pneumococcal conjugate vaccination program compared to no vaccination program in Nigeria over a period of twenty years (2014-2033). This model changes the input parameters over the years. The parameters (demography, disease burden, health services utilization and costs, vaccination coverage, vaccine efficacy, and vaccination costs) used are from published and grey literatures for PCV-13.[14]

Two main cost-effective analyses of PCV-13 vaccination program in Nigeria were evaluated in comparison with no vaccination program (for a period of 2014 - 2025; 2026 - 2033). A discount rate of 3% was applied for both future health outcomes and future costs based on WHO recommendations.[15-18] Monetary rates were estimated based on the year 2017 conversion rates of N305.25 naira to $1.[19,20]

The model estimated the number of (community) cases, deaths and sequelae due to *S.pneumoniae*, as well as associated costs in scenarios with and without vaccination.[14] These estimates were then used to calculate health impact/benefit (outpatient visit, inpatient admission/DALYs averted), economic impact (e.g., net costs, incremental program costs and treatment costs averted), cost-effectiveness (e.g., cost-per-death averted) and cost-utilities (e.g., cost-per-DALY averted). The results from each cohort were combined and used to report both the cumulative and annual health benefits and costs associated with each scenario.[14] Numbers of deaths and life expectancy (obtained from UNWPP yearly data) were used to calculate years of life lost (YLL).[21,22] While the disability rate for each disease states (Table 1) was multiplied by the prevalence of each disease. States cases were used to calculate years of life with disability (YLD). DALYs were estimated by adding YLL and YLD.[22] Net cost of vaccine introduction was obtained by subtracting health service cost avoided from the vaccine program cost.[14,23] The DALY averted was calculated by subtracting the DALY lost in the vaccinated cohort from the DALY lost in the unvaccinated cohort.[14,23] Finally, net cost of vaccine introduction was divided by total DALY averted to provide an incremental cost-effectiveness ratio (ICER) estimate from both governmental and societal cost perspectives in United States dollars (US$) per DALY averted.[14,23]

Demography and burden of disease used

The focus was on the following pneumococcal diseases: SP acute otitis media, SP pneumonia (severe), SP pneumonia (non-severe), SP meningitis, SP non-pneumonia / non-meningitis NPNM (severe), SP NPNM (non-severe), SP meningitis sequel as the demographic data used are number of live births per year, incidence rate, disability weights, mean duration of illness (in days), life expectancy at birth and mortality rate in children under-five age.

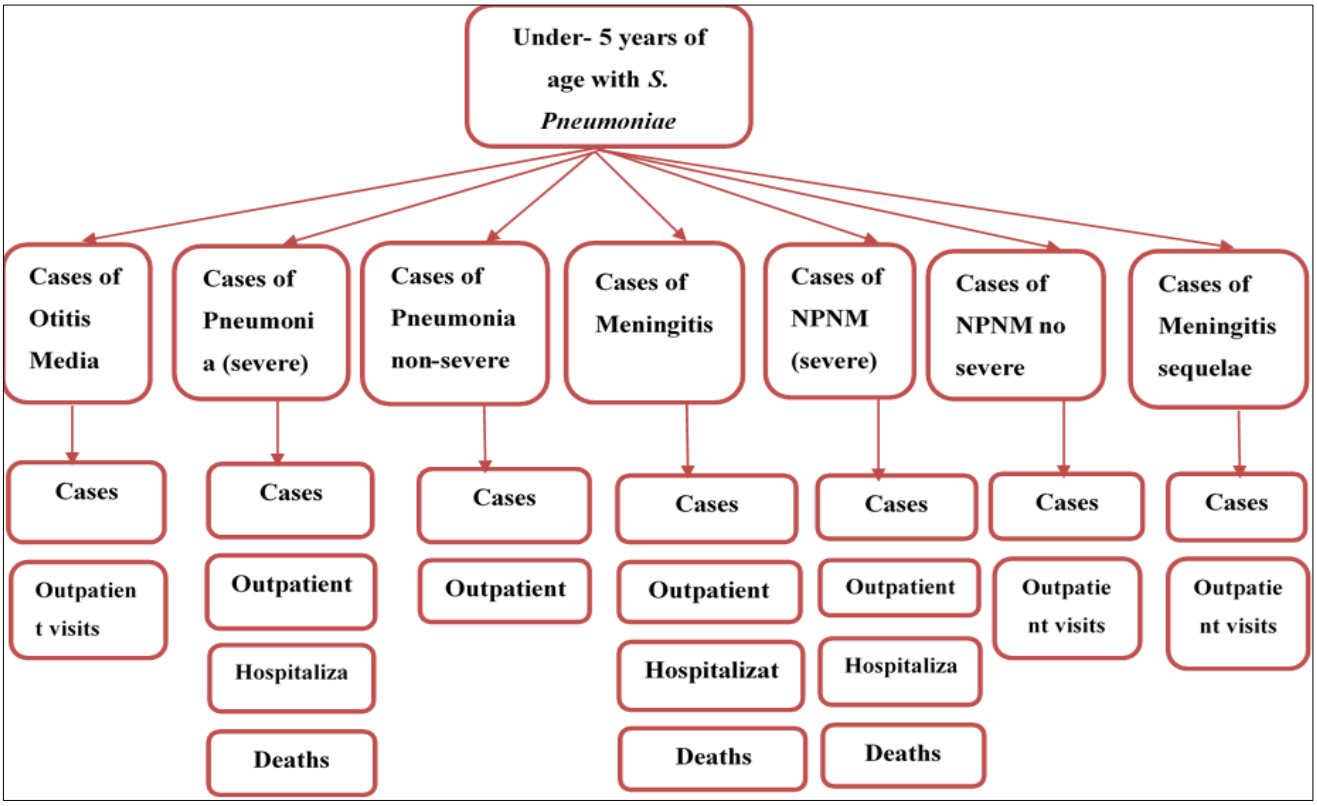

Figure 1: Schematic diagram for health states and outcomes of *S. pneumoniae* considered.

Table 1: Base case parameters input used in the model.

Input parameter	Estimated	Scenarios		Source
Incidence rate		**Low**	**High**	
***Streptococcus* otitis media**				
Incidence rate <5 years (per 1,00,000)	11555	11423	11688	(29)
Outpatient visits <5 years (per 1,00,000)	5801	5734	5867	(30)
Streptococcus pneumonia (non-severe form)				
Incidence rate <5 years (per 1,00,000)	1385	1293	1688	(31)
Outpatient visits <5 years (per 1,00,000)	695	649	847	(30)
Streptococcus pneumonia (severe form)				
Incidence rate <5 years (per 1,00,000)	860.34	644.56	981.30	(31)
Outpatient visits <5 years (per 1,00,000)	432	324	493	(30)
Hospitalizations <5 years (per 1,00,000)	431.89	323.57	492.61	(30)
Deaths <5 years (per 1,00,000)	145.07	102.87	151.19	(31)
***Streptococcus* meningitis**				
Incidence rate <5 years (per 1,00,000)	24.52057	8.598552	55.13146	(31)
Outpatient visits <5 years (per 1,00,000)	12.30933	4.316473	27.67599	(30)
Hospitalizations <5 years (per 1,00,000)	12.30933	4.316473	27.67599	(30)
Deaths <5 years (per 1,00,000)	17.30879	6.069619	38.91666	(31)
Sequelae cases <5 years (per 1,00,000)	2.502489	0.713159	7.312872	(32)
Sequelae visits <5 years (per 1,00,000)	1	0	4	(30)
***Streptococcus* NPNM (non-severe)**				
Incidence rate <5 years (per 1,00,000)	74.04231	25.96419	166.4749	(31)
Outpatient visits <5 years (per 1,00,000)	37.16924	13.03402	83.57042	(30)
***Streptococcus* NPNM (severe)**				
Incidence rate <5 years (per 1,00,000)	9.835202	3.448879	22.11323	(31)
Outpatient visits <5 years (per 1,00,000)	4.937272	1.731337	11.10084	(30)
Hospitalizations <5 years (per 1,00,000)	4.937272	1.731337	11.10084	(30)
Deaths <5 years (per 1,00,000)	5.441853	1.908277	12.23533	(31)

Continued.

Input parameter	Estimated	Scenarios		Source
Incidence rate		**Low**	**High**	
Disability weights				
Streptococcus acute otitis media	2.0%			(33)
Streptococcus pneumonia (non-severe)	4.0%			(33)
Streptococcus pneumonia (severe)	28.0%			(33)
Streptococcus meningitis	62%			(33)
Streptococcus NPNM (non-severe)	5%			(33)
Streptococcus NPNM (severe form)	28%			(33)
Streptococcus meningitis sequelae	24%			(33)
Mean duration of illness (in days)				
Streptococcus acute otitis media	7	6	9	Expert opinion
Streptococcus pneumonia (non-severe)	7	6	9	Expert opinion
Streptococcus pneumonia (severe)	10	7	21	Expert opinion
Streptococcus meningitis	10	7	21	Expert opinion
Streptococcus NPNM (non-severe)	7	6	9	Expert opinion
Streptococcus NPNM (severe form)	10	7	21	Expert opinion

Table 2: Input parameters for estimating health service utilization and costs.

Parameter	Estimate ($)	Scenarios ($)		Source/s
Government cost		**Low**	**High**	
Government cost per outpatient visit				
Streptococcus acute otitis media	50	25	75	
Streptococcus pneumonia (non-severe)	50	25	75	
Streptococcus pneumonia (severe)	50	25	75	
Streptococcus meningitis	50	25	75	
Streptococcus NPNM (non-severe)	50	25	75	
Streptococcus NPNM (severe form)	50	25	75	
Streptococcus meningitis sequelae	150	100	200	Expert opinion
Government cost per inpatient admission				
Streptococcus pneumonia (severe)	150	100	200	
Streptococcus meningitis	150	100	200	
Streptococcus NPNM (severe form)	150	100	200	
Household cost				
Household cost per outpatient visit				
Streptococcus acute otitis media	3.684	0.59	64.01	(34-38)
Streptococcus pneumonia (non-severe)	3.684	0.59	64.01	(34-38)
Streptococcus pneumonia (severe)	3.684	0.59	64.01	(34-38)
Streptococcus meningitis	3.684	0.59	64.01	(34-38)
Streptococcus NPNM (non-severe)	3.684	0.59	64.01	(34-38)
Streptococcus NPNM (severe form)	3.684	0.59	64.01	(34-38)
Streptococcus meningitis sequelae	3.684	0.59	64.01	(34-38)
Household cost per inpatients admission				
Streptococcus pneumonia (severe)	3.684	0.59	64.01	(34-38)
Streptococcus meningitis	3.684	0.59	64.01	(34-38)
Streptococcus NPNM (severe form)	3.684	0.59	64.01	(34-38)

All costs are presented in 2017 US $.

Table 3: Input parameters for estimating PCV vaccine coverage and timeliness.

Parameter	Estimate	Scenarios		Source/s
Vaccine coverage		**Low**	**High**	
Coverage of DTP1				
Year 2014	48.0%	45.5%	50.5%	(39)
Year 2015	55.0%	52.5%	57.5%	(39)
Year 2016-2033	70.0%	67.5%	72.5%	(39)

Continued.

Parameter	Estimate	Scenarios		Source/s
Coverage of DTP2				
Year 2014	48.0%	45.5%	50.5%	(39)
Year 2015	55.0%	52.5%	57.5%	(39)
Year 2016-2033	70.0%	67.5%	72.5%	(39)
Coverage of DTP3				
Year 2014	25.0%	21.3%	28.7%	(39)
Year 2015	36.0%	32.3%	39.7%	(39)
Year 2016-2033	57.0%	53.3%	60.7%	(39)
Vaccine efficacy				
Dose 1	29.0%	14.5%	37.5%	(40)
Dose 2	58.0%	29.0%	75.0%	(40)
Dose 3	58.0%	29.0%	75.0%	(40)
Vaccine efficacy duration for each dosage				
Parameter 1 (Mean in months)	10000.0	10000.0	10000.0	Expert opinion
Parameter 2 (alpha or shape)	100.0	100.0	100.0	Expert opinion
Vaccine dose price projection				
2014-2025	3.30	0.13	50.69	(41)
2026-2033	11.55	0.13	50.69	(41)

All costs are presented in 2017 US $.

Vaccine coverage, efficacy, and other impact assumptions

The vaccine coverage estimates used are 48.0% in 2014, 55.0% in 2015 and 70% in 2016 for DTP1 and DTP2, while PCV dose 3 covered 25% (survey estimate), 36% and 57% in 2014, 2015 and 2016 respectively.[24] There was no coverage information for 2017 upward, therefore 70% coverage was assumed for DTP1 and DTP2 and 57% for DTP3 from 2017 to 2033 (Table 3). Meanwhile lower and upper limit of 95% confidence interval for mid coverage value was used to estimate low and high scenario respectively. The assumed vaccine efficacy is 29% after first dose and 58% after second and third dose (Table 3).

Vaccination program cost

This study considered the total vaccination cost per dose as a summation of the vaccine price per dose, fixed price assumption for safety box/bag price per dose ($0.03), estimated (0%) wastage and also the incremental health system costs ($1) per dose (based on personnel, transportation, cold chain equipment, and other activities).[2,25-27] Considering the intervention of GAVI and the Pfizer to reduce the financial cost of PCV13 total program cost, the vaccine price per dose was reduced to $3.30 and will run for a period of twelve years, effective from 2014 to 2025.[11,13,28] However, UNICEF 2017 revealed that without Pfizer subsidy, the price per dose will increase from $3.30 to $7.[11] The projected calculated cost after year 2026 to year 2033 for PCV 13 is $11.55 and Gamma function of second kind was used to estimate low and high scenario (Table 3).

Scenario analysis

The base case cost-effectiveness result (ICER) was gotten with the mid-level estimate. However, we ran an additional (scenario) analysis to test for the robustness /and uncertainty of our major parameters: vaccine coverage, treatment (health service utilization) cost, vaccine efficacy, disease incidence rate, and vaccine schedule. One-way sensitivity analysis was carried out by changing these parameters one at a time. ICER for different scenarios of each parameter was noted across the periods. Two-way sensitivity analysis of vaccine cost per dose was done against treatment cost, vaccine efficacy and coverage. Probability sensitivity analysis was done to determine the uncertainty of the above listed parameter. The PSA was run 1000 times and the median ICER with 95% CI was recorded for each period.

RESULTS

Estimated reduction in the burden of pneumococcal disease

PCV-13 vaccination in Nigeria was estimated to prevent approximately 18 million discounted episodes of total pneumococcal illness, 9 million outpatients, 590,543 inpatients and 189,755 deaths over the period 2014–2025. While 14 million discounted episodes of total pneumococcal illness, 7 million outpatients, 453,075 inpatients and 108,177 deaths would be prevented over the period 2026–2033. In all, the vaccine would have an approximated 31.4% and 30% reduction of the total burden of pneumococcal diseases over the period of 2014-2025 and 2026-2033 respectively (Table 4).

Table 4: Estimated reduction in the burden of disease.

	2014-2025			2026-2033		
	No vaccine	**With vaccine**	**Averted**	**No vaccine**	**With vaccine**	**Averted**
Total cases <5 years	58,221,154	39,918,608	18,302,546	45,733,532.00	31,691,471.00	14,042,060.00
All-cause acute otitis media	48,356,023	33,154,704	15,201,319	37,984,333.00	26,321,593.00	11,662,740.00
Pneumococcal pneumonia (non-severe)	5,796,027	3,973,974	1,822,053	4,552,860.00	3,154,946.00	1,397,914.00
Pneumococcal pneumonia (severe)	3,600,400	2,468,569	1,131,831	2,828,165.00	1,959,803.00	868,361.90
Pneumococcal meningitis	104,621	71,732	32,889	82,181.60	56,948.49	25,233.10
Pneumococcal NPNM (non-severe)	309,679	212,328	97,352	243,257.50	168,567.50	74,689.98
Pneumococcal NPNM (severe)	41,849	28,693	13,156	32,872.64	22,779.40	10,093.24
Meningitis sequel	12,555	8,608	3,947	9,861.79	6,833.82	3,027.97
Total outpatient visits	29,222,857	20,036,287	9,186,569	22,954,963.00	15,906,853.00	7,048,110.00
All-cause acute otitis media	24,276,356	16,644,780	7,631,575	19,069,417.00	13,214,328.00	5,855,089.00
Pneumococcal pneumonia (non-severe)	2,908,476	1,994,160	914,316	2,284,648.00	1,583,168.00	701,480.30
Pneumococcal pneumonia (severe)	1,807,858	1,239,535	568,323	1,420,098.00	984,069.90	436,028.00
Pneumococcal meningitis	50,218	34,432	15,787	39,447.17	27,335.28	12,111.89
Pneumococcal NPNM (non-severe)	154,840	106,164	48,676	121,628.80	84,283.77	37,344.99
Pneumococcal NPNM (severe)	20,924	14,346	6,578	16,436.32	11,389.70	5,046.62
Meningitis sequel	4,185	2,869	1,316	3,287.26	2,277.94	1,009.32
Total inpatient admissions	1,878,540	1,287,998	590,543	1,475,620.00	1,022,544.00	453,075.50
Pneumococcal pneumonia cases	1,807,398	1,239,220	568,178	1,419,736.00	983,819.40	435,917.00
Pneumococcal meningitis	50,218	34,432	15,787	39,447.17	27,335.28	12,111.89
Pneumococcal NPNM	20,924	14,346	6,578	16,436.32	11,389.70	5,046.62
Total deaths <5 years	608,049	418,294	189,755	354,652.00	246,474.30	108,177.70
Pneumococcal pneumonia cases	527,980	363,212	164,768	307,951.00	214,018.30	93,932.72
Pneumococcal meningitis	61,871	42,563	19,308	36,087.18	25,079.69	11,007.49
Pneumococcal NPNM	18,197	12,519	5,679	10,613.88	7,376.38	3,237.50

Economic benefits

The total health cost reduction when under-five children are vaccinated with PCV13 from 2014-2025 is estimated to be about $455 million and $485 million from both government and societal perspective respectively. However, the cost reduction was about $420 million and $448 million from government and societal perspective respectively in 2026-2033 (Table 5).

Table 5: Economic benefits.

	2014-2025			2026-2033		
	No vaccine (status quo)	With vaccine	Averted	No vaccine (status quo)	With vaccine	Averted
Total gov. health service costs	1,462,329,869	1,007,174,453	455,155,417	1,369,419,860.79	948,952,087.65	420,467,773.15
Total outpatient visits costs	1,225,887,803	844,325,827	381,561,975	1,148,076,883.46	795,570,435.73	352,506,447.74
All-cause acute otitis media	1,213,817,776	832,239,015	381,578,760	953,470,866.28	660,716,406.25	292,754,460.03
Pneumococcal pneumonia (non-severe)	145,423,781	99,708,001	45,715,779	114,232,417.18	79,158,404.13	35,074,013.05
Pneumococcal pneumonia (severe)	90,392,911	61,976,772	28,416,139	71,004,898.16	49,203,497.24	21,801,400.92
Pneumococcal meningitis	2,510,914	1,721,577	789,337	1,972,358.28	1,366,763.81	605,594.47
Pneumococcal NPNM (non-severe)	7,741,985	5,308,195	2,433,789	6,081,438.04	4,214,188.42	1,867,249.62
Pneumococcal NPNM (severe)	1,046,214	717,323	328,890	821,815.95	569,484.92	252,331.03
Meningitis sequelae	627,728	430,394	197,334	493,089.57	341,690.95	151,398.62
Total inpatient admission costs	236,442,067	162,848,625	73,593,441	221,342,977.33	153,381,651.92	67,961,325.41
Pneumococcal pneumonia cases	271,109,684	185,882,972	8,522,671	212,960,454.63	147,572,905.72	65,387,548.91
Pneumococcal meningitis	7,532,742	5,164,731	2,368,011	5,917,074.85	4,100,291.44	1,816,783.41
Pneumococcal NPNM	3,138,642	2,151,971	986,671	2,465,447.85	1,708,454.77	756,993.09
Total societal health service costs	1,558,121,439	1,073,150,553	484,970,886	1,459,422,128.58	1,011,319,986.87	448,102,141.67
Total outpatient visit costs	1,316,005,422	906,394,015	409,611,408	1,232,642,967.68	854,171,281.57	378,471,686.11
All-cause acute otitis media	1,303,251,870	893,558,386	409,693,483	1,023,722,599.71	709,397,991.06	314,324,608.65
Pneumococcal pneumonia (non-severe)	156,138,605	107,054,487	49,084,118	122,649,061.68	84,990,795.34	37,658,266.34
Pneumococcal pneumonia (severe)	97,053,061	66,543,220	30,509,840	76,236,539.06	52,828,810.92	23,407,728.14
Pneumococcal meningitis	2,695,918	1,848,422	847,495	2,117,681.64	1,467,466.97	650,214.67
Pneumococcal NPNM (non-severe)	8,312,414	5,699,303	2,613,111	6,529,518.39	4,524,689.82	2,004,828.57
Pneumococcal NPNM (severe)	1,123,299	770,176	353,123	882,367.35	611,444.57	270,922.78
Meningitis sequelae	643,145	440,964	202,180	505,199.85	350,082.88	155,116.97
Total inpatient admission costs	242,116,017	166,756,538	75,359,479	226779160.9	157148705.3	69630455.56
Pneumococcal pneumonia cases	277,768,138	190,448,259	87,319,879	218190763.4	151197296.3	66993467.11
Pneumococcal meningitis	7,717,746	5,291,576	2,426,170	6062398.205	4200994.595	1861403.611
Pneumococcal NPNM	3,215,727	2,204,823	1,010,904	2525999.252	1750414.414	775584.8377

Costs are discounted at 3% per year and all costs are presented in 2017 US $.

Table 6: Base cost-effectiveness results.

	2014-2025		2026-2033	
	Government perspective	**Societal perspective**	**Government perspective**	**Societal perspective**
Summary of base-case cost				
Net cost of vaccine introduction	232,597,851	202,689,795	184,878,026	160,513,936
Costs of vaccine introduction	687,660,681	687,660,681	555,587,218	555,587,218
Health service costs avoided	455,062,830	484,970,886	370,709,192	395,073,282
Result for daly averted				
Dalys averted (extracted from model)	4,376,668	4,376,668	2697312.294	2697312.294
Base-case cost-effectiveness results				
US$ per Daly averted (extracted from model)	54	47	69	60
Cost-effectiveness threshold				
1 × GDP per capita (2017) - WHO threshold for 'highly cost-effective	1,968.56			
3 × GDP per capita (2017) - WHO threshold for 'cost-effective'	5, 905.68			

Costs and Dalys are discounted at 3% per year and all costs are presented in 2017 US $.

Table 7: ICER for scenario analysis results.

Parameters	**2014-2025**		**2026-2033**	
Scenario analysis	**Govt. perspective**	**Societal perspective**	**Govt. perspective**	**Societal perspective**
DTP1+DTP2 schedule	53	46	54	41
Low disease incidence	93	83	54	41
Low efficacy	210	203	54	41
Low treatment cost	102	95	54	41
Low vaccine coverage	52	45	54	41
Base case (most probable) scenario	54	47	69	60
High vaccine coverage	55	48	1426	1419
High treatment cost	4	2	1426	1419
High efficacy	17	11	1426	1419
High disease incidence rate	38	32	1426	1419
3+1 schedule (Including PCV-13 in the 3 doses of DTP and Measles dose schedule)	53	46	1426	1419
5% discount rate	77	68	1426	1419
Probabilistic sensitivity analysis				
Median ICER	443	446	446	443
Lower 95%	4	2	4	2
Upper 95%	875	875	875	875

Table 8: Two-way sensitivity analysis evaluating PCV dose price against vaccine efficacy, treatment cost and vaccine coverage.

Price per dose	**Low vaccine efficacy**	**High vaccine efficacy**	**Low treatment cost**	**High treatment cost**	**Low vaccine coverage**	**High vaccine coverage**
2026-2033	**Govt. (societal)**	**Govt. (societal)**	**Govt. (societal)**	**Govt. (societal)**	**Govt. (societal)**	**Govt. (societal)**
$0.13	Cost-saving	Cost-saving	Cost-saving	Cost-saving	Cost-saving	Cost-saving
$50.69	4886 (4877)	1809 (1800)	2468 (2459)	2338 (2329)	2355 (2345)	2403 (2394)

Costs and Dalys are discounted at 3% per year.

Base cost-effectiveness results

From the analysis conducted, it was observed that cost of vaccine introduction and DALY averted was the same for government and societal perspective. However, net cost of vaccine introduction was higher from government perspective compared to societal due to difference in health service cost avoided from both perspectives.

Moreover, it was found that the discounted cost required for averting one DALY to be US$ 54 (governmental perspective) and US$ 47 (societal perspective) in 2014-2025. Also, US$ 69 (governmental perspective) and US$ 60 (societal perspective) would be required to avert one DALY in 2026-2033 (Table 6).

Scenario analysis results

Higher ICER was deduced from governmental perspective compared to societal perspective because health care cost averted from societal was greater than that of governmental perspective. It was discovered that low vaccine efficacy had highest ICER, followed by treatment cost and disease incidence rate from both governmental and societal perspective. Moreover, ICER obtained in 2014-2025 was lower compared to 2026-2033. Which indicated that PCV13 was highly cost-effective from 2014-2025 compared to 2026-2033 (Table 7).

Two-way sensitivity analysis result

Increased vaccine price per dose ($50.69) resulted to a higher ICER compared to a vaccine price per of $0.13 in 2026-2033. In this period, ICER sharply increased to US $4886 per DALY averted (highest ICER) when the vaccine price per dose was US$50.69 with a low efficacy. Meanwhile, a low vaccine price per dose (with either low or high efficacy, treatment cost and coverage,) will avert more health care cost vaccine compared to the program cost. Therefore, ICER would be negative and it was stated as cost saving in the UNIVAC model. There was no two-way sensitivity analysis conducted for the period 2014-2025 as there is certainty for the price-per-dose during that period (Table 8).

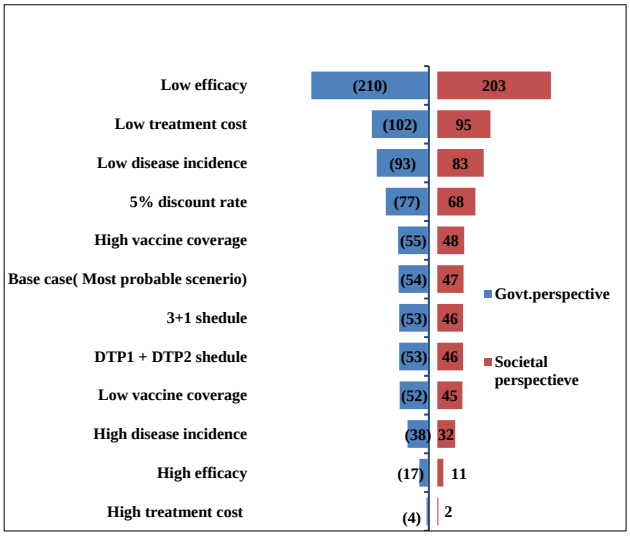

Figure 2: Tornado graph showing different discounted ICER estimates (US$ per Daly averted) comparing PCV-13 under-5 children vaccination with no vaccination in Nigeria from 2014-2025.

DISCUSSION

The study investigated the cost-effectiveness of the PCV-13 national vaccination from 2014 to 2025 and also 2026-2033, acknowledging the vaccine cost per dose from 2026 when there may be no more funding support from Pfizer and GAVI. The result showed that, based on the estimated health and economic benefits among under-five children in Nigeria, the ICER estimates within these periods (both with and without GAVI's support and Pfizer subsidy) is less than 1-3 times the country's GDP per capital (WHO CET) and also, less than the most recent proposed CET ($239 - $1545) for public health interventions in Nigeria.[41] Additionally, the study estimated that, the incremental net monetary benefit of the PCV-13 vaccination program in Nigeria will exceed zero from 2014 to 2025, and also 2026-2033.

Our study also showed that vaccine efficacy was the most sensitive parameter followed by disease incidence rate and treatment cost. Increase in ICER was influenced by low vaccine efficacy and ICER was very low when vaccine efficacy scenario was high. This confirms that high vaccine efficacy would make the immunization program more cost-effective, implying that if the vaccine is efficient, there would be low adverse effect following immunization and the uptake will increase, which will reduce disease incidence. Removal of DTP3 brought insignificant changes to ICER from both perspectives; but this could be as result of low coverage and high-dropout rates for DTP3 in Nigeria.[42]

Our findings are similar to other global cost-effectiveness estimates. A pooled African study which assessed the ICER of PCV13 introduction for 30 birth cohorts (2015 to 2045) up to age 5 years in 180 countries globally, show that PCV introduction throughout Africa requires only 12% of global PCV investments but accounts for 69% of the lives saved and 63% of the DALYs averted globally.[9] With few exceptions, our study also corroborates other national PCV-vaccination program CEA (UNIVAC-used) studies conducted in Croatia, India, Paraguay, Peru and Georgia respectively.[22,23,43-46] The only exception was the study done in Croatia which show PCV introduction is unlikely to be cost-effective. However, this difference could be as a result of the huge differences in the incidence rate of the pneumococcus diseases and consumption cost in these countries. Furthermore, this difference could have also resulted to the difference in the total vaccine program cost (India: $4,791,339,140, Peru: $455,484,409 and Nigeria: $1,951,782,730).[43,45]

Among all the CEA studies on PCV-13, India is likely to have the highest total vaccine program cost (for 10 years cohorts), excluding societal cost.[43] While Nigeria is estimated to have a very high total vaccine program cost. The main suggested reason for this comparison between India and Nigeria is the similarity in their GDP per capital estimates. Also, the two countries were amongst five countries with highest burden of pneumococcal diseases in the world.[2,31] A critical review of all these studies

suggests that the total PCV program cost will be high in countries with the highest burden of pneumococcal disease and not the GDP per capita of the country. The GAVI and Pfizer funded project has successfully supported the implementation of PCV-13 vaccination program in Nigeria. This study has further established the cost-effectiveness of the PCV-13 vaccination program in Nigeria, emphasizing the importance of adopting prevention over treatment strategies.

Beyond the ICER estimate which is suggesting that the national PCV program in Nigeria will be cost-effective, this study also suggest to policy-makers adopting this study's result to additionally consider the budget and equity impact of the national PCV program in Nigeria. Even though, evidence validates the submission of proposal by Nigerian government to GAVI for funding to support the introduction of PCV into Nigeria's immunization schedule, there is still a need for harmonization and regularization of all relevant stakeholders to be involved with the implementation of this proposal to enable the achievement of its full benefits.[12] Other wider health systems issues that needs to be addressed include availability of human resources for health (HRH) for scale-up, addressing equity issues in the PCV-13 (DTP -1, 2, 3) coverage in the country, strengthening the delivery system of the PCV-13 program including the safety of vaccines which will reduce the wastage of PCVs at the local level, incorporating PCV-13 vaccination program evaluation both at national and state level, increased funding and decentralization of the budgetary funding system.

A limitation of the UNIVAC model used is that it is not a dynamic model. This means that this study assumed that there was no change in the risk of pneumococcal infection in the susceptible(s). Passive population-based surveillance was used in this study which may have likely underestimated the pneumococcal disease burden arising from lower case detection, reporting or testing. Deaths due to pneumococcal may also have been underestimated because children may have died prior to collecting specimens for laboratory confirmation. There was no household cost for low and high scenarios, an estimated cost was used. Health cost from governmental perspective was also based on conservative assumptions alone which may likely cause it to be less cost-effective.

However, this herd immunity effect (as a result of changes in risk of pneumococcal infection from the PCV-13 vaccination) could have exaggerated the result of this study. Another limitation of the UNIVAC model is that it assumed a linear relationship between the size of the program and its effect. In another words, the cost-effectiveness ratio (CER) of this study was insensitive to the size of the PCV-13 vaccination program in Nigeria. Due to limited CEA studies done for Nigeria, we could not compare the estimated ICER with the cost-effective ICER of a set of existing vaccination programs for Nigeria as a fixed-price cut-off point representing the assumed social willingness to pay for an additional unit of health. Also, as vaccine cost per dose, healthcare cost and disease burden estimate in Nigeria are likely to be different from the present estimates in most African countries, our study is also limited in generalizability. We used fixed rates and figures for indices that are likely to vary with time (e.g. incidence rates and GDP) which may have over or underestimated some of the figures and conclusions. Percentage decrease in dose efficacy was based on conservative assumptions alone which could likely make cost to be less cost-effective. Vaccine efficacy was obtained from past experimental study, which may be accurate but outdated because the efficiency of the vaccine might have changed.[40] Recent clinical trial study on the efficiency of the vaccine would be better and give more reliable information. In addition, we assumed the vaccine efficacy for each of the disease states to be of equal estimate, which could have had a limitation in estimating the true ICER value for the analyses done.

CONCLUSION

This study shows that the PCV-13 vaccination of under-five children would reduce morbidity and mortality caused by pneumococcal diseases. The study results also indicated that PCV-13 vaccination would be cost-effective in a range of scenarios. This study has provided a platform towards finding the true efficacy and cost-effectiveness estimate of PCV-13 in Nigeria. Beyond the estimated ICER, health impact and monetary benefit, this study also suggest to policy-makers adopting this study's result to additionally consider the budget and equity impact of the PCV-13 vaccination in Nigeria.

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