



Published in final edited form as:

Pediatr Infect Dis J. 2025 February 01; 44(2 Suppl): S75–S79. doi:10.1097/INF.0000000000004638.

Effect of the Ten-valent Pneumococcal Conjugate Vaccine on Invasive Pneumococcal Disease and Pneumonia in Infants Younger Than Ten Weeks of Age in Southern Mozambique:

A Population-based Prospective Surveillance Study

Sérgio Massora, PhD^{*}, Hélio Mucavele, MD^{*}, Maria da Gloria Carvalho, PhD[†], Inácio Mandomando, PhD^{*}, Alberto Chaúque, MSc^{*}, Benild Moiane, MSc^{*}, Nelson Tembe, PhD^{*,‡}, Saad B. Omer, MD, PhD[§], Quique Bassat, MD, PhD^{*,¶,||,**,††}, Jennifer R. Verani, MD, MPH[†], Clara Menéndez, MD, PhD^{*,¶,††}, Llorenç Quintó, MSc^{*,¶,††}, Betuel Sigaúque, MD, PhD^{*,‡‡}, Azucena Bardají, MD, PhD^{*,¶,††}

^{*}Centro de Investigação em Saúde de Manhiça (CISM), Maputo, Moçambique

[†]Centers for Disease Control and Prevention, National Center for Immunization and Respiratory Diseases, Division of Bacterial Diseases, Respiratory Diseases Branch, Atlanta, Georgia

[‡]Instituto Nacional de Saúde, Ministério de Saúde, Maputo, Mozambique

[§]Peter O'Donnell Jr School of Public Health, Dallas, Texas

[¶]ISGlobal, Hospital Clínic – Universitat de Barcelona, Barcelona, Spain

^{||}ICREA, Barcelona, Spain

^{**}Pediatrics Department, Hospital Sant Joan de Déu, Universitat de Barcelona, Barcelona, Spain

^{††}Consorcio de Investigación Biomédica en Red de Epidemiología y Salud Pública (CIBERESP), Madrid, Spain

^{‡‡}John Snow Inc. (JSI) on the Maternal and Child Survival Program–MCSP (USAID Grantee), Maputo, Mozambique.

Abstract

Background: Mozambique introduced 10-valent-pneumococcal conjugate vaccine (PCV10) in 2013. We aimed to evaluate the indirect effect of PCV10 on invasive pneumococcal disease (IPD) and clinical severe pneumonia (CSP) in infants aged less than 10 weeks.

Methods: Routine surveillance data for IPD and CSP among admitted infants less than 10 weeks of age were analyzed to compare IPD and CSP incidence using demographic surveillance data from pre- and post-PCV10 periods. IPD was defined as isolation of pneumococcus from blood or cerebrospinal fluid, and CSP according to World Health Organization criteria.

Address for correspondence: Sérgio Massora, PhD, Centro de Investigação em Saúde de Manhiça (CISM), Road 12. P.O. Box 1929, Manhiça, Maputo, Mozambique. sergio.massora@manhica.net.

The authors have no conflicts of interest to disclose.

Supplemental digital content is available for this article. Direct URL citations appear in the printed text and are provided in the HTML and PDF versions of this article on the journal's website (www.pidj.com).

Results: The incidence of IPD and CSP among infants less than 10 weeks decreased by 87% [incidence rate ratio (IRR): 0.13; 95% confidence interval (CI): 0.02–0.95] from 283/100,000 in the pre-PCV to 36/100,000 children year at risk (CYAR) post-PCV, and by 62% (IRR: 0.38; 95% CI: 0.27–0.52) from 4100/100,000 pre-PCV to 1550/100,000 CYAR post-PCV periods, respectively. Vaccine-type IPD incidence declined by 92% (IRR: 0.18; 95% CI: 0.02–1.34) from 205/100,000 pre-PCV to 36/100,000 CYAR post-PCV, though the reduction was not statistically significant. The mortality rate due to IPD among infants less than 10 weeks declined from 47/100,000 CYAR in the pre-PCV to 0 in the post-PCV period. Mortality due to CSP declined by 29% (IRR: 0.71; 95% CI: 0.34–1.50), from 457/100,000 CYAR in the pre-PCV to 324/100,000 in the post-PCV periods.

Conclusions: PCV10 introduction led to substantial declines in the incidence of IPD, CSP and associated mortality in infants too young to be vaccinated (less than 10 weeks) in Mozambique, suggesting indirect protection.

Keywords

invasive pneumococcal disease; severe clinical pneumonia; 10-valent-pneumococcal conjugate vaccine impact; young children

Streptococcus pneumoniae (pneumococcus) is an important cause of severe pneumonia, sepsis and meningitis among children worldwide.¹ Pneumococcal conjugate vaccine (PCV) introduction in routine immunization programs globally resulted in the prevention of an estimated 250,000 cumulative pneumococcal-related deaths from 2000 to 2015.^{1–3} Despite this achievement, in the year 2015, the total pneumococcal deaths continued to account for at least 10% of all mortality among HIV-uninfected children 1–59 months of age, with highest incidence in sub-Saharan Africa.¹ Studies from the prevaccine era indicated that, in Africa, pneumococcus was responsible for up to 47% of cases of culture-proven meningitis during the first 3 months of life,^{4,5} and 16.5% of cases of community-acquired neonatal sepsis, second only to *Staphylococcus aureus*.⁶ The use of PCV has been shown to lead to indirect protection among unvaccinated individuals mediated by a reduction in colonization and transmission of vaccine serotypes.⁷ Substantial indirect effect of PCV in adults and in infants too young to receive vaccination have been proven in high-income countries.^{8–10} However, little is known about indirect protection against invasive pneumococcal disease (IPD) in young infants in low-income settings.

Since 2001, the Centro de Investigação em Saúde de Manhica (CISM) has conducted routine surveillance for invasive bacterial disease among children in rural Mozambique.¹¹ In the prevaccination era, pneumococcus was a leading agent of meningitis and sepsis in the country with a peak of reported incidence of IPD in infants of 479 per 100,000 children year at risk (CYAR).¹² Data from this surveillance platform were instrumental in prompting the Mozambican Ministry of Health to apply for support from Gavi, the Vaccine Alliance, to introduce 10-valent pneumococcal conjugate vaccine (PCV10) in 2013 using a 3+0 schedule (at 2, 3 and 4 months of age) with no booster or catch-up campaign. Coverage of 3 PCV doses among children 12–23 months old from 2015 to 2018, based on World Health Organization and United Nations International Children's Emergency Fund estimates, was at least 80% each year.¹³ Recent data have shown that PCV10 introduction in Mozambique led

to a remarkable decrease in IPD and pneumonia in children under 5 years of age,^{14,15} but indirect effects of PCV on children too young to be vaccinated (<10 weeks of age) have not been shown. We focused on the age group less than 10 weeks because the first PCV dose is given at 2 months of age, and we assumed that there is no direct PCV effect during the first 2 weeks after the first dose. In this study, we characterized the burden of IPD and clinical severe pneumonia (CSP) in infants younger than 10 weeks of life before and after PCV10 implementation to assess indirect effect of PCV10 effects.

MATERIALS AND METHODS

Study Area and Population

We analyzed data from ongoing surveillance for IPD and pediatric pneumonia routinely conducted by CISM at the Manhiça District Hospital (MDH), a referral district hospital in Southern Mozambique. Within the district, CISM has maintained a continuous demographic surveillance system (DSS) since 1996. Since 2014, the DSS covers the entire district, which includes a population of approximately 200,000 inhabitants and covers approximately 2300 km².¹⁶ Manhiça has a predominantly young population, with 13.5% aged less than 5 years of age.¹⁷

The area is rural, malaria-endemic and bears a high HIV burden, with HIV prevalence among pregnant women estimated at 21.7% in 2021 (Mendes et al., unpublished data), and overall community-based HIV prevalence among adults of 33.6% in 2015.¹⁸ Acute respiratory infections and malaria are major causes of neonatal, infant and child mortality in the area.¹⁹

Morbidity Surveillance and Sample Collection

As part of the ongoing morbidity surveillance at MDH, trained clinical personnel perform physical examination and gather demographic data, presenting signs and symptoms, and clinical outcomes. Data collection, cleaning and management were conducted using the OpenClinica open-source software (version 3.1, Copyright OpenClinica LLC and collaborators, Waltham, MA, www.OpenClinica.com), and the REDCap platform (REDCap, Vanderbilt University Medical Center, Nashville, TN). Blood for cultures was obtained by venipuncture upon admission and before administration of antimicrobials for all children less than 2 years old requiring hospitalization and for those 2 to <15 years old with axillary temperature $\geq 39^{\circ}\text{C}$ or other signs of severe disease (except trauma) according to the admitting clinician. Lumbar puncture to collect cerebrospinal fluid (CSF) was systematically performed on all children or infants <29 days old admitted with suspected meningitis.

Study Population and Case Definitions

The study included all children less than 10 weeks with CSP and/or IPD admitted to MDH from January 1, 2003, to December 31, 2018. IPD was defined as the isolation of pneumococcus from blood or CSF, identified by culture or quantitative polymerase chain reaction (PCR). Cases of IPD caused by a serotype included in PCV10 (1, 4, 5, 6B, 7F, 9V, 14, 18C, 19F and 23F) were classified as vaccine-type IPD (VT-IPD). All other serotypes were classified as non-VTs, with serotypes 3, 6A and 19A being classified as PCV13 unique

serotypes. Cases with *S. pneumoniae* detected in CSF (CSF only or in both CSF and blood) were classified as meningitis; all other cases with *S. pneumoniae* in the blood were classified as bacteremia. Among bacteremia cases, those with cough and/or breathing difficulties plus tachypnea were classified as bacteremia with pneumonia. CSP was defined according to World Health Organization classification as the presence of history of cough for up to 2 weeks or difficulty breathing, increased respiratory rate according to age group and chest wall indrawing.²⁰

Laboratory Methods

Pediatric blood culture bottles (Pedibact1, Becton Dickinson, Franklin Lakes, NJ) were inoculated with 1–3 mL of whole blood and incubated in an automated system (BACTEC 9050, Franklin Lakes, NJ) for 5 days. Positive blood culture bottles with a Gram stain compatible with pneumococcus were subcultured onto blood agar and incubated overnight at 37°C and 5% CO₂. CSF specimens were first stained by Gram and subsequently cultured onto blood agar, chocolate blood agar and brain heart infusion broth for 5 days, followed by incubation at 37°C in an atmosphere of 5% CO₂. Brain heart infusion broths were subcultured on blood agar media and incubated for 72 hours in case of turbidity appearance. Typical colony morphology and α -hemolysis, confirmed by optochin (BBL Taxo; Becton Dickinson) sensitivity and bile solubility 2% (Sodium deoxycholate, Sigma-Aldrich, Steinheim, Germany), were used to identify pneumococcus isolates. In addition, CSF samples were processed at a Centers for Diseases Control and Prevention (CDC) laboratory by quantitative-PCR for the detection of pneumococcal *lytA* gene and serotyping.^{21,22} All pneumococcal isolates were serotyped at CISM laboratory by sequential multiplex PCR. Quality control and resolution of serogroups that could not be differentiated by PCR were done at the CDC by Quellung reaction.

Statistical Analysis Methods

We analyzed data for all cases admitted to MDH, and for the incidence calculation, we restricted to DSS catchment area. We calculated incidence rates for overall IPD, PCV10 type IPD, non-VT-IPD and CSP among children aged less than 10 weeks residing in the study area for the periods pre- and post-PCV10 introduction. The calendar year of vaccine introduction (April 2013–March 2014) was excluded from the vaccine impact analyses as it was considered a transition period to full implementation of the PCV program. Time at risk for incidence rates was calculated as the number of person-years at risk from the beginning of the time at risk until the end of follow-up. In calculating person-year at risk, individuals were excluded during a lag period of 15 days after each episode. Children did not contribute to the time at risk or to the number of episodes during the lag periods or during the migration periods detected through the DSS.

Negative binomial regression models were estimated to determine incidence rate ratios (IRRs) between post- and pre-PCV periods. Serotype distributions between pre- and post-PCV periods were compared using chi-square or Fisher's exact test when appropriate. For additional information on statistical analysis methods, see text, Supplementary Digital Content 1, <http://links.lww.com/INF/F839>. All analyses, data manipulation and implementations were done in Stata version 15.0 (StataCorp, College Station, TX).

Ethical Considerations

The protocol for population-based invasive pneumococcal surveillance described in this study was reviewed and approved by the Mozambican National Bioethics Committee (006CNBS/02), the Institutional Review Board of the Clinic Hospital of Barcelona (Barcelona, Spain), and was reviewed by CDC, deemed research not involving human subjects, and was conducted consistent with applicable federal law and CDC policy.

RESULTS

Characteristics of Participants

From January 2003 to December 2018, there were 4754 admissions to MDH among infants less than 10 weeks of age. Among them, 3307 and 1217 admissions in this age group occurred during pre- and post-PCV periods, respectively, and 230 admissions during the transition period. Blood culture was performed for 90.7% (2999) and 74.9% (911) of admitted infants with criteria for blood culture in the pre- and post-PCV periods, respectively; 74.9% (172) of admissions had blood culture performed during the transition period. CSF culture was performed for 37.2% (940/2524) and 28.2% (304/1080) of infants with criteria for lumbar puncture in the pre- and post-PCV periods, respectively, and 32.8% (60/183) during the transition period.

A total of 45 IPD cases were identified among infants aged less than 10 weeks admitted to MDH; 38 and 7 cases from the pre- and post-PCV periods, respectively. No cases occurred during the transition period. Of the 45 IPD cases, 42.2% (19/45) were from the Manhiça DSS catchment area; 18/38 (47.4%) and 1/7 (14.3%) cases from the pre- and post-PCV periods, respectively.

A total of 966 MDH admissions were due to episodes of CSP; 669 in the pre-PCV and 261 in the post-PCV periods, respectively, and 36 admissions during the transition period. Of the total CSP episodes, 32.6% (315/966) occurred in the DSS catchment area, 260/669 (38.9%) in the pre- and 43/261 (16.5%) in the post-PCV periods, respectively, and 12/36 (33.3%) during the transition period. Of infants with IPD, 66.7% (30/45) presented as bacteremic without clinical features of pneumonia or meningitis, and of all CSP episodes, 89.8% (867/966) included clinical pneumonia without confirmed bacteremia (Table, Supplemental Digital Content 2, <http://links.lww.com/INF/F840>).

Impact of PCV10 on Invasive Pneumococcal Disease and Clinical Severe Pneumonia

A decrease in the incidence of IPD and CSP among infants less than 10 weeks of age was observed from the pre- to post-PCV periods. The incidence of IPD declined by 87% [IRR: 0.13; 95% confidence interval (CI): 0.02–0.95], from 283/100,000 to 36/100,000 CYAR (Table, Supplemental Digital Content 3, <http://links.lww.com/INF/F841>). No case of IPD was observed in this age group during the last 2 years of the study after PCV10 introduction (Figure, Supplemental Digital Content 4, <http://links.lww.com/INF/F842>). Despite the decline in blood culture collection, no significant impact was observed in IPD incidence (Table, Supplemental Digital Content 5, <http://links.lww.com/INF/F843>). Comparing the pre-PCV and post-PCV implementations, though not statistically significant, the incidence

of PCV10 serotypes declined by 82% (IRR: 0.18; 95% CI: 0.02–1.34), from 205/100,000 to 36/100,000 CYAR (Table, Supplemental Digital Content 3, <http://links.lww.com/INF/F841>). The incidence of non-PCV10 serotypes IPD was 63 per 100,000 CYAR in the pre-PCV period. No non-PCV10 IPD case was observed in this age group after PCV introduction. The incidence of CSP decreased by 62% (IRR: 0.38; 95% CI: 0.27–0.52), from 4100/100,000 to 1550/100,000 CYAR between pre- and post-PCV10 periods.

Impact of PCV10 on Mortality due to IPD and CSP

Overall case fatality rate due to IPD in all infants less than 10 weeks of age admitted to MDH during the study period was 22.2% (10/45), of which 23.7% (9/38) occurred during pre- and 14.3% (1/7) during post-PCV introduction periods, respectively. Of the IPD deaths that occurred in the pre-PCV period, 33.4 (3/9) cases were due to vaccine serotypes; the 1 death observed in the post-PCV was non-VT. The incidence of death due to IPD among infants aged less than 10 weeks and residents in the DSS area declined from 47/100,000 CYAR in the pre-PCV to 0 in the post-PCV periods (Table, Supplemental Digital Content 3, <http://links.lww.com/INF/F841>). Among CSP, the overall case fatality rate during the study period was 14.2% (137/966), 13.9% (93/669) and 14.5% (38/261) in the pre- and post-PCV10 periods, respectively, and 16.7% (6/36) during the transition period. The incidence of death due to CSP declined by 29% (IRR: 0.71; 95% CI: 0.34–1.50), from 457/100,000 CYAR in the pre-PCV to 324/100,000 in the post-PCV periods (Table, Supplemental Digital Content 3, <http://links.lww.com/INF/F841>).

Serotype Distribution of IPD Isolates

During the 16-year study period, there were 45 isolates of IPD identified from infants aged less than 10 weeks, including both infant residents and nonresidents in the DSS catchment area; 43 (96%) had known serotypes. No IPD cases caused by PCV10 serotypes were observed among infants aged less than 10 weeks in the post-PCV period, except for serotypes 1 and 23F which increased. The proportion of serotype 19A (included in PCV13 but not in PCV10) and of non-VTs increased in the post-PCV period; however, neither increase was statistically significant (Figure, Supplemental Digital Content 6, <http://links.lww.com/INF/F844>).

DISCUSSION

We observed a significant decline of IPD and CSP among infants aged less than 10 weeks 5 years after the introduction of PCV10 in the expanded program of immunization in Mozambique. Furthermore, we observed in this same age group a reduction in mortality related to IPD and CSP. Overall, these results show that infants who were too young to be vaccinated benefited from pneumococcal vaccination following the introduction of PCV10 in Mozambique using a 3-dose schedule without booster or catch-up campaign.

Indirect protection of PCV vaccination among infants too young to be vaccinated has been documented in high-income countries. A population-based study conducted in the United States in young infants, before and after the introduction of PCV7 in 2000 using a 3+1 schedule for infants at ages 2, 4, 6 and 12–15 months, showed a 40% reduction in the

incidence of IPD due to all serotypes, providing the first evidence that neonates and infants too young to receive PCV benefited from herd immunity.⁹ In England and Wales, where PCV7 was introduced in 2006 using 2, 4 and 12–13 months of age (2+1) schedule including a catch-up campaign for all children less than 2 years old, the incidence of PCV7 IPD declined by 83% among infants less than 90 days old and a declining trend in overall IPD was observed.¹⁰

Yet, despite pneumococcus being a major cause of illness and death in children worldwide, and a recognized pathogen in young infants, data from developing settings examining the indirect effects of PCV in early infancy are scarce. A study conducted in Kilifi, Kenya, where PCV10 was introduced with a 3+0 schedule with catch-up vaccination among children under 5 years of age, provided evidence of indirect protection against IPD in young unvaccinated infants. In this study, a notable reduction was observed among infants 0–2 months of age with VT-IPD incidence rates declining from 173.2 in the prevaccine to 0.0 per 100,000 CYAR in the postvaccine period.²³ Indirect effects through declining incidence of VT-IPD were also observed among individuals >5 years old. In Malawi, the incidence of VT-IPD among infants aged less than 90 days went from 148/100,000 in the pre-PCV13 to 36/100,000 in the post-PCV13 periods.²⁴ Similarly, to what was observed in Kenya and Malawi, in our study, the IPD incidence declined from 283/100,000 CYAR in the pre-PCV to 36/100,000 CYAR in the post-PCV periods, with no case of IPD admission in this age group documented during the last 2 years of the study period. We also observed that both VT-IPD and non-VT-IPD incidence rates decreased drastically among infants aged less than 10 weeks, though these declines did not show statistical significance. The decline of non-VT-IPD observed in this age group suggests that there are other socioeconomic and epidemiologic factors, including improved access to HIV care that contribute to lessening the risk of IPD. However, despite the decline of VT-IPD and non-VT-IPD, evidence of circulation of VT-carriage among vaccinated children raises the potential for ongoing pneumococcal transmission in our setting.²⁵

We observed a notable 62% reduction in the incidence of CSP among infants aged less than 10 weeks following PCV introduction. The indirect effect of PCV on the risk of pneumonia in older children and adults has been documented in high-income countries.^{26,27} However, data on indirect effect of PCV in young infants from low-income settings were limited.

The incidence of death due to IPD and CSP among young infants aged less than 10 weeks observed in this study decreased from 47 to 0.0 cases per 100,000 CYAR, and from 457 to 324 cases per 100,000 CYAR in the pre- to post-PCV10 periods, respectively. Some evidence exists on the effect of PCV introduction on child mortality, especially in high- and middle-resource settings. In Denmark, a nationwide population-based cohort study looking at the impact of the introduction of PCV7 and PCV13 showed a substantial decline (28%) in pneumococcal-related mortality across all age groups (from <2 to ≥65 years); mainly among the nonvaccinated population.²⁸ In addition, data from South Africa showed a reduction of 23% in mortality in children 8–18 years of age who are not eligible to receive vaccination.²⁹ However, most studies of PCV impact on mortality reflect a direct effect or a mix of direct and indirect effects. This study adds to the literature by showing a reduction in IPD and pneumonia-related mortality in infants too young for vaccination.

Our findings should be interpreted considering some potential limitations. First, data on HIV status were not systematically measured and were not included in the analysis. Improvements in the access to antiretroviral drugs for maternal prophylaxis and prevention of mother-to-child transmission of HIV occurred over the study period³⁰; data from Malawi and South Africa documented a significant decline of IPD after the implementation of antiretroviral treatment programs.^{31,32} Therefore, some of the reduction in IPD incidence observed in our study is likely attributable to reductions in pediatric HIV infections. Second, the before–after study design for the evaluation of the population effect of vaccines is susceptible to bias due to the potential impact of other public health interventions deployed in the study area, such as the massive investment in malaria control strategies (indoor residual spraying and bed net distribution), the introduction of rotavirus vaccine in the country and the overall improvement of socioeconomic and health care. Taking all this into account, it is recognized that the overall reduction of IPD and pneumonia, including mortality observed in this study, cannot be attributed solely to the effect of vaccine introduction. Third, the passive case detection approach may have missed IPD episodes occurring in the community and not seeking health care or with difficulties in accessing the health system. Also, the differences in the proportion of eligible cases having blood culture and CSF done between the pre- and post-PCV periods might influence incidence rate calculations. Moreover, some cases from the study area may not have been identified during the first days of life due to a delay in the allocation of permanent identification numbers from the surveillance system in both the pre- and post-PCV periods. The combination of these factors could have led to an underestimation of the true number of episodes in both periods. Therefore, incidences can be considered in fact as “minimum community-based incidence rates (MCBIR).” Finally, the small case count may also have had an impact on our findings.

In conclusion, our data provide further evidence that routine infant PCV use can result in indirect protection among infants too young for vaccination, and potentially reduce IPD mortality in this age group. Ensuring the long-term continuation of PCV vaccination programs with high coverage in LMIC is essential for the reduction of childhood morbidity and mortality, and advancing toward the ending of preventable deaths in young infants.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

ACKNOWLEDGMENTS

The authors are grateful to the children and their parents for participating in the study. The authors thank all clinicians and laboratory technicians from the CISM and the Manhica District Hospital for their contribution to the conduct of the study. The authors also thank the health authorities from Manhica District and the Ministry of Health of Mozambique for their continued support and collaboration with the research activities ongoing at the Manhica District Hospital. The authors acknowledge support from the Spanish Ministry of Science and Innovation through the “Centro de Excelencia Severo Ochoa 2019–2023” _Program (CEX2018–000806-S) and support from the Generalitat de Catalunya through the CERCA Program.

This work received support from the Program for Appropriate Technology in Health (PATH) through the pneumonia and Pneumococcus surveillance study (GAT.770–790-01350-LPS), Bill and Melinda Gates Foundation through Center for Vaccine Development, University of Maryland, School of Medicine (Grant: S00957), GAVI Alliance through the Hib Initiative (Award No. 90022369), GAVI Full Country Evaluation through Institute

for health Metrics and Evaluation-IHME (University of Washington-Subcontract No. 759940 and 760010) and from the U.S. Agency for International Development (Fixed Obligation Grant: AID-656-f-12-00001 and TFA-656-12-000003) through the Surveillance for Paediatric Pneumonia and Invasive Pneumococcal Disease in Mozambique. The routine clinical, microbiological and demographic surveillance ongoing at the MDH run by the CISM receives support since its beginning from the core funding provided by the Spanish Agency for International Development and Cooperation (Ministry of Foreign Affairs, Spain). A.B. was supported by the Ministry of Science, Innovation and Universities, Government of Spain through a Ramon y Cajal Grant (RYC-2013-14512). The authors acknowledge support from the Spanish Ministry of Science and Innovation through the “Centro de Excelencia Severo Ochoa 2019–2023” _Program (CEX2018-000806-S), and support from the Generalitat de Catalunya through the CERCA Program.

The findings and conclusions in this report are those of the authors and do not necessarily represent the official position of the Centers for Disease Control and Prevention.

REFERENCES

1. Wahl B, O'Brien KL, Greenbaum A, et al. Burden of *Streptococcus pneumoniae* and *Haemophilus influenzae* type b disease in children in the era of conjugate vaccines: global, regional, and national estimates for 2000–15. *Lancet Global Health*. 2018;6:e744–e757. [PubMed: 29903376]
2. Mackenzie GA, Hill PC, Jeffries DJ, et al. ; Gambia Pneumococcal Surveillance Group. Impact of the introduction of pneumococcal conjugate vaccination on invasive pneumococcal disease and pneumonia in the Gambia: 10 years of population-based surveillance. *Lancet Infect Dis*. 2021;21:1293–1302. [PubMed: 34280357]
3. Simonsen L, Taylor RJ, Young-Xu Y, et al. Impact of pneumococcal conjugate vaccination of infants on pneumonia and influenza hospitalization and mortality in all age groups in the United States. *MBio*. 2011;2:1–10.
4. Swann O, Everett DB, Furyk JS, et al. Bacterial meningitis in Malawian infants <2 months of age: etiology and susceptibility to World Health Organization first-line antibiotics. *Pediatr Infect Dis J*. 2014;33:560–565. [PubMed: 24378940]
5. Mulholland EK, Ogunlesi OO, Weber M, et al. Etiology of serious infections in young Gambian infants. *Pediatr Infect Dis J*. 1999;18:S35–S41. [PubMed: 10530572]
6. Waters D, Jawad I, Ahmad A, et al. Aetiology of community-acquired neonatal sepsis in low- and middle-income countries. *J Glob Health*. 2011;1:154–170. [PubMed: 23198116]
7. Cheung Y, Zaman SMA, Nsekpong ED, et al. Nasopharyngeal carriage of *Streptococcus pneumoniae* in Gambian children who participated in a 9-valent pneumococcal conjugate vaccine trial and in their younger siblings. *Pediatr Infect Dis J*. 2009;28:990–995. [PubMed: 19536041]
8. Moore MR, Link-Gelles R, Schaffner W, et al. Effect of use of 13-valent pneumococcal conjugate vaccine in children on invasive pneumococcal disease in children and adults in the USA: analysis of multisite, population-based surveillance. *Lancet Infect Dis*. 2015;15:301–309. [PubMed: 25656600]
9. Poehling KA, Talbot TR, Griffin MR, et al. Invasive pneumococcal disease among infants before and after introduction of pneumococcal conjugate vaccine. *JAMA*. 2006;295:1668–1674. [PubMed: 16609088]
10. Ladhani SN, Andrews NJ, Waight P, et al. Impact of the 7-valent pneumococcal conjugate vaccine on invasive pneumococcal disease in infants younger than 90 days in England and Wales. *Clin Infect Dis*. 2013;56:633–640. [PubMed: 23175560]
11. Sigauque B, Roca A, Mandomando I, et al. Community-acquired bacteremia among children admitted to a rural hospital in Mozambique. *Pediatr Infect Dis J*. 2009;28:108–113. [PubMed: 19131902]
12. Sigauque B, Verani J, Massora S, et al. Burden of invasive pneumococcal disease among children in rural Mozambique: 2001–2012. *PLoS One*. 2018;13:1–13.
13. WHO. Summary, WHO vaccine-preventable diseases: monitoring system. 2018 global summary. Coverage time series for Mozambique. Available at: https://apps.who.int/immunization_monitoring/globalsummary. 2018. Accessed May 25, 2020.
14. Mucavele H, Massora S, Lessa FC, et al. Impact of 10-valent pneumococcal conjugate vaccine (PCV10) on radiologically confirmed pneumonia among children in Mozambique. In: Present 11th

- International Symposium on Pneumococci & Pneumococcal Diseases (ISPPD); 2018; Melbourne, Australia.
15. Massora S, Mucavele H, Lessa FC, et al. Impact of 10-valent pneumococcal conjugate vaccine (PCV10) on invasive pneumococcal disease among children in Mozambique, 2008–2016. In: Present 11th International Symposium on Pneumococci & Pneumococcal Diseases (ISPPD); 2018; Melbourne, Australia.
 16. Nhacolo A, Jamisse E, Augusto O, et al. Cohort profile update: Manhica health and demographic surveillance system (HDSS) of the Manhica Health Research Centre (CISM). *Int J Epidemiol*. 2021;50:395. [PubMed: 33452521]
 17. Instituto Nacional de Estatística (INE). 2017. QUADRO 3. POPULAÇÃO POR IDADE, SEGUNDO DISTRITO, ÁREA DE RESIDÊNCIA E SEXO. MAPUTO PROVÍNCIA.xlsx. Available at: <http://www.ine.gov.mz/iv-rgph-2017/maputo-provincia/quadro-3-populacao-por-idade-segundo-distrito-area-de-residencia-e-sexo-maputo-provincia-2017.xlsx/view>. Accessed April 20, 2020.
 18. Lopez-Varela E, Augusto O, Fuente-Soro L, et al. Quantifying the gender gap in the HIV care cascade in southern Mozambique: we are missing the men. *PLoS One*. 2021;16(2 February):e0245461–e0245415.
 19. Sacarlal J, Nhacolo AQ, Sigaque B, et al. A 10 year study of the cause of death in children under 15 years in Manhica, Mozambique. *BMC Public Health*. 2009;9(January 1997):1–10. [PubMed: 19121216]
 20. Cherian T, Mulholland E, Carlin J, et al. Standardized interpretation of paediatric chest radiographs for the diagnosis of pneumonia in epidemiological studies. *Bull World Heal Organ*. 2004;83:353–359.
 21. Carvalho GS, Tondella ML, Mccaustland K, et al. Evaluation and improvement of real-time PCR assays targeting *lytA*, *ply*, and *psaA* genes for detection of pneumococcal DNA. *J Clin Microbiol*. 2007;45:2460–2466. [PubMed: 17537936]
 22. Pimenta FC, Roundtree A, Soysal A, et al. Sequential triplex real-time PCR assay for detecting 21 pneumococcal capsular serotypes that account for a high global disease burden. *J Clin Microbiol*. 2013;51:647–652. [PubMed: 23224094]
 23. Hammit LL, Etyang AO, Morpeth SC, et al. Effect of ten-valent pneumococcal conjugate vaccine on invasive pneumococcal disease and nasopharyngeal carriage in Kenya: a longitudinal surveillance study. *Lancet*. 2019;393:2146–2154. [PubMed: 31000194]
 24. Koenraads M, Swarthout TD, Bar-Zeev N, et al. Changing incidence of invasive pneumococcal disease in infants less than 90 days of age before and after introduction of the 13-valent pneumococcal conjugate vaccine in Blantyre, Malawi. *Pediatr Infect Dis J*. 2022;41:764–768. [PubMed: 35703302]
 25. Valenciano SJ, Moiane B, Lessa FC, et al. Effect of 10-valent pneumococcal conjugate vaccine on *Streptococcus pneumoniae* nasopharyngeal carriage among children less than 5 years old: 3 years post-10-valent pneumococcal conjugate vaccine introduction in Mozambique. *J. Pediatric Infect. Dis. Soc*. 2021;10:448–456. [PubMed: 33245124]
 26. Mackenzie GA, Hill PC, Sahito SM, et al. Impact of the introduction of pneumococcal conjugate vaccination on pneumonia in The Gambia: population-based surveillance and case-control studies. *Lancet Infect Dis*. 2017;17:965–973. [PubMed: 28601421]
 27. Griffin MR, Zhu Y, Moore MR, et al. U.S. hospitalizations for pneumonia after a decade of pneumococcal vaccination. *N Engl J Med*. 2013;369:155–163. [PubMed: 23841730]
 28. Harboe ZB, Dalby T, Weinberger DM, et al. Impact of 13-valent pneumococcal conjugate vaccination in invasive pneumococcal disease incidence and mortality. *Clin Infect Dis*. 2014;59:1066–1073. [PubMed: 25034421]
 29. Kleynhans J, Tempia S, Shioda K, et al. Estimated impact of the pneumococcal conjugate vaccine on pneumonia mortality in South Africa, 1999 through 2016: an ecological modelling study. *PLoS Med*. 2021;18:e100353 7–e1003515.
 30. UNAIDS. Evaluation of the Joint Programme on HIV Mozambique 2016–2020. 2021. Available at: https://www.unaids.org/sites/default/files/media_asset/evaluation-UN-Joint-Programme-HIV-Mozambique_en.pdf. Accessed May 11, 2024.

31. Everett DB, Mukaka M, Denis B, et al. Ten years of surveillance for invasive *Streptococcus pneumoniae* during the era of antiretroviral scale-up and cotrimoxazole prophylaxis in Malawi. *PLoS One*. 2011;6:e17765–e17769.
32. Nunes MC, Von Gottberg A, De Gouveia L, et al. The impact of antiretroviral treatment on the burden of invasive pneumococcal disease in South African children: a time series analysis. *AIDS*. 2011;25:453–462. [PubMed: 21178754]

Author Manuscript

Author Manuscript

Author Manuscript

Author Manuscript