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Article

Effectiveness of Pneumococcal Vaccines (PCV13) Against Mortality from Clinical Pneumonia and Meningitis in Children Under Five Years in Ghana After PCV13 Introduction Into the Routine Immunisation System

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Abstract

Background: *Streptococcus pneumoniae* is a major cause of mortality from pneumonia and meningitis among children under five in West Africa. A systematic review in 2018 showed that 81% of pneumonia deaths in Africa were caused by pneumococcus. The 13-valent pneumococcal conjugate vaccine (PCV13) was introduced into Ghana's routine immunisation programme (EPI) in 2012, using the 3+0 schedule. However, few studies have assessed the impact of PCV13 on pneumonia and meningitis outcomes in Ghana and Africa. This study assessed the effectiveness of PCV13 in lowering mortality from clinical pneumonia and meningitis among children under five in the Kassena Nankana districts of Ghana. Methods: This was a retrospective observational study using longitudinal mortality and vaccination data of children younger than 5 years from the Navrongo Health and Demographic Surveillance System (NHDSS) database. The NHDSS monitors the health and demographics of 160,000 individuals across two districts. Secondary data on mortality and vaccinations from 1 January 2007 to 31 December 2017 were extracted. Mortality (non-traumatic) from pneumonia and all-cause mortality in children under five years in the study were assessed through verbal autopsies using the WHO tool. Mortality rates (MR) were calculated as the number of deaths per 1,000 live births. Results: Mortality from pneumonia fell by 50% in both males and females after the introduction of PCV13 vaccination. All-cause mortality for both sexes was reduced by 60%. PCV13 vaccine coverage increased from 85.9% in 2014 to 95.7% by 2017. Furthermore, mortality rates from pneumonia and meningitis combined showed a marked reduction from approximately 15% to 8% in children under five years old. Conclusion: PCV13 has been effective in lowering mortality from clinical pneumonia and meningitis in this study population.

Keywords: effectiveness; pneumonia; meningitis; pneumococcal vaccines; health and demographic surveillance system; Ghana

Key Messages

1. What is already known on this topic?

Pneumococcal vaccines are safe and effective, reducing pneumonia morbidity and mortality in infants, with most studies carried out in the global North. Few pneumococcal vaccine effectiveness studies have been conducted in Africa, including Ghana, following the introduction of PCV13 into infant immunisation programmes.

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2. What this study adds

This study used longitudinal mortality data from a health and demographic surveillance system (HDSS) to assess the effectiveness of pneumococcal vaccines. The study found that pneumonia and meningitis mortality rates decreased by more than 50% five years after the introduction of PCV-13.

3. How this study might affect research, practice, or policy

The HDSS can be utilised to evaluate the effectiveness of newly introduced vaccines over time and acts as an additional tool for monitoring vaccine safety and effectiveness. This enhances the monitoring of vaccine safety and effectiveness in lower- and middle-income countries (LMICs) such as Ghana, which have HDSS zones. This is especially significant with the introduction of vaccines such as MenAfrivac and malaria vaccines, which are predominantly used in LMICs.

1. Introduction

Pneumonia is a significant cause of under-five mortality in the West African sub-region, with a high disease burden; it is estimated to cause 17% of deaths in young children in West and Central Africa, and 15% of deaths globally in 2015[1,2]. Streptococcus pneumoniae is a major cause of bacterial pneumonia in children worldwide [3,4]. Additionally, pneumococcal disease was the leading cause of vaccine-preventable deaths worldwide [4,5], accounting for ~800,000 deaths annually among children <5 years of age in 2017 [5–7].

Consequently, the 13-valent pneumococcal conjugate vaccine (PCV13) was introduced into Ghana's routine immunisation programme (EPI) on 1 April 2012, using the 3+0 vaccination schedule (administered to infants at 6, 10, and 14 weeks of age) [8]. There was no catch-up campaign when PCV13 was first introduced. The official country report estimated PCV13 coverage to be 99% in 2017. Since the introduction of PCV13 vaccines in 2012, few studies have assessed their impact on pneumonia in Ghana and across Africa. This is likely because it is challenging and costly to determine the aetiology of pneumonia [9].

Additionally, it is difficult to measure the impact of PCV13 on reducing pneumococcal pneumonia. It is much easier to estimate the effect on all-cause pneumonia[10] . In Senegal, pneumonia hospitalisations declined significantly (−3.8%, 95% confidence interval [CI] −1.5 to −5.9%) among children less than 12 months, two years after PCV13 introduction [11]. Notwithstanding this, there was no reduction in pneumonia hospitalisations among children aged 12-59 months [11]. The decline in the younger age group could be attributed to vaccine-induced direct protection [11]. Vaccine uptake may not have reached optimal levels to provide adequate indirect protection among children aged 12-59 months [11]. Other studies in Africa have found a reduction in hospitalisations for pneumonia in children under five after PCV13 introduction, although only two were significant [12–16].

This study was conducted to assess the impact of PCV13 on both all-cause mortality and mortality from clinical pneumonia in children under five years of age in Ghana within five years of introduction.

Furthermore, it demonstrates that the Navrongo Health and Demographic Surveillance System (NHDSS) can be used for passive post-marketing surveillance of newly introduced vaccines, such as PCV-13.

2. Methodology

2.1. Setting

The study area is the two Kassena Nankana districts in the Upper East Region of Ghana (see Figure 1). This area has been under health and demographic surveillance since 1992. Geographically, the surveillance area lies between latitude 10.300 and 11.100 North and longitude 1.10 west and covers a total land area of 1675 sq. km. Operationally, it is divided into five zones (North, South, East, West and Central) and further divided into 247 clusters. The total population under surveillance as

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of June 2018 was 167,000, residing in 42,000 households [17,18]. The population density of the districts is 91.5 sq. km, and the major ethnic groups are the Nankana and Kassena. The area is characterised by Guinea Savannah vegetation dominated by semi-arid conditions and vast grassland integrated with short trees. The study area is typical of many rural areas in sub-Saharan Africa, where agriculture is the mainstay of the local economy; Approximately 90% of the population are subsistence farmers and engage in animal rearing[17,18].

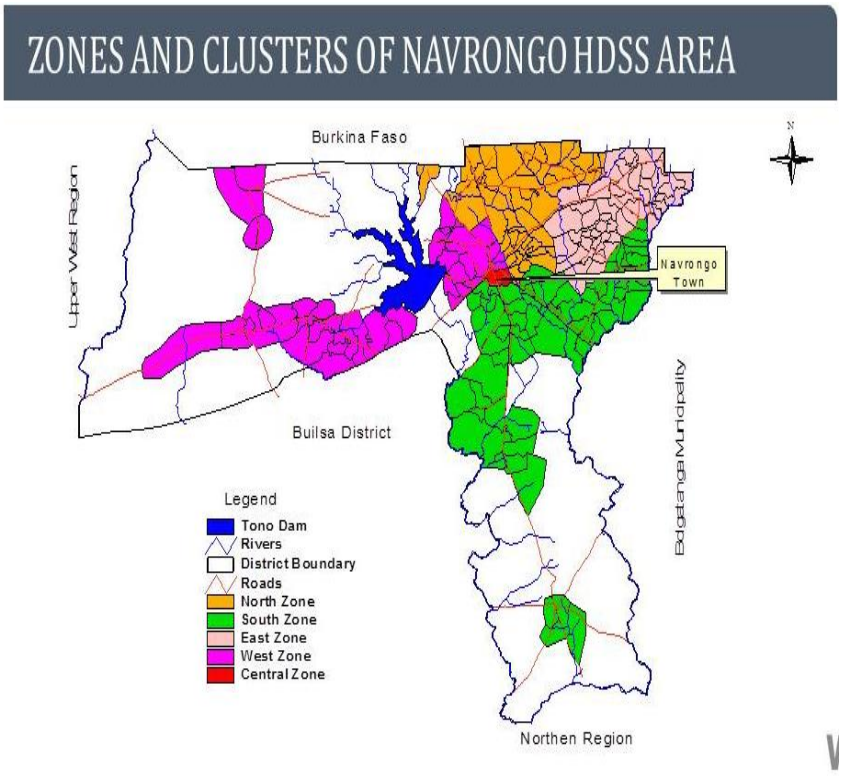

Figure 1. Map of Kassena Nankana Districts - Study Area.

2.2. Navrongo Health and Demographic Surveillance System

The Navrongo Health and Demographic Surveillance System (NHDSS) monitors the health and demographics of the two Kassena Nankana districts (Kassena Nankana Municipal and West) and assesses morbidity and mortality [17].

The NHDSS provides a platform for assessing health and social interventions in Northern Ghana.

2.3. Study Design

This was a retrospective observational cohort study that utilised longitudinal mortality and vaccination data from the NDHSS database. The study area had a population of 744,266 as of December 2022. The study population consisted of children under five years of age (n = 22,658) registered in the NHDSS database between 1 January 2007 and 31 December 2017. All under-five mortality data, including recorded causes of death, and vaccination data were extracted from the NDHSS database for the period from 1 January 2007 to 31 December 2017. No sample size was calculated; all observed under-five mortality cases in the database during this period were included.

2.4. Case Ascertainment

The NHDSS trains fieldworkers who visit each compound every six months to carry out interviews with household heads. In the context of HDSS, a compound refers to a single hut for each ever-married woman, along with additional huts for unmarried adult sons and the compound head.

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Routinely collected data include pregnancies, live births and stillbirths, morbidity, mortality, in- and out-migration (from one compound to another within the communities or to areas outside the NHDSS catchment), and childhood vaccinations. Community volunteers gather data on births and deaths in their communities in near-real-time. Verbal autopsies (VAs) using the World Health Organisation (WHO) tool (version 2022) are performed on all deaths. Each year, information such as educational status, marital status, religion, and access to national health insurance coverage is collected. Household socio-economic characteristics are updated every other year. The system also acts as a control for other health indicators in Ghana, aiding the evaluation of national public health interventions.

Secondary data on all children under five years old were extracted from the NDHSS database covering the period from 1 January 2007 to 31 December 2017. 1 April 2012, the day of vaccine introduction, was used as the reference date for comparisons before and after the introduction of the vaccines.

2.5. Variable Definitions

1. The case definition of pneumonia was based on the cause of death identified through verbal autopsies. According to the WHO (2022), the case definition for pneumonia includes recognising respiratory symptoms such as cough, difficulty breathing, rapid breathing, chest pain, and abnormal lung sounds during interviews with family members or caregivers of the deceased. These symptoms are used to classify the cause of death as pneumonia when there is no clinical or laboratory confirmation.
2. The WHO case definition for meningitis includes a sudden onset of fever, neck stiffness, altered consciousness, and other meningeal signs (e.g., headache, confusion, photophobia). In infants: bulging fontanelle, unusual behaviour (irritability), or poor feeding.

The outcome under investigation is mortality (non-traumatic infant mortality) from pneumonia, meningitis and all-cause mortality in children younger than five years in the study area.

Demographic characteristics extracted included age, sex, birth order of child, number of siblings, the mother's level of education, and immunisation status of child.

2.6. Data Sources

Data on mortalities over ten years (2007 to 2017) from the Navrongo Health Demographic Surveillance System (NHDSS) were used to estimate vaccine coverage (a full three-dose schedule) among those age-eligible each year, as well as mortality rates from pneumonia and all causes in children under five before and after the introduction of PCV13.

The Navrongo HDSS began in 1993, when all residents of 45 rural communities within the NHDSS area were surveyed for the first time. Everyone is assigned a unique identification number, along with their name, date of birth, sex, and relationship to the household head. After the baseline census, every household is visited quarterly by a well-trained interviewer to record births, deaths, in- and out-migrations, and pregnancies. Each visit is known as an HDSS round. All data is entered into a database system. Currently, the database used for capturing HDSS information is the Household Registration System II (HRS2).

The HRS2 is a structured system, designed and programmed using the relational database package Visual FoxPro. A person is registered in the HDSS if they have resided within the Demographic Surveillance Area (DSA) for at least four months before an update round. Such a person is classified as an external in-migrant, and they are coded as "Entry" in the database. Those who were present during the baseline were coded as "Enumerated."

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2.7. Outcome Definitions and Ascertainment

The primary outcome of interest in this study is mortality among children under five years old. Mortality rates (MR) were calculated as the number of deaths per 1,000 live births. The study population consisted of males and females living in urban and rural areas. Mortality data were gathered through routine surveillance systems and vital registration records. The cause of death was determined only through verbal autopsy interviews with the caregivers of the deceased children. The causes of mortality examined in this study include pneumonia and meningitis.

2.8. Exposure Definitions and Ascertainment

The exposure of interest in this study is PCV13 (pneumococcal conjugate vaccine) immunisation. Exposure was defined as the presence or absence of PCV13 immunisation in children under five years of age. The vaccination status was determined through individual child vaccination records obtained from caregivers during household visits. Children were classified as exposed if they received the recommended doses of PCV13 according to the Ghana Expanded Programme on Immunisation (EPI) schedule. Unexposed children either did not receive these vaccines or received them partially or on a different schedule.

2.9. Data Analysis

The analysis aimed to evaluate the impact of PCV13 introduction on mortality rates due to pneumonia and meningitis in children under five. Descriptive statistics, including proportions and percentages, were used to present the socio-demographic characteristics of the study participants and their vaccination coverage. Mortality rates before and after the introduction of the vaccines were calculated along with their respective 95% confidence intervals (CI). To assess the effect of PCV13 introduction on mortality rates, data were prepared for survival analysis, and mortality rates were compared before and after vaccination. Stratified analyses using Cox proportional hazards models were performed to examine the effect of vaccination on mortality across subgroups defined by sex, area of residence (urban and rural), and place of delivery (health facility or home). Kaplan-Meier survival curves were utilised to illustrate the overall survival experience of the under-five cohort.

2.10. Study Design

This was a retrospective observational study that used longitudinal mortality and vaccination data from the NDHSS database.

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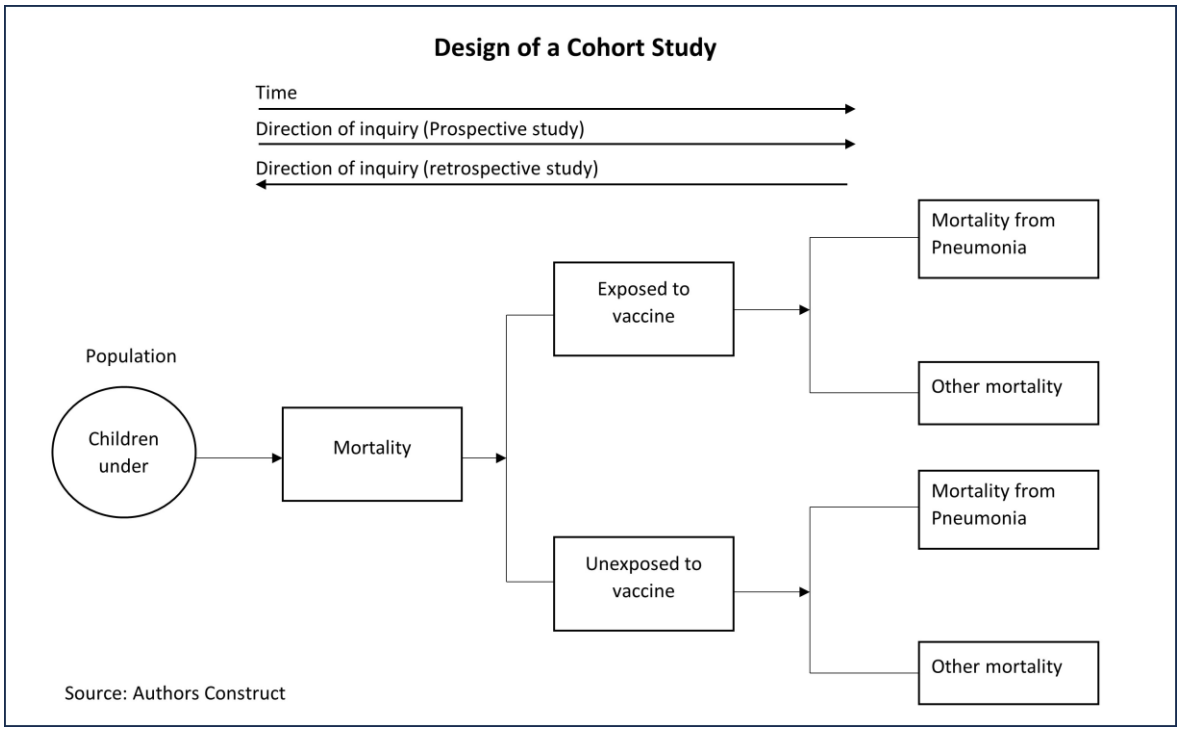

3. Results

3.1. Background Characteristics

This section presents the socio-demographic characteristics of the study participants. The proportion of deaths was distributed across all sociodemographic groups within the study population. Out of a total number of 48,351 children, males constituted 50.2% of the study population (24,287) and experienced more deaths (4.2%). The majority (68.9%) of the participants had mothers aged between 20 and 34 years, and children with mothers aged 35 years and above contributed 5.0% of deaths. Vaccine coverage of the third dose of PCV13 ranged between about 85% the first year after introduction and about 96% in 2017. PCV13 is given at six weeks, ten weeks and fourteen weeks in Ghana. A high percentage of deaths (7.8%) occurred among participants whose mothers had only primary education (54.5%) and resided in rural areas (84.9%). Additionally, a greater percentage of deaths (6.8%) occurred among participants who were delivered at home or elsewhere outside a health facility. Furthermore, the data indicate that the poorest participants (28.3%) experienced the highest death rate (4.9%) (Table 1). Information was accessed at baseline.

Table 1. Background characteristics (at time of childbirth).

Variable	Number (%)	Death of child (%)
Sex children		
Female	24,064 (49.8)	858 (3.6)
Male	24,287 (50.2)	1,014 (4.2)
Mother's Age		
<19	5,919 (12.2)	243(4.1)
20-34	33,295 (68.9)	1,170(3.5)
35+	9,137 (18.9)	459(5.0)
Maternal Education		
No formal Education	10,245(21.2)	549(5.4)
Primary/JSS	26,370(54.5)	1031(7.8)

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Secondary/Tertiary	9,025(18.7)	229(4.8)
Missing	2,711(5.6)	63(2.3)
Place of Residence of mother		
Urban	7,316 (15.1)	221 (3.0)
Rural	41,035 (84.9)	1,651 (4.0)
Delivery Place		
Health Facility	32,560 (67.3)	1,137(3.5)
Home/Elsewhere	8,511 (17.6)	576(6.8)
Missing	7,280 (15.1)	159(2.2)
Wealth Quantiles		
Poorest	12,177(28.3)	591(4.9)
Poorer	9,886(23.0)	412(4.2)
Poor	8,054(18.7)	334(4.2)
Less Poor	8,051(18.7)	268(3.3)
Least poor	4,881(11.3)	125(2.6)
Multiple		
Singleton	46,022(95.2)	1,718(3.7)
Multiple	2,329(4.8)	154(6.6)
Period		
Before	23,002(47.6)	1,232(5.4)
After	25,349(52.4)	640(2.5)
Total	48,351	1,872(3.9)

Objective 1: All-cause mortality in children under five before and after PCV13 introduction

All-cause mortality in children under five before and after the introduction of the PCV13 immunisation is presented in Table 2. Generally, the data reveal a decrease in mortality rate (MR) after the introduction of the PCV13 immunisation. For instance, there was a decrease in the MR in males (MR = 8.8, 95% CI = 8.1-9.7) and females (MR = 7.6, 95% CI = 6.9-8.4) after the introduction of the PCV13 immunisation. Similarly, there was a decrease in the MR in participants who resided in urban areas (MR = 6.5, 95% CI = 5.4-7.9) and rural areas (MR = 8.5, 95% CI = 7.9-9.2) after the introduction of the PCV13 immunisation (Table 2).

Table 2. Mortality rate in children under five before and after PCV13 immunisation.

Variable	Before PCV13 immunization (2007-2012)		After PCV13 immunization (2012-2017)	
	Deaths	MR (95%CI)	Deaths	MR (95%CI)
Sex				
Female	470	19.8 (18.1 - 21.7)	338	7.6 (6.9 - 8.4)
Male	559	23.4 (21.5 - 25.4)	455	8.8 (8.1 - 9.7)
Mother's Age				
<19	139	26.6 (22.5 - 31.4)	104	8.9 (7.3 - 10.8)
20-34	619	19.4 (18.0 - 21.0)	551	7.8 (7.2 - 8.5)
35+	271	25.6 (22.7 - 28.8)	188	9.2 (7.9 - 10.6)
Maternal Education				
No formal Education	356	24.5 (22.0 - 27.1)	193	9.2 (8.0 - 10.5)
Primary/JSS	549	42.5 (37.7 - 48.0)	482	16.7 (14.7 - 18.9)
Secondary/Tertiary	110	32.0 (24.2 - 42.3)	119	11.3 (8.7 - 14.8)
Missing	14	39.4 (23.3 - 66.5)	49	11.6 (8.7 - 15.3)
Place of Residence				
Urban	121	18.7(15.7 - 22.4)	100	6.5(5.4 - 7.9)

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Rural	908	22.0(20.6 - 23.5)	743	8.5(7.9 - 9.2)
Delivery Place				
Health Facility	482	21.1(19.3 - 23.1)	655	8.6(8.0 - 9.3)
Home/Elsewhere	445	23.4(21.3 - 25.6)	131	9.3(7.8 - 11.0)
Missing	102	17.7(14.6 - 21.5)	57	4.6(3.5 - 5.9)
Wealth Quantiles				
Poorest	331	26.1(23.4 - 29.1)	260	10.1(8.9 - 11.4)
Poorer	225	22.3(19.6 - 25.4)	187	8.9(7.7 - 10.3)
Poor	175	21.5(18.6 - 25.0)	159	9.3(8.0 - 10.9)
Less Poor	138	17.6(14.9 - 20.8)	130	7.5(6.3 - 8.9)
least poor	61	13.9(10.8 - 17.9)	64	6.0(4.7 - 7.6)
Multiple				
Singleton	946	20.7(19.5 - 22.1)	772	7.9(7.3 - 8.5)
Multiple	83	40.8(32.9 - 50.6)	71	16.1(12.8 - 20.4)
Period				
Before	1,029	21.6(20.3 - 22.9)	203	4.8(4.2 - 5.5)
After			640	10.6(9.8 - 11.5)

Figure 2 shows the survival probability of children under five in the study area. Children who were introduced to PCV13 had a higher chance of survival compared with those before PCV13 introduction. This difference was statistically significant using the log-rank test for the equality of survival functions (p<0.0001) (see Figure 2)

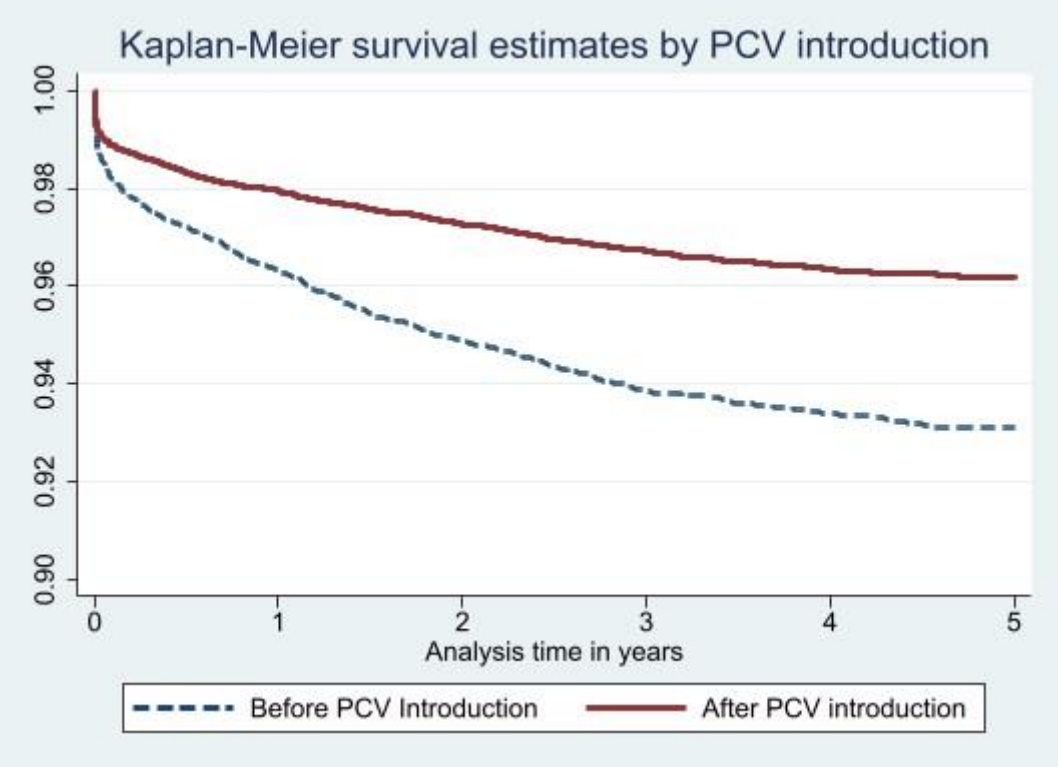

Figure 2. Kaplan-Meier survival estimates by PCV introduction.

3.2. Mortality Due to Pneumonia, Meningitis, and Diarrhoea Before and After PCV13 Immunisation

Overall, there was a substantial reduction in MR for the above causes of death after the introduction of the PCV13 vaccine (Table 3). There was a greater reduction in the mortality rate from pneumonia than from meningitis.

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Table 3. Cause-specific mortality rates per 1000 person-years(pyrs) before and after PCV13 introduction.

Cause of Death	Before PCV13 introduction		After PCV13 introduction	
	Death	MR (95%CI)/1000 pyrs	Death	MR (95%CI)/1000 pyrs
Pneumonia	54	11.3(8.7 - 14.8)	88	5.9(4.8 - 7.2)
Meningitis	17	3.6(2.2 - 5.7)	31	2.1(1.5 - 2.9)
Pneumonia and Meningitis	71	14.9(11.8 - 18.8)	119	7.9(6.6 - 9.5)
Diarrhoea	73	15.3(12.2 - 19.3)	107	7.1(5.9 - 8.6)

3.3. Mortality Rate of Pneumonia in Children Under Five Before and After PCV13 Immunisation

According to the data, under-five mortality rates (MR) from pneumonia decreased significantly after the introduction of the PCV13 vaccine across all parameters. A reduction in pneumonia MR was observed for both sexes (MR=0.6, 95% CI=0.4-0.8) following the introduction of the PCV13 immunisation. Similarly, there was a decline in pneumonia MR among children born in health facilities (MR=0.5, 95% CI=0.4-0.7) and at home (MR=0.8, 95% CI=0.6-1.2) after the introduction of the PCV13 immunisation. (Table 4).

Table 4. Mortality rate of Pneumonia in children under five before and after PCV13 vaccination.

Variable	Before PCV13 immunization		After PCV13 immunization	
	Deaths	MR (95%CI)	Deaths	MR (95%CI)
Sex				
Female	27	1.1(0.8 - 1.7)	45	0.6(0.4 - 0.8)
Male	27	1.1(0.8 - 1.6)	43	0.6(0.4 - 0.8)
mother's Age				
<19	5	1.0(0.4 - 2.3)	11	0.7(0.4 - 1.2)
20-34	35	1.1(0.8 - 1.5)	56	0.5(0.4 - 0.7)
35+	14	1.3(0.8 - 2.2)	21	0.7(0.4 - 1.0)
Maternal Education				
No formal Education	20	1.4(0.9 - 2.1)	27	0.8(0.5 - 1.1)
Primary/JSS	25	1.8(1.0 - 3.3)	44	1.0(0.7 - 1.6)
Secondary/Tertiary	8	2.2(0.8 - 6.6)	11	0.8(0.3 - 2.0)
Missing	1	2.8(0.4 - 20.0)	6	1.3(0.6 - 2.9)
Place of Residence				
Urban	8	1.2(0.6 - 2.5)	13	0.6(0.3 - 1.0)
Rural	46	1.1(0.8 - 1.5)	75	0.6(0.5 - 0.7)
Delivery Place				
Health Facility	24	1.0(0.7 - 1.6)	52	0.5(0.4 - 0.7)
Home/Elsewhere	23	1.2(0.8 - 1.8)	28	0.8(0.6 - 1.2)
Missing	7	1.2(0.6 - 2.6)	8	0.4(0.2 - 0.9)
Wealth Quantiles				
Poorest	17	1.3(0.8 - 2.2)	27	0.7(0.5 - 1.0)
Poorer	12	1.2(0.7 - 2.1)	20	0.6(0.4 - 1.0)
Poor	8	1.0(0.5 - 2.0)	13	0.5(0.3 - 0.9)
Less Poor	6	0.8(0.3 - 1.7)	10	0.4(0.2 - 0.7)
least poor	7	1.6(0.8 - 3.4)	12	0.8(0.5 - 1.4)
Multiple				
Singleton	51	1.1(0.9 - 1.5)	81	0.6(0.5 - 0.7)
Multiple	3	1.5(0.5 - 4.6)	7	1.1(0.5 - 2.3)

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3.4. Mortality Rate of Meningitis in Children Under Five Before and After PCV13 Vaccination

The analysis of data on the mortality rate (MR) from meningitis among under-fives is summarised in Table 5. The results show a marked decline in meningitis MR across all variables after the introduction of the PCV13 vaccine. For instance, there was a great decline in meningitis MR for males (MR=0.2, 95% CI=0.1-0.4), females (MR=0.1, 95% CI=0.0-0.4), urban residents (MR=0.2, 95% CI=0.2-0.3), and rural residents (MR=0.6, 95% CI=0.4-0.8) after the introduction of the PCV13 immunisation. Likewise, there was a decline in pneumonia MR in children who were delivered in health facilities (MR=0.2, 95% CI=0.1-0.3) and homes (MR=0.3, 95% CI=0.1-0.5) after the introduction of the PCV13 immunisation (Table 5).

Table 5. Cause-specific Meningitis death rate in children under five before and after PCV13 vaccination by background characteristics.

Variable	Before PCV13 immunization		After PCV13 immunization	
	Deaths	MR (95%CI)	Deaths	MR (95%CI)
Sex				
Female	10	0.4(0.2 - 0.8)	17	0.2(0.1 - 0.4)
Male	7	0.3(0.1 - 0.6)	14	0.2(0.1 - 0.3)
Mother's Age				
<19	2	0.4(0.1 - 1.5)	6	0.4(0.2 - 0.8)
20-34	11	0.3(0.2 - 0.6)	20	0.2(0.1 - 0.3)
35+	4	0.4(0.1 - 1.0)	5	0.2(0.1 - 0.4)
Maternal Education				
No formal Education	5	0.3(0.1 - 0.8)	8	0.2(0.1 - 0.4)
Primary/JSS	8	0.7(0.2 - 1.7)	17	0.4(0.2 - 0.8)
Secondary/Tertiary	3	0.7(0.2 - 2.0)	4	0.2(0.1 - 0.6)
Missing	1	2.8(0.4 - 20.0)	2	0.4(0.1 - 1.7)
Place of Residence				
Urban	2	0.3(0.1 - 1.2)	3	0.1(0.0 - 0.4)
Rural	15	0.4(0.2 - 0.6)	28	0.2(0.2 - 0.3)
Delivery Place				
Health Facility	7	0.3(0.1 - 0.6)	20	0.2(0.1 - 0.3)
Home/Elsewhere	9	0.5(0.2 - 0.9)	9	0.3(0.1 - 0.5)
Missing	1	0.2(0.0 - 1.2)	2	0.1(0.0 - 0.4)
Wealth Quantiles				
Poorest	5	0.4(0.2 - 0.9)	10	0.3(0.1 - 0.5)
Poorer	3	0.3(0.1 - 0.9)	5	0.2(0.1 - 0.4)
Poor	3	0.4(0.1 - 1.1)	4	0.2(0.1 - 0.4)
Less Poor	4	0.5(0.2 - 1.4)	6	0.2(0.1 - 0.5)
least poor	1	0.2(0.0 - 1.6)	3	0.2(0.1 - 0.6)
Multiple				
Singleton	17	0.4(0.2 - 0.6)	30	0.2(0.1 - 0.3)
Multiple	0	0	1	0.2(0.0 - 1.1)

Objective 2: Cause-specific pneumonia and meningitis under-five death rates since the introduction of PCV-13

This section shows the cause-specific pneumonia and meningitis death rates since the introduction of PCV-13 in children under five. Under-five mortality rates (MR) from pneumonia and meningitis decreased substantially after the introduction of the PCV13 vaccine for all the independent variables. For example, a reduction in MR from pneumonia and meningitis was observed for males (MR = 0.8, 95% CI = 0.6-1.1), females (MR = 0.8, 95% CI = 0.6-1.0), urban residents (MR = 0.7, 95% CI =

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0.5-1.2), rural residents (MR=0.8, 95% CI = 0.7-1.0), delivery in health facility (MR = 0.7, 95% CI = 0.6-0.9) and delivery in homes (MR = 1.1, 95% CI = 0.8-1.5) after the introduction of the PCV13 immunization (Table 6).

Table 6. Cause-specific Meningitis and Pneumonia death rates in children under five years of age before and after PCV13 vaccination by background characteristics.

Variable	Before PCV13 immunization		After PCV13 immunization	
	Deaths	MR (95%CI)	Deaths	MR (95%CI)
Sex				
Female	37	1.6(1.1 - 2.2)	62	0.8(0.6 - 1.1)
Male	34	1.4(1.0 - 2.0)	57	0.8(0.6 - 1.0)
Mother's Age				
<19	7	1.3(0.6 - 2.8)	17	1.0(0.6 - 1.6)
20-34	46	1.4(1.1 - 1.9)	76	0.7(0.6 - 0.9)
35+	18	1.7(1.1 - 2.7)	26	0.8(0.6 - 1.2)
Maternal Education				
No formal Education	25	1.7(1.2 - 2.5)	35	1.0(0.7 - 1.4)
Primary/JSS	33	2.5(1.5 - 4.1)	61	1.4(1.0 - 2.1)
Secondary/Tertiary	11	2.9(1.3 -7.4)	15	1.0(0.5 - 2.3)
Missing	2	5.6(1.4 - 22.5)	8	1.7(0.9 - 3.5)
Place of Residence				
Urban	10	1.5(0.8 - 2.9)	16	0.7(0.5 - 1.2)
Rural	61	1.5(1.2 - 1.9)	103	0.8(0.7 - 1.0)
Delivery Place				
Health Facility	31	1.4(1.0 - 1.9)	72	0.7(0.6 - 0.9)
Home/Elsewhere	32	1.7(1.2 - 2.4)	37	1.1(0.8 - 1.5)
Missing	8	1.4(0.7 - 2.8)	10	0.5(0.3 - 1.0)
Wealth Quantiles				
Poorest	22	1.7(1.1 - 2.6)	37	1.0(0.7 - 1.3)
Poorer	15	1.5(0.9 - 2.5)	25	0.8(0.5 - 1.2)
Poor	11	1.4(0.7 - 2.4)	17	0.7(0.4 - 1.1)
Less Poor	10	1.3(0.7 - 2.4)	16	0.6(0.4 - 1.0)
least poor	8	1.8(0.9 - 3.7)	15	1.0(0.6 - 1.7)
Multiple				
Singleton	68	1.5(1.2 - 1.9)	111	0.8(0.6 - 0.9)
Multiple	3	1.5(0.5 - 4.6)	8	1.2(0.6 - 2.5)

Objective 3: To estimate vaccine coverage of PCV-13 in children under five in the Kassena Nankana districts.

Table 7. Vaccination coverage among children aged 12-23 months in Kassena Nankana East and West Districts in Ghana: 2007-2017.

Survey Year	BCG	OPV0	OPV1	OPV2	OPV3	Penta1	Penta2	Penta3	Measles 1
2007	98.9	70.2	99.3	98.7	97.8	99.5	99.2	98.1	93.2
2008	97.8	72.6	99.3	98.5	97.9	99.4	99.0	98.2	95.3
2009	99.3	73.6	99.8	99.5	98.9	99.9	99.8	99.3	96.3
2010	99.1	90.0	99.1	98.7	98.1	99.0	98.6	98.5	95.9
2011	99.6	93.3	99.8	99.7	98.8	99.8	99.7	99.4	97.3
2012	99.7	95.7	100.0	99.9	98.9	99.9	99.9	99.6	96.4
2013	99.1	97.2	99.6	99.4	97.6	99.6	99.5	99.0	95.1
2014	98.2	96.4	99.0	98.9	97.4	99.0	98.9	98.3	93.9

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2015	98.6	97.2	99.0	99.3	98.2	99.0	99.2	99.0	95.1
2016	97.7	97.0	98.7	98.6	97.6	98.6	98.5	97.7	94.6
2017	97.5	96.3	98.3	98.2	97.8	97.7	97.9	97.5	94.7

The vaccination coverage among children aged 12-23 months in Kassena Nankana East and West from 2007 to 2017 is summarised in Table 1. The data reveal that BCG, OPV1, OPV2, OPV3, Penta1, Penta2, Penta3, and Measles1 had a vaccination coverage of at least 93% during this period. However, OPV0 had less than 75% coverage in the districts in 2007, 2008, and 2009. Notably, OPV1 had 100% coverage in 2012, which was higher than that of BCG, OPV0, and Penta1 (Table 7).

Table 8. Vaccination coverage for vaccines introduced into Ghana EPI schedule in 2012: Children aged 12-23 months in Kassena Nankana East and West Districts in Ghana: 2013-2017.

Survey Year	PCV1	PCV2	PCV3	Rota1	Rota2
2013	25.3	23.4	19.6	25.8	21.2
2014	94.1	92.9	85.9	93.9	90.9
2015	97.2	97	95.4	96.6	96.2
2016	96.8	96.5	95.4	96.3	95.7
2017	96.1	96.1	95.7	95.6	95.8

In 2012, pneumococcal conjugate vaccine (PCV), rotavirus vaccine and a second dose of measles-containing vaccine (MCV2) were introduced into the Expanded Program on Immunisation (EPI) in Ghana. According to Ghana's EPI schedule, PCV and rotavirus vaccine are given in the first year of life and MCV2 in the second year of life (2YL) at 18 months. In the first year of the introduction, the coverage rate was low (2013). However, coverage with the last doses of PCV and rotavirus vaccine reached almost 90% coverage within four years of introduction.

4. Discussion

This study demonstrated that the PCV13 vaccine is effective in reducing mortality from clinical pneumonia in a resource-poor setting. Mortality from pneumonia decreased by about 50% in both males and females after the introduction of PCV13 vaccination. All-cause mortality for both sexes was reduced by 60%. Along with high PCV13 vaccine coverage, which increased from 85.9% in 2014 to 95.7% by 2017, these data indicate that PCV13 has been effective in reducing mortality from clinical pneumonia in this population. Additionally, mortality rates from pneumonia and meningitis combined showed a marked reduction from about 15% to 8% in children younger than five years.

Our study was unable to distinguish among the types of strains causing pneumonia mortality, unlike studies in Europe and North America. However, since PCV13 strains account for most pneumonia cases, we assume that any reduction in pneumonia mortality is due to the prevention of infection by strains included in PCV13 [19–21].

Mortality from clinical pneumonia in children under five years within the demographic surveillance area was 11.3% of deaths before the introduction of PCV13. This aligns with the findings reported in a study by O'Brien et al., which estimated the mortality rate from invasive disease caused by S. pneumoniae at 11%[22]. Our results showed that mortality from pneumonia declined by 50% after the introduction of PCV13, demonstrating the vaccine's effectiveness. These results are consistent with findings from England and Wales, which indicated a 32% further reduction in vaccine-type invasive disease following the deployment of PCV13 after the initial use of PCV7 [19]. Waight P. A et al. projected that in the coming years in England and Wales, disease attributable to PCV13, including non-bacteraemia pneumonia, will become almost extinct [19]. This projection was based on the premise that eight years of PCV use in England caused an 86% reduction in vaccine-type pneumococcal invasive disease[19].

PCV-13 was developed after PCV-7 to protect against key additional serotypes common in Africa and other regions with high incidence[19]. The reduction in mortality from clinical pneumonia

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in our study area confirms the effectiveness of PCV13 in a low- and middle-income country setting. In a modelling study, Cynthia Chen et al. projected that, in Africa from 2020 to 2030, using real-world vaccine coverage data, invasive pneumococcal disease (IPD) pneumonia deaths in children under 5 years would decrease by 19.9% [23]. This was due to reduced vaccine coverage[23]. The high levels of vaccine coverage in the study area resulted in a significantly lower mortality rate from vaccine-preventable clinical pneumonia.

The decrease in meningitis deaths may partly be attributed to the introduction of PCV13 alongside the MenAfrivac vaccine. The MenAfrivac vaccine is used to prevent Meningococcus A infection, which usually causes epidemics in the meningitis belt of Africa [24]. The verbal autopsies could not differentiate between deaths from pneumococcal meningitis and other types of meningitis. However, a study conducted in Burkina Faso in 2014 and 2015 indicated a decrease in the overall incidence of pneumococcal meningitis after the introduction of PCV13, with a more pronounced reduction in cases caused by vaccine-serotype strains[22]. This suggests that the vaccine is effectively reducing the burden of pneumococcal disease, including meningitis, in the targeted population. In a study by PM Faye et al. in Senegal, the effectiveness of the pneumococcal vaccine was also observed across both meningitis and pneumonia, two serious illnesses caused by pneumococcal bacteria[25]. A retrospective study in Rwanda, using hospital records, showed a decline in both pneumonia and meningitis after the introduction of PCV13, as observed in this study, which utilised demographic surveillance data[26].

A study of pneumococcal carriage by Nicholas T K D Dayie et al. showed that PCV-13 introduced in Ghana did not eliminate PCV-13-covered serotypes, with a carriage rate of 54%, like the rates from the pre-PCV-13 period. However, this does not match the decline in pneumonia and meningitis deaths seen in most studies on PCV vaccine effectiveness [20,23,25,27–33]. These findings show that PCV13 reduces mortality from vaccine-type invasive diseases, such as pneumonia and meningitis, in resource-limited settings like northern Ghana, regardless of sex, socioeconomic status, or age. Achieving high levels of vaccine coverage in such settings can enhance the vaccine's effectiveness and promote herd immunity.

5. Limitations

One inherent limitation of this study is that it was conducted using a single health and demographic surveillance system catchment area (Kassena Nankana East and West), which made assessing nationwide trends difficult. No laboratory tests were used to confirm diagnoses.

Additionally, diagnoses are based on results from verbal autopsies, which may not be very accurate because information obtained from relatives of the deceased may not be reliable. It is impossible to determine whether a particular bacterial strain caused the pneumonia. Another limitation worth noting is that PCV13 was not the only vaccine introduced in Ghana in 2012. Rotavirus vaccine, Meningitis A vaccine, and a second dose of measles-containing vaccine (MCV2) were also added to Ghana's EPI. These likely contributed to a reduction in all-cause mortality. There is minimal risk that a child under five was not included in the NHDSS database because a robust numbering system with GPS and community volunteers is used. However, some vaccination data were missing due to errors in vaccination records and the absence of individual vaccination cards.

6. Conclusions

This study demonstrated that PCV-13 coverage increased annually, with a slight decrease in third-dose coverage compared to the second dose. PCV-13 is effective in reducing mortality from pneumonia and meningitis. Newly introduced childhood vaccines are well-received in Ghana, as evidenced by high vaccination coverage. The HDSS can be successfully used for vaccine effectiveness studies. Linking data to hospital records will enhance data robustness and ensure that morbidity data can be included in effectiveness studies. The NHDSS system has been operational for 32 years and

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remains sustainable with sufficient funding, particularly in the absence of robust longitudinal data systems in Africa.

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Abbreviations

The following abbreviations are used in this manuscript:

NHDSS	Navrongo Health and Demographic Surveillance System
EPI	Expanded Programme on Immunisation
PCV	Pneumococcal Vaccine
MCV	Measles Containing Vaccine

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