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COST-EFFECTIVENESS ANALYSIS OF PNEUMOCOCCAL CONJUGATE VACCINE (PCV) AMONG CHILDREN UNDER FIVE YEARS IN GHANA

BY

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DECLARATION

I, Abdul-Mumin Ibrahim, declare that this study is a product of my independent thought under the guidance of Professor Justice Nonvignon. I further declare that specific references used in the work have been duly acknowledged. As far as I know, no part of this work wholly or partially, has been submitted somewhere for another certificate.

Abdul-Mumin Ibrahim Signature: ..... Date: 07.02.2023

(Student)

Professor Justice Nonvignon Signature: ..... Date:… 07.02.2023

(Supervisor)

DEDICATION

I dedicate this work to the mercy of Allah for sustaining me with a peaceful mind, sound health, divine protection and adequate provision to undertake this task.

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ABSTRACT

Background: Streptococcus pneumonia is responsible for 18% of infant deaths in Ghana. With co-financing from Gavi in 2012, Ghana introduced the PCV13 into the childhood immunisation programme to reduce the burden of Streptococcus pneumonia. However, Ghana graduated to the Gavi accelerated transition phase in 2021, which spans five years before the nation assume full responsibility of paying for the PCV13. This research aims to evaluate the health effects and cost-effectiveness of PCV13 immunisation in Ghana since its implementation and after the cessation of support from Gavi.

Methods: This study utilized the UNIVAC tool to evaluate two main scenarios of cost-effectiveness, from vaccine introduction (2012 – 2025) and after Gavi transition (2026 – 2031) in comparison with no vaccination. The sources of data include national data, international estimates and expert opinion. Cost was considered from the perspectives of both the government and society. Health outcomes were discounted at three percent and currency values were stated in US Dollars with 2022 Cedis equivalence. The robustness of the base case results was tested by performing sensitivity analysis.

Results: PCV13 will reduce the pneumococcal disease burden by 48% from 2012 to 2031. The vaccination programme costs are USD 130 million and USD 275 million in 2012 – 2025 and 2026 – 2031 respectively. The incremental cost-effectiveness ratios are USD 89 and USD 73 from the perspectives of government and society respectively in 2012 – 2025. The incremental cost-effectiveness ratios are USD 530 and USD 510 respectively from the perspectives of government and society in 2026 – 2031.

Conclusion: The PCV13 vaccination programme in Ghana is highly cost-effective under any cost-effectiveness threshold even when Ghana does not benefit from Gavi co-financing from 2026 onwards.

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LIST OF ABBREVIATIONS

AMC	Advance Market Commitment
CBA	Cost-benefit Analysis
CEA	Cost-effectiveness Analysis
CR	Credible Range
CUA	Cost-utility Analysis
DALYs	Disability-Adjusted Life Years
DE	Direct Effects
DHS	Demographic and Health Survey
DPs	Development Partners
DTP	diphtheria/tetanus/pertussis
EPI	Expanded Programme on Immunisation
GBD	Global Burden of Disease
GDP	Gross Domestic Product
GHS	Ghana Health Service
HiB	Haemophilus Influenza B
HTA	Health Technology Assessment
ICER	Incremental Cost-effectiveness Ratio
IPD	Invasive Pneumococcal Disease

LMIC	Low and Middle Income Country
LYG	Life Years Gained
MDAs	Ministries, Departments and Agencies
MICS	Multiple Indicator Cluster Survey
MMDAs	Metropolitan, Municipal and District Assemblies
MOH	Ministry of Health
NITAG	National Immunisation Technical Advisory Group
NPNM	Non-pneumonia Non-meningitis
ODA	Official Development Assistance
PCV	Pneumococcal Conjugate Vaccine
PSA	Probabilistic Sensitivity Analysis
QALYs	Quality-Adjusted Life Years
RVV	Rotavirus Vaccine
SSA	Sub-Sahara African
UNICEF	United Nations Children's Fund
UNWPP	United Nations World Population Prospects
USD	United States Dollars
VPD	Vaccine Preventable Disease
WHO	World Health Organization

WHO-CHOICE	World Health Organization's Choosing Interventions Cost-effective
YLD	Years of Life with Disability
YLLs	Years of Life Lost

CHAPTER ONE

INTRODUCTION

1.1 Background

There has been a significant decline in the global burden of Streptococcus pneumoniae following the introduction of the pneumococcal conjugate vaccine (PCV) in many countries (Chen et al., 2019). In Africa, pneumococcal deaths have fallen by 63% from 447,000 to 166,000 between 2000 and 2015. This can be attributed primarily to the introduction of PCV in childhood immunisation programmes (Pecenka et al., 2021). The vaccine gives immunity to children from Streptococcus pneumonia and its associated conditions (WHO, 2019). Apart from giving direct immunity to vaccinated children, PCV also provides herd immunity to unvaccinated individuals. PCV is therefore an effective method for preventing pneumococcal disease in children (Lucero et al., 2009).

For the first time in 2007, the World Health Organisation (WHO) recommended PCV to be included in childhood immunisation programmes worldwide to prevent pneumococcal disease. Consequently, PCV immunisation has been implemented in more than 140 countries globally (Whitney, 2017; Knoll et al., 2021). Many high-income countries have therefore adopted the PCV vaccine to immunize children under five years. Through the Advance Market Commitment (AMC), Gavi, the Vaccine Alliance has supported many African countries to introduce PCV where the price per dose is reduced (Bloomberg, 2016). Based on the co-financing policy of Gavi, countries initially pay USD 0.20 per dose whereas GAVI pays the remaining amount (Pecenka et al, 2021).

As the GDP per capita of countries increase, they move from self-financing phase to preparatory transition, accelerated transition and finally to the fully self-financing phase.

Countries pay a higher proportion of the full AMC price upon graduating to each stage. They eventually pay the full price for the PCV when they reach the fully self-financing stage. Countries that get co-financing support from Gavi are however confronted with how to sustain PCV immunisation programmes after Gavi exits (Pecenka et al., 2021).

1.2 Problem Statement

Pneumococcal disease is the leading global cause of mortality from contagious diseases in children under five years (WHO, 2019). An estimated 920,000 children under than five years died from pneumonia in 2015 (Knoll et al., 2021). Africa and Asia are reported to have the highest burden of invasive pneumococcal disease (IPD) (Wahl et al., 2018). Pneumonia is responsible for 18% of deaths in children under 5 years in Ghana (Abbey et al., 2018). Annual pneumonia and meningitis cases are estimated to be 6,441 and 286 respectively in Northern Ghana alone. The pneumococcal disease has a substantial economic burden on families in Ghana estimated at USD 777 per case (Kobayashi et al., 2021).

To reduce the burden of the pneumococcal disease in children under five years, Ghana introduced the PCV13 into the infant immunisation programme in 2012. However, the country is faced with substantial reduction in official development assistance (ODA) as a result of attaining a lower middle income country (LMIC) status back in 2010. Consequently, financial support from development partners fell by 30% between 2011 and 2013. The proportion of health aid from the Netherlands which hitherto was 40% has significantly declined to as low as one percent in recent times (Nonvignon et al., 2018).

The withdrawal of development partner support adversely affects a country's health system in terms of service delivery, health technologies and finance. This becomes more problematic in situations where financial and technical assistance are simultaneously withdrawn as Ghana is currently experiencing (Mao et al., 2021).

A cross-programmatic efficiency analysis undertaken by the WHO in 2017 revealed that Ghana had defaulted on two occasions regarding co-financing commitments to Gavi. Ghana also moved to the Gavi accelerated transition phase in 2021 which will span a period of five years before getting to fully self-financing phase. The implication of this analysis is that Ghana might fully finance the childhood vaccines programme from 2026 onwards (WHO, 2017). This comes at a time Ghana is facing economic challenges coupled with limited fiscal space for health financing.

1.3 Research Questions

a) What are the health effects of PCV vaccination in Ghana?
b) What are the incremental costs of PCV vaccination in Ghana?
c) Is PCV vaccination in Ghana cost-effective?

1.4 Research Objectives

1.4.1 General Objective

To assess the cost-effectiveness of PCV by comparing with a scenario of no vaccination among children under five years in Ghana from introduction through implementation (2012 – 2025) and six years after the exit of Gavi (2026 – 2031).

1.4.2 Specific Objectives

a) To assess the health effects of PCV vaccination in Ghana
b) To estimate the incremental costs of PCV vaccination in Ghana
c) To assess the cost-effectiveness of PCV vaccination in Ghana

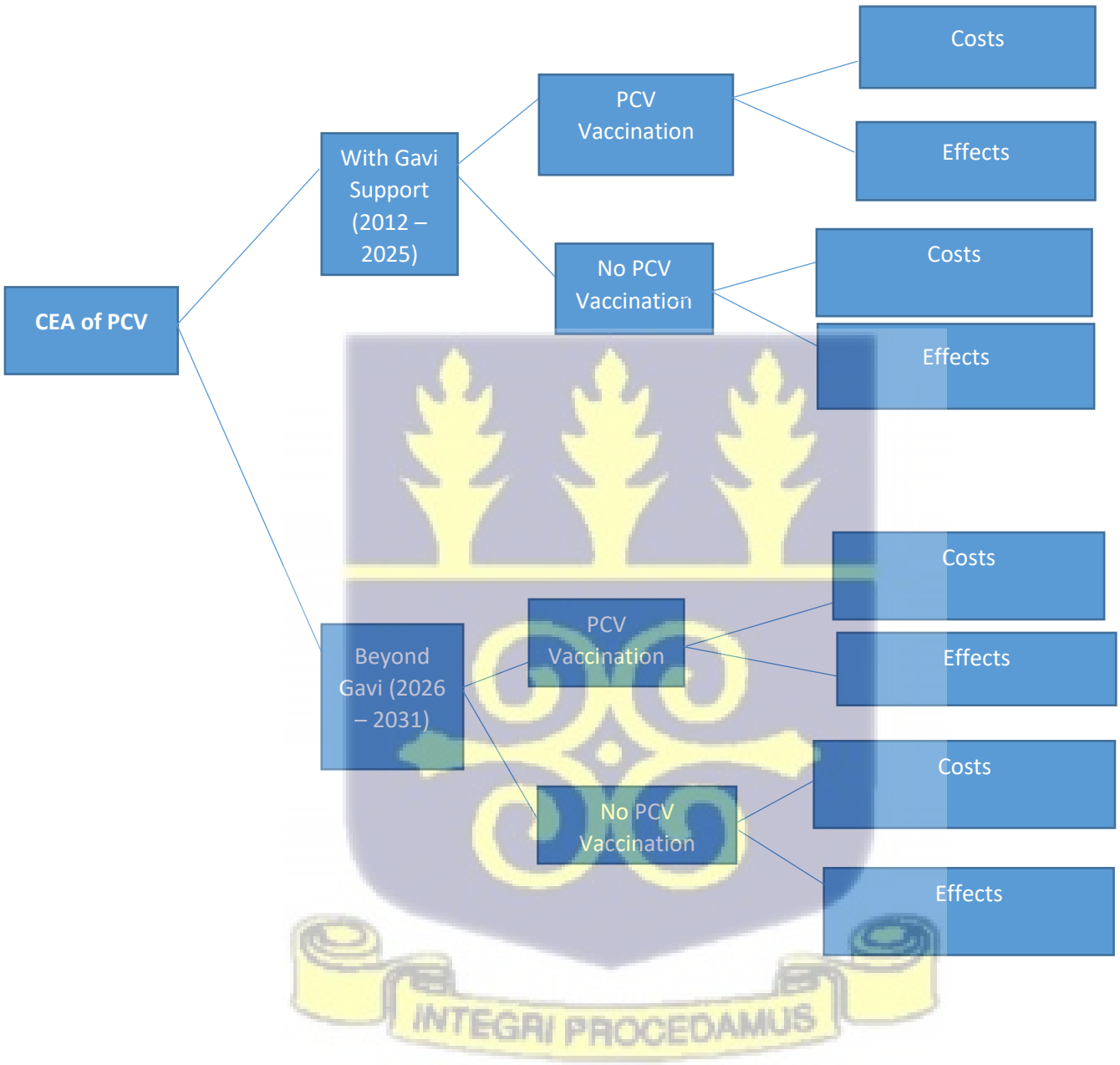
1.5 Conceptual Framework of Cost-Effectiveness of PCV Vaccination

Figure 1 illustrates the conceptual framework for this study. The framework compares two periods of PCV immunisation of children below five years in Ghana. The first period examines

the current PCV immunisation programme from introduction (2012 to 2025) with a hypothetical scenario of "No PCV immunisation." The second period compares PCV immunisation beyond the Gavi transition (2026 to 2031) with a scenario of "No immunisation" in Ghana within the same period of time.

The health effects and costs of vaccination are estimated under two scenarios. In the first scenario, cost-effectiveness is analyzed based on only the price per dose Ghana pays during the 14 years of Gavi co-financing support. The second scenario assesses cost-effectiveness according to the full cost Ghana may incur to continue with PCV immunisation six years without Gavi co-financing support. The analysis considers cost from the perspectives of both government and the society. The second scenario really gives a clearer picture of cost-effectiveness as the price per dose will dramatically increase when support from Gavi discontinues.

Figure 2: Conceptual Framework of Cost-effectiveness of PCV Vaccination



CHAPTER TWO

LITERATURE REVIEW

2.1 Introduction

This chapter discusses the incidence of pneumococcal disease and pneumococcal conjugate vaccines (PCVs). It also examines the role of economic evaluation, especially, cost-effectiveness of healthcare interventions in general. It finally highlights cost-effectiveness studies of PCVs in some middle-income and lower middle-income countries (LMICs) with particular emphasis on African countries.

2.2 Epidemiology of Pneumococcal Disease

Streptococcus pneumoniae is the causative agent which regularly inhabits the human nasopharynx and is spread primarily through respiratory droplets. The main reservoir of this organism are infants and young children. Streptococcus pneumoniae has more than 90 known serotypes (WHO, 2019).

Prior to the introduction of PCVs in the different WHO regions, six to eleven serotypes accounted for at least 70% of all invasive pneumococcal disease (IPD) in children under five years (Rudan et al., 2013). Most ailments occur at uneven intervals. Nursing homes, child-care centres and other closed institutions are places where outbreaks of pneumococcal diseases occur. The African “meningitis belt” records large outbreaks of meningitis caused by serotype 1 (Kobayashi et al., 2021).

In 2015, pneumococcal infections caused 294,000 out of 5.83 million deaths among children under five years of age in in the world (Wahl et al., 2018). Developing countries in Africa and Asia record higher rates of disease and mortality than high income countries (WHO, 2019).

Since 2006, the reported mean annual incidence of IPD in children under two 2 years before the widespread introduction of PCVs into national vaccination programmes was 44.4 per 100,000 in Europe and 167 per 100,000 in the United States of America (Isaacman et al., 2008). In contrast, the annual incidence of IPD in children under two years in Africa ranged from 60 per 100,000 in South Africa to 797 per 100,000 in Mozambique (WHO, 2019).

Although disparities in the sensitivity of case ascertainment and surveillance could partly be responsible for differences in the reported incidence, nevertheless, Africa largely recorded higher incidence than Europe or North America. Asia and Latin America however report incidence rates range between these extremes (Knoll et al., 2021).

2.3 Pneumococcal Conjugate Vaccines

The incidence of pneumococcal meningitis has been considerably reduced with the introduction of PCVs (Knoll et al., 2021). During the period 1980 and 2007, a systematic review and meta-analysis of data on IPD serotypes from children under five years showed that the serotypes in PCV10 and PCV13 cover at least 70% of IPD in each geographical region (Rudan et al., 2013).

The WHO has licensed PCV10 and PCV13 for active immunisation for the prevention of Streptococcus pneumoniae in infants and children aged from 6 weeks to 5 years albeit with differences in details of labeling with respect to the various countries (WHO, 2019). The manufacturers of PCV10 and PCV13 recommend three primary doses at an interval of at least four weeks, plus a booster dose at least six months after the third dose. The first dose can be given as early as six weeks of age whilst the booster dose is given preferably between 9 and 15 months of age. Alternatively, two primary doses can be administered two months separately, starting at two months of age. This is followed by a booster dose at least six months after the second dose for PCV10 and at 11 to 15 months of age for PCV13 (WHO, 2019).

The increase in the number of serotypes in PCVs signifies substantial improvement in combating Streptococcus pneumoniae in LMICs. This therefore guarantees the safety and effectiveness of currently available PCVs (WHO, 2019). It is based on this evidence that the WHO has recommended for PCVs to be included in global infant vaccination programmes.

2.4 Economic Evaluation in Healthcare

A perennial economic problem facing the world is the scarcity of resources. This is the reason policy-makers in the health sector are often confronted with decisions on how to allocate resources to competing healthcare needs. Economic evaluation is becoming an essential element in resource allocation for the health sector. To optimize the use of scarce resources, economic evaluation is used as a tool to allocate resources in healthcare (Drummond et al., 2008).

Various interventions are systematically compared in relation to their costs and effects in economic evaluation. As a result, an assessment is carried out on both the inputs and outputs of the pertinent alternative interventions. Cost is mostly measured in monetary value in various economic evaluations. There are however variations in how the health impact of an intervention are measured (Drummond et al., 2008).

The health impact of an intervention are converted into monetary units in cost-benefit analysis (CBA). Natural units such as deaths averted and life-years gained are used to measure health effects in cost-effectiveness analysis (CEA). Health effects are measured using combined changes in the quality and quantity of life known as Quality-Adjusted Life Years (QALYs) gained in cost-utility analysis (CUA). The most credible measure for evaluating the effectiveness of healthcare interventions is the number of QALYs gained (Drummond et al., 2008). The use of QALYs as a measure of effectiveness is however limited in developing countries due to poor quality of data. In this case, disability-adjusted life years (DALYs)

averted are employed in many economic evaluations in the developing world (Pecenka et al., 2021).

2.5 Cost-Effectiveness Analysis in Healthcare

Cost-effectiveness analysis (CEA) is an important mechanism for determining priorities and the allocation of scarce resources in healthcare (Drummond et al., 2008). Policy-makers use CEA as a tool to assess competing priorities in the allocation of limited resources. A fundamental concern in CEA is whether an intervention offers the optimal health gains relative to its costs to allow for its adoption. Information on CEA can be used together with clinical information to aid in healthcare policy-making (Woods et al., 2016).

Cost-effectiveness is important in the health policy space as it gives a quantitative measure of the overall efficiency of the health system. It could be used by policy-makers as a tool to prioritise and to allocate resources in a manner that obtains better health outcomes for the population and to give the best value for money as one of the primary objectives in health planning (Bertram et al., 2021). Cost-effectiveness analysis could also be used as evidence to support the inclusion of additional interventions in a health benefit package (Griffiths et al., 2022). Thus, cost-effectiveness analysis will guarantee efficient use of limited resources in the health budget to achieve the greatest health gain for the population (Bertram et al., 2021).

Case studies from many countries have supported the use of information on cost-effectiveness together with clinical data in healthcare decision-making. On the other hand, factors such as political convenience, social preferences and systemic obstacles to implementation adversely affect the use of CEA in the prioritization of healthcare interventions in many countries (Hutubessy et al., 2003). To make CEA assessments across regions more meaningful, costs are presented in US Dollars. DALYs averted are used to measure effectiveness and the primary

outcome measure of cost-effectiveness is the cost per DALY averted. DALYs simplify population-level improvement as a fraction of the current burden of disease.

For an intervention to be considered cost-effective, the WHO uses the following threshold: if the cost per DALY averted by an intervention is less than the GDP per capita of the country under discussion, it is considered highly cost effective. Even if the cost per DALY averted by an intervention is less than three times the GDP per capita of the country, it is still considered cost effective. However, if the cost per DALY averted by an intervention is greater than three times the GDP per capita of the country, then it is not cost-effective (Hutubessy et al., 2003).

Hutubessy et al (2003) identified serious weaknesses in economic evaluation of health interventions such as limited data, discrepancies in various methods of economic evaluations and the lack of generalizability and transferability of results to locations other than the original research. To address these limitations, the authors have outlined methods in which analysts can conduct CEA based on country-specific information on cost and burden of disease using the World Health Organization's Choosing Interventions that are Cost-Effective (WHO-CHOICE) project. The WHO-CHOICE has gained popularity in many economic evaluations and in policy dialogues in countries such as Argentina, Ethiopia and Estonia for the past two decades (Hutubessy et al., 2003).

2.6 Tools for Cost-Effectiveness Analysis of PCV

Chaiyakunapruk et al (2011) analytically assessed three cost-effectiveness modelling tools namely, TRIVAC (upgraded to UNIVAC), PneumoADIP and GlaxoSmithKline's SUPREMES based on the guidelines for conducting economic evaluations in infant vaccination programmes as spelt out by the WHO. Nationwide introduction of PCV was compared with no PCV vaccination in the models.

In spite of the differences in the features, configuration and data requirements, similar range of diseases were captured by the models. Each model uses different methods to estimate herd effects. It was observed that vaccine efficacy, vaccine price, burden of disease, serotype coverage and vaccine coverage were the most influential parameters in the models. It was also seen that the TRIVAC and PneumoADIP tools produced similar health outcomes, incremental costs and incremental cost-effectiveness ratios when cohort modelling was done with a homogenous set of input parameters (Chaiyakunapruk et al., 2011).

Chaiyakunapruk et al (2011) noted that the variances in the models were as a result of the methodology, data requirements and subtle differences in the absence of user-friendly manuals. However, users can easily interpret research results using the UNIVAC tool because of its comprehensible functions.

2.7 Cost-effectiveness Analysis of PCV in Low and Middle Income Countries

There is a general understanding of the medical and scientific benefits of vaccines. According to many researches that have been reviewed, vaccination strategies in low and middle-income countries are generally cost-saving, cost-effective or both cost-saving and highly cost-effective based on various assumptions. On the other hand, a strong investment case has not been made on the economic benefits of vaccination programmes in LMICs (Njau & Cairns, 2016).

Njau & Cairns (2016) undertook a systematic review to assess the narrow and broad economic benefits of vaccines in low and middle income countries. Out of 177 studies reviewed, 86% dealt with the direct effects and herd protection of vaccines whilst 18% considered broader economic benefits of vaccination programmes. Some related factors include willingness to pay, productivity gains arising from vaccination outcomes and cost savings made as a result of vaccine-preventable diseases (VPD) being averted.

In recent times, policy-makers are gradually combining information on clinical effectiveness with cost-effectiveness analysis when new vaccines are included in infant immunisation programmes (Nakamura et al., 2011). However, factors such as product choice, serotype prevalence and vaccination coverage in the country have a significant influence on the cost-effectiveness of the vaccine in question (WHO, 2019).

Some cost-effectiveness studies have been criticized for giving so much preference to economic benefits of vaccination programmes. Another criticism is the difficulty in making cross-country comparisons as a result of wide variations in methodology and underlying assumptions (Njau & Cairns, 2016).

Owing to the high prices of PCVs, it is difficult to introduce them in some countries. Even in other settings that they have been introduced, their sustainability is being threatened by limited budgets for healthcare. This is mostly the case in countries that are steadily moving to the Gavi self-financing phase where they would need to bear the full cost of PCV vaccination (Chen et al., 2019).

The sustainability of national immunisation programmes of PCV largely depends on the health benefits, cost-effectiveness and budget impacts in those countries. This information is also important for countries that are yet to introduce PCV into their childhood vaccination (Chen et al., 2019). Several factors such as vaccine efficacy, disease burden, vaccine price, delivery costs, herd protection, vaccination coverage and schedule determine the cost-effectiveness of PCV (Chaiyakunapruk et al., 2011).

Meanwhile, there still exist a significant number of countries where the cost-effectiveness of PCV has not been thoroughly assessed and in a manner that is universally acceptable (Saokaew et al., 2016; Wu et al., 2015). The prevailing gap in this area is that research in cost-effectiveness of PCVs exists in only a few number of countries. Another problem is that current

studies fail to address such issues as indirect effects of PCV vaccination and serotype replacement, among others (Nakamura et al., 2011).

Chen et al (2019) attempted to address this knowledge gap by conducting a global cost-effectiveness analysis of PCV immunisation. They used post-vaccination data from 180 countries that have introduced PCV and also accounted for regional epidemiology of pneumococcal disease. An ecological model was used to forecast a range of clinical presentations whilst a decision tree model was used to evaluate the economic outcomes of considering a strategy of PCV vaccination and a scenario of no PCV vaccination. These two models were integrated to obtain the incremental cost-effectiveness ratio of PCV immunisation.

Chen et al estimated that global PCV vaccination could avert 400,000 deaths and about 55 million annual cases of pneumococcal diseases. Over USD 3 billion and USD 2.6 billion savings respectively from the health system and society could be offset with USD 15.5 billion global cost of vaccines. With 83% of vaccine-preventable deaths in the world, annual global PCV vaccination cost in 71 countries is USD 16 billion accounting for 18% of total vaccination costs. This makes PCV immunisation likely cost-effective in all the six UN regions (Chen et al., 2019).

In a similar approach, Nakamura et al (2011) estimated the cost-effectiveness of introducing PCV vaccination in 72 poor countries eligible for Gavi support. An incidence-based approach was used to construct decision-analytic models which evaluated a three-dose immunisation schedule of children under five years for 10 birth cohorts. A no vaccination scenario was compared to each of PCV7, PCV10 and PCV13 vaccination. The results showed that 294,000 to 603,000 annual pneumococcal deaths could be averted with PCV immunisation. Also, 9.3 million to 17.6 million DALYs could be averted on an annual basis with PCV vaccination. It

is noteworthy that 91% of the DALYs averted is as a result of direct effects of PCV immunisation in children under five years.

Out of the 72 Gavi-eligible countries, PCV is highly cost-effective in 69 of them based on the cost-effectiveness thresholds of the WHO. This finding remained robust when assumptions on disease burden and vaccine efficacy were varied in the sensitivity analyses. The cost-effectiveness analysis therefore support the introduction and sustainability of PCV immunisation in Gavi-eligible countries as a result of its potential to prevent significant number of deaths at fairly low costs (Nakamura et al., 2011).

From the perspectives of government and public health providers, Sibak et al (2015) used the TRIVAC model to evaluate the cost-effectiveness of PCV13 in the Egyptian national vaccination programme. Compared to a scenario of no PCV immunisation, the cost per DALY averted was estimated to be USD 3,916 from the perspective of government. The PCV vaccination programme was estimated to incur a total incremental cost of over USD 1 billion. With 10 cohorts evaluated, Sibak et al (2015) estimated that over 8,000 deaths would be averted by the PCV immunisation programme. The PCV immunisation programme in Egypt is considered as a high impact intervention. Its implementation would give good value for money whilst reducing the burden of pneumonia and child mortality as enunciated in the resolution of the National Immunisation Technical Group (NITAG) of Egypt. Alongside the results of the cost-effectiveness analysis is the recommendation to strengthen surveillance activities in order to generate national level data that is of high quality, use evidence-based analysis to introduce other vaccines in the future and monitor the impact of the interventions (Sibak et al., 2015).

From the perspectives of government and society, Ezoji et al (2019) estimated over 18 million children in Iran would be affected by the pneumococcal disease within a period of five years when there is no PCV immunisation. Almost five million deaths would be averted with PCV

vaccination in the same period. In a scenario of no PCV vaccination, the number of hospitalizations and deaths would be about 300,000 and 29,000 respectively. However, introduction of PCV in the national immunisation programme would avert over 105,000 hospitalizations and approximately 10,000 deaths. The cost per DALY averted by PCV immunisation from government and societal perspectives would be USD 1,890 and USD 1,538 respectively (Ezoji et al, 2019).

On a limited scale albeit with large populations; Li et al (2021) adopted a unique approach where they considered both direct and indirect effects of PCV immunisation in their cost-effectiveness study. A previous model was localized in the Chinese cities of Beijing, Chengdu, Karamay, Qingdao, Shanghai, Shenzhen and Suzhou to estimate the cost-effectiveness of PCV vaccination compared to a scenario of no vaccination among children under five years. Another peculiar approach adopted by Li et al (2021) is the incremental cost-effectiveness ratios (ICERs) being reported in QALY gained in spite of the preponderance of DALYs averted outcome measure in LMICs. The ICERs range from 1,145 CNY in Shenzhen to 15,422 CNY in Qingdao per QALY gained in the base case analysis. This makes PCV13 a cost-effective intervention in each of the seven cities studied. Shanghai recorded lower incremental costs and higher QALYs gained making PCV13 the dominant strategy in that city. With regard to the direct effects (DE)-only, all ICERs in each of the seven cities fell below a cost-effectiveness threshold of three times GDP per capita of China making PCV13 vaccination a cost-effective strategy in reducing the disease burden of Streptococcus pneumonia in the seven Chinese cities (Li et al., 2021).

Dilokthornsakul et al (2019) developed a Markov model with a life-time horizon to assess the cost-effectiveness of PCV10 and PCV13 in comparison with no PCV immunisation from a societal perspective. This was against the backdrop of a previous study which showed both

PCV10 and PCV13 not to be cost-effective interventions in tackling the burden of pneumococcus in children under five years in Thailand. Dilokthornsakul et al (2019) therefore considered changes in vaccine efficacy, herd protection and price in their analysis. Without considering indirect effects, the results of the base case analysis indicated ICERs of 170,437 THB per QALY gained for PCV10 and 73,674 THB per QALY gained for PCV13. In comparison with no PCV immunisation, both PCV10 and PCV13 recorded lower costs and higher QALYs when herd protection is considered. The results imply that whilst PCV13 is cost-effective, PCV10 is not cost-effective at the prevailing price. However, both PCV10 and PCV13 are cost-effective when herd protection is considered (Dilokthornsakul et al., 2019).

Urueña et al (2011) assessed the incremental costs, health impact and cost-effectiveness of PCV10 and PCV13 at the time both vaccines were licensed for immunisation of children under five years in Argentina. Each of the vaccines was compared to a 'do-nothing' approach by using the TRIVAC tool to model 20 birth cohorts. The analysis considered cost from both the health system and societal perspectives. Urueña et al (2011) adopted an unusual approach where the number of life years gained (LYG) was examined separately from the number of life years gained after adjusting for DALY morbidity weights. The results showed that PCV13 will have at least 10 percent increase in the number of LYG as compared to PCV10. In the case of PCV10, the number of LYG is approximately 57,000 and the number of LYG after adjusting for DALY morbidity weights is over 64,000. As for PCV13, the number of LYG is over 65,000 whilst the number of LYG after adjusting for DALY morbidity weights is about 72,000.

The costs per DALY averted by PCV10 and PCV13 are respectively USD 8,973 and USD 10,948 from the perspective of the health system. From the societal perspective, the costs per DALY averted by PCV10 and PCV13 are USD 8,546 and USD 10,510 respectively. With direct comparison of PCV10 and PCV13, there is an additional USD 28,147 cost per DALY

averted in favour of PCV13. The findings also revealed that the most influential parameters on cost-effectiveness are price of vaccines, serotype replacement, pneumonia mortality and discount rate (Urueña et al., 2011).

Vučina et al (2015) used the TRIVAC model to evaluate the cost-effectiveness of PCV10 and PCV13 compared to a scenario of no PCV immunisation in Croatia for the period of 2014 to 2033. This was aimed at introducing PCV into the infant vaccination programme whilst ensuring judicious use of limited healthcare resources by the Ministry of Health in Croatia. The study found ICER of USD 69,000 per averted DALY from the perspective of government. From the societal perspective, an ICER of USD 77,000 per DALY would be averted. One of the scenarios that was marginally cost-effective was mainly based on the 2008 WHO estimates of Streptococcus pneumonia in Croatia. The second scenario was based on the assumption that there would be a significant reduction in the price of PCV during the period of study.

In order to have both PCV10 and PCV13 to be cost-effective under the base case results, the Croatian government needs to pay a maximum of USD 20 per vaccine. From the base case analysis, PCV13 is less cost-effective than PCV10 based on the sensitivity of vaccine price. The study concluded that PCV13 is likely not to be cost-effective in Croatia based on direct effects of PCV vaccination in children alone. It was recommended that further analysis be conducted on herd protection of PCV13 immunisation in adults (Vučina et al., 2015).

Studies from 22 low income countries prove PCV immunisation to be a cost-effective intervention from the health system and societal perspectives (Saokaew et al., 2016). Whilst PCV immunisation is highly cost-effective in many low income countries, studies have shown that it is only cost-saving in a few countries like The Gambia and Mongolia, among others (Pecenka et al., 2021; Sundaram et al., 2017)

Ayieko et al (2013) compared either of PCV10 or PCV13 with no vaccination using a decision analytic model. The aim was to evaluate the cost-effectiveness of either of the vaccines in Kenya, from a societal perspective. Data from a population-based surveillance system in Kilifi Hospital was used to extrapolate the burden of Streptococcus pneumonia where adjustments were made for variable access to healthcare in Kenya. The study adopted an approach where data on herd protection and serotype replacement was extrapolated from the USA.

With an annual vaccination cost of USD 14 million, PCV10 will reduce the incidence of pneumococcus by 43%. It will also reduce healthcare cost by almost USD 2 million. PCV10 will reduce infant deaths by 6.1% on an annual basis. The cost per DALY averted is USD 59 whilst the cost per death averted is USD 1,958 from the societal perspective. The cost-effectiveness ratios improved by 20% with the introduction of PCV13. The cost-effectiveness ratios improved by 43% to 56% further with the inclusion of herd effects of PCV13 immunisation (Ayieko et al., 2013).

Examining the health benefits and cost-effectiveness of PCV in India, Krishnamoorthy et al (2019) compared PCV vaccination to a scenario of no PCV vaccination. The UNIVAC tool was used to model 10 birth cohorts of children under five years from 2018 to 2027. Crucially, the study considered cost only from the perspective of government. Krishnamoorthy et al (2019) used a willingness to pay (WTP) threshold equal to the GDP per capita to determine the cost-effectiveness of PCV immunisation in India. The PCV immunisation would cost the Indian government an amount of USD 467 per DALY averted, making it a highly cost-effective intervention in India. The PCV vaccination remains cost-effective in India even with the most unfavourable scenario where the cost per DALY averted is USD 2,323 (Krishnamoorthy et al., 2019).

From the healthcare provider and societal perspectives, Farooqui & Jit (2019) evaluated the cost-effectiveness of PCV10 and PCV13 by comparing with a scenario of no PCV immunisation in India. In contrast to the methodology adopted by Krishnamoorthy et al (2019), an age-stratified static tool was used to model 30 birth cohorts of children under five years in India. Apart from the direct effects of the vaccine on immunized children, the model also examined indirect effects on children who were unvaccinated.

The costs per DALY averted from the societal perspective are USD 295 and USD 224 respectively for PCV10 and PCV13. From the perspective of the healthcare provider however, the costs per DALY averted for PCV10 and PCV13 are USD 527 and USD 470 respectively. Notably, the ICER of PCV13 from the perspective of the healthcare provider corroborates the finding of Krishnamoorthy et al (2019) albeit with a marginal difference.

In terms of the health effects, the number of deaths averted by PCV10 and PCV13 are 62,000 and 78,000 respectively. The number of inpatients averted are 681,000 and 827,000 respectively for PCV10 and PCV13. The PCV vaccination programme would save healthcare costs of USD 979 million to USD 1,227 million. The costs saved from the societal perspective range from USD 3,748 million to USD 3,659 million. The ICERs are robust for the base case analysis. The ICERs remain robust when alternative scenarios are considered (Farooqui & Jit, 2019). Based on the findings of the two studies, the PCV vaccination programme in India is highly cost-effective compared to a scenario of no vaccination from government, healthcare provider and societal perspectives (Farooqui & Jit, 2019; Krishnamoorthy et al., 2019).

Nigeria has the highest burden of Streptococcus pneumonia in Africa. Whilst the country comes third after India and China in the global ranking of pneumococcal disease, Nigeria is also faced with a threat of the exit of GAVI upon attaining the self-financing stage in 2025. The sustainability of the national PCV programme is therefore a matter of concern for policy-

makers in Africa's most populous nation. In assessing the sustainability of the PCV immunisation programme, Idris et al (2020) used the UNIVAC tool to conduct a cost-effectiveness study for 20 birth cohorts of children below five years from both government and societal perspectives. Idris et al (2020) modelled separately for 2014 to 2025 and also for 2026 to 2031, which respectively represent the period that Nigeria gets co-payment support from Gavi and the period that the country is expected to be weaned from Gavi support.

The national PCV immunisation programme will reduce the disease burden of pneumococcus by 31.4% for the 2014 – 2025 period. The disease burden is expected to reduce by 30% in the 2026 – 2033 period. The most sensitive parameters obtained from a one-way sensitivity analysis are vaccine efficacy, burden of disease and cost of treatment in that order. From the base case analysis, the costs per DALY averted for the 2014 – 2025 period are USD 54 and USD 47 respectively from the perspectives of government and society. For the 2026 – 2033 period, the costs per DALY averted are USD 69 and USD 60 from the perspectives of government and society respectively. The ICERs obtained from the two time frames therefore suggest that the PCV vaccination programme will not only be highly cost-effective during the period Nigeria gets support from Gavi, but also after the Gavi transition (Idris et al., 2020).

Pecenka et al (2021) conducted a cost-effectiveness analysis for the PCV immunisation programme in The Gambia from both government and societal perspectives. The UNIVAC tool was used to model 20 birth cohorts of children below five years spanning the 2011 – 2030 period. The findings of Pecenka et al revealed that the Gambian PCV vaccination programme will avert 117,000 cases; 9,000 outpatient visits; 88,000 inpatient admissions; 3,300 deaths and 100,000 DALYs resulting from Streptococcus pneumonia. With an investment of USD 2 million in the PCV vaccination programme, The Gambian government is expected to save USD

4 million from outpatient visits and inpatient admissions alone. In the same vein, an amount of USD 7.3 million worth of savings will be accrued to the society from 2011 to 2030.

Hence the PCV immunisation programme is not only highly cost-effective, but also cost-saving. It is expected to remain cost-saving until the country pays USD 2.95 per dose. At that point, the PCV immunisation programme will still be cost-effective but certainly not cost-saving. The Gambian government will therefore get good value for money for PCV vaccination of children under five years should Gavi support ends in the unforeseeable future (Pecenka et al., 2021).

Using an age-stratified cohort model, Sundaram et al (2017) evaluated the cost-effectiveness and budget impact of PCV13 vaccination in Mongolia from the perspectives of the health system and the society. This was at a time that the Ministry of Health in Mongolia considered introducing PCV into the childhood immunisation programme to reduce the incidence of pneumococcal disease in children below the age of five years. A scenario of PCV13 vaccination was therefore compared with a scenario of no PCV13 vaccination for 30 birth cohorts. Indirect effects of PCV13 immunisation were also considered in the analysis.

The cost per DALY averted from the perspective of the health system was USD 52 whilst it was cost-saving from the perspective of society. Excluding indirect effects of PCV13 vaccination gives ICERs of USD 79 per DALY averted and USD 19 per averted DALY from the health system and societal perspectives respectively. The PCV13 immunisation programme will cost the Mongolian government USD 920,000 in the first year of introduction. The annual incremental cost will be USD 820,000. Conversely, the PCV13 vaccination programme will reduce healthcare cost to the government by USD 440,000 in the first year of introduction, and an annual USD 510,000 afterwards (Sundaram et al., 2017). Sundaram et al (2017) concluded that the introduction of PCV13 in the child immunisation programme was therefore cost-saving

from the societal perspective, and a highly cost-effective intervention in Mongolia in spite of uncertainties around some of the input parameters.

2.8 Conclusion

Based on WHO-recommended thresholds for interpreting cost-effectiveness, there is evidence in the literature to show that PCV vaccination in children under 5 years is generally a cost-effective intervention in low and middle-income countries. This is especially true when compared with a scenario of no vaccination. On the other hand, there is evidence that indicates that it is not a cost-effective intervention in countries such as Croatia and Thailand, among others.

Given that each country has its distinctive characteristics in terms of epidemiology of Streptococcus pneumonia and socio-economic environment. Hence, cost-effectiveness analysis needs to be assessed on a contextual basis. While literature is replete on the incidence of streptococcus pneumoniae in Ghana and the African meningitis belt in general (Abbey et al., 2018; Dadzie et al., 2020; Kobayashi et al., 2021), little is known about the cost-effectiveness of PCV vaccination in Ghana.

An earlier study to estimate cost-effectiveness of the rotavirus vaccine, which was introduced simultaneously with the PCV in Ghana, shows that rotavirus vaccination is a highly cost-effective intervention. It will remain cost-effective even after Ghana pays for the full price of the vaccine when co-financing support from Gavi ends (Nonvignon et al., 2018).

There is therefore the need to generate empirical evidence on the cost-effectiveness of PCV vaccination to provide decision-makers with the needed evidence to prioritise the intervention, considering the health and economic impact of this investment in an era of donor transition in Ghana.

CHAPTER THREE

METHODS

3.1 Introduction

In this chapter, an overview is provided on the methods of assessing the health effects and cost-effectiveness of PCV13 vaccination programme in Ghana. Issues addressed under this chapter are the study design, study variables, sources of data and inputs for base case analysis, among others.

3.2 Study Design

The study adopted a static cohort model where an analysis of the base case input parameters compares the health effects and incremental costs of PCV13 immunisation to a scenario where there is no immunisation for 20 birth cohorts starting from 2012. PCV13 immunisation was introduced in Ghana in 2012, hence the choice of the starting year for the analysis. Ghana has also developed a roadmap to attain universal health coverage (UHC) by 2030. The study therefore evaluates the cost-effectiveness of PCV13 to coincide with the UHC Roadmap in Ghana. Two main scenarios of cost-effective analyses of PCV13 vaccination in Ghana (for a period of 2012 to 2025; 2026 - 2031) were evaluated in comparison with no vaccination programme.

The UNIVAC (version 1.4) model was used to evaluate the cost-effectiveness of PCV13 compared to a scenario of no vaccination programme in Ghana from 2012 to 2025 and from 2026 to 2031. UNIVAC is a proportionate outcomes model which was developed in the London School of Hygiene and Tropical Medicine. It is a Microsoft Excel spreadsheet software designed to calculate the ICERs and other pertinent indicators for Haemophilus Influenza B

(HiB), Rotavirus vaccine (RVV) and Pneumococcal Conjugate Vaccine (PCV) (Clark et al., 2013; Jauregui et al., 2015).

3.2 Study Area

This is a national-level study conducted in Ghana starting from the implementation of PCV13 vaccination programme in 2012 to 2025 and beyond the GAVI transition (2026 to 2031). Ghana is located on the coast of West Africa between latitude 5°33' North and 0°12' West and longitude 5.550° North and 0.200° West with a landmass of 238,537 square kilometres. Ghana is bordered in the North and Northwest by Burkina Faso, in the East by Togo, in the West by Cote d'Ivoire and in the South by the Gulf of Guinea. The 2021 Population and Housing Census records the total population of Ghana to be 30,832,019. Ghana has sixteen administrative regions which include: Upper East, North East, Upper West, Savannah, Northern, Bono, Bono East, Ahafo, Ashanti, Oti, Volta, Eastern, Western, Western North, Central and Greater Accra Regions (GSS, 2021).

The health sector of Ghana mainly comprises the Ministry of Health (MOH) and its twenty-three (23) agencies. The MOH collaborates with other Ministries, Departments and Agencies (MDAs); Metropolitan, Municipal and District Assemblies (MMDAs); Development Partners (DPs) and the private sector to achieve its vision and goals. Whilst the MOH is responsible for policy formulation, the agencies implement the policies through service delivery, financing, regulation, training and research. The Ghana Health Service (GHS) is the largest service delivery agency in Ghana. Tertiary and specialist services are carried out by the Teaching Hospitals. There are also many private health institutions complementing the services being provided by the public sector (MOH, 2018).

3.3 Study Population

The 2021 Population and Housing Census records the population of children below the age of five years in Ghana as 3,773,723. This study simulates health outcomes and cost of PCV immunisation in children under five years for 20 successive birth cohorts.

3.4 Study Variables

The input parameters for the UNIVAC model include demography, burden of disease, health services utilization and treatment costs, vaccination coverage, vaccine efficacy and vaccination costs. The cost per DALY averted denotes the weighted combination of morbidity and mortality effects of the PCV immunisation programme and hence, it is the primary outcome measure of this study. DALYs are more preferable outcome measures in LMICs and are therefore utilized in this study. Another reason for the use of DALYs in this study is the paucity of QALY weights for every disease and country (Hutubessy et al., 2003). The study also evaluated such outcomes as averted cases and deaths, outpatient visits and inpatient admissions avoided, incremental cost of PCV immunisation programme and reduced treatment costs.

3.5 Eligibility Criteria

3.5.1 Inclusion Criteria

The inclusion criteria is children less than five years of age in Ghana constituting over Three Million of the population. Only direct vaccine effects were considered. Cost was also examined from the perspective of both government and society.

3.5.2 Exclusion Criteria

The study excludes data on suspected pneumococcal deaths in children less than five years which were not reported at health facilities. Data collected on pneumococcal cases before the introduction of the PCV vaccination in Ghana was also excluded in the analysis.

3.8 Data and Data Sources

3.8.1 Disease Burden and Healthcare Utilisation

The study considered the various disease conditions of Streptococcus pneumonia such as acute otitis media (AOM), pneumonia (non-severe), pneumonia (severe), meningitis, meningitis (sequelae), non-severe non-pneumonia non-meningitis (NPNM) and severe NPNM. For each category, there were estimates for the number of cases, outpatient visits, inpatient admissions and deaths. Particularly, this study did not attribute deaths to pneumonia (non-severe) and non-severe NPNM (Appiah-Korang et al., 2014; Edmond et al., 2010; Monasta et al., 2012).

The study also examined outcomes for outpatient pneumonia (non-severe), inpatient pneumonia (severe) and Streptococcus meningitis. Pneumonia (non-severe) was assumed to result in outpatient visit followed by recovery. Severe pneumonia on the other hand results in inpatient admission followed by recovery or death. Streptococcus meningitis results in inpatient admission followed by recovery with or without sequelae or death (Appiah-Korang et al., 2014; Edmond et al., 2010; Monasta et al., 2012).

Data was primarily obtained from the 2014 Demographic and Health Survey (DHS) and the 2017 Multiple Indicator Cluster Survey (MICS) (GSS, 2018). Data from international estimates, particularly from the Maternal and Child Epidemiology Estimation (MCEE) by Wahl et al (2017), were used in instances where there was paucity of local data on some disease episodes at the national level. In calculating years of life lost (YLLs), data on number of deaths and life expectancy were obtained from the annual data of the United Nations World Population Prospects (UNWPP).

3.8.2 Estimates for Disability-Adjusted Life Years

Disability weights on Streptococcus pneumonia were obtained from the Global Burden of Disease (GBD) study conducted by Salomon et al (2015). The GBD disability weights allowed for the use of a common data source to evaluate health states (Salomon et al., 2015).

3.8.3 Vaccination Coverage

In Ghana, PCV13 is administered along with the first and third doses of diphtheria/tetanus/pertussis (DTP) vaccine during two, three and four months of age. Coverage levels of PCV13 were accessed from the immunisation coverage database of the WHO and UNICEF with the assumption that it was constant during the course of the 20 birth cohorts.

3.8.4 Vaccine Efficacy

Data on vaccine efficacy was obtained from Lucero et al (2009). The evidence from this systematic review is reported to be of high quality based on Cochrane risk of bias tool. The vaccine efficacy after the first dose is 29%. However, the vaccine efficacy after the second and booster doses is 58%. In the UNIVAC model, the period of efficacy is assumed to be lifelong.

3.8.5 Vaccination Programme Costs

The data on price per dose and costs of delivery were taken from the database of the UNICEF Vaccine Supply Division. For the purpose of this study, the total vaccination cost was estimated as a sum of vaccine price per dose, fixed price assumption for safety box (USD 0.03), estimated wastage and incremental health system costs per dose.

As the vaccination programme is already functioning under the Expanded Programme on Immunisation (EPI), cold chain and other start-up costs were excluded as they are sunk costs. Data on cost of treatment was obtained from a recent cost study conducted by Kobayashi et al (2021) on Estimating the Economic Burden of Pneumococcal Meningitis and Pneumonia in Northern Ghana and the African Meningitis Belt Post-PCV13 Introduction.

3.8.6 Costs on Outpatient Visits and Inpatient Admissions

Costs were only applicable to cases that sought care at the health facility. A discount rate of 3% was applied to future health outcomes based on WHO recommendation (Hutubessy et al., 2003). All the monetary units were reported in US Dollars due to the volatility in the exchange rate of the Ghana Cedi.

Table 1 shows the input parameters for the UNIVAC tool.

Table 1: Inputs for Base Case Parameters

Input Parameter	Mid Value	Low	High	Source
Acute Otitis Media				
Incidence rate <5 years (per 100,000)	11555	11422	11687	Monasta et al (2012)
Outpatient visits <5 years (per 100,000)	5801	5734	5867	DHS/MICS stratum
Hospitalizations <5 years (per 100,000)	277	127	351	Appiah-Korang (2014)
Deaths <5 years (per 100,000)	91	85	98	Monasta et al (2012)
Streptococcus pneumonia (non-severe)				
Incidence rate <5 years (per 100,000)	851	796	1038	MCEE (Wahl et al 2017)
Outpatient visits <5 years (per 100,000)	427	400	521	DHS/MICS stratum
Streptococcus pneumonia (severe)				
Incidence rate <5 years (per 100,000)	546	409	623	MCEE (Wahl et al 2017)
Outpatient visits <5 years (per 100,000)	274	206	313	DHS/MICS stratum
Hospitalizations <5 years (per 100,000)	274	206	313	DHS/MICS stratum
Deaths <5 years (per 100,000)	64	46	67	MCEE (Wahl et al 2017)
Streptococcus meningitis				
Incidence rate <5 years (per 100,000)	16	6	34	MCEE (Wahl et al 2017)
Outpatient visits <5 years (per 100,000)	8	3	17	DHS/MICS stratum
Hospitalizations <5 years (per 100,000)	8	3	17	DHS/MICS stratum
Deaths <5 years (per 100,000)	9	3	19	MCEE (Wahl et al 2017)
Sequelae cases <5 years (per 100,000)	3	1	7	35% of survivors (Edmond et al, (2010)
Streptococcus NPNM (non-severe)				
Incidence rate <5 years (per 100,000)	48	18	104	MCEE (Wahl et al 2017)
Outpatient visits <5 years (per 100,000)	24	9	52	DHS/MICS stratum
Streptococcus NPNM (severe)				
Incidence rate <5 years (per 100,000)	18	7	39	MCEE (Wahl et al 2017)
Outpatient visits <5 years (per 100,000)	9	3	2	DHS/MICS stratum
Hospitalizations <5 years (per 100,000)	9	3	2	DHS/MICS stratum
Deaths <5 years (per 100,000)	8	3	17	MCEE (Wahl et al 2017)

Disability Weights				
Acute Otitis Media	1%	1%	2%	Salomon (2015)
Streptococcus pneumonia (non-severe)	5.10%	3.20%	7.40%	Salomon (2015)
Streptococcus pneumonia (severe)	13.30%	8.80%	19%	Salomon (2015)
Streptococcus meningitis	13.30%	8.80%	19%	Salomon (2015)
Streptococcus NPNM (non-severe)	5.10%	3.20%	7.40%	Assumption (same as non-severe pneumonia)
Streptococcus NPNM (severe form)	13.30%	8.80%	19%	Assumption (same as meningitis)
Streptococcus meningitis sequelae	26%	15.30%	36.40%	Assumption
Vaccine Coverage				
Dose 1 (with DTP1)	94%	85%	100%	WHO UNICEF Estimates (2017) for Ghana
Dose 2 (with DTP2)	94%	84%	100%	WHO UNICEF Estimates (2017) for Ghana
Dose 3 (with DTP3)	93%	84%	100%	WHO UNICEF Estimates (2017) for Ghana
Vaccine Efficacy				
1st Dose	29%	14.5%	37.5%	Assumption (half of full efficacy)
2nd Dose	58%	29%	75%	Systematic review by Lucero et al (2009)
Booster Dose	58%	29%	75%	Systematic review by Lucero et al (2009)
Mean Duration of Illness (in days)				
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
Vaccine Programme & Health System Costs (USD)				
Vaccine price per dose (2012 – 2022)	USD 2·90			UNICEF Supply Division Vaccine Price
Vaccine price per dose (2023 – 2025)	USD 2.75			UNICEF Supply Division Vaccine Price
Vaccine price per dose (After 2025)	USD 14·50			UNICEF Supply Division Vaccine Price
Syringe price per dose	USD 0·03	USD 0·03	USD 0·03	UNICEF Supply Division Vaccine Price
Vaccine and syringe wastage	5%	5%	5%	Assumption

Government Cost per Outpatient (USD)				
Acute Otitis Media	USD 1.3	USD 0.00	USD 2.9	Kobayashi et al., (2021)
Streptococcus pneumonia (non-severe)	USD 1.3	USD 0.00	USD 2.9	Kobayashi et al., (2021)
Streptococcus pneumonia (severe)	USD 1.3	USD 0.00	USD 2.9	Kobayashi et al., (2021)
Streptococcus meningitis	USD 1.3	USD 0.00	USD 2.9	Kobayashi et al., (2021)
Streptococcus NPNM (non-severe)	USD 1.3	USD 0.00	USD 2.9	Kobayashi et al., (2021)
Streptococcus NPNM (severe)	USD 1.3	USD 0.00	USD 2.9	Kobayashi et al., (2021)
Streptococcus meningitis sequelae	USD 1.3	USD 0.00	USD 2.9	Kobayashi et al., (2021)
Government Cost per Hospitalization (USD)				
Acute Otitis Media	USD 128.5	USD 115	USD 200	Kobayashi et al., (2021)
Streptococcus pneumonia (severe)	USD 128.5	USD 115	USD 200	Kobayashi et al., (2021)
Streptococcus meningitis	USD 141.1	USD 112.6	USD 324	Kobayashi et al., (2021)
Streptococcus NPNM (severe form)	USD 128.5	USD 115	USD 200	Kobayashi et al., (2021)
Household Cost per Outpatient (USD)				
Acute Otitis Media	USD 12.7	USD 3.2	USD 47.5	Kobayashi et al., (2021)
Streptococcus pneumonia (non-severe)	USD 12.7	USD 3.2	USD 47.5	Kobayashi et al., (2021)
Streptococcus pneumonia (severe)	USD 12.7	USD 3.2	USD 47.5	Kobayashi et al., (2021)
Streptococcus meningitis	USD 12.7	USD 3.2	USD 47.5	Kobayashi et al., (2021)
Streptococcus NPNM (non-severe)	USD 12.7	USD 3.2	USD 47.5	Kobayashi et al., (2021)
Streptococcus NPNM (severe form)	USD 12.7	USD 3.2	USD 47.5	Kobayashi et al., (2021)
Streptococcus meningitis sequelae	USD 12.7	USD 3.2	USD 47.5	Kobayashi et al., (2021)
Household Cost per Hospitalization (USD)				
Streptococcus pneumonia (severe)	USD 141.1	USD 112.6	USD 324	Kobayashi et al., (2021)
Streptococcus meningitis	USD 141.1	USD 112.6	USD 324	Kobayashi et al., (2021)
Streptococcus NPNM (severe form)	USD 141.1	USD 112.6	USD 324	Kobayashi et al., (2021)

3.9 Data Processing

This examined the health effects and the expected costs of the vaccination programme to Ghana. A discount rate of 3% was applied for future health outcomes based on WHO recommendations (Edejer et al., 2005).

3.10 Base Case Analysis

The mid values in Table 1 were considered the best estimates and were therefore used in the base case analysis.

3.10.1 Health Impact

The number of cases, deaths and sequelae due to meningitis together with costs in scenarios with or without PCV13 immunisation were estimated in the model. The estimates were used to calculate the health effects such as outpatient visit, inpatient admission and DALYs 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.

3.10.2 Disability-Adjusted Life Years Averted

The years of life lost (YLL) were calculated from the number of deaths and life expectancy. The disability weight for each condition was multiplied by the prevalence rate of the disease. Cases were then used to calculate years of life with disability (YLD). DALYS are calculated from the sum of YLL and YLD. The DALYs averted was calculated by subtracting the DALYs lost in the immunized cohort from the DALYs lost in the cohort not immunized.

3.10.3 Incremental Cost-effectiveness Ratio

Averted treatment costs were subtracted from the vaccination programme costs to obtain the net cost of vaccine introduction. The incremental cost-effectiveness ratio was obtained by dividing the net cost of vaccine introduction by the total averted DALY.

3.10 Scenario and Sensitivity Analysis

The mid values were used to estimate the base case results. To test the robustness of the base case results however, a scenario analysis was undertaken. Values for the parameters with the most uncertainty were changed one after the other in a one-way sensitivity analysis and the ICER of each parameter was recorded. A two-way sensitivity analysis was also conducted in which the vaccine price per dose was paired with each of the influential parameters namely vaccine efficacy, cost of treatment and vaccination coverage. In addition to the one-way scenario analysis, a probabilistic sensitivity analysis (PSA) was performed with 1000 iterations where median, lower 95% and higher 95% ICERs were noted for each period.

3.12 Ethical Consideration

3.12.1 Ethical Clearance:

The study relied on secondary data from published literature and international estimates ha are available in the public domain. Moreover, it posed no harm on human subjects. Ethical clearance was therefore not required.

3.12.2 Description of Subject:

Secondary data on children below the age of five years was collected for this study.

3.12.3 Potential Risk/Benefit:

The results and findings of this study could be used by the Government of Ghana through the Ministries of Health and Finance to develop an investment case for funding PCV13 vaccination in particular and health financing in general. It would also serve as a guide for GAVI, UNICEF and other development partners to prioritise their country programmes on childhood vaccination.

3.12.4 Data Quality Control:

Any error identified was noted and validated by comparing with other datasets in order to get the right measure of the parameter. This enhanced the reliability in the data. It also produced a credible analysis of the data. The data extracted is stored into hard disk drive and protected with password to prevent any tampering which might affect consistency in the results. A copy of the data is also saved on Google Drive to enable access to the data to forestall any unforeseen circumstance that might lead to loss of data.

3.12.5 Declaration of Competing Interest:

There are no competing interests in this study.

3.13 Limitations of Study

This study used a model that is not dynamic which assumed that there was no change in the disease infecting the vulnerable population. The model does not also account for indirect effects of the vaccine in adult population. There is also limited data on some input parameters such as disease burden at the national level, hence the study relied heavily on published literature and international estimates.

CHAPTER FOUR

RESULTS

4.1 Introduction

The findings of this cost-effectiveness analysis of PCV13 vaccination in Ghana are presented in this chapter. The UNIVAC model (version 1.4) was used to model 20 birth cohorts separately for 2012 – 2025 and from 2026 – 2031 from the perspectives of government and society. The results are presented in tables preceded with the interpretation of the outputs based on the health impact, cost of vaccination programme, base case cost-effectiveness results, ICERs for scenario analysis and two-way sensitivity analysis.

4.2 Health Impact of PCV13 Vaccination in Ghana

PCV13 vaccination is estimated to avert 3,666,153 discounted episodes of total pneumococcal illness including 1,840,409 outpatient visits, 159,890 hospitalizations and 40,317 deaths over the period 2012 to 2025. While 1,692,582 discounted episodes of total pneumococcal illness including 849,676 outpatient visits, 73,818 hospitalizations and 19,024 deaths would be averted over the period 2026 to 2031. In particular, PCV13 vaccination would avert 91% of Acute Otitis Media cases which constitutes 89% of cases of Streptococcus pneumonia. Severe pneumonia contributes 37% to the total pneumococcal deaths and hence, PCV13 vaccination will avert almost 50% of severe pneumonia deaths from 2012 to 2031. In total, the PCV13 vaccination programme will reduce the pneumococcal disease burden by 48% from 2012 to 2031 compared to a scenario of no vaccination.

Table 2 shows the results of the estimated reduction in the burden of streptococcus pneumonia in under-five children between the period of 2012 – 2025 and 2026 – 2031.

Table 2: Estimated Reduction in the Burden of Streptococcus pneumonia in Ghana

	2012-2025			2026-2031		
Disease Burden	**No Vaccine**	**With Vaccine**	**Averted**	**No Vaccine**	**With Vaccine**	**Averted**
Total Cases	7,659,030	3,992,877	3,666,153	3,536,005	1,843,423	1,692,582
Acute Otitis Media	6,787,591	3,538,571	3,249,020	3,133,681	1,633,680	1,500,001
Pneumococcal pneumonia (non-severe)	500,251	260,796	239,455	230,955	120,404	110,551
Pneumococcal pneumonia (severe)	321,145	167,422	153,723	148,266	77,295	70,970
Pneumococcal meningitis	9,422	4,912	4,510	4,350	2,268	2,082
Pneumococcal NPNM (non-severe)	28,449	14,831	13,618	13,134	6,847	6,287
Pneumococcal NPNM (severe)	10,701	5,579	5,122	4,940	2,576	2,365
Meningitis sequelae	1,471	767	704	679	354	325
Total Outpatient Visits	3,844,388	2,004,424	1,840,409	1,775,074	925,398	849,676
Acute Otitis Media	3,407,371	1,776,362	1,631,008	1,573,108	820,107	753,000
Pneumococcal pneumonia (non-severe)	251,126	130,919	120,207	115,939	60,443	55,497
Pneumococcal pneumonia (severe)	161,215	84,046	77,169	74,429	38,802	35,627
Pneumococcal meningitis	4,730	2,466	2,264	2,184	1,138	1,045

Pneumococcal NPNM (non-severe)	14,281	7,445	6,836	6,593	3,437	3,156
Pneumococcal NPNM (severe)	5,372	2,801	2,571	2,480	1,293	1,187
Meningitis sequelae	739	385	354	341	178	163
Total Inpatient Admissions	334,029	174,139	159,890	154,214	80,396	73,818
Acute Otitis Media	162,713	84,827	77,886	75,121	39,163	35,958
Pneumococcal pneumonia (severe)	161,215	84,046	77,169	74,429	38,802	35,627
Pneumococcal meningitis	4,730	2,466	2,264	2,184	1,138	1,045
Pneumococcal NPNM (severe)	5,372	2,801	2,571	2,480	1,293	1,187
Total Deaths	84,228	43,910	40,317	39,743	20,719	19,024
Acute Otitis Media	44,746	23,327	21,814	21,114	11,007	10,106
Pneumococcal pneumonia (severe)	31,356	16,347	15,009	14,796	7,713	7,082
Pneumococcal meningitis	4,299	2,241	2,051	2,028	1,057	971
Pneumococcal NPNM (severe)	3,827	1,995	1,832	1,806	941	864
DALYs (Discounted)	2,623,383	1,370,135	1,253,248	1,049,523	548,147	501,376
DALYs (Undiscounted)	6,981,303	3,641,831	3,339,472	2,556,397	1,333,614	1,222,783

4.3 Total Healthcare Costs

Compared with a scenario of no vaccination, averted outpatient visits and hospitalizations will lead to a reduction in healthcare cost by USD 18,350,140 and USD 9,504,246 in 2012 – 2025 and 2026 - 2031 respectively from the perspective of government. The healthcare costs averted from the societal perspective are USD 37,897,274 and USD 19,628,461 respectively in 2012 – 2025 and 2026 – 2031 as shown in Table 3.

In a scenario of no vaccination, healthcare cost incurred by government on hospitalization constitutes 92% of total government health cost whilst outpatient cost is 51% of total societal health cost of pneumococcal diseases. The healthcare costs averted from the societal perspective are higher than the cost averted from the government perspective in the two timeframes under study. This could be attributed to the addition of out-of-pocket costs incurred by households.

Table 3: Total Healthcare Costs

	2012 - 2025			**2026 - 2031**		
	Without	**With**	**Averted**	**Without**	**With**	**Averted**
Gov't Costs	38,403,054	20,052,915	18,350,140	19,890,424	10,386,178	9,504,246
Outpatient	3,186,270	1,663,774	1,552,496	1,650,292	861,733	788,559
Hospitalizations	35,216,785	13,389,141	16,827,644	18,240,132	9,524,446	8,715,686
Total Societal Health Costs	79,311,172	41,413,898	37,897,274	41,078,317	21,449,856	19,628,461
Outpatient	40,767,792	21,287,709	19,480,083	21,115,213	11,025,726	10,089,487
Hospitalizations	38,543,380	20,126,188	18,417,191	19,963,104	10,424,130	9,538,974

4.4 Cost of Vaccination Programme

Table 5 shows the total costs of the PCV vaccination programme to be USD 130 million and USD 275 million respectively for the periods of 2012 – 2025 and 2026 – 2031 at an annual discount rate of 3%. The PCV13 vaccination programme will have incremental costs of approximately USD 2 million and USD 2.6 million for the periods of 2012 – 2025 and 2026 – 2031 respectively after discounting at 3% per year. Also, the cost of vaccine introduction and DALYs averted are the same from the perspectives of government and society. The net cost of vaccine introduction is however higher from the perspective of government than that from the societal perspective. This is as a result of higher health service cost averted from the perspective of society than that of government.

4.5 Cost-effectiveness of PCV13 Vaccination

Table 5 shows that the discounted costs required to avert one DALY from the perspectives of government and society are respectively USD 118 and USD 97 representing 4% and 5% of 2022 GDP per capita (USD 2,445.30) from 2012 to 2025. However, the discounted costs for averting one DALY from 2026 to 2031 are USD 530 and USD 510 representing 22% and 21% of per capita GDP respectively from the perspectives of government and society.

The undiscounted ICERs show costs per DALY averted in 2012 – 2025 to be USD 40 and USD 33 respectively from the perspectives of government and society. In the case of the 2026 – 2031 period, the undiscounted ICERs are USD 234 and USD 225 from the government and societal perspectives respectively.

The costs per DALY averted are higher in the latter scenario because Ghana would be expected to pay for the full price per dose of the vaccine from 2026 onwards without support from Gavi.

From the base case analysis, the PCV13 immunisation programme in Ghana is highly cost-effective with respect to the GDP per capita of USD 2,445.3 both with co-financing support from Gavi and even if Gavi exits in 2026 as envisaged.

Table 4: Base Cost-effectiveness

	2012-2025		2026-2031	
Summary of Base Case Cost	**Government Perspective**	**Societal Perspective**	**Government Perspective**	**Societal Perspective**
Net Cost of Vaccination	111,467,257	91,920,123	265,649,021	255,524,806
Cost of Vaccine Introduction	129,817,397	129,817397	275,153,267	275,153,267
Health Service Costs averted	18,350,140	37,897,274	9,504,246	19,628,461
Base Case Cost-effectiveness Results				
Cost per DALY Averted (Discounted)	118	97	530	510
Cost per DALY Averted (Undiscounted)	40	33	234	225

*All costs are in US Dollars (USD)

4.6 Scenario Analysis

Table 6 shows that the parameter with the highest ICER is low vaccine efficacy, followed by low disease incidence and low treatment cost both from the perspectives of government and society. All other parameters have the same ICER as the base case (most probable) scenario from both government and societal perspectives. Furthermore, ICERs obtained in the period 2012 – 2025 are lower than those obtained within the period of 2026 – 2031 from both perspectives. When individual parameters are varied across scenarios for uncertainty, the highest costs per DALY averted are USD 1,079 and USD 1,058 representing 44% and 43% of per capita GDP respectively from the perspectives of government and society.

The results also show that the most influential parameters are vaccine efficacy, disease incidence and treatment costs in descending order. Low vaccine efficacy resulted in ICERs of USD 193 and USD 177 respectively from the perspectives of government and society in the period of 2012 – 2025. It also resulted in ICERs of USD 1,079 and USD 1,058 respectively from the perspectives of government and society in 2026 – 2031.

It can also be deduced from the results that low vaccine efficacy led to an increase in the ICER whereas high vaccine efficacy led to a decrease in the ICER. This implies that for the vaccination programme to be more cost-effective, the vaccine efficacy needs to be high. The results from the scenario analysis also show that the cost per DALY averted even from the most unfavourable scenario to the vaccine is highly cost-effective when compared to the 2022 GDP per capita of Ghana.

4.7 Probabilistic Sensitivity Analysis

Table 6 shows the results of the probabilistic sensitivity analysis (PSA) that was undertaken with 1000 iterations for each of the scenarios. The parameters used to account for uncertainties in the model include vaccination coverage, vaccine efficacy, disease burden and treatment costs. For the 2012 – 2025 period, the median ICER is USD 91 with 95% Credible Range (CR) of USD 68 – USD 144 per DALY averted. This represents 2.8 – 5.9% of GDP per capita from the government perspective. The median ICER from the perspective of society is USD 73 with 95% CR of USD 45 – USD 128 per DALY averted representing 1.8 – 5.2% of GDP per capita. In the case of the 2026 – 2031 period, the median ICERs is USD 550 with 95% CR of USD 433 – USD 747 per DALY averted representing 17.7 – 30.5% of GDP per capita. However, the median ICER is USD 524 with 95% CR of USD 405 – USD 716 per DALY averted which represents 16.6 – 29.3% of GDP per capita from government and societal perspectives respectively.

The results obtained from the PSA support the evidence from the base case and scenario analyses that the PCV13 vaccination programme in Ghana is highly cost-effective from the perspectives of government and society even six years after the withdrawal of co-financing support by GAVI.

Table 5: Incremental Cost-effectiveness Ratio for Scenario Analysis

Parameters	**2012 – 2025**		**2026 - 2031**	
Scenario Analysis	**Government Perspective**	**Societal Perspective**	**Government Perspective**	**Societal Perspective**
Low disease incidence	119	101	680	655
Low efficacy	193	177	1079	1058
Low treatment cost	92	88	533	529
Low vaccine coverage	89	73	530	510
Base case scenario	89	73	530	510
High vaccine coverage	89	73	530	510
High treatment cost	89	73	530	510
High efficacy	89	73	530	510
High disease incidence rate	89	73	530	510
Probabilistic Sensitivity Analysis				
Median ICER	91	73	550	524
Lower 95%	68	45	433	405
Upper 95%	144	128	747	716

4.8 Two-way Sensitivity Analysis

When the price per dose increases to USD 14.5, it results in higher ICERs than a price per dose of USD 2.75 in the period of 2026 – 2031. Hence, the ICER rises to USD 1,026 and USD 1,006

per DALY averted when the price per dose increases to USD 14.5 with a low efficacy as shown in Table 5. However, evaluating a low vaccine price per dose against either low or high efficacy, treatment cost or coverage will result in USD 111 USD 91 per DALYs averted respectively from the government and societal perspectives in three of the scenarios. The only exceptions are low vaccine efficacy and high treatment costs. In the case of higher treatment cost, it results in the highest ICER of USD 517 and USD 431 per averted DALY from the perspectives of government and society respectively. Since there is certainty in the price per dose during the period of 2012 – 2025, there was no need to conduct a two-way sensitivity analysis for that timeframe.

Table 7 shows results of assessing PCV13 price per dose against vaccine efficacy, vaccine coverage and treatment costs from a two-way sensitivity analysis. PCV13 vaccination is highly cost-effective in all the scenarios evaluated.

Table 6: Two-way Sensitivity Analysis

Price per dose	Low vaccine efficacy	High vaccine efficacy	Low treatment cost	High treatment cost	Low vaccine coverage	High vaccine coverage
2026 - 2031	Government (Societal)	Government (Societal)	Government (Societal)	Government (Societal)	Government (Societal)	Government (Societal)
USD 2.75	241 (221)	111 (91)	115 (110)	517 (431)	111 (91)	111 (91)
USD 14.5	1026 (1006)	405 (385)	533 (529)	490 (404)	504 (483)	531 (511)

CHAPTER FIVE

DISCUSSION

5.1 Introduction

The research examined the cost-effectiveness of PCV13 immunisation in Ghana since its introduction in 2012 to 2025 and from 2026 to 2031 compared with a scenario of no vaccination from government and societal perspectives. The study considered the vaccine price per dose during the period of co-financing support from Gavi compared to when Government of Ghana may be purchasing vaccines without assistance from Gavi.

The analysis shows that the continuation of PCV13 vaccination programme will significantly reduce burden of disease due to Streptococcus pneumonia in children under-five years in Ghana. PCV13 vaccination is also estimated to be a highly cost-effective intervention in Ghana both during the period of support from Gavi and also after the period that Ghana is expected to fully finance the vaccination programme.

5.2 Health Impact of PCV Vaccination in Ghana

It is estimated that PCV13 vaccination can avert about 3.7 million and about 1.7 million cases of diseases associated with Streptococcus pneumonia over the periods 2012 – 2025 and 2026 – 2031 respectively. Cumulatively, the PCV13 vaccination programme is estimated to avert about 48% of the disease burden of Streptococcus pneumonia in Ghana from 2012 to 2031. These findings align with the results of a research undertaken in Accra and Tamale which revealed PCV13 to have 48 – 51% coverage of pneumococcal isolates in Ghana (Dayie et al., 2015). Similar findings were also obtained from a study in the Islamic Republic of Iran where Ezoji et al (2019) assessed that PCV13 vaccination would avert over 4.5 million cases and 38% of deaths from 2014 to 2023.

The findings of this study also corroborate many studies in LMICs. In assessing the health effects of PCV13 in children less than five years for 30 birth cohorts (2015 – 2045), results from 180 countries show that 12% of global investments are required to introduce PCV in the whole of Africa. This will save 69% of lives and avert 63% of DALYs on a global scale (Chen et al., 2019).

5.3 Cost of PCV Vaccination Programme in Ghana

The total costs of introducing PCV13 programme in Ghana are approximately USD 130 million and USD 275 million for the periods of 2012 – 2025 and 2026 – 2031 respectively. The incremental health system costs of PCV13 vaccination are approximately USD 2 million and USD 2.6 million for the periods of 2012 – 2025 and 2026 – 2031 respectively. Hence, Ghana is expected to incur more than twice the cost of PCV13 vaccines for the next six years after Gavi exits as compared to the 14 years of support from Gavi. This is mainly attributable to a sharp increase in the price per dose of PCV13 from USD 2.75 to USD 14.50.

The Government of Ghana would spend an additional USD 145 million representing 53% increase to purchase PCV13 in the years following Gavi transition compared to the 14 years of partnership with Gavi. This finding is comparable to the study of Vodicka et al (2022) that Ghana's share of Gavi co-financing of price per dose will increase from 32% to 100% as the country moves towards Gavi self-financing phase.

Furthermore, the societal cost of Streptococcus pneumonia during 2012 – 2025 is USD 79.3 million, out of which USD 39.7 million (50%) would be averted by vaccination. The cost to the government within the same period is USD 38.4 million, out of which USD 18.5 million (48%) would be averted by vaccination. During the 2026 – 2031 period, the economic burden to society is USD 41 million, out of which USD 19.6 million (49%) would be averted by

vaccination. In the same period, government will avert USD 9.5 million (48%) out of a cost of USD 19.9 million through vaccination.

The PCV13 vaccination programme in Ghana is not necessarily a cost-saving intervention. This is due to the fact that the vaccine programme costs are greater than the government cost savings attributable to averted disease. This finding is in line with a study from Kenya showing that continuing the PCV programme after transitioning from the support of Gavi is highly cost-effective although not cost-saving (Ayieko et al., 2013).

However, findings from another study based in The Gambia show that the PCV programme is likely to be cost-saving between 2011 and 2030, with projected reductions in disease burden and savings of USD 4 million for medical care. The findings also indicate that the PCV programme will remain cost-saving until The Gambia pays approximately USD 0.66 per dose. Even after The Gambia incurs the full cost of vaccine purchase, the PCV programme is likely to remain highly cost effective (Pecenka et al., 2021).

5.4 Cost-effectiveness of PCV Vaccination in Ghana

At a discount rate of 3%, results from the base case analysis find ICERs to be USD 97 and USD 118 per DALY averted respectively from government and societal perspectives in 2012 – 2025; and USD 530 and USD 510 per DALY averted respectively from government and societal perspectives in 2025 – 2031. It is worthy of note that the undiscounted ICERs are lower than the discounted ICERs for both timeframes and perspectives making the former to be highly cost-effective than the latter. Undiscounted ICERs are useful when policy makers want to examine short-term budget impacts of an intervention.

The scenario analysis shows that the ICERs obtained from the government perspective are higher than those obtained from the societal perspective. This is due to the fact that the healthcare costs averted from the government perspective are lower than those from the societal

perspective. Also, the most influential parameters are vaccine efficacy, incidence of pneumococcal disease and treatment costs.

Each of the ICERs from the two time frames and perspectives are less than the 2022 GDP per capita of Ghana (USD 2,445.30), hence could be considered highly cost-effective. However, the WHO thresholds have been a subject of intense academic debate in recent times (Leech et al., 2018). Meanwhile, Ghana currently does not have an established threshold to determine the cost-effectiveness of an intervention. Nonetheless, contemporary econometric modelling based on opportunity costs and income elasticity recommends probable cost-effectiveness thresholds of 4 – 40% GDP per capita for Ghana (Woods et al., 2016). Based on this model, only the parameter on low vaccine efficacy (USD 1,079/USD 1,058 per DALY averted) exceeds the threshold of good value for money from the perspectives of both government (44%) and society (43%) under a scenario when Ghana fully transitions from the support of GAVI in 2026. In spite of the controversy surrounding the WHO thresholds for considering an intervention as cost-effective, it is sufficient to consider the PCV13 vaccination programme as highly cost-effective based on the fact that even the most unfavourable scenario (low vaccine efficacy) is less than the 2022 GDP per capita of Ghana (USD 2,445.3).

The findings are also similar to other national level studies on PCV13 vaccination where the UNIVAC model was used to conduct cost-effectiveness analyses in Nigeria, India, The Gambia and Croatia (Idris et al., 2020; Krishnamoorthy et al., 2019; Pecenka et al., 2021; Vučina et al., 2015) respectively. Croatia happens to be the only exception where PCV13 vaccination is likely not to be cost-effective. This is as a result of a difference in modelling where PCV10 and PCV13 were compared to one another. In such a scenario, PCV10 was more cost-effective than PCV13 based on the price of the vaccines (Vučina et al., 2015). This is attributable to the vast differences in the disease burden of Streptococcus pneumonia and consumption cost in these countries. India has the highest total vaccine programme cost (USD 4,791,339,140 in 10 birth

cohorts, excluding societal cost) among all the CEA studies on PCV13 (Krishnamoorthy et al., 2019). This is followed by Nigeria which is estimated to have a very high total vaccine programme cost (USD 1,951,782,730 in 20 birth cohorts) from the perspectives of both government and society (Idris et al., 2020). Apart from the similarity in the estimates of GDP per capita of India and Nigeria, these two countries are on top of the list of countries in the world with the highest burden of Streptococcus pneumonia (Wahl et al., 2018).

Comparing with the cost-effectiveness of other vaccination programmes where UNIVAC was used for modelling, PCV13 is more cost-effective (USD 97 – USD 118 per DALY averted) in the period that Ghana is in partnership with Gavi than Rotavirus vaccination (USD 238 – USD 332 per DALY averted) and Human Papillomavirus (HPV) vaccination (USD 152 – USD 488 per DALY averted) in Ghana (Nonvignon et al., 2018; Vodicka et al., 2022). However, PCV13 is less cost-effective (USD 510 – USD 530 per DALY averted) if Ghana assumes full responsibility of purchasing the vaccines from 2026.

These differences could be attributed to variation in model inputs such as vaccine price per dose, vaccine efficacy, disease burden, disability weights and cost of treatment, among others. The huge differences could also be as a result of the modelling approach used in the various studies. Whereas Nonvignon et al (2018) estimated costs under a scenario of the price per dose Ghana pays for the Rotavirus vaccine whilst benefiting from Gavi co-financing, and a second scenario where Ghana pays fully for the vaccines for 20 years in either cases; this study rather modelled based on the price per dose borne by Ghana during the period (2012 – 2025) of partnership with Gavi and separately for the period that Ghana might pay fully for the vaccine after the exit of Gavi support (2026 – 2030).

5.5 Limitations of the Model used

This UNIVAC model used in this study has some limitations. First of all, as a static model assumes that there will be no change in the population that is susceptible to infection of Streptococcus pneumonia. Thus, it does not consider complicated health transition states of the disease. Also, the model does not take indirect effects or herd protection of the vaccine on the unvaccinated population into consideration and hence, the cost-effectiveness might be underestimated (Pecenka et al., 2018; Vodicka et al., 2022). Furthermore, the number of cases were based on published literature and international estimates. This has the potential to underestimate the disease burden of Streptococcus pneumonia due to low case detection and instances where some children might have died before their specimens were taken to the laboratory for confirmation (Krishnamoorthy et al., 2019). However, the model has several advantages that allowed for its use in this study. Some of these include its transparency and ease of interpretation to policy makers, use of minimal set of data inputs, ability to make standardised comparison between different vaccine policies and flexibility as it can easily be adapted to assess interventions in a judicious manner (Clark et al., 2013; Nonvignon et al., 2018).

CHAPTER SIX

CONCLUSION AND RECOMMENDATIONS

6.1 Conclusion

In spite of variations in the results of the scenarios in terms of costs and ICERs, the findings consistently indicate that PCV13 vaccination is a high impact and highly cost-effective intervention in Ghana. However, it is not necessarily cost-saving. Hence, PCV13 vaccination gives value for money under any cost-effectiveness threshold.

In a context where many LMICs including Ghana are on the verge of paying fully for vaccines after the exit of Gavi and are facing economic challenges partly as a result of the effects of the COVID-19 pandemic, it is essential to assist governments and policy-makers to derive the best value for money by allocating resources based on diseases with high morbidity, disability and mortality whilst considering interventions that are cost-effective.

6.2 Recommendations

1. The results of this study could serve as a guide for the Health Technology Assessment (HTA) Unit of the Ministry of Health (MOH) to replicate in cost-effectiveness of other routine immunisation programmes in Ghana.
2. The HTA Unit of MOH could conduct a budget and equity impact of PCV13 vaccination in Ghana in addition to this cost-effectiveness study.
3. Policy-makers at the Ministry of Health could make a strong investment case using the results from this study and the budget impact analysis to inform efficient resource allocation in the health sector of Ghana.
4. The Government of Ghana should sustain the PCV13 vaccination programme by increasing the proportion of health spending on routine immunisation even after the exit

of Gavi as PCV13 vaccination is currently the most potent public health tool to combat Streptococcus pneumonia in Ghana, whilst researchers continue to explore other less expensive and more cost-effective solutions to pneumococcal diseases in Ghana

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